Genetics of Model Organisms
BIOSC 2130 ~ Fall 2014
Thurs 10-11:50 a.m. Langley A219B

Instructors
Debbie Chapman (dlc7@pitt.edu) *course organizer
Jeff Hildebrand (jeffh@pitt.edu) *course organizer
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The basic principles of genetics have been elucidated largely by studies using a small number of species: from the peas used by Mendel to more recent examples such as the zebrafish. In this course we will investigate many of these key species that have become model organisms, including the yeast, Saccharomyces cerevisiae, the nematode, *Caenorhabditis elegans*, the fruit fly, *Drosophila melanogaster*, and the mouse, *Mus musculus*. Why were these species chosen to study genetics? What important findings in genetics have these studies yielded? How do you 'do' genetics in these model systems? How can experiments with these species help us to understand the basis of human genetic disease? These questions will be addressed by presentations from experts in the field and by discussions of classic and current literature.

This course is open to all graduate students at the University of Pittsburgh. It is assumed that students participating in the class have taken an introductory genetics class at undergraduate level (e.g. BIOSC 0350 here at Pitt).

Schedule

	Date	Subject	Instructor
1	Aug 28	Introduction to Genetics and *Drosophila* as a Genetic Model Organism	DLC
2	Sept 4	*Drosophila* genetic screens – ectopic eyes – Tribute to Walter Gehring	DLC
3	Sept 11	*Drosophila* genetics – More eyes – Ras signaling pathway Enhancer and Suppressor screens	DLC
4	Sept 18	*Drosophila* genetic screen for cancer Mouse as a genetic model system	DLC/JDH
5	Sept 25	Mouse genetic screens	JDH
6	Oct 2	Mouse genetic screens. Mouse dosage compensation in mammals Oct 3 - Jeannie Lee, Science 2014	JDH
7	Oct 9	Mouse genomic imprinting	JDH
8	Oct 16	Mouse genomic imprinting Genomic Editing – ZFNs, TALENs, CRISPR-Cas9	DLC/JDH
9	Oct 23	Genomic Editing – Paper Discussion	DLC/JDH
10	Oct 30	Genomic Editing – Paper Discussion Yeast Genetics	DLC/CEC
11	Nov. 5	11 am – Introduction to *C. elegans* as a Model System	LAJ
12	Nov 6	Yeast Genetics	CEC
13	Nov 13**	RNAi: discovery, function and its use as a genetic tool in *C. elegans* – Paper Discussion (Phil Sharp lecture begins at 11 am (Langley 219B)	DLC/JDH
14	Nov 20	Student Presentations	Students
	Nov 27	*THANKSGIVING*	
15	Dec 4	Student Presentations - Using model organisms to study human disease	Students
16	Dec. 11	Student Presentations	Students

**Class to be held in Langley 219A, beginning at 9 am

Coursework and Grades

Participation: 40%

Students must play an active part in the course by reading the set papers in advance and contributing to the discussion during class.

Homework: 30%

Each instructor will set a short assignment for specific classes. For most paper discussion days, a Figure facts template will be assigned for each paper. These are due by midnight on the Wednesday before the paper discussion class. Students should upload their filled in templates to the Course web site under Assignments.

Final Presentation: 30%

Toward the end of the semester, each student will choose a paper that uses one of the discussed organisms to model a human disease*. Each student will give a 30 minute (roughly) oral presentation to the class with 5-10 additional minutes for questions. This final presentation should include introductory material, focus should be given to the human disease and how this model organism is a great system to study this disease. The presenter will then lead the discussion of the research article for the entire group (i.e. this is what the instructors did for the first set of papers – now you get to do it!). The presenter will prepare a Powerpoint presentation including all of the figures from the paper, assuring that the figures are of decent resolution. As the presenter, you will not be able to go through each figure in detail in the time allotted; you will need to focus on the most important parts of each figure. Each student is expected to have read the papers and contribute to the discussion. Although the group as a whole will discuss future directions for the research (coming to class prepared with ideas – or ready to shoot down the ideas that the authors may have included in their discussion), the presenter should include his/her own ideas at the end of the presentation. These should not be a reiteration of the authors' discussion.

