Genome Sciences and Technology I: Genetics and Genomics
Fall Semester, 2002
Lecture/Discussion Schedule

The time-use format that will be followed in this course is as follows: a 2-hr. session on Fridays (9:05-11:00) will be devoted to a lecture illustrating general principles and themes important in mammalian genetics and genomics; Mondays (9:05-9:55) will be devoted to a discussion session led by the TA (Ling Li), reviewing relevant points from lecture and any necessary background genetics; Wednesdays (9:05-9:55) will be devoted to an open discussion of a research paper that illustrates the principles of the preceding lecture. All students must read the paper in advance and be prepared to answer questions on it and participate in discussion.

Date			Topic	Instructor
Part I. Genetics, genomics, and gene discovery				
Aug	21	W	Overview and themes	Handel
Purpose of course; merging genetics and genomics; identifying "disease genes;" also using genetics/genomics to investigate biological mechanisms, etc., meiosis and segregation/family analyses; practical differences between human and model organisms				
	23	F	Meiosis and segregation	Handel
Family analyses and segregation, following a disease; how segregation analysis may help in gene identification; utility of "markers;" types of variation.				
	26	M	Discussion	Li
	28	W	Paper 1	Rinchik
Stewart GD et al. 1988. Trisomy 21 (Down syndrome): Studying nondisjunction and meiotic recombination by using cytogenetic and molecular polymorphisms that span chromosome 21. Am J Hum Genet 42:227-236.				
Purpose: to introduce molecular markers (RFLPs, SSLPs, FISH) for segregation analysis				
	30	F	Mapping/co-segregation	Rinchik
Markers and co-segregation as prelude to positional cloning.				
Sept.	2	M	No Class (Labor Day)	
	4	W	Paper 2	Culiat

Aniskter et al. 2001 Mutation of a new gene causes a unique form of Hermansky-Pudlak syndrome in a genetic isolate of central Puerto Rico. Nature Genetics 28:376-380.

Purpose: to show model of mapping a disease gene, to answer questions about segregation and co-segregation

6	F	Cytogenetics	Johnson

Chromosome aberrations as medically important and as a means to “short-circuit” mapping ordeal, especially in humans; mapping tools such as deletions, translocations, inversions, mapping, breakpoint fragment

9	M	Discussion	Li
11	W	Paper 3	Johnson

Tassabehji M et al. 1999. Williams syndrome: Use of chromosomal microdeletions as a tool to dissect cognitive and physical phenotypes. Am J Hum Genet 64: 118-125.

Purpose: illustrates use of chromosomal aberrations to map phenotypes

13	F	Basic techniques for DNA and RNA analysis	Culiat

Basic molecular techniques such as nucleic acid hybridization, physical mapping, cloning, construction and screening of libraries and common gene expression assays; integration of these techniques for positional cloning will be emphasized

16	M	Discussion	Li
18	W	Paper 4 (same as Paper 2)	Culiat

Aniskter et al. 2001 Mutation of a new gene causes a unique form of Hermansky-Pudlak syndrome in a genetic isolate of central Puerto Rico. Nature Genetics 28:376-380.

Purpose: use of molecular techniques for identifying and confirming candidate genes for disease phenotypes

20	F	Generating, interpreting & using genome sequence	Culiat

BACs and YACs, assembly of contigs, sequencing techniques, shotgun vs. contig approach, analysis of sequence information and application to recent positional candidate approaches

23	M	Discussion	Li
25	W	Paper 5	Culiat

DeSilva U et al. 2002. Generation and comparative analysis of approximately 3.3 Mb of mouse genomic sequence orthologous to the region of human chromosome 7q11.23 implicated in Williams syndrome. Genome Res 12:3-15.

Purpose: to illustrate the generation and use of comparative sequence information for identifying candidate genes for a human disease (Williams Syndrome); since the critical region was defined by cytogenetic abnormalities, this will also serve as a follow-up of Dr. Johnson's lectures

Take-home Exam #1: to be provided at end of class Friday Sept. 27; due Wednesday Oct. 2; covers material from Aug. 21 through Sept. 25.

Part II. Altering the genome for mutational analysis

	27	F	Experimental Mutagenesis	Rinchik

Types of variation, how to induce mutations, mutation screens in mice.

