Genetics
Biology 310
Spring 2010
Lecture: MWF 9 – 9:50 in A254
Laboratory: M 1:30 – 4:20 in K201
T 1:30 – 4:20 in K208

Instructors: Maureen Peters (lecture & Monday lab); Katherine Cullen (Tuesday lab)
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Office hours: Peters, T 10:30 – 11:30, W 10 – 11, and by appointment.

Course goals:
1) To provide a solid understanding of the principles of classical & molecular genetics.
2) To increase your appreciation of the role of genetics in all areas of the biological sciences.
3) To improve your ability to critically read primary scientific literature in molecular genetics.
4) To improve your ability to communicate scientific information effectively.

Textbook: Readings for lectures are primarily from Griffiths et al., An Introduction to Genetic Analysis, 9th edn (W. H. Freeman & Co.). The text website, http://bcs.whfreeman.com/iga9e/, has extra material that you may find helpful such as animations, exercises & practice tests.

Blackboard: The syllabus, lecture readings, problem sets, answer keys, discussion and supplemental papers will be made available on Blackboard.

Problems: This course is heavily based on problem solving. You must be able to apply the material that you have learned to solve these problems. The best way to learn problem solving is to practice it! Practice problems will be assigned at most lectures – do them promptly.
Problems solving/help sessions: Problem solving/help sessions will be held some Wednesday evenings from 7 – 8 in K201 (see class schedule).

Discussion papers: We will read & discuss several research articles throughout the semester. Groups of 2 or 3 students will be responsible for leading discussion of one article. Participants will complete short written assignments for 3 of the articles. More information about the article discussions and article-related assignments will be provided during the 2nd or 3rd week of class.

GRADING		
Problem sets	5 @ 30 pts e.	150 pts
Paper discussions (Group of 2 or 3 will lead discussion. Everyone presents once)		
Participants (3 Assignments)	3 @ 10 pts. e. *(skip 3)*	30 pts
Paper Leaders (x 1)	Prep. meeting with me	15 pts
	Introduction/class discussion	35 pts
Hour Exams	2 @ 100 pts each	200 pts
Final Exam	100/170 pts will be cumulative	170 pts
Lab portion	(*details in lab syllabus*)	150 pts
TOTAL		750 pts

Exam policy: No make-up exams will be given without prior consent, except in the case of unexpected emergency (e.g., illness with doctor's note, death in the family).
Late assignment policy: All problem sets & written assignments must be handed in **before** class begins. 10% will be deducted for each day that an assignment is late.
Honor System: Exams will be given under the Honor System as described at www.oberlin.edu/students/links-life/rules-regs.html#honor.