*Make every effort to select papers unrelated to research in the department. Papers should be selected from the last 2-3 years. Once you have a paper or papers in mind, please send them to us so that we can approve them. dlc7@pitt.edu and jeffh@pitt.edu.

Short oral presentations: Each student will give one short introductory presentation as part of the faculty-lead discussions of the assigned research papers. These presentations are short, 10-minute introductions to one or two of the assigned papers. The presenter will be responsible for preparing slides and presenting relevant background information for the paper. This should include knowledge about the topic at the time the paper was published, the goals of the paper, the hypothesis being tested, and may include a brief introduction to a new or interesting technique used. Students will volunteer for (or be assigned to) specific papers on the first day of class.

Students with Disabilities

If you have a disability for which you are or may be requesting an accommodation, you are encouraged to contact both your instructor and the Office of Disability Resources and Services, 216 *William Pitt Union, 412-648-7890/412-383-7355 (FTY), as early as possible in the term. Disability Resources and Services will verify your disability and determine reasonable accommodations for this course.*

Academic Integrity Policy on cheating/plagiarism

Academic Integrity Policy: Cheating/plagiarism will not be tolerated. Students suspected of violating the University of Pittsburgh Policy on Academic Integrity, noted below, will be required to

participate in the outlined procedural process as initiated by the instructor. A minimum sanction of a zero score for the quiz, exam or paper will be imposed.

E-mail Communication Policy

Each student is issued a University e-mail address (username@pitt.edu) upon admittance. This e-mail address may be used by the University for official communication with students. Students are expected to read e-mail sent to this account on a regular basis. Failure to read and react to University communications in a timely manner does not absolve the student from knowing and complying with the content of the communications. The University provides an e-mail forwarding service that allows students to read their e-mail via other service providers (e, g., Hotmail, AOL, Yahoo). Students that choose to forward their e-mail from their pitt.edu address 'to another address do so at their own risk. If e-mail is lost as a result of forwarding, it does not absolve the student from responding to official communications sent to their University e-mail address. To forward e-mail sent to your University account, go to http://accounts.pitt.edy,logintoyouraccount,click on Edit Forwarding Addresses, and follow the instructions on the page. Be sure to log out of your account when you have finished.

Introduction to Genetics of Model Organisms
Drosophila as a Genetic Model Organism
Debbie Chapman

Review Papers for August 28th

Introduction to Genetics of Model Organisms:

1) Davis, RH. (2004) The age of model organisms *Nature Rev Gen* **5**:69-76.

2) Hunter P. (2008) The paradox of model organisms. *EMBO Reports*. **9**:717-719.

3) Fields S, Johnston M. (2005) Cell biology. Whither model organism research? *Science* **307**(5717):1885-6.

Drosophila as a Genetic Model Organism:

4) Roberts DB. (2006) *Drosophila melanogaster*: the model organism. *Entomologia Experimentalist Applicata* **121**:93-103.

5) Beckingham KM, Armstrong JD, Texada MJ, Munjaal R, Baker DA. (2005) *Drosophila melanogaster* – the model organism of choice for the complex biology of multi-cellular organisms. *Gravit Space Biol Bull.* **18(2)**:17-29.

Review Papers for Drosophila genetics – September 4-18th

1) Thomas BJ, Wassarman DA. (1999) A fly's eye view of biology. *Trends Genet.* **15(5)**:184-90.

2) St. Johnston D. (2002) The Art and Design of Genetic Screens: *Drosophila melanogaster. Nat Rev Gen* **3**:176-188.

Papers for Discussion

Tribute to Walter Gehring and understanding master regulatory genes – September 4th

3) Halder G, Callaerts P, Gehring WJ. (1995) Induction of ectopic eyes by targeted expression of the eyeless gene in Drosophila. *Science* **267(5205):**1788-92.

