Instructor  Steve Mount  smount@umd.edu  301-405-6934
Meetings  MWF 9:00 AM  PLS 1117.  Sept. 3 through December 12.

We will not meet Oct. 6 or Nov. 28. There is no final exam.

Prerequisites:
Genetics and at least one advanced course in either Genetics, Biochemistry or Molecular Genetics at the undergraduate level. Those without these prerequisites are encouraged to take BSCI 410 first.

Readings
11 papers from the primary literature in molecular genetics are required reading. Papers and supplemental readings will be available online. I will provide links through the course web page at http://www.life.umd.edu/classroom/mocb630. One copy of some papers will be placed on reserve in the Chemistry library (White Memorial Chemistry Library), but the website (not the reserve materials) should be regarded as the definitive source of information about the readings.

Texts and background literature
In the book store:
- Gibson and Muse  A Primer of Genome Science. 2002. This text is required.
- Hawley and Walker  Advanced Genetic Analysis. 2003. This text is required.
  This text is strongly recommended, and I will refer you to it for background reading. The first edition is an acceptable alternative.
- Young  Exploring Genomes. 2003
  This text is recommended. A nice "split-screen" tutorial for online resources.

On reserve in Chemistry (White Memorial) library:
  This excellent book is a nice supplement for human genetics.
Coverage. Methods of genetic analysis in various species commonly used for molecular genetics (model organisms) will be discussed. The primary species are the yeast *Saccharomyces cerevisiae*, the worm *Caenorhabditis elegans*, the plant *Arabidopsis thaliana*, the fruit fly *Drosophila melanogaster*, the mouse, and humans. For each species we will consider methods for the identification of informative mutations revealing new genes or new gene functions. We will also discuss methods for testing the expression of modified genes, usually by genetic transformation of organisms. We will bear in mind throughout the application of information from model organisms to organisms which are not in this group.

The course will also involve a great deal of information about gene expression, cell biology and development (especially gene expression). These topics will be woven into a survey of methods for genetic analysis.

Permission is required for this course. Anyone who has been accepted into the MOCB or CBMG graduate program will automatically be granted permission by the department or program. Students in other Ph.D. programs will be granted permission from the instructor on an individual basis until the class is full (the class was full as of Aug. 28, 2003). Everyone else must wait until the start of classes, when permissions for registration up to a total of 30 students will be granted. This policy is described in even more detail at www.life.umd.edu/classroom/MOCB630/permissions.html. Keeping the class small is important for the paper presentations.

Grading
Your grade will be determined as described below. +/- grading will be used (i.e. grades of A+, A-, B+, C-, etc. are possible). In general, you will not be directly tested on the lecture material except as it applies to the papers, or is reflected in the homework. However, the lectures and homework are designed to work together with the papers. Consider what was written by one student last year: "Halfway through the semester, I began closely reading the journal articles a week before presentation of them, before you began a set of lectures following the previous presentation day. It made the lectures much more interesting and fulfilling." You are encouraged to write the Honor Pledge on your assignments ("I pledge on my honor that I have not given or received any unauthorized assistance on this assignment/examination." See http://www.jpo.umd.edu/aca/honorpledge.html). You are expected to prepare your own homework and you are responsible for your own answers, but I encourage you to work together to prepare your presentations and to discuss the papers and homework.

Papers
The goal is to learn how to extract from a paper:
- what claims are being made
- how the results were obtained (i.e. which experiments were done)
- why the experiments were done the way they were
- whether the data justify the conclusions and what caveats remain
- why these experiments were done at all; and why we should care
Papers
On the date that a paper is to be discussed, come to class familiar with the paper, and with a copy of the paper in hand. Your familiarity with the papers will be judged by your presentations, your contributions to the overall discussion, and by your grade on quizzes.

Presentations (20%)
When papers are covered in class, I may call on you to present a defined section of the paper (usually one figure, or a part of a figure). Your presentation will be graded based on the clarity with which you cover the following four things:

1) the overall point of the figure or section
2) the techniques used
3) the results
4) the interpretation.

Each presentation will be given a specific time limit (5 minutes unless specified), and you will know this in advance.

I will give you a grade on your presentation and a summary by email after class (within a few days). Everyone is subject to being called on at every paper presentation, except that you will be called on only once for a single paper, and you are exempt from presentation on the very next paper. For example, if you are selected to present a figure in paper 2, you will be exempt from presentation for paper 3. This will exempt you from presentations on that day, but not from quizzes (you still have to read the paper). Those scheduled to present on a particular day will be informed at the beginning of class. The selection of students for presentation will be essentially random except that I will ensure that everyone presents at least two times during the course of the semester, you can be removed from the list (if you want to be), when and if you have presented three times, and no one will present more than four times. For papers presented over two days, figures assigned to specific presenters on the first day of a paper scheduled will be reassigned if they have not been presented. Those who present on the first day will be removed from the pool for the second day and for the next paper (remember, no one is exempt from quizzes). If we don't finish a paper on the assigned day, we will not continue that paper; papers will be presented only on the days stated in the syllabus (any changes would be made well in advance, announced in class and posted on the web site).

