

Syllabus

PHG 513, Winter 2009

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Course description

This course will draw from multiple disciplines to provide a general understanding of molecular approaches to genotyping, as well as the understanding of genotype/phenotype relationships and gene-environment interactions as determinants of disease susceptibility. Instruction will cover the application of array technologies for the identification of low penetrance disease susceptibility genes and the identification of potential gene targets for novel pharmacotherapeutic treatments of disease. It will also examine the molecular basis for interindividual differences in drug/xenobiotic disposition and application of that information for individualized drug treatment regimens and disease prevention strategies.

Learning Objectives

At the end of this course students should be able to:

1. explain the various technologies used to identify genetic polymorphisms, with particular emphasis on genes of pharmacological and environmental relevance.
2. be able to identify and understand the conceptual basis behind basic methodologies used to identify genetic variability in human DNA samples
3. explain the significance of genetic polymorphisms in the development, progression, and treatment of human disease.
4. appreciate the public health importance of genetic variability in specific multigene families of enzymes involved in metabolism of drugs and non-drug chemicals in the environment
5. describe the connection between environmental exposures, genetic polymorphisms, and risk for diseases of public health importance.
6. understand the role of genetic polymorphisms as determinants of adverse drug reactions and pharmacological efficacy.
7. read critically original scientific literature relating to 'gene-environment interactions'

8. have the technical background necessary to appreciate the ethical, legal and social implications that arise out of pharmaco- and toxicogenomic research.
9. write professionally about one area of 'gene-environment' interaction with public health importance
10. integrate basic concepts of ethics into arguments for and against genotyping of populations for 'environmental susceptibility' genes.

Grading

The course will include 3 exams (multiple choice / short answer) over materials covered in class and assigned readings that will count for 75% of your grade (25% for each of 3 exams). The remaining 25% of your grade will be based on your class term paper. An average numeric score of 80 will be approximately equal to a grade point score of 3.0, a score of 90 will be a 3.5 and average scores of 95 and above will be 4.0.

Reading

Textbook: We recommend that students use the textbook, "Gene-Environment Interactions: Fundamentals of Ecogenetics (LG Costa and DL Eaton, Editors, Wiley Press, 2006) for selected background reading, although it is not required. Some reading assignments will be from this textbook, although some additional background or supplemental reading may be provided. For students who feel that their background in basic molecular biology and genetics requires updating, we recommend any basic textbook in molecular genetics or medical genetics. A particularly good text is: "Principles of Medical Genetics", 2nd Edition, TD Gelherter, FS Collins and D Ginsburg, Williams & Wilkins, 1998 (about \$40), although it is getting out dated (third edition is due in 2008). A more recent textbook would be Strachan and Read's "Human Molecular Genetics" (2003).

Hard copies of lecture notes will be provided on the day of the lecture in class (as available). Extras will be placed in the PHG 513 folder in the file cabinet outside of room F363.

Term Paper

You will be asked to choose a particular disease that has both a genetic and an environmental component to it, and write a brief paper (10-15 pages, double spaced) describing what is known

about the etiology of the disease. In the paper, you should cover:

1. the fundamental biology of the disease, including which genes are involved
2. identify candidate genes that might act as susceptibility genes, and discuss their function
3. review the basic epidemiology of the disease that has led to discoveries that genetic factors are involved
4. identify and discuss any environmental factors that have been implicated in the etiology of the disease; environmental factors are defined in their broadest terms, and include diet, viruses and other microbiological factors, occupation, lifestyle factors, etc.
5. identify and discuss at least one "ELSI" problem – real or potential- that has surfaced in your study of the disease.
6. Include all appropriate references

Possible diseases for discussion include, but are not limited to:

- Parkinson's Disease
- Amyotrophic Lateral Sclerosis (ALS: Lou Gehrig's Disease)
- Alzheimer's Disease
- basically ANY kind of cancer, especially:
 - Colon Cancer
 - Breast Cancer
 - Brain Cancers (several forms)
 - Malignant Melanoma
 - Leukemia
- Diabetes
- Alcoholism
- Certain birth defects that may have a genetic component
- Heart disease
- Lung diseases such as asthma, COPD, pulmonary fibrosis, etc.
- Genetically determined adverse drug responses
- Just about any other chronic disease that is not purely genetic

Lecture Schedule, Winter 2008

Date	Topic	Lecturer	Book@
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Jan 6#	Introduction: genes, environment and disease	Eaton	Chp. 1 & 2
Jan 8	Technological approaches to understanding genotype-phenotype relationships I – DNA analysis	Eaton	Chp. 3
Jan 13	Technological approaches to understanding genotype-phenotype relationships II – RNA analysis	Ed Kelly	Chp. 3
Jan 15*	Technological approaches to understanding genotype-phenotype relationships III – Proteomics and metabolome analyses	Thummel	handout
Jan 20	Technological approaches to understanding genotype-phenotype relationships IV- metabolomics & Review	Thummel, Eaton	handout
Jan 22	Basic concepts of xenobiotic metabolism & disposition	Thummel	Chp 6; handout
Jan 27	EXAM 1 (through Jan 20)		
Jan 29*	Polymorphisms and enzyme kinetics	Thummel	Chp. 7
Feb 3#	Polymorphism in Phase I enzymes: pharmacogenetics	Eaton	handout
Feb 5#	Polymorphisms in Phase I enzymes: toxicogenetics	Eaton	Chp. 7
Feb 10#	Polymorphism in Phase II biotransformation enzymes (GSTs, mEH, NQ01)	Eaton	Chp. 8, 9
Feb 12*	Phase II, continued (UGTs, SLTs), phase III transporters	Thummel	Chp. 8
Feb 17	Receptor polymorphisms and drug efficacy/toxicity	Thummel	Chp. 11
Feb 19	Polymorphisms in DNA repair	Eaton	Chp. 10
Feb 24	EXAM 2 (from Jan 22- Feb 17)		
Feb 26*	Pharmacogenomics and new drug development	Thummel	
March 3	G x E interactions and Acute Lymphocytic Leukemia	Thummel	handout

March 5#	G x E interactions and Diabetes	Karen Edwards	Chp. 17
March 10	ELSI case study - TBD	Felecia Cerrato	Chp. 21-23
March 12	ELSI related to Pharmaco- and toxicogenomics	Wylie Burke	handout
March XX	EXAM 3 (from Feb 19 –March 12) 10:30 – 12:20		
	Term paper – due 4 PM, Friday March 20		

* Days that Dr. Eaton is out of town; # Days that Dr. Thummel is out of town

@ Textbook: Costa, LG and Eaton DL. *Gene-Environment Interactions: Fundamentals of Ecogenetics*, Wiley Press, 2006.

NOTE: Lecture notes will be on the web page at least 24 hours before class if available. If they are not posted by 1 PM on Tuesday, hard copies will be provided on the day of the lecture in class. Any additional readings will be on the website if links are available. Otherwise, hard copies will be provided at least 1 week before the lecture.

Students With Disabilities

To request academic accommodations due to a disability, please contact Disability Resources for Students, 448 Schmitz Hall, 206-543-8924 (V/TTY). If you have a letter from Disability Resources for Students indicating that you have a disability which requires academic accommodations, please present the letter to me so we can discuss the accommodations you might need in this class.

Send mail to: fcerrato@u.washington.edu
Last modified: 1/20/2009 10:43 AM