GNET/BIOL 621 Fall 2019

Course Policies

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
	Dr. Shawn Ahmed	shawn@med.unc.edu
Teaching Assistant:	Rami Major	ramim@live.unc.edu

See Sakai site for office hours.

Course meetings

11:30 – 12:45 pm Tues & Thurs

Recitation: 2:40 – 3:30 pm Fridays

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.

Attendance at synchronous sessions is highly recommended but is not mandatory. You do not need to have your video on, but you may if you wish. Questions should be sent through the chat box. The TA will then call on you. If you prefer to ask questions anonymously, you may use the private chat function to send your question to the TA.

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Grading

Final grades will be based on:

- 36% Exams: two midterms and a comprehensive final
- 40% Problem sets
- 24% Recitation (participation and paper presentation)

Exams

There will be three take-home exams. The first two will each be worth 100 points and count for 8% of your final grade. There will also be a comprehensive final exam that will have150 points from the final third of the course and 50 points from each of the 1st and 2nd parts; it will be 20% of the final 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 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.

Problem Sets

Each instructor will assign approximately two 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 Sakai Assignment tool or Gradescope (accessible through Sakai). Problem sets will be graded and returned. Late problem sets will not be accepted. Problem sets count as 40% of your grade.

Diversity Statement

The instructors of this course value 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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Schedule of class meetings

Part I: Genetic Principles (Copenhaver)

Aug	11	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
	13	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
	14	Fri	*Discussion (TAs present first paper)*
	18	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
	20	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
	21	Fri	*Discussion*
	25	Tues	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)
	27	Thurs	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.
	28	Fri	*Discussion*
Sept	1	Tues	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
	3	Thurs	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.
	4	Fri	*Discussion*
	8	Tues	Association mapping
	10	**Thurs**	**Exam I**
	11	Fri	*No discussion this week*

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Pat II: Genetic Analysis (Sekelsky)

Sept	15	Tues	Experimental Genetics
	17	Thurs	Genetic Screens Driever, W., *et al*. (1996) A genetic screen for mutations affecting embryogenesis in zebrafish. *Development* 123: 37-46.
	18	Fri	*Discussion* (Driever article)
	22	Tues	Mutations and Mutagenesis Boettcher *et al.* (2019) A dominant-negative effect drives selection of TP53 missense mutations in myeloid malignancies. *Science* 365: 599-604.
	24	Thurs	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.
	25	Fri	*Discussion* (Boettcher article)
	29	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.
Oct	1	Thurs	Genetic interactions Feng, W., *et al.* (2019) Genetic determinants of cellular addiction to DNA polymerase theta. *Nature Comm.* 10: 4286.
	2	Fri	*Discussion* (Yook article)
	6	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.
	8	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.
	9	Fri	*Discussion* (Conradt article)
	13	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.
	15	Thurs	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.
	16	Fri	*Discussion* (Eisenstein and Babic articles)
Oct	**20**	**Tues**	**Exam 2**

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Part III: Non-Mendelian Genetics (Ahmed)

Oct 22 Thurs DNA transposons

Ivics, Z. *et al.* (1997) Molecular reconstruction of Sleeping Beauty, a Tc1-like transposon from fish, and its transposition in human cells. *Cell* 91: 501-510.

Cell 128: 1089-1103.

23 Fri *Discussion*

27 Tues Retrotransposons

Brennecke, J. *et al.* (2007) Discrete small RNA-generating loci as master regulators of transposon activity in Drosophila.

29 Thurs Gene targeting

Sandler, J.D. *et al.* (2011) Selection-free zinc-finger-nuclease engineering by context-dependent assembly (CoDA). *Nature Methods* 8: 67-69.

30 Fri *Discussion*

Nov 3 Tues RNAi I

Fire, A. *et al.* (1998) Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. *Nature* 391: 806-811.

5 Thurs RNAi II

Boutros, M. *et al.* (2008) The art and design of genetic screens: RNA interference. *Nature Reviews Genetics* 9: 554-566.

6 Fri *Discussion*

10 Tues Non-Mendelian inheritance

Starr, D.J. and T. Cline (2002) A host parasite interaction rescues Drosophila oogenesis defects. *Nature* 418: 76-79.

12 Thurs Epigenetics I

Gottschling, D.E. *et al.* (1990) Position effect at S. cerevisiae telomeres: reversible repression of Pol II transcription. *Cell* 63: 751-762.

13 Fri *Discussion*

17 Tues Epigenetics II

Avner, P. and E. Heard (2004) X-chromosome inactivation: counting, choice and initiation. *Nature Reviews Genetics* 2: 59-67.

Bartolomei, M.S. *et al.* (1991) Parental imprinting of the mouse H19 gene. *Nature* 351: 153-155.

Nov 24 Tues CUMMULATIVE FINAL EXAM (take home)

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