DAY	TOPIC	READINGS (*it.*=classics **)
2/8	Introduction	Ch. 1
2/10	Autosomal inheritance	Ch. 2, 2.1-2.4; *Mendel, 1865*
2/12	Sex linked inheritance	Ch. 2, 2.5; *Bridges, 1914*
2/15	Human genetics: pedigrees	Ch. 2, 2.6
2/17*	Pedigree problems & Independent assortment	Ch. 3, 3.1-3.4
2/19	Cytoplasmic inheritance & genetic testing discussion **Problem set #1 due**	Ch. 3, 3.5; Ch. 16, 16.3; 20, 20.5; Harmon, 2006
2/22	Gene mapping I	Ch. 4, 4.1-4.2; *Sturtevant, 1913*
2/24*	Gene mapping II	Ch. 4, 4.3, 4.8
2/26	Gene mapping III problems	
3/1	Mapping human ancestry & diseases **Problem set #2 due**	Drayna, 2005
3/3*	Allelic interactions	Ch. 6, 6.1
3/5	**EXAM 1(up to & including 3/1 material)**	
3/8	Gene interactions	Ch. 6, 6.2, 6.3
3/10	**PAPER 1**: Evolution of cavefish	Protas et al., 2005; Ch. 19, 19.6
3/12	Forward genetic screens I	Ch. 1, 1.3; Ch. 20, 20.4
3/15	Forward genetic screens II	Ch. 20; p.745
3/17*	Mutation	Ch. 15, 15.1-15.3, *Muller, 1927*
3/19	**PAPER 2**: Yeast that can't secrete.	Novick, et al., 1980
3/22	DNA recombination **Problem set #3 due**	Ch. 15, 15.4 & 15.5
3/24	Reverse genetics: siRNA	Ch. 13, p. 479-482; Ch. 8, p.312-314; Fire et al., 1998
3/26	**PAPER 3**: *C. elegans* keep track of time?	Dal Santo et al., 1999
	SPRING BREAK	
4/5	Targeted mutations in mice I	Ch. 20, p.747-753
4/7*	Targeted mutations in mice II	Mak, 2007
4/9	**PAPER 4**: Recovery from neurodegeneration?	Yamamoto et al., 2000
4/12	Mobile genetic elements **Problem set #4 due**	Ch. 14
4/14*	Gene dosage	Ch. 16, p. 565-580
4/16	**PAPER 5**: Modeling cancer in mice	Zhang et al., 2004
4/19	**EXAM II (up to & including 4/14 material)**	
4/21	Genomics I	Sup. Readings, meet @ Mac lab
4/23	Genomics II	meet @ Mac lab
4/26	Genomics III (Alexa Sharp, Computer Science)	
4/28	Genomics IV (Alexa Sharp, Computer Science)	
4/30	Eukaryotic gene regulation I **Problem set #5 due**	Ch. 11, 11.1-11.3
5/3	Eukaryotic gene regulation II	Ch. 11, 11.4
5/5	Eukaryotic gene regulation III: microRNA's	Reinhart et al., 2000; Seydoux, 2006
5/7	**PAPER 6**: How to make one specific cell	Wenick & Hobert, 2004
5/10	Epigenetics	Ch. 11, 11.6
5/12	**PAPER 7**:What's so special about stem cells?	Meshorer et al., 2006
5/14	Topic to be determined	

Thursday 5/20– FINAL EXAM – 9 AM!

- Problem solving/help session 7– 8 PM in K201; ** I will post (on Blackboard) all additional reading material including classic papers describing the original experiments that led to major breakthroughs in Genetics.

Genetics Laboratory Syllabus
and
General Information

Spring 2010
M 1:30 – 4:20 PM in K201 (Peters)
T 1:30 – 4:20 PM in K208 (Cullen)

Goals: The laboratory component of Genetics is designed to complement the material presented in the lecture portion of the class, to introduce you to *Caenorhabditis elegans*, a model genetic organism; to improve your ability to plan and analyze experiments; and to build scientific communication skills.

Philosophy: The major portion of this laboratory course is designed to simulate a research laboratory experience in a *C. elegans* genetics laboratory. You will perform multiple experiments that involve several consecutive genetic crosses of mutant animals. These animals develop at their own pace making it impossible to fit the experiments into weekly three-hour segments. Thus, **you will need to spend time in the lab in addition to our regularly scheduled meetings *but* will probably not need to be in lab for entirety of every scheduled meeting**.

The lab will be open from ~9 AM until 4 PM Monday to Friday. You can access the lab on any day from 8 AM until 10 PM by picking up the appropriate keys from the Oberlin Office of Safety and Security (150 W. Lorain St.). You will be required to leave your Oberlin ID card at the Office of Safety and Security until you return the keys.

We do expect you to come to lab each scheduled lab meeting, i.e. Monday or Tuesday, but depending on the state of your experiments, you may not need to stay the entire laboratory session.

Required Laboratory Materials:
1. Indelible **extra fine** marking pen (e.g., "Sharpie") *Dark colors are most legible. This may be purchased at the bookstore.*
2. Lab notebook. You may use one from a previous lab course, as long as you have about 40 blank pages.

Collaboration: You and your lab partner will work together on the experiments. In most cases, you will perform experiments in parallel and share the data. If handled properly, scientific collaborations such as this can be rewarding both professionally and personally. To insure a pleasant and productive collaboration you need to communicate effectively with each other and divide the work equally. You are encouraged to work together on assignments but you must always submit **an individual lab report or assignment, one have written entirely on your own**. Each person's lab notebook should contain all of the primary data. If anyone besides your lab partner makes a significant contribution to your work you must acknowledge the person when you turn in your assignment.