Quizzes (40%)
A quiz may be given on a paper on presentation day. In some cases, there may be a brief quiz before our discussion of the paper. In other cases, the discussion may be replaced by a full one-hour quiz, or the quiz will come at the end. Some quizzes will count more than others. This weighting will be reflected in the total number of points in the quiz.

Discussion (10%)
Contributions to the discussion that aid everyone's understanding of the paper will help your grade. Good questions are especially encouraged. I will never grade anyone down for asking honest questions about the paper.
Homework (30%).
Homework will be assigned at least four days (two class meetings) before the due date. Homework is due at the beginning of class. In many cases, homework questions will direct your reading to essential points of the paper. However, not all papers will have homework, and not all homework will be specifically related to a paper. (For some papers, background information will be provided on a handout which is not homework or on the web site). There will be 14 homework assignments, each of which will count 20 points. Your lowest four grades (including any not turned in) will be dropped before averaging. Whether or not I accept late homework, and how much it is discounted, will vary depending on many factors, including whether the homework was discussed in class before the late homework was turned in, and why it was not turned in on time.

Your gene. Each of you will be assigned a gene by email (based on what you tell me about your interests). I will send you the refseq accession number for the yeast version of your gene. You will be required to answer questions about that gene and its homologs in other species for Homework 5 (due Oct. 1) and on homework assignments throughout the remainder of the semester.

At the end of the year, the overall scores for homework and quizzes will be normalized before summing. Presentation grades will be averaged as is. I generally give roughly equal numbers of A's and B's and only a few C's, but I do have a sense of what it takes to get an A that is independent of your performance relative to the rest of the class.

Because evaluation during class when papers are presented will count for 70% of your grade, you should be sure to attend class on those days! If you must be absent from class on days when papers are presented (dates in bold on the syllabus) you should let me know (by email or telephone), in advance if possible, and explain your absence. If there is a legitimate reason why you cannot present on a particular day, you will be taken out of the pool. If you are assigned a presentation and are not present, or decline to present, you will be given a presentation grade of C. In the case of conflicts that you know about in advance, try to let me know as soon as you learn that you will be missing the class. Unanticipated absences will be dealt with on a case-by-case basis.

Office hours: I will normally be available immediately after class on Mondays and Wednesdays. We can chat in the hall or walk back to my office. I am also happy to set up an appointment to meet with you in my office at other times. I prefer that you do this by email.

I like to address questions via email so that I can disseminate my answers to the entire class. If you send questions to me at smount@umd.edu, I will generally remove your name and send my answer to the class mail reflector so that everyone can see the question and its answer. Of course, not all questions are of a public nature; you should tell me if you don't want the question posted on the class mail reflector. I will also exercise judgment about what matters call for a public answer.
Section 1: www.life.umd.edu/classroom/MOCB630/section1.html

Sept. 3  Lecture 1 - General Introduction
Outline of the course.
Principal species; Major techniques of molecular biology;
The flow of genetic information from DNA to RNA to protein.
-- Hawley and Walker, Ch. 2

Sept. 5  Lecture 2 - Techniques in molecular biology I: cloning & hybridization.
Hartwell, Ch. 9

Sept. 8  Lecture 3 - Techniques in molecular biology II: Amplifying and
Mutagenizing genes. Nucleic acid biochemistry and manipulation.
(PCR, SELEX, etc.)

large pool of random sequences. Science 261: 1411-1418.
* Homework 1 (on background) is due.

Sept. 12  Paper 1, continued.

Section 2: www.life.umd.edu/classroom/MOCB630/section2.html

Sept. 15  Lecture 4 - Techniques in molecular biology III: Sequencing genomes.
Gibson and Muse, Ch. 2, pp. 78-91
-- Fleischmann et al. (>30 authors). 1995. Whole-genome random sequencing and
-- Venter et al. 1998. Shotgun sequencing of the human genome. Science 280:
1540-1542.
287:2196-2204.
- International Human Genome Sequencing Consortium. 2001. Initial sequencing
and analysis of the human genome. Nature 409:860-921

Sept. 17  Lecture 5 - Techniques in molecular biology IV:
Genome analysis, protein domains, types of homology.
- "Exploring Genomes" by Paul G. Young.
Hartwell, Ch. 11
- The Arabidopsis Genome Initiative. 2000. Analysis of the genome sequence of
the flowering plant Arabidopsis thaliana.
19: 345-351.

