BIOL 425: HUMAN GENETICS

Course Description

Biology 425 serves both as an advanced genetics course and a survey of the exciting and rapidly evolving field of human genetics. The course includes lectures, problem solving, and analysis of published research articles. An introductory course in genetics and molecular biology is a prerequisite. If you did not do well in introductory genetics, you should consider carefully whether this course is appropriate for you. We will assume an understanding of basic genetic and molecular principles; you will be responsible for reviewing appropriate topics on your own before lectures, using online sources, your intro genetics text, or any of the texts currently used in BIOL 202.

Course Goals

1. Gain a broad knowledge of modern human genetics, including what is known, what is unknown, and what approaches are used to expand our understanding. Along the way, a deeper understanding of fundamental genetics should be attained.
2. Learn how to read and assess the scientific literature dealing with human genetics research and discovery, including different types of articles and critical analysis of research approaches.
3. Understand modes of inheritance and expression of traits ranging from Mendelian to multifactorial.
4. Learn about the human genome, from its organization into chromosomes (structure, function, behavior, and abnormalities) to the DNA content (how entire genomes were and are sequenced, major components of the genome, the field of genomics).
5.

Staff

Instructors: Dr. Jeff Sekelsky, sekelsky@unc.edu; Dr. Greg Copenhaver, gcopenhaver@bio.unc.edu

Teaching Assistant: Natalie Rittenhouse, nrittenhouse@unc.edu

See Sakai site for office hours.

Course meetings

9:45 – 11:00 am, Tues & Thurs

See Sakai for Zoom link.

SARS-COV-2 (COVID-19) Special Circumstances

At the time this syllabus is being written the SARS-COV-2 pandemic is still active and we anticipate having to make adjustments to our normal procedures for the course. We will be using a “remote learning” model. Synchronous sessions will meet by Zoom during normal class time. These will be recorded and made available via the Sakai site. These recordings are intended for the private use of our class and may not be distributed outside of class (including posting to websites) in whole or in part; doing so is a violation of copyright laws and the UNC Honor Code.

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Grading

Final grades will be based on:

- 20% Exam I (Thursday, Sept 27)
- 20% Exam II (Tuesday, Dec. 11, 8 am [final exam period])
- 30% Problem sets
- 10% Response papers for assigned reading and quizzes
- 20% Group projects

Exams

There will be two exams: Both exams will be take-home and open-book. They are to be taken alone (without consulting anyone else either in-person or electronically) and the UNC honor code will apply. You will have 24 hours to return your exam (instructions will be given at the time). Exam I will be on September 24th, and Exam II will be given on the day of the scheduled final exam (Nov 20). Make-up exams (including early exams) will not be given. Exams will consist of questions similar to those on problem sets, which emphasize conceptual understanding of human genetics. You will not need to know details from assigned articles, but you may be given a reminder of the essential data from an article and asked what main conclusions were drawn from the data, or you may be asked how an assigned reading fit into the principles being discussed at the time.

Problem Sets

Problem sets will be assigned approximately every two weeks, and will include problems and questions related to lectures and reading. Our goals with problems sets are to both reinforce and apply the material that was covered and, in some cases, extend beyond what we covered in class. Problem sets will involve a substantial effort. You may work collaboratively to solve the problems, but each student must write and turn in his or her own answers. Late problem sets will not be accepted or graded. Problem sets must be turned in as a hardcopy, a Word document, a PDF document, or electronically through Sakai – other file formats (JPG, Pages etc) will NOT be accepted.

Readings

Many lectures will have an assigned reading in the form of a published research article. Assigned articles will be discussed in class. You should bring your copy of the article to class and be prepared to contribute to discussions. To facilitate participation, each student must post a response by 9 am *before class* on the day the article is being discussed. We will give instructions regarding different responses. Examples might be asking you to describe you actual response (what you thought of it, what it made you think of, etc.), describing figures in your own words, or listing questions you had.

