Molecular Genetics, BIO 462/662 Fall 2007

M 8/27 RR Course Overview
Content and aims: Molecular Genetics: Theory < course topics > Practice
Format and grading: discussion, papers, exams, projects
Overview of gene expression - Gene structure and function
Strachan & Read, sections 1.3-1.5

W 8/29 RR Regulation of gene expression – *cis*- and *trans*-acting elements, RNA splicing; Strachan & Read, sections 10.1-10.3
Methods for studying gene expression
Strachan & Read, sections 6.1-6.3, 7.1-7.3.

F 8/31 RR Transcriptomics – Global mRNA profiling
Strachan & Read, section 19.3.
Genome structure and mutation Strachan & Read: Ch. 9 (reference only)
Bioinformatics I. *Handout of Arabidopsis Database exercise due 9/26)*

M 9/3 **No class (Labor Day)**

W 9/5 RR Proteomics – Global protein profiling
Strachan & Read, section 19.4.

F 9/7 RR Discussion of DeRisi et al. paper

M 9/10 RR Using transcription factors to study protein interactions – Yeast Two Hybrid
Song and Fields (1989)
Epigenetic mechanisms of gene regulation – Chromatin, DNA methylation and genomic imprinting
Wolffe and Matzke, 1999. Strachan & Read, sections 10.4-10.5

W 9/12 RR GMOs; Transgenic plants for crop improvement

F 9/14 RR Guest Lecture – Anthony Garza, SU Biology
Databases and their application to genome-wide approaches to determining gene function in prokaryotes

M 9/17 SE Review of genetic principles Strachan & Read: Ch. 4
Heritability Strachan & Read: Ch. 16.1-16.3; 16.8
Mendelism
Polygenic Inheritance
Muller's Definitions of allele types

W 9/19 SE More about alleles –
Wertman *et al.* Systematic mutational analysis of the yeast ACT1 gene
Use of plasmids to alter gene dosage and create libraries
Concept: Dosage suppression and methods to study genes whose function is essential to cellular replication – Liu et al. paper

F 9/21 SE Complementation and non-complementation
Genome structure and mutation Strachan & Read: Ch. 9 (reference only)
Types and locations of DNAs
Cot curves
Coding fraction
mutagenesis methods and hit rates
types of mutation with respect to gene structure and protein folding

M 9/24 SE Discussion of Winzeler et. al and Giaever et al. papers

W 9/26 RR/SE **Exam 1** Material through 9/24
Arabidopsis Database Exercise--**Due at beginning of class**

F 9/28 SE Genetic Interactions
Suppression
Enhancement
Synthetic lethals; Second site non-complementation (SSNC)

M 10/1 SE Discussion of Tong *et al*.: Genome wide synthetic lethality screening in the systematic deletion set; construction of gene networks
Bioinformatics II. *Handout of GO take home assignment (due 10/29)*

W 10/3 SE Discussion of Halsell and Kiehart paper on SSNCs

F 10/5 SE/EM Group topic assignment – topic selection and organization of literature search

M 10/8 EM RNAi interference (RNAi): What it is and how is it useful? Strachan & Read: 20.2.7; 20.3.3.

W 10/10 EM Endogenous RNAi-related mechanisms repress gene expression at the post-transcriptional level. Strachan & Read: 9.2.3; 10.2.6.

F 10/12 **No class – Eid Ul-Fitr**

M 10/15 EM EM –Post-transcriptional silencing as a defense against transposon activity in the germ line: Discussion of Sijen & Plasterk (2003).

W 10/17 EM Guest Lecture – Prof. Melissa Pepling, SU Biology
Mouse methodologies

F 10/19 EM Guest Lecture – Prof. Craig Albertson, SU Biology
Applications of Quantitative Genetics to Development and Evolution

M 10/22 EM RNA-mediated mechanisms of transcriptional silencing: histone and DNA modification. Strachan & Read: 10.2.1; 10.4; 10.5.6.

W 10/24 EM RNAi-related mechanisms of viral defense in plants and animals.

