

# BIOL 425: HUMAN GENETICS

## Course Goals

Biology 425 serves both as an advanced genetics course and a survey of the exciting and rapidly evolving field of human genetics. Through lectures and reading of published research articles, our aim to have students acquire an in-depth understanding of human genetics and research methods in human genetics. We also hope that students will improve their critical reading skills.

## Prerequisites

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.

## Staff

<b>Instructors:</b>	Dr. Jeff Sekelsky 303 Fordham Hall <a href="mailto:sekelsky@unc.edu">sekelsky@unc.edu</a>	Dr. Greg Copenhaver 4161 Genome Science Building <a href="mailto:gcopenhaver@bio.unc.edu">gcopenhaver@bio.unc.edu</a>
<b>Teaching Assistant:</b>	Sarah Brotman <a href="mailto:sbrotman@email.unc.edu">sbrotman@email.unc.edu</a>	

See Sakai site for office hours.

## Course meetings

9:30 – 10:45 am, Tues & Thurs, 128 Wilson Hall

You should come to course meetings prepared, having read any lecture notes, perused PowerPoint slides, and of course read any articles to be discussed. We may sometimes begin class with a short quiz to assess comprehension of class materials. These will count in the Problem Sets grade.

## Grading

Final grades will be based on:

- 25% Exam I (Thursday, Sept 27)
- 25% Exam II (Tuesday, Dec. 10, 8 am [final exam period])
- 30% Problem sets
- 10% Response papers for assigned reading and quizzes
- 10% Group projects

## Exams

There will be two exams: Exam I will be in class and Exam II will be given during the scheduled final exam period. Please note that the second exam is very late in the exam period – plan your travel accordingly, as 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.

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## 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 your 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. Five 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 a graduate research coordinator (GRC). The GRC Program is sponsored by the [Office for Undergraduate Research](#). We encourage you to visit the OUR website to see other ways that you might engage in research, scholarship and creative performance while you are at Carolina. Please note that the GRC is *not* a TA; his sole responsibility is to assist groups with their presentations. He is not involved in grading decisions, but may provide information to the instructors regarding effort and group dynamics.

Each group will select an article that we discussed in class, or another article in human genetics (subject to the approval of the GRC; 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 GRC to go over their plan and revise it. They will then put together a presentation for the class, meet with the GRC to go over their presentation, and give the presentation to the class.

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 and guidance are available on the Group Projects section of the Assignments page.

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## 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 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.**
- **Recording of lectures is prohibited** unless explicit permission has been granted by the instructor (separate permission for each instructor). Use of cell phones during class is prohibited, except when part of a class activity. Computers are allowed, but only for taking notes or viewing PowerPoints and readings during discussion. Students caught using computers for other tasks (email, surfing, other reading, etc.) will lose computer privileges for the remainder of the semester.

## 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 20, 22, 27)

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.

- Tues Aug 27 Woolf and Dukepoo (1969) [Hopi Indians, inbreeding, and albinism](#). *Science* 164: 30-37.
- Tues Aug 27 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 29 Sicherer et al. (2000) [Genetics of peanut allergy: A twin study](#). *J. Allerg. Clin. Immunol.* 106: 53-56.

### HUMAN CHROMOSOMES (AUG 29, SEPT 3, 5)

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

Readings:

- Tues Sept 3 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.
- Thurs Sept 5 Strong *et al.* (1981) [Familial retinoblastoma and chromosome 13 deletion transmitted via an insertional translocation](#). *Science* 213: 1501-3.

### THE HUMAN GENOME (SEPT 10 – OCT 1)

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

*note: Thurs Sept 12 will be a guest lecturer, Dr. Julie Korda Holsclaw*

Readings:

- Tues Sept 17 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 24 Choi *et al.* (2010) [Genetic diagnosis by whole exome capture and massively parallel DNA sequencing](#). *PNAS* 106: 19096–19101.

**Thurs Oct 3 EXAM I (in class)**

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

- Tues Oct 8 **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 10 **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 16 **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 17 FALL BREAK
- Tues Oct 22 **Topic:** Ethics & Genetics  
**Reading:** none
- Thurs Oct 24 **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.
- Tues Oct 29 **Topic:** Epigenetics  
**Reading:** Jang, 2015 Histone H3.3 maintains genome integrity during mammalian development. *Genes & Development* 29: 1377-1392.
- Thurs Oct 31 **Topic:** Forensic Genetics  
**Reading:** none
- Tues Nov 5 **Topic:** Cancer genetics  
**Reading:** Turner, 2017 Extrachromosomal oncogene amplification drives tumour evolution and genetic heterogeneity. *Nature* 543: 122-125.

## BIOL 425: HUMAN GENETICS

- Thurs Nov 7 **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.
- Tues Nov 12 **Topic:** Gene therapy  
**Reading:** Ribeil, 2017 Gene Therapy in a Patient with Sickle Cell Disease. *The New England Journal of Medicine* 376: 848-855.
- Thurs Nov 14 **Topic:** **Guest Lecture by Dr. Bradford Powell: Personal genetics in the clinic**  
**Reading:** none

### Section III. Student Presentations

- Tues Nov 19 **STUDENT PRESENTATIONS – Groups 1 & 2**  
Thurs Nov 21 **STUDENT PRESENTATIONS – Groups 3 & 4**
- Tues Nov 26 **STUDENT PRESENTATIONS – Groups 5 & 6**  
Thurs Nov 28 THANKSGIVING BREAK
- Tues Dec 3 **STUDENT PRESENTATIONS – Groups 7 & 8**
- Tues Dec 10 **EXAM II: 8:00 am - 11:00 am**