Response papers will count for 10% of your final grade. Each response paper will be graded on a scale of 0-5. A response that shows only that you read the article will get a 3. If we can't even tell you read it, you will be given a lower score. Responses that show that you were conscious, engaged, and thinking while reading (which doesn't mean you have to understand it all) will get 4 or 5. We anticipate having 12-15 articles assigned. Your top ten scores will be counted toward your grade.

Group Projects and Presentations

Enrolled students will be placed into groups of 4-5 sometime after the second week of classes. Each group will conduct a research project and present the project to the class. Four class meetings at the end of the semester have been set aside for presentations, two per meeting. The Group Projects section of the Assignments page has more information.

Group projects will be overseen by the TA. Each group will select an article that we discussed in class, or another article in human genetics (subject to the approval of the TA; you may not select a paper that is related

to research that any group member is currently or has been engaged in). The group will develop a plan for future research in the area, addressing questions left unanswered in the publication or raised by results in the publication. The group will meet with the TA to go over their plan and revise it. They will then put together a presentation for the class, meet with the TA to go over their presentation, and give the presentation to the class. **Because of the special SARS-COV-2 (COVID-19) consideration, all groups should anticipate holding their group project development sessions, and final presentations online via Zoom.**

Showing up for and paying attention at the presentations of other groups is important. Students in the audience will fill out evaluation forms, which we also use to take attendance. Points are deducted from your total for each presentation that you miss or for which you are late. Additional details, guidance on developing projects, and the grading rubric are available on the Group Projects section of the Assignments page.

Other Policies

- All aspects of the **UNC Honor Code** will be enforced.
- Re-grade requests must be made in writing within one week of receiving a grade (returned problem set, exam, etc.). Only errors in grading are considered, not requests for additional partial credit. We reserve the right to regrade the entire exam or problem set.
- We make various course materials available to you, including PowerPoint files, lecture notes, problem sets, and exams. These materials are copyrighted. **It is a violation of the honor code to distribute course materials outside of the classroom without written permission from the instructors. This includes posting or sharing of recorded lectures.** This also includes depositing in fraternity or sorority files or contributing to online repositories. **It is also a violation of the honor code to access or consult any course documents that may have been deposited by others.**

Diversity Statement

This course values the perspectives of individuals from all backgrounds reflecting the diversity of our students. We broadly define diversity to include race, gender identity, national origin, ethnicity, religion, social class, age, sexual orientation, political background, and physical and learning ability. We strive to make this classroom an inclusive space for all students.

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The schedule of classes provided below is subject to change. Human genetics is an exciting and fast-moving field. We strive to incorporate the latest advances, but sometimes this means we have to cut or reduce a topic that was scheduled. Also, since this is in part a discussion-based course, we often have to make small adjustments in response to discussions that are longer than anticipated.

Section I. Human Transmission and Molecular Genetics (Sekelsky)

HUMAN HEREDITY AND INHERITANCE (AUG 11, 13, 18)

Topics: Pedigrees, simple and complex inheritance

Readings. Links take you to PubMed entries, but annotated PDFs will be posted to Sakai. Dates are dates on which we discuss articles; these are also subject to change, so don't get too far ahead.

Thurs Aug 13 — Woolf and Dukepoo (1969) Hopi Indians, inbreeding, and albinism. *Science* 164: 30-37.

Tues Aug 18 — Lipton et al. (2001) Apparent Mendelian inheritance of breast and colorectal cancer: chance, genetic heterogeneity, or a new gene? *Familial Cancer* 1: 189-195.

Thurs Aug 20 — Sicherer et al. (2000) Genetics of peanut allergy: A twin study. *J. Allerg. Clin. Immunol.* 106: 53-56.

HUMAN CHROMOSOMES (AUG 20, 25, 27)

Topics: Chromosomes and chromatin, mitosis and meiosis, aneuploidy, chromosome rearrangements, the *X* and *Y* chromosomes

Readings:

Tues Aug 25 — Bourthoumieu *et al.* (2005) Monozygotic twins concordant for blood karyotype, but phenotypically discordant: A case of "mosaic chimerism". *Am. J. Med. Gen.* 135: 190-4.

