GNET/BIOL 621 Fall 2019

Course Policies

Lecture: **Tues & Thurs 11:00 am - 12:15 pm, 128 Wilson Hall**
Recitation: **Fridays, 2:30 - 3:20 pm, 128 Wilson Hall**
Instructors: See Sakai site

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, and discussion. We have not assigned a textbook, but you may wish to consult one if you need to review introductory genetics. Any textbook used for BIOL 202 is okay.

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 two in-class midterm exams. Each will be 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 will consist of questions similar to those on problem sets, and are meant to emphasize conceptual understanding of genetics. No makeup exams will be given; this includes the final! We are required to have a final exam at the time scheduled by the University. If your other courses decide to have an exam at some time of the instructors' choosing and it conflicts with this final, you must arrange for a different time with the other instructor.

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 (yes, asking questions counts, too, even questions about not understanding parts of the article – it's important to be willing to do this), responding to comments by other students, explaining figures or text from the article being discussed, etc. 12% of your grade will be based on your participation in recitation.

Problem Sets

Problem sets will be assigned most weeks. These will include problems and questions about the lectures and reading. You are encouraged to work collaboratively to solve the problems, but each student must write and turn in his or her own answers. You can turn them in at class or post them to Sakai through the Assignment tool. 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	20	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
	22	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
	23	Fri	*Discussion (TAs present first paper)*
	27	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
	29	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
	30	Fri	*Discussion*
Sept	3	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)
	5	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.
	6	Fri	*Discussion*
	10	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
	12	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.
	13	Fri	No Discussion due to Genetics Retreat
	17	Tues	Association mapping
	19	**Thurs**	**Exam I**
	20	Fri	*No discussion this week*

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Part II: Genetic Analysis (Sekelsky)

Sept 24 Tues — Genetic Screens

Driever, W., *et al*. (1996) A genetic screen for mutations affecting embryogenesis in zebrafish. *Development* 123: 37-46.

26 Thurs — Mutations and Mutagenesis

Sivanantharajah L. and A. Percival-Smith (2009) Analysis of the sequence and phenotype of Drosophila Sex combs reduced alleles reveals potential functions of conserved protein motifs of the Sex combs reduced protein. *Genetics* 182: 191-203.

27 Fri — *Discussion* (Driever article)

Oct 1 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.

3 Thurs — 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.

Simon, M.A., *et al.* (1991) Ras1 and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the sevenless protein tyrosine kinase. *Cell* 67: 701-16.

4 Fri — *Discussion* (Yook article)

8 Tues — Genetic interactions

Simon, M.A., *et al.* (1991) Ras1 and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the sevenless protein tyrosine kinase. *Cell* 67: 701-16.

10 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.

11 Fri — *Discussion* (Eisenstein and Babic articles)

15 Tues — 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 Thurs — No class: Fall Break

18 Fri — *No discussion this week*

22 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.

24 Thurs — 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.

25 Fri — *Discussion* (Conradt article)

29 Tues — Review

Oct 31 Thurs — Exam 2

Nov 1 Fri — No discussion this week

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Part III: Non-Mendelian Genetics (Ahmed)

Nov 5 Tues — 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.

7 Thurs — Retrotransposons

Brennecke, J. *et al.* (2007) Discrete small RNA-generating loci as master regulators of transposon activity in Drosophila. *Cell* 128: 1089-1103.

8 Fri — *Discussion*

12 Tues — Gene targeting

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

14 Thurs — RNAi I

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

15 Fri — *Discussion*

19 Tues — RNAi II

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

21 Thurs — Non-Mendelian inheritance

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

22 Fri — *Discussion*

26 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.

28 Thurs — THANKSGIVING

29 Fri — THANKSGIVING

Dec 3 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.

12 Thurs — **CUMMULATIVE FINAL EXAM 12:00 – 3:00 pm**

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