			Can RNAi be used as an effective clinical tool to treat disease? Strachan & Read: 21.6.
F	10/26	EM	An example of RNA-mediated viral defense in human cells: Discussion of Lecellier *et al*. (2005)
M	10/29	SE/EM	**Exam 2** – lectures through 10/26. GO take-home assignment—**Due at beginning of class**
W	10/31	JB	Studying human disease in the Drosophila model system Tickoo and Russell (2002) Curr. Opin. Pharmacol. 2: 555-560. Strachan & Read, Ch. 7, p. 192; Ch. 8, pp. 229-236, Ch. 19, pp. 541-545 *Hand out homework assignment –* Bioinformatics III. *OMIM, BLAST and Wormbase due on 11/19*
F	11/2	JB	Overview and discussion of genetic tools St. Johnson (2002) Nature Reviews P element insertional mutagenesis Cloning by plasmid rescue & Inverse PCR
M	11/5	JB	Genetic trickery (continued) FLP/FRT system for mosaics; UAS/GAL4 system
W	11/7	JB	Study of human disease in Drosophila - Cancer Strachan & Read, Ch. 17, pp. 488-506; Xu, *et al*. (1995) Development
F	11/9	JB	Study of human disease in Drosophila , cancer continued Tao, et al. (1999) Nature Genetics
M	11/12	JB	Neurodegeneration in man and flies Min and Benzer (1999) Science
W	11/14	JB	Trinucleotide repeats and neurodegeneration; Strachan & Read, Ch. 11, pp. 337-340 Marsh, et al. (2000) Human Mol. Genet. 9: 13-25.
F	11/16	JB	Discussion of Marsh, et al. (2000)
M	11/19		**Exam 3** Material through 11/17 *Assignment (OMIM, BLAST ...)* --**Due at beginning of class**
W	11/21		**No Class (Thanksgiving Break)**
F	11/23		**No Class (Thanksgiving Break)**

M	11/26	Student presentations – In class group organization time; Reference lists due
W	11/28	Student presentations
F	12/30	Student presentations
M	12/3	Student presentations
W	12/5	Student presentations
F	12/7	Course review

Bio 462/662 Molecular Genetics
Course Policies and Grading
Fall 2005

Course coordinator: Dr. Scott Erdman, BRL 609, seerdman@syr.edu, 443-3748
Lecturers: Dr. Ramesh Raina, BRL 601A, raraina@syr.edu, 443-4546
Dr. Eleanor Maine, Lyman 426, emmaine@syr.edu, 443-9169
Dr. John Belote, BRL 304, jbelote@syr.edu, 443-3695

Reader: Bio 462/662 - Molecular Genetics; Erdman, Raina, Maine and Belote
Textbook: Human Molecular Genetics, 3rd edition; Strachan & Read; Garland Publishing

The reader is required, while the textbook is optional, but highly recommended.

I. Bio 462

(A) Faculty: There will be four primary faculty involved in teaching this course, Drs. S. Erdman, E. Maine, R. Raina and J. Belote. Please refer any questions regarding content or materials directly to the faculty presenting that material. Any additional questions or problems—see Dr. Erdman. For matters that are likely to require some appreciable amount of time it is generally preferred that you make an appointment, rather than 'show-up' at a faculty member's office.

(B) Evaluation: The course will be divided into several evaluation components. Your grade will be determined based on your performance on three exams, three take home assignments and a group project. There will be a total of 200 points possible in the course. The three take home assignments for the course are due on the dates of the exams and you should therefore plan your studies and work on them accordingly. Take home assignments, lecture notes and announcements related to the course will be made available through the course site in Blackboard.

Please note the following:

(i) **No exams will be dropped and participation in the group project cannot be waived. Assignments submitted late will be subject to an automatic discounting of 50% of the possible points before grading.**

(ii) **There will be no final exam.**

(iii) **No additional or extra credit assignments will be considered.**

(C) Format:

(iv) The course will follow a general format of **lectures** and **discussions** on specific topics. Background material for these will be found in papers that have been selected for a "Bio 462 Molecular Genetics Reader" available in the bookstore as well as in the recommended readings from the textbook by Strachan and Read. Some concepts may be elaborated on in lecture and you will be responsible for any material presented in lecture, hence attendance is expected and essential for success in the course. Provision of lecture notes to students is at each lecturer's discretion.

(v) Students will be required to **read, analyze and discuss a selection of scientific papers** that typify molecular genetics research and illustrate the concepts we are covering. Reading scientific literature in the form of

primary papers is an essential skill, as is being able to clearly summarize and effectively evaluate their content. You will also be guided by some general questions that are intended to help you analyze the papers. These papers are all contained in the Reader for the course available in the SU Bookstore. The papers must be read in advance of the class discussion. Approximately 1/2 of the class period will be devoted to discussing the paper in randomly assigned small groups. The task of each of these groups will be to "tear apart" one specific part of the Results section of the paper. Your job will be to understand and judge the quality of the experiments used in that specific section of the paper and to determine how the various experiments support (or fail to support) one another and the conclusions of that section of the paper and the paper as a whole. During the final half of the class period we will discuss as a class the interrelationships of these Results sections and identify particularly brilliant, or, perhaps sometimes, missing, experiments.