Tues Sept 1 — Strong *et al.* (1981) Familial retinoblastoma and chromosome 13 deletion transmitted via an insertional translocation. *Science* 213: 1501-3.

THE HUMAN GENOME (SEP 1, 3, 8, 10, 15, 17, 22)

Topics: Sequencing the genome, the structure and content of the genome, genomics, variation

Readings:

Tues Sept 8 — Lander *et al.* (2001) Initial sequencing and analysis of the human genome. *Nature* 409: 860-921.

Venter *et al.* (2001) The sequence of the human genome. *Science* 291: 1304-51.

Note that these are long papers. We will only read part of each - see Sakai for instructions.

Tues Sept 15 — Choi *et al.* (2010) Genetic diagnosis by whole exome capture and massively parallel DNA sequencing. *PNAS* 106: 19096–19101.

Thurs Sep 24 EXAM I (take-home)

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Section II. Topics in and Applications of Human Genetics (Copenhaver)

Tues Sep 29 ***Topic***: Recombination
Reading: Tran & Schimenti, 2018 A putative human infertility allele of the meiotic recombinase DMC1 does not affect fertility in mice. *Human Molecular Genetics* 27: 3911-3918.

Thurs Oct 1 ***Topic***: Segregation mapping
Reading: Sobreria, 2010 Whole-Genome Sequencing of a Single Proband Together with Linkage Analysis Identifies a Mendelian Disease Gene. *PLOS Genetics* 6(6): e100099.

Tues Oct 6 ***Topic***: Association mapping
Reading: Chen, 2018 A genome-wide association study identifies a susceptibility locus for biliary atresia on 2p16.1 within the gene EFEMP1. *PLOS Genetics* 14(8): e1007532.

Thurs Oct 8 ***Topic***: Mitochondrial genetics
Reading: Cree, 2008 A reduction of mitochondrial DNA molecules during embryogenesis explains the rapid segregation of genotypes. *Nature Genetics* 40: 249-254.

Tues Oct 13 ***Topic***: Identifying human disease genes
Reading: Burns, 2018 Variants in EXOSC9 Disrupt the RNA Exosome and Result in Cerebellar Atrophy with Spinal Motor Neuronopathy. *The American Journal of Human Genetics* 102: 858–873.

Thurs Oct 15 ***Topic***: Epigenetics
Reading: Jang, 2015 Histone H3.3 maintains genome integrity during mammalian development. *Genes & Development* 29: 1377-1392.

Tues Oct 20 ***Topic***: Forensic Genetics
Reading: none

Thurs Oct 22 ***Topic***: Cancer genetics
Reading: Turner, 2017 Extrachromosomal oncogene amplification drives tumour evolution and genetic heterogeneity. *Nature* 543: 122-125.

Tues Oct 27 ***Topic***: Pharmacogenetics
Reading: Yang, 2016 Genome-Wide Pharmacogenomic Study on Methadone Maintenance Treatment Identifies SNP rs17180299 and Multiple Haplotypes on CYP2B6, SPON1, and GSG1L Associated with Plasma Concentrations of

Methadone R- and S-enantiomers in Heroin-Dependent Patients. *PLOS Genetics* 12(3): e1005910.

Thurs Oct 29 ***Topic***: Gene therapy
Reading: Ribeil, 2017 Gene Therapy in a Patient with Sickle Cell Disease. *The New England Journal of Medicine* 376: 848-855.

Tues Nov 3 ***Topic***: **Guest Lecture by Dr. Bradford Powell: Personal genetics in the clinic**
Reading: none

Section III. Student Presentations

Thurs Nov 5 STUDENT PRESENTATIONS – Groups 1 & 2
Tues Nov 10 STUDENT PRESENTATIONS – Groups 3 & 4
Thurs Nov 12 STUDENT PRESENTATIONS – Groups 5 & 6
Tues Nov 17 STUDENT PRESENTATIONS – Groups 7 & 8

Nov 20 EXAM II: Take-home