GENETICS 410. Analytical Genetics. Spring 2015

Class Meeting: MWF 9 AM in Industrial Education II, Room 0101

Instructors:
Dr. Phil Becraft, 2116 Molecular Biology Building. 294-2903; becraft@iastate.edu
Dr. Tom Peterson, 2258 Molecular Biology Building. 294-6345; thomasp@iastate.edu

Office hours: Tues., Thurs 10:00-11:00, or by appointment.

Grader: Bryan Gontarek gontarek@iastate.edu

Text: GENETICS: From Genes to Genomes, 5th ed. By Leland Hartwell, et al.

Course materials will be available on Blackboard, including additional required reading.

Grading: Course grade will be based on the following:
Assignments (200 points)
4 Midterm exams (100 points each) and one Final Exam (*cumulative,* 100 points)
Course Total = 700 points. The final grade will be based on 600 points, derived by dropping the lowest 100-point score among the 1-hour exams.
There will be no make-up exams without prior approval or a medical excuse.

Academic Dishonesty: The class will follow Iowa State University's policy on academic dishonesty. Anyone suspected of academic dishonesty will be reported to the Dean of Students Office.
http://www.dso.iastate.edu/ja/academic/misconduct.html

Students with Disabilities: Iowa State University is committed to assuring that all educational activities are free from discrimination and harassment based on disability status. All students requesting accommodations are required to meet with staff in Student Disability Resources (SDR) to establish eligibility. A Student Academic Accommodation Request (SAAR) form will be provided to eligible students. The provision of reasonable accommodations in this course will be arranged after timely delivery of the SAAR form to the instructor. Students are encouraged to deliver completed SAAR forms as early in the semester as possible. SDR, a unit in the Dean of Students Office, is located in room 1076, Student Services Building or online at www.dso.iastate.edu/dr/. Contact SDR by e-mail at disabilityresources@iastate.edu or by phone at 515-294-7220 for additional information.

Dead Week: This class follows the Iowa State University Dead Week policy:
http://www.provost.iastate.edu/help/academic-policies-and-procedures/dead-week

Harassment and Discrimination: Iowa State University strives to maintain our campus as a place of work and study for faculty, staff, and students that is free of all forms of prohibited discrimination and harassment based upon race, ethnicity, sex (including sexual assault), pregnancy, color, religion, national origin, physical or mental disability, age, marital status, sexual orientation, gender identity, genetic information, or status as a U.S. veteran. Any student who has concerns about such behavior should contact his/her instructor, Student Assistance at 515-294-1020 or email dso-sas@iastate.edu, or the Office of Equal Opportunity and Compliance at 515-294-7612.

Religious Accommodation: If an academic or work requirement conflicts with your religious practices and/or observances, you may request reasonable accommodations. Your request must be in writing, and your instructor or supervisor will review the request. You or your instructor may also seek assistance from the Dean of Students Office or the Office of Equal Opportunity and Compliance.

Contact Information: If you are experiencing, or have experienced, a problem with any of the above issues, email academicissues@iastate.edu.

Course Learning Goals

1. Students will understand genetic principles that underpin modern genetic analyses, and be able to apply those principles to solve genetic problems.
2. Students will acquire a fundamental knowledge of genetic/genomic databases, how they can be queried, and how bioinformatics can facilitate genetic analyses.
3. Students will learn key approaches for performing genetic analyses at a genome-wide scale and be able to interpret data in the context of a biological problem.
4. Students will understand how genetic material is packaged, replicated, recombined and segregated in both mitotic and meiotic divisions.
5. Students will learn how changes in structure and number of chromosomes can impact gene expression, genome stability, and phenotype.
6. Students will develop skills for evaluation of genetic research and apply these skills to the critical analysis of primary research papers.

TENTATIVE SCHEDULE

P. Becraft lectures (1st half)

Dates	**Topics**	**Reading**
1/12	Introduction	Chap.1
1/14 – 1/21	Advanced Mendelian Principles	Chap. 2,3
1/23-1/28	Mutational Analysis	Activities on Blackboard Chap. 9
1/30 – 2/2	Bioinformatics: Intro to databases, BLAST, Multiple sequence alignments, phylogenetic analysis	Chap. 7, 17 Reverse genetics reading on Blackboard
2/4	Genetic Analysis of Processes I: biochemical pathway	p. 233-235 Epistasis reading on Blackboard
2/6 - 2/9	Genetic Analysis of Processes II: regulatory pathway	Chap. 18
2/11	Genome Mapping I: linkage	Chap. 5.1-5.4
2/13	**Exam I : material through 2/9**	
2/16 – 2/18	Genome Mapping II: DNA markers	9.4, 9.5, 10.1-10.3
2/20 – 2/25	Genome Mapping III: human, physical, comparative	9.6, 10.4, 11.6
2/27 – 3/2	Genomics and Systems Analysis	10.3, 10.5
3/2-3/6	Genomics class discussions	Readings on Blackboard
	Exam II : TAKEHOME	**Due 3/11**

T. Peterson Lectures (2nd half)

Tentative Schedule and Assigned Readings:

March 9: Mitosis, Meiosis, and Tetrad Analysis (Hartwell Chapter 5, pages 135 – 146)

March 11: Tetrad Analysis in Yeast, Neurospora, and Arabidopsis (Francis et al. 2007 paper).
March 13 Maize Genetics Conference—no class

March 16 – 20: Spring Break!