	30	M	NO CLASS (work on take-home exam)	
Oct	2	W	Paper 6	Michaud

TBA

	4	F	Genome manipulation I	Michaud

Various methods and applications used to alter the mouse genome for the purpose of determining the whole-animal biological functions of genes and proteins. The methods discussed will include: transgenics, gene targeting, gene-trapping, chromosome engineering, and chemical mutagenesi; knowledge of these methods and their applications will facilitate critical reading of the primary literature in mouse genetics and genomics.

	7	M	Discussion	Li
	9	W	Genome manipulation II	Michaud
	11	F	NO CLASS - FALL BREAK	
	14	M	Discussion	Li
	16	W	Paper 7	Michaud

Chen, Y., Schimenti, J. and Magnuson, T. 2000. Towards the yeastification of mouse genetics: chemical mutagenesis of embryonic stem cells. Mamm Genome 11:598-602.

Purpose: A review on the recent progress of chemical mutagenesis in embryonic stem cells, and the application of cell-based, phenotype-driven and genotype-driven mutagenesis screens for functional genomics in the mouse.

Part III. Genome-wide techniques

	18	F	Microarrays and data analysis	Jones

Principles and practice of microarray analysis of whole genome expression, complexities of data analysis, understand the principle behind microarrays, pros and cons of different technical methodologies, important issues in designing an experiment, novel pitfalls of microarray data analysis

21	M	Discussion	Li
23	W	Paper 8	Jones

Wurmbach E, Yuen T, Ebersole BJ, Sealfon SC. 2001. GrRH-receptor-coupled gene network organization. JBC 276: 47195-47201.

Purpose: to illustrate the power of microarray, genome-wide analysis

25	F	Complex traits	Johnson

Basic QTL analyses, polygenes, interval mapping, association, linkage disequilibrium

28	M	Discussion	Li
30	W	Paper 9	Johnson

Roberts J, Watters J, Ballard J, Dietrich W. 1998. *Ltx1*, a mouse locus that influences the susceptibility of macrophages to cytolysis caused by intoxication with *Bacillus anthracis* lethal factor, maps to chromosome 11. Mol Microbiol 29: 581-591.

Purpose: to illustrate mapping of a quantitative trait

Take-home Exam #2: to be provided at end of class Friday Nov. 1; due Wednesday Nov. 6; covers material from Sept. 27 through Oct. 30.

Part IV. Model pathways (cellular and developmental) and model organism genetics/genomics

Nov	1	F	Yeast: Pathway dissection	Becker

Yeast as a model organism and models of complex pathways of cellular interactions

4	M	NO CLASS (work on take-home exam)	
6	W	Paper 10	Becker

Tong AH et al. 2001. Systematic genetic analysis with ordered arrays of yeast deletion mutants. Science. 294:2364-2368.

Purpose: to illustrate practice of yeast genetics for whole genome analysis

8	F	Fly genetics & genomics: Sex determination	McKee

Introduction to *Drosophila* as a genetic model system and overview of fly genomics

11	M	Discussion	Li
13	W	Paper 11	McKee

Parkhurst SM, Bopp D, Ish-Horowicz D (1990) X:A ratio, the primary sex-determining signal in Drosophila, is transduced by helix-loop-helix proteins. Cell 63: 1179-1191.

Purpose: To illustrate the use of *Drosophila* genetic methods to dissect a developmental pathway (sex-determination)

15	F	Mouse genetics & genomics: Sex determination	Rinchik

The laboratory mouse as a model organism, genetic and cellular dissection of sex determination

18	M	Discussion	Li
20	W	Paper 12	Handel

Schmahl J., Eicher EM, Wahsburn LL, Capel B. 2000. *Sry* induces cell proliferation in the mouse gonad. Development 127:65-73.

Purpose: to show the utility of mouse for analysis of sex determination using genetic conditions, and developmental and cellular appraoches

22	F	Human genetics & genomics: Sex determination	Handel

The human as a model organism, genetic dissection of sex determination and fertility

25	M	Discussion	Li
27	W	Paper 13	Handel

Sinclair AH et al. 1990. A gene from the human sex-determining region encodes a protein with homology to a conserved DNA-binding motif. Nature 346:240-244.

Purpose: to illustrate positional cloning strategy in human families, false starts and success

3	M	Pulling it all together: Summary	Handel

Take-home Exam #3: to be provided at end of class Monday Dec. 3; due Thursday Dec. 5; covers material from Nov. 1 through Dec. 3.