Honor System: The course assignments and assessments should be performed under the Honor System's guidelines. For further information please see the documents available at www.oberlin.edu/students/links-life/rules-regs.html#honor.

Grading

	Due date/suggested completion date	
MAPPING EXPERIMENTAL SEQUENCE		
Assignment 1: Mating plate	Due 2/15 or 16; 2/22 or 23	5
Assignment 2: Progress report on mutant	Due by 3/15 or 16	20
Experiment 1: Dominance testing of mutant	*Complete by 3/8 or 9*	*10*
Experiment 2: Mapping of mutant	*Completed by 3/25 or 26*	*30*
Experiment 3: Complementation test of mutant	*Completed by 4/26 or 27*	*10*
Manuscript Summary of data from expts 1-3, *graded now* Written report itself	Due 5/14 (Friday)	 20
Quizzes #1: Basic *C. elegans* i.d., anatomy #2: Mapping your mutant (take-home)	 In lab on 2/22 or 23 Due 4/9 (Friday)	 10 10
RNAi INTERFERENCE SCREEN		
Assignment 3 Assignment 4	Due 4/16 (Friday) Due 5/3 or 4	10 15
Genetics in the News		5
Lab citizenship/participation/cleanliness		5
GRAND TOTAL		**150**

Late policy: Late assignments will be penalized 10% per day late. If you are having experimental problems and you discuss your situation with your instructor several days **before** the due date, you may be given an extension.

MORE DETAILS ON ASSESSMENTS (and how they help us to achieve the course goals):

Goal: Learn to see and manipulate worms

Assignment #1: Mating worms.
Submit one "perfect" mating plate directly to your instructor during lab.
You simply cannot do genetic analysis without mating worms reliably. It is tough at first but gets much easier as you practice!

Due: 2/15 or 16, 2/22 or 23

Quiz: Practicum testing ability to identify hermaphrodites, males, "simple" mutants; also testing basic knowledge of nomenclature, and anatomy.
By preparing for the quiz you will develop the identification skills required for the subsequent experiments.

Date: 2/22 or 23

Goal: Characterizing your mutant: preparation, execution, & follow-up

Assignment #2: Progress report for Experiment #2.
You will report your phenotypic characterization in a short summary paragraph. Characterizing the mutant phenotype will help to you to identify traits that will allow you to recognize your mutant in a mixed population of normal and mutant worms. The ability to find your mutant in a mixed population is necessary to complete the mapping experiments.
You will deepen your understanding of experiment #2 by answering some questions about the protocol and drawing out genetic crosses.

Due by 3/15 or 16

Experiment #1: Testing the dominance of your mutant.
Determine whether your mutant is dominant or recessive and X-linked or not by analyzing a genetic cross to wild-type.
This information will be of use in planning for experiment #2. The process also increases your ability to mate mutant worms and identify your mutant.

Graded as part of manuscript.
Finish by 3/8 or 3/9

Experiment #2: Finding and mapping your mutant with visible markers.
Map your mutant to a chromosome. Submit a marked allele to me.
This long experiment gives you hands-on experience with mapping. Since it is a long sequential experiment you will learn how to plan and monitor your experiments. You will grow to appreciate the dictates of working with a multi-cellular laboratory animal.

Graded as part of manuscript.
Finish by 3/25 or 26

Experiment #3: Complementation testing your mutant.*
Based on results from experiment #2 you will identify and order an appropriately marked allele from the *C. elegans* worm repository. Then you will perform a complementation test.
The complementation test will allow you to determine the accuracy of your chosen candidate mutant gene.

Finish by 4/26 or 27

Goal: Gain familiarity with RNAi and screens

Experiment #4: RNAi screen, focus on defecation defects
You will be responsible for performing a "mini-screen" using clones from a *C.elegans* RNAi library and reporting your results. You will use bioinformatic resources to determine the size of your RNAi insert and to compare your observations to those of others. You will also answer some general questions about the protocol. This process will familiarize you with the pros and

cons of RNAi as a technique and screens in general. Your results will be organized in a "work sheet" format rather than manuscript form.

