GNET/BIOL 621 Fall 2023

Course Description

BIOL/GNET 621 is an upper-level genetics course intended for graduate students and advanced undergraduates. Undergraduates must have taken BIOL 202 or the equivalent; there are no pre-requisites for graduate students. The course covers genetic principles and tools through lectures, reading of research articles, problem solving, and discussion.

Course Goals

1. Understand fundamental aspects of genetics, including the structure, function, and behavior of genes and chromosomes.
2. Become familiar with the use of genetics as a tool for analysis, including complementation, pathway elucidation, and mosaic analysis.
3. Learn about non-Mendelian areas of genetics, such as transposable elements, RNA interference, etc.
4. Gain experience in reading and assessing the scientific literature of genetics.

Staff

Instructors:	Dr. Greg Copenhaver	gcopenhaver@bio.unc.edu
	Dr. Jeff Sekelsky	sekelsky@unc.edu
Teaching Assistants:	Alejandro Gomez	alegomez@email.unc.edu
	Rachel Szymanski	raszyman@email.unc.edu

See Canvas site for office hours.

Course meetings

11:00 – 12:45 pm Tues & Thurs	128 Wilson Hall
Recitation: 2:30 – 3:30 pm Fridays	128 Wilson Hall

Attendance and participation are strongly recommended during lectures and required in recitations.

We will record lectures using Panopto. These will be available on the Canvas site (Panopto link on left). Panopto records two channels, one of the blackboard and one of the Powerpoint. The latter allows skipping ahead by slide. Panopto does an automated transcription. Although these will have many errors, especially when scientific terms and names are used, we do not edit the transcripts. Due to unanticipated technology or instructor issues, it is possible that some recordings will be unavailable. Note that Panopto does not allow for remote participation like Zoom does. We intend class recordings to be useful in reviewing material or if you miss one or more meetings, but it is not a substitute for in-person attendance.

Grading

Final grades will be based on:

- 36% Exams
- 40% Problem sets
- 24% Recitation (participation and paper presentation)

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Exams

There will be two exams, one after each instructor's section. Each counts as 18% of your grade. Exams are intended to emphasize conceptual understanding of genetics and ability to solve problems like those on problem sets.

Paper presentation

One or two original research papers will be assigned as reading to accompany each lecture. Each week, a group of 2-3 students (depending on class size) will present one of these papers during recitation. Dates will be assigned/chosen at the first recitation meeting. Your presentation counts as 12% of your grade.

When other students are presenting, you will be expected to pay attention and contribute to discussion by asking or answering questions, responding to comments by other students, explaining figures or text from the article being discussed, etc. We encourage you to ask questions about parts of the reading you may not have understood – this is one of the best ways to learn. Participation in recitation counts as 12% of your grade.

Problem Sets

Each instructor will assign 2-3 problem sets. These will include questions about the material and problems to be solved based on lecture material and readings. You are encouraged to work collaboratively to solve the problems, but each student must write and turn in their own answers. We will use either the Canvas Assignment tool or Gradescope (accessible through Canvas). Problem sets will be graded and returned. Late problem sets will not be accepted. Problem sets (combined) count as 40% of your grade.

Other Policies

- Students are bound by the Honor Code in taking exams and in written work. The Honor Code of the University is in effect. Please consult with us if you have any questions. Plagiarism will not be tolerated. For problem sets, students may share tips and questions on a shared site; however, **it is a violation of the honor code to post answers on any site, private or public**.
- 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 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.**
- 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.
- Although COVID-19 remains endemic, the indoor mask requirement has been lifted for most of campus. If you feel more comfortable wearing a mask, you are free to do so. There are many reasons why a person may decide to continue to wear a mask; we respect that choice and we expect all students in the class to be respectful of their classmates. If you are ill or if you test positive, please do not come to class. We are not providing a synchronous participation option, but we are providing recordings of each meeting (see above).
- Please see the related document on additional UNC policies and resources.

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Schedule of class meetings

Part I: Genetic Principles (Copenhaver)