March 23 Tetrad Analysis in Arabidopsis (Francis et al. 2007 paper).
March 25 Tetrad Analysis: Finish, review, questions and problems.
March 27 Mitotic Recombination in Drosophila (Hartwell Chapter 5, pages 146 – 149)

March 30 Mitotic Recombination in Humans (Choate et al. 2010 paper).

April 1 Catch up and Review
April 3: **Exam III, in class.**

April 6: Chromosomal Genetics: (Hartwell Chapter 12, Pages 405 – 413; 417 - 424)
April 8 Chromosomal Genetics and Position Effect (413 – 417)
April 10 Position Effect in Plants?: (Rosin et al. 2008)

April 13 Position Effect in Plants? (Rosin et al. 2008); Student Presentations
April 15 Chromosome Aberrations (Hartwell Chapter 13, pages 429 – 447)
April 17 Aneuploidy (Hartwell Chapter 13, pages 454 – 465; New Scientist paper)

April 20 Cancer genetics (Hartwell Chapter 17, pages 586 – 609)
April 22 Does Aneuploidy cause Cancer? (Duesberg 2007)
April 24 Does Aneuploidy cause Cancer? (Weaver et al. 2007)
Exam IV (TAKEHOME; due 9 AM Friday May 1)

April 27 Chromothripsis and chromosome breakage; catch up and review
April 29 Transposable Elements (Hartwell Chapter 13, pages 447 – 454)
May 1 Transposable Elements (McClintock 1984; Jones 2005)

May 4 (Mon) Final Exam, 7:30 – 9:30 AM. (Comprehensive).

Assigned papers for Genetics 410, Spring 2012 Second-half (papers are posted on WebCT):

Hawley, 2007. Meiosis in living color: Fluorescence-based tetrad analysis in *Arabidopsis.* Proc. Natl. Acad Sci. 104: 3673 – 3674. *This is a short paper that reviews the highlights of Francis et al.*

Francis, Lam, Harrison, Bey, Berchowitz and Copenhaver, 2007. Pollen tetrad-based visual assay for meiotic recombination in *Arabidopsis.* Proc. Natl Acad Sci. 104: 3913 – 3918. *This paper shows how tetrad analysis can be done in the plant Arabidopsis, using a mutation called quartet in which the four pollen grains of a single meiosis are held together. The figures show the results of using transgene markers that give different fluorescent colors. Very nice work!*

Choate et al., 2010. Mitotic Recombination in Patients with Ichthyosis Causes Reversion of Dominant Mutations in KRT10. Science 330: 94 – 97. *Mitotic recombination—not just in Drosophila!*

McClintock, 1984. The significance of responses of the genome to challenge. Science 226: 792 – 801.
This paper represents McClintock's Nobel address; it contains some history of her research, as well as discussions regarding the possible significance of transposable elements.

Jones, R.N., 2005. McClintock's controlling elements: the full story. Cytogenet Genome Research 109: 90 – 103. *This is a review paper containing an excellent basic genetic description of McClintock's research, beginning with her induction of chromosome breaks.*

Rosin FM, Watanabe N, Cacas JL, Kato N, Arroyo JM, Fang Y, May B, Vaughn M, Simorowski J, Ramu U, McCombie RW, Spector DL, Martienssen RA, Lam E. (2008) Genome-wide transposon tagging reveals location-dependent effects on transcription and chromatin organization in Arabidopsis. Plant J. 55(3):514-25. *Genetics textbooks regularly contain vivid illustrations of Position Effect Variegation (PEV) in Drosophila. Left unsaid is whether PEV occurs in other organisms, such as plants. This paper attempts to experimentally test for position effect using a novel transgenic system.*

Duesberg, 2007. Chromosomal Chaos and Cancer. Sci. American May 2007, pages 53 – 59. *Peter Duesberg (an accomplished researcher AND a notorious HIV/Aids Denialist) describes the hypothesis that aneuploidy resulting in massive gene imbalances is the primary event in tumorigenesis.*

Weaver and Cleveland, 2006. Does Aneuploidy cause Cancer? Current Opinion in Cell Biology 2006, 18:658–667. *A short review of the evidence for the aneuploidy hypothesis.*

Weaver et al., 2007. Aneuploidy Acts Both Oncogenically and as a Tumor Suppressor. Cancer Cell 11, 25–36. *The authors manipulated levels of the mitosis-specific, centromere-linked motor protein CENP-E to induce aneuploidy and chromosomal instability in vitro and in vivo. The results are in some ways very surprising! But how meaningful are their conclusions?*

Maher and Wilson, 2012. Chromothripsis and Human Disease: Piecing together the Shattering Process. Cell 148: 29 – 32. *Chromothripsis is a phenomenon by which specific regions of the genome are shattered and then stitched back together, resulting in highly rearranged chromosomes that are the hallmark of very aggressive cancers. How does this happen and what does it mean?*

Crasta et al., 2012. DNA breaks and chromosome pulverization from errors in mitosis. Nature 482: 53-58. *The authors identify a possible cause of chromothripsis.*

If time permits: *Paper: New Scientist, "The stranger within":* "EXPLAIN this. You are a doctor and one of your patients, a 52-year- old woman, comes to see you, very upset. Tests have revealed something unbelievable about two of her three grown-up sons. Although she conceived them naturally with her husband, the tests say she isn't their biological mother. Somehow she has given birth to somebody else's children….." *Is this true? If so, how can it be?*