Assignment 3 due 4/16 (Friday)
Assignment 4 due 5/3 or 4

Goal: Building written & oral scientific communication skills

Lab meetings: We will have several lab meetings during which you will present and discuss your experimental progress. You will also share some new research findings related to molecular genetics during the "Genetics in the News" segment.

Manuscript: Characterization of an uncoordinated mutant.

Scientists communicate their research findings primarily by writing articles that are published in scientific journals. To learn to communicate using this format, you will write a research article to summarize your mutant analyses. The manuscript will include: an abstract, brief introduction, results: data & analysis from assignment 2, experiments 1 - 3, and a brief discussion. You should include several figures.

Mapping your mutant manuscript: 70 pts. (50 pts on completion of experiments, and experimental results, 20 pts on presentation of data with particular focus on clarity of figures)

Lab Notebook
The purposes of a keeping a lab notebook are to prepare for performing an experiment, to track experimental observations and modifications, to analyze results and, finally, to record conclusions. Your notebook should always be up to date, coherent and legible. It may be monitored during the semester.

Format:
I will not require a specific notebook format but you should follow these guidelines. Each lab exercise should start with the date and a sentence describing the overall goal of the assignment or experiment. You should enter any materials prepared, necessary calculations, and drawing of genetic crosses.

If you write in a dark colored pen, do NOT use both sides of the paper. It shows through and makes it difficult to read. Do NOT scribble out mistakes. Simply draw one line or one big "X" through it.

It is *essential* to update lab notebooks as you go through the experiment, writing down any observations or results, and recording any changes in procedures that differ from those that were intended. It is important to accurately record what really occurred during an experiment, rather than what you wish had occurred, in order to be able to honestly evaluate the result or to trouble shoot experiments that didn't work. At the conclusion of an experiment data analyses & brief conclusions must be entered.

Special considerations for *C. elegans* experiments:
In preparing for a genetic experiment **you must draw out all crosses**!

You will be performing several assignments/experiments concurrently. Therefore, a chronological entry format is not the best option for this notebook. Instead you should estimate how many notebook pages are required for the entire assignment/experiment when you begin and reserve the necessary pages in your notebook.

Maintenance of worms, maintaining strains & mating plates, should be noted in your notebook.

Lab Guidelines.
During the semester we will be working with living organisms, toxic substances, finely calibrated (and thus expensive) instruments, and unfamiliar equipment. We will be sharing limited space, sharing equipment, and all of us will be constrained by limited time. If we are to succeed, each student must come to lab prepared.

- Before coming to lab you should have read the lab protocol sufficiently well that you have a good idea of what procedures you will be doing and what the ultimate goal of the exercise is. Using a lab notebook is standard practice in research labs, and helps scientists ensure that they have fully planned out experiments and have all materials on hand. It also keeps the protocol fresh in your mind, allowing the experiments to be carried out without mistakes, in a smooth and efficient manner. Being prepared (and organized!) in advance saves time in the long run.

- As in other biological and chemical laboratories, there should be no eating or drinking in the room. Also, avoid touching or wiping your face and eyes with your hands during an experiment. Do not chew your pencil or apply Chapstick. If your hair is long, it is a good idea to pull it back away from your face. The last thing you should do before leaving the lab for the day is wash your hands with soap and water.

- Please keep your lab space clean and tidy. Take measures to avoid contamination of your worm plates (discussed in worm handbook).

- Place your backpack and coat out of the way along the windows in the laboratory. Because we will be moving about the laboratory extensively, you should not place them near the lab benches or on the floor where they could trip someone.

- Do not leave your lab stool/chair in the middle of an aisle. It is inconsiderate and dangerous.

- During the semester you will be instructed in the use of particular equipment. It is your responsibility to make certain that you understand how this equipment works.

- You must **attend all lab periods** but may leave early depending on the state of your experiments.