Aug	22	Tues	Introduction, DNA & chromosome structure Gaffney, DJ, et al., (2012) Controls of nucleosome positioning in the human genome. PLOS Genetics 8(11): e1003036. doi: 10.1371/journal.pgen.1003036
	24	Thurs	Meiosis & mitosis Lutes, AA, et al. (2010) Sister chromosome pairing maintains heterozygosity in parthenogenetic lizards. Nature 464(7286):283-6. doi: 10.1038/nature08818
	25	Fri	*Discussion (TAs present first paper)*
	29	Tues	Mendelian basics Tory et al. (2104) Mutation-dependent recessive inheritance of NPHS2-associated steroid-resistant nephrotic syndrome. Nature Genetics 46(3) 299-304. doi:10.1038/ng.2898
	31	Thurs	Molecular biology basics Long, C, et al. (2014) Prevention of muscular dystrophy in mice by CRISPR/Cas9–mediated editing of germline DNA. Science. 345(6201):1184-8. doi: 10.1126/science.1254445
Sept	1	Fri	*Discussion*
	6	Tues	No class: Well-being day
	7	Thurs	Recombination 1. Baudat, F., *et al.* (2010) PRDM9 is a major determinant of meiotic recombination hotspots in humans and mice. *Science* 327:836-40. 2. McVean, G. & S. Myers (2010) PRDM9 marks the spot. *Nature Genet* 42: 821-2. (review)
	8	Fri	*Discussion*
	12	Tues	Chromosome aberrations Sasaki, M., J. Lange, & S. Keeney (2010) Genome destabilization by homologous recombination in the germ line. *Nature Reviews Mol. Cell Biol.* 11:182-95.
	14	Thurs	Linkage and mapping Kirby et al. (2013) Mutations causing medullary cystic kidney disease type 1 lie in a large VNTR in MUC1 missed by massively parallel sequencing. Nature Genetics 45(3) 299-305. doi:10.1038/ng.2543
	15	Fri	*Discussion*
	19	Tues	Pedigrees, tetrads & LODs Sobreira, N.L., *et al.* (2010) Whole-genome sequencing of a single proband together with linkage analysis identifies a Mendelian disease gene. *PLoS Genet.* 17: e1000991.
	21	Thurs	No class (Genetics retreat)
	22	Fri	No recitation (Genetics retreat)

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	26	Tues	Association mapping
	28	Thurs	Non-Mendelian inheritance
	29	Fri	*Discussion*
	3	Tues	Epigenetics
	5	Thurs	TA presentation / review
	31	Fri	*Discussion*
Oct	**10**	**Tues**	**Exam I (take home)**

Part II: Genetic Analysis (Sekelsky)

Oct	12	Thurs	No class – University Day
	13	Fri	*Discussion?*
	17	Tues	The Genetic Method Driever, W., *et al*. (1996) A genetic screen for mutations affecting embryogenesis in zebrafish. *Development* 123: 37-46.
	19	Thurs	No class: Fall Break
	19	Thurs	Mutations and Mutagenesis Boettcher *et al.* (2019) A dominant-negative effect drives selection of TP53 missense mutations in myeloid malignancies. *Science* 365: 599-604.
	20	Fri	*Discussion* (Boettcher article)
	18	Tues	Complementation Strathdee, C.A., A.M. Duncan, and M. Buchwald (1992) Evidence for at least four Fanconi anaemia genes including *FACC* on chromosome 9. *Nature Genet.* 1: 196-198.
	21	Fri	No recitation: Fall Break
	25	Tues	Bacterial genetics Eisenstein, B.I. *et al.* (1997) Conjugal transfer of the gonococcal penicillinase plasmid. *Science* 195: 998-1000. Babic, A. *et al.* (2008) Direct visualization of horizontal gene transfer. *Science* 319: 1533-6.
	21	Fri	*Discussion* (Eisenstein and Babic articles)
	31	Tues	TBD
Nov	2	Thurs	TBD
	3	Fri	*Discussion*

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Nov	7	Tues	Complementation complexities Yook, K.J., S.R. Proulx, & E.M. Jorgensen (2001) Rules of nonallelic noncomplementation at the synapse in *Caenorhabditis elegans*. *Genetics* 158: 209–220.
	9	Thurs	Genetic interactions Feng, W., *et al.* (2019) Genetic determinants of cellular addiction to DNA polymerase theta. *Nature Comm.* 10: 4286.
	10	Fri	*Discussion* (Yook article)
	14	Tues	Epistasis and pathway analysis Conradt, B. & H.R. Horvitz (1999) The TRA-1A sex determination protein of *C. elegans* regulates sexually dimorphic cell deaths by repressing the *egl-1* cell death activator gene. *Cell*. 98: 317–327
	16	Thurs	Mosaicism Choate, K.A. *et al.* (2010) Mitotic recombination in patients with ichthyosis causes reversion of dominant mutations in *KRT10.* *Science* 330: 94-97.
	17	Fri	*Discussion*
	21	Tues	Mosaic analysis Xie, T. and Spradling, A.C. (1998) *decapentaplegic* is essential for the maintenance and division of germline stem cells in the *Drosophila* ovary. *Cell* 94: 251-260.
	23	Thurs	No class : Thanksgiving
	24	Fri	No recitation : Thanksgiving
	21	Tues	Transposable elements
	17	Thurs	RNAi
	18	Fri	*Discussion*
	22	Tues	Jeff's failed thesis project
	29	Tues	
Dec	**3**	**Sat**	**EXAM 2 (take home)**

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