4) Jang CC, Chao JL, Jones N, Yao LC, Bessarab DA, Kuo YM, Jun S, Desplan C, Beckendorf SK, Sun YH. (2003) Two Pax genes, eye gone and eyeless, act cooperatively in promoting Drosophila eye development. *Development* **130(13):**2939-51.

Genetic dissection of the Ras pathway – September 11th

5) Simon MA, Bowtell DD, Dodson GS, Laverty TR, Rubin GM. (1991) Ras1 and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the sevenless protein tyrosine kinase. *Cell* **67**, 701-16.

6) Karim FD, Chang HC, Therrien M, Wassarman DA, Laverty T, Rubin GM. (1996) A screen for genes that function downstream of Ras1 during Drosophila eye development. *Genetics* **143(1)**:315-29.

Genetic screen for cancer – September 18th

7) Pagliarini RA, Xu T. (2003) A genetic screen in *Drosophila* for metastatic behavior. *Science* **302**:1227-31.

Mouse as a Genetic Model Organism
Jeffrey Hildebrand

Background papers:

1. Zohn E, Anderson KV, Niswander L. (2005) Using genomewide mutagenesis screens to identify the genes required for neural tube closure in the mouse. *Birth Defects Res A Clin Mol Teratol.* 73(9):583-90.

2. Eggenschwiler JT, Anderson KV. (2007) Cilia and developmental signaling. *Annu Rev Cell Dev Biol*. 23:345-73

For class:

September 25th

3. García-García MJ, Eggenschwiler JT, Caspary T, Alcorn HL, Wyler MR, Huangfu D, Rakeman AS, Lee JD, Feinberg EH, Timmer JR, Anderson KV. (2005) Analysis of mouse embryonic patterning and morphogenesis by forward genetics. *PNAS.* 102(17):5913-9.

4. Huangfu D, Liu A, Rakeman AS, Murcia NS, Niswander L, Anderson KV. (2003) Hedgehog signalling in the mouse requires intraflagellar transport proteins.*Nature.* 426(6962):83-7.

5. Caspary T, Larkins CE, Anderson KV. (2007) The graded response to Sonic Hedgehog depends on cilia architecture. *Dev Cell*. 12(5):767-78.

October 2nd

6. Yoshiba S, Shiratori H, Kuo IY, Kawasumi A, Shinohara K, Nonaka S, Asai Y, Sasaki G, Belo JA, Sasaki H, Nakai J, Dworniczak B, Ehrlich BE, Pennekamp P, Hamada H. (2012) Cilia at the node of mouse embryos sense fluid flow for left-right determination via Pkd2. *Science.* 338(6104):226-31

Imprinting/Dosage Compensation
Jeffrey Hildebrand

Reviews:

1. Bartolomei and Ferguson-Smith. (2011) Mammalian Genomic Imprinting. *Cold Spring Harb Perspect Biol. 3:a002592*

2. Lee and Bartolomei (2013) X-Inactivation, Imprinting, and Long Noncoding RNAs in Health and Disease. Cell. 152, 1308-1323

papers for class:

October 9th:

3. Ciccone et al. (2009) KDM1B is a histone H3K4 demethylase required to establish maternal genomic imprints. *Nature.* 461, 415-418.

4. Sleutals et al (2002) The non-coding Air RNA is required for silencing autosomal imprinted genes. *Nature*. 415, 810-813.

October 16th:

5. Lee (2000) Disruption of Imprinted X Inactivation by Parent-of-Origin Effects at Tsix. *Cell*. 103, 17–27

Genomic Editing – ZFNs, TALENs, CRISPR-Cas9
Debbie Chapman

Review Papers for October 16th

1) Urnov FD, Rebar EJ, Holmes MC, Zhang HS, Gregory PD. (2010) Genome editing with engineered zinc finger nucleases. *Nat Rev Genet.* **11**(9):636-46.