Safety

You will receive instructions on the handling of toxic substances and on the disposal of hazardous waste. In general, you should be aware that Federal law mandates that information on lab chemicals be available to those working with the chemicals. The physical and chemical properties of these chemicals as well as any special handling precautions, health hazard data and disposal information are all described on what is known as an MSDS (Material Safety Data Sheet). These sheets are available in the chemical stockroom of the Biology Department. Information may also be obtained by consulting the MSDS solutions center via the Internet at

http://www.msds.com

In the provided search box enter the name of the chemical of interest. If in doubt about a substance, *ask questions*!

When you enter a laboratory for the first time, note the location of fire extinguishers, eye wash stations and safety showers. Chances are excellent that you will never need to use these items, but if you do, you will not want to waste time searching for them! And remember, this information and attitude toward your own safety applies not only to this course, but to other lab courses at Oberlin and to other laboratories in which you may work in the future.

Suggested lab progress.

DATE	CLASS TIME	DUE
LAB 1 2/8 or 9	Learn to use the microscope, handle pick, move worms, work on identifying different sexes and stages.	
LAB 2 2/15 or 16	**Assignment #1**: Set up a mating plate, turn in. Work on worm handling and identification of sexes, developmental stages, & mutant identification. Obtain your Unc mutant, become familiar with its phenotype. ***Between now and next week:*** Maintain your N2 and mutant worms. Prepare for quiz next week: L4 hermaphrodite and male plates available daily. Have lots of L4 mutants ready for class on 2/22 or 23 so that you can start assignment #2 and experiment #1.	
LAB 3 2/22 or 23	**Quiz #1**- during lab Begin **assignment #2**: phenotypic description part. **Experiment #1**: Begin, if possible ***Between now and next week:*** Maintain your N2's, mating plates and mutants. Start/continue assignment #2, experiment #1.	**Assignment #1** (if not already completed last week.)
LAB 4 3/1 or 2	Lab Meeting: Progress Reports, Genetics in the News Begin/continue **assignment #2**, **experiment #1**. **Experiment #2:** Begin, if possible. Obtain mapping strains. ***Between now and next week:*** You should be able to plan this on your own from now on. It will vary depending upon your progress through the experiments. Please talk to your instructor if you have questions.	
LAB 5 3/8 or 9	Lab Meeting: Progress Reports, Genetics in the News **Experiment #2:** Begin! Get individual marker strains.	***(Experiment #1 completed by now)***
LAB 6 3/15 or 16	Lab Meeting: Progress Reports, Genetics in the News Continue **experiment #2**.	**Assignment #2**
LAB 7 3/22 or 23	Continue/finish **experiment #2**. Begin data analysis. **Experiment #3:** Prepare by finding complementation strains using Wormbase. Ask Prof. to order it.	***(Experiment #2 completed by 3/26)***
	SPRING BREAK! Don't let your worms die!	

LAB 8 4/5 or 6	**Experiment 4**: RNAi experiment begins, obtain worms, review Con phenotype Begin **experiment #3**? (Depends on arrival of complementation strain.) *Continue/complete experiment #2, if you could not before spring break.* **Quiz #2** given out. ***Between now and next week:*** Turn in Quiz on Friday. Continue **experiment 3 & 4**. Practice identifying Con worms.	**Quiz #2 due on FRIDAY**
LAB 9 4/12 or 12	Lab meeting: Progress reports, Genetics in the News Continue/complete **experiment #3 & 4.** ***Between now and next week:*** Continue/complete **experiment 3 & 4**.	**Assignment #3 due FRIDAY**
LAB 10 4/19 or 20	Lab meeting: Progress reports, Genetics in the News Continue/complete **experiment 3.** **Experiment #4:** Perform PCR (experiment 4), complete screen.	***(Experiment #4 completed by now)***
LAB 11 4/26 or 27	Lab meeting: Progress reports, Genetics in the News **Experiment #4:** run PCR gel.	**Assignment #4 due** ***(Experiment #3 completed by now)***
LAB 12 5/3 or 4	Wrap-up and clean-up. Finish any remaining experiments.	
LAB 13 5/10 or 11	No scheduled lab – work on your manuscripts.	**Manuscript due FRIDAY** (includes data and analysis of Experiments #1–3)