(vi) **A group assignment** at the end of the course will involve presentation of a specific "advanced" technique or unique paper/topic to the class. You will receive this assignment before Thanksgiving break and the last four class periods will be reserved for these presentations and discussions. Evaluation of these projects will be centered on your understanding of the material, clarity of presentation and self-evaluation by group members. Some of these topics may involve the molecular basis of inherited diseases. If your group chooses such a topic, remember that the *majority of the focus of your presentation should be on the genetics and molecular mechanisms,* **not** simply symptoms, disease etiology and treatments.

(II) Bio 662

The graduate level section of this class will involve <u>two components in addition</u> to the 462 material covered by the take home assignments and exams. However, Bio662 students will **not** be included in the final group presentations.

(A) There will be one additional discussion section or tutorial beyond the Bio 462 class discussions with each faculty member. These discussions will center on an additional paper or perhaps a more "in-depth" introduction to the methodologies surrounding the papers being read that week. Materials for these discussions (1 paper, usually) will be handed out in advance of the discussion day.

(B) A series of assignments will entail your identifying, researching and organizing a research grant proposal outline on a topic related to the material covered during the course and then developing a set of specific aims addressing this topic. Organization of the aims of a proposal requires extensive thought and this will be the focus of this assignment – you will not be required to write a full proposal, only the aims section and one part of the experimental plan. For this project you will work both individually and in groups. There will be group discussion and critique of approaches and participation in these activities will constitute a portion of your final course grade.

<u>Graduate grades will not be a part of the undergraduate curve or grade distribution; grading of graduate students will be done using the undergraduate curve or grade distribution as a reference only.</u>

A general guide to reading and understanding scientific papers:

It is important to view a scientific paper as a formal argument of a point. Most reasonable points can be supported by more than a single observation or argument; although, in some cases one strong experiment may be worth much more than several weak ones. If you look carefully at a well-written paper you will find that the basic points the paper makes are found in a) the Abstract and, sometimes b) the last paragraph of the Introduction. Evidence in the form of experiments will be found in the Results. Details, some of which being nonetheless very important, regarding how the experiments were done are found in the Materials and Methods. Finally, the Introduction and Discussion sections serve to introduce and discuss the experimental findings of the work. We will seek to systematically analyze a paper by having different groups each focus first on a single section of the Results or Discussion.

The questions you will try to answer as groups are:

I. Results:

1) What is the primary working hypothesis (question to be addressed-may be found in the Introduction or beginning of the Results/Discussion sections)?
2) What are the different pieces of data/experiments presented in this section?
3) Which are the strongest findings? Which are the weakest data?
4) How do these points relate to one another? Do any of them support each other?
5) How do these points support the main points(s) or hypothesis of the paper?
6) Regarding (#4) above, rank your section relative to the other sections of the Results.

II. Discussion:

1) What results do the authors choose to focus on and discuss at greater length in this section?
2) Does the point being discussed by the authors seem well supported in the Results or not?
3) Do the authors make any speculations? How valuable are they likely to be if correct and if incorrect?

(1) Approximately 1/2 of the class period may be devoted to discussing the paper in randomly assigned small groups. The task of each of these groups will be to "tear apart" one specific part of the Results or Discussion sections of the paper. Your job will be to understand and judge the quality of the experiments used in that section of the paper to support (or fail to support) one another and the conclusions of that section of the paper as a whole.
(2) During the last 20 min. of the class period we will discuss as a class the interrelationships of these sections and identify particularly brilliant, or, perhaps sometimes, missing, experiments.
(3) The aim of the discussion 'structure' will facilitate your ability to construct a well-supported scientific argument or set of proposed experiments. Obviously, for this mechanism to work you will have to have read the paper *before class begins* as there will not be time for this in class. While it may seem that not reading the paper and simply "following along" would be an easy way to approach this part of the class, we will incorporate three evaluation criteria that will make this a less-than-wise option for you to consider.

(i) Some content from this part of the course will appear on the exams.
(ii) Students will be called on at random to discuss their interpretations of the literature and help further the discussion in the class as a whole.
(iii) Your *individual contributions* to the efforts of different groups in which you participate throughout the course of the semester will be considered to help determine your final grade—both peer and faculty evaluations may be used.