2) Joung JK, Sander JD. (2013) TALENs: a widely applicable technology for targeted genome editing. *Nat Rev Mol Cell Biol.* **14**(1):49-55.

3) Sander JD, Joung JK. (2014) CRISPR-Cas systems for editing, regulating and targeting genomes. *Nat Biotechnol.* **32**(4):347-55.

Papers for Discussion October 23rd

4) Jiang J, Jing Y, Cost GJ, Chiang JC, Kolpa HJ, Cotton AM, Carone DM, Carone BR, Shivak DA, Guschin DY, Pearl JR, Rebar EJ, Byron M, Gregory PD, Brown CJ, Urnov FD, Hall LL, Lawrence JB. (2013) Translating dosage compensation to trisomy 21. *Nature* **500**(7462):296-300.

5) Yen ST, Zhang M, Deng JM, Usman SJ, Smith CN, Parker-Thornburg J, Swinton PG, Martin JF, Behringer RR. (2014). Somatic mosaicism and allele complexity induced by CRISPR/Cas9 RNA injections in mouse zygotes. *Dev Biol.* **393**(1):3-9.

Papers for Discussion October 30th

6) Long C, McAnally JR, Shelton JM, Mireault AA, Bassel-Duby R, Olson EN. (2014) Prevention of muscular dystrophy in mice by CRISPR/Cas9-mediated editing of germline DNA. *Science* **345**(6201):1184-8.

Christine Cucinotta
Yeast as a Model System

Reviews (To be discussed Oct. 30 - Nov. 6):

1) Budding Yeast for Budding Geneticists: A Primer on the Saccharomyces cerevisiae Model System, Duina, Miller, and Keeney 2014

2) The art and design of genetic screens: yeast, Forsburg 2001

3) Yeast: Experimental Organism for 21st Century Biology, Botstein and Fink 2011

Articles:

4) (To be discussed **Oct. 30**) Healing for destruction: tRNA intron degradation in yeast is a two-step cytoplasmic process catalyzed by tRNA ligase Rlg1 and 5 ′-to-3′ exonuclease Xrn1, Wu and Hopper, 2014

5) (To be discussed **Nov. 6**) From structure to systems: high-resolution, quantitative genetic analysis of RNA polymerase II. Braberg et al. 2013.

Read the first four articles and be prepared to discuss them in class on **October 30th**.

The 5th paper is for discussion on **November 6th**.

Introduction to C. elegans as a Model System
RNAi: discovery, function and its use as a genetic tool in C. elegans
Lew Jacobson

Review paper for November 5th

*RNAi and C. elegans as a model system **if you read only one review article, the Lehmann et al. (2012) paper is probably the most relevant.*

1) Boutros M, Ahringer J. (2008). The art and design of genetic screens: RNA interference. *Nat Rev Genet.* **9(7):**554-66.

2) Lehmann S, Shephard F, Jacobson LA, Szewczyk NJ. (2012) Using Multiple Phenotype Assays and Epistasis Testing to Enhance the Reliability of RNAi Screening and Identify Regulators of Muscle Protein Degradation. *Genes* **3(4):**686-701.

3) Ankeny RA. (2001). The natural history of *Caenorhabditis elegans* research. *Nat Rev Genet.* **2(6):**474-9.

Papers for Discussion – November 13th

4) Fire A, Xu S, Montgomery MK, Kostas SA, Driver SE, Mello CC. (1998) Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. *Nature* **391(6669)**:806-11.

5) Gally C, Wissler F, Zahreddine H, Quintin S, Landmann F, Labouesse M. (2009) Myosin II regulation during *C. elegans* embryonic elongation: LET-502/ROCK, MRCK-1 and PAK-1, three kinases with different roles. *Development* **136(18):**3109-19.

Supplemental Data for Gally et al. can be found at:

http://dev.biologists.org/content/136/18/3109/suppl/DC1