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Section 3: www.life.umd.edu/classroom/MOCB630/section3.html

Sept. 19  Lecture 6 - Molecular genetics I: Genetic maps and markers.  
SNP detection methods.  
Gibson and Muse -- pp. 271-294.  
Hawley and Walker "Advanced Genetic Analysis" - Chap. 7

Sept. 22  Lecture 7 - Molecular genetics II: Humans I:  
Genomics, human gene mapping and positional cloning.  
Gibson and Muse "A Primer of Genome Science" - Chap. 5  
* Homework 2 (on NCBI) is due.

* Homework 3 (on paper 2 and SNP detection) is due.

Sept. 26  Lecture 8 - Molecular genetics III: humans II: complex traits, advanced mapping

Sept. 29  Paper(s) 3 -- Lai et al. 2001. A forkhead-domain gene is mutated in a severe speech and language disorder. Nature 413:519-523. and  
* Homework 4 (on paper 3 and gene mapping) is due.

Section 4: www.life.umd.edu/classroom/MOCB630/section4.html

Oct. 1  Lecture 9 - Gene expression I: DNA recombination, repair, transposition  
* Homework 5 (on your gene) is due.

Oct. 3  Lecture 10 - Molecular genetics IV: Mouse I: Transgenics, knock-outs.  
-- Hartwell Reference E

* Homework 6 (on paper 4 and the mouse) is due.

Oct. 10  Lecture 11 - Molecular genetics V: Mouse II: Inbred lines, QTLs, RDA.  
Lisitsyn. Representational Difference Analysis: finding the difference between genomes. TIGs. 11: 303.  
Gibson and Muse -- pp. 258-271.

*  **Homework 7 (on paper 5) is due.**

Oct. 15  **Paper 5**, continued.

**Section 5**: www.life.umd.edu/classroom/MOCB630/section5.html

Oct. 17  Lecture 12 - **Molecular genetics VI: Yeast**
-- Ch. 13 of *Recombinant DNA: Using yeast to study eukaryotic gene function.*
-- **Hartwell Reference A**

Oct. 20  Lecture 13 - **Gene expression II: Transcription.**
-- **Hartwell, Ch. 17**

Oct. 22  Lecture 14 - **Gene expression III: Regulation of transcription.**
-- **Hartwell, Ch. 17**

Oct. 24  Lecture 15 - **Gene expression IV: Microarrays and parallel genetic analysis**


*  **Homework 8 (on paper 6, microarrays and transcription) is due.**

**Section 6**: www.life.umd.edu/classroom/MOCB630/section6.html

Oct. 29  Lecture 16 - **Genetic concepts I: Redundancy and synthetic phenotypes.**
-- **Hawley and Walker, Chs. 3 and 4**

Oct. 31  Lecture 17 - **Molecular Genetics VII: Arabidopsis thaliana**
-- **Hartwell Reference B**


*  **Homework 9 (on paper 7, redundancy and Arabidopsis) is due.**
Nov. 5 Lecture 18 - Genetic concepts II: Epistasis.
-- Hawley and Walker, Ch. 5
-- Hartwell, Ch. 19

Section 7: www.life.umd.edu/classroom/MOCB630/section7.html

Nov. 7 Lecture 19 - Molecular genetics VIII: Drosophila I: Introduction, nomenclature, basics.
-- Hartwell Reference D

Nov. 10 Lecture 20 - Molecular genetics IX: Drosophila II: The many uses of P elements

Nov. 12 Lecture 21 - Molecular genetics X: Binary systems
-- Hawley and Walker, Ch. 5


Nov. 17 Lecture 22 - Genetic concepts III: The nature of alleles and mutations.
-- Hawley and Walker, Ch. 1

Section 8: www.life.umd.edu/classroom/MOCB630/section8.html

Nov. 19 Lecture 23 - Molecular genetics XI: C. elegans
-- Hartwell Reference C
* Homework 10 (on binary systems, alleles and Drosophila) is due.

Nonsense-mediated decay, cytoplasmic polyadenylation, RNA editing.

* Homeworks 11 AND 12 (on paper 9, C. elegans and epistasis) are due.

Nov. 26 Paper 9, continued.
Dec. 1  Lecture 25 - Gene expression VI: Post-transcriptional regulation II: Hartwell Sex determination in Drosophila (Ch. 17)

*  Homework 13 (on paper 10 and post-transcriptional regulation) is due.

Section 9: www.life.umd.edu/classroom/MOCB630/section9.html

Dec. 5  Lecture 26 - Gene expression VII: Post-transcriptional regulation II: RNA interference and microRNAs

Dec. 8  Lecture 27 - Gene expression VIII: Epigenetic phenomena I. Methylation, imprinting, heterochromatin and maintenance of active or inactive states.


*  Homework 14 (on paper 11, RNAi and epigenetics) is due.