Human Genetics 2034
Biochemical and Molecular Genetics of Complex Diseases
Fall Term 2015; Tuesday and Thursday, 2:00-3:25 PM
A215 Crabtree Hall

Instructors: M. Ilyas Kamboh, PhD  F. Yesim Demirci, MD
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Course Description:
This course provides students with an understanding of the molecular and biochemical genetic approaches to understanding genetically determined susceptibility to common disease. This will be presented using selected examples of complex human diseases (cardiovascular disease, neurodegenerative diseases, diabetes, lupus, age-related macular degeneration, and mental health diseases). Risk of common, complex diseases is determined by genotypes at multiple genetic loci and the complex interaction of genetic variation and environmental exposures. Risk of almost every common disease is influenced by genes, but the relationship between genotype and disease phenotype is weak compared to that observed with rare Mendelian traits. However, understanding the contribution of genes to common disease susceptibility is important to public health.

Course Objectives:
At the end of this course the student will be able to:

• Describe the underlying genetic architecture and environmental risk factors that influence genetic susceptibility to a variety of common, complex diseases ranging from cardiovascular disease to neurological disorders

• Explain the role of epigenetics on susceptibility to common disease

• Describe and discuss the public health impact of a variety of common, complex diseases, including potential pharmacogenomics applications

Purpose of Course:
The goal of this course is to provide students with an understanding of the molecular and biochemical genetic approaches to understanding genetically determined susceptibility to common diseases. This goal will be achieved by using selected examples of complex human diseases (cardiovascular disease, neurodegenerative diseases, mental health diseases, autoimmune diseases and eye diseases).

Risk of common and complex diseases is determined by the genotypes at multiple genetic loci and their complex interaction with environmental exposures. Understanding the contribution of genetic factors to common disease susceptibility is important to public health because these diseases account for a large fraction of morbidity and mortality in the general population.
This course will also cover the importance of pharmacogenomics and epigenetics to show how genetic differences can affect individual’s response to drugs (pharmacogenetics) and how changes in gene expression can occur without changes in the DNA sequence due to DNA methylation, histone modification or RNA interference (epigenetics) as these factors can also play a role in the development of common diseases.

Text Book:

There is no text book for this course. Handouts are used extensively. Much of the background information can be found in the appropriate sections of “The Metabolic and Molecular Basis of Inherited Disease” Shriver et al. (eds.), available in Falk Library.

Lecture slides and reading are available on Courseweb.

Grading:

Grades will be assigned based on paper writing (20%), mid-term exam (40%) and the final exam (40%). The grading scale is:

- 90-100% A
- 80-89%  B
- 70-79%   C
- 60-69%   D
- < 60%    F

Academic Integrity:

All students are expected to adhere to the school’s standards of academic honesty. Any work submitted by a student for evaluation must represent his/her own intellectual contribution and efforts. The Graduate School of Public Health’s policy on academic integrity, approved by EPCC on 10/14/08, which is based on the University policy, is available online in the Pitt Public Health Academic Handbook (www.publichealth.pitt.edu/home/academics/academic-requirements). The policy includes obligations for faculty and students, procedures for adjudicating violations, and other critical information. Please take the time to read this policy.

Students committing acts of academic dishonesty, including plagiarism, unauthorized collaboration on assignments, cheating on exams, misrepresentation of data, and facilitating dishonesty by others, will receive sanctions appropriate to the violation(s) committed. Sanctions include, but are not limited to, reduction of a grade for an assignment or a course, failure of a course, and dismissal from the school.

All student violations of academic integrity must be documented by the appropriate faculty member; this documentation will be kept in a confidential student file maintained by the Office of Student Affairs. If a sanction for a violation is agreed upon by the student and instructor, the record of this agreement will be expunged from the student file upon the student’s graduation. If the case is referred to the Pitt Public Health Academic Integrity Hearing Board, a record will remain in the student’s permanent file.

Plagiarism:
University of Pittsburgh policy: “Integrity of the academic process requires that credit be given where credit is due. Accordingly, it is unethical to present as one's own work the ideas, representations, words of another, or to permit another to present one's own work without customary and proper acknowledgement of sources.

A student has an obligation to exhibit honesty and to respect the ethical standards of the profession in carrying out his or her academic assignments. Without limiting the application of this principle, a student may be found to have violated this obligation if he or she:*
10. Presents as one's own, for academic evaluation, the ideas, representations, or words of another person or persons without customary and proper acknowledgment of sources.
11. Submits the work of another person in a manner which represents the work to be one's own.”

Source: http://www.bc.pitt.edu/policies/policy/02/02-03-02.html

Therefore, you must clearly indicate which thoughts are yours and which thoughts belong to others by citing your sources. If you are uncertain, please contact the instructor. Plagiarism detection software will be used in this course. If plagiarism is detected, you will automatically receive a grade of zero for that assignment.

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 Disability Resources and Services, 140 William Pitt Union, 412-648-7890 or 412-383-7355 (TTY) as early as possible in the term.

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<tr>
<td>9/1</td>
<td>Introduction and course overview</td>
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<td>9/3</td>
<td>Genetic basis of common diseases – Background and introduction</td>
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<td>9/8</td>
<td>Principal of multifactorial inheritance and application of genetics in medicine</td>
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<td>9/10</td>
<td>Genetic approaches to dissect the architecture of common diseases</td>
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<td>9/15</td>
<td>Epidemiology of coronary artery disease (CAD) and the role of genes involved in lipid metabolism in relation to CAD</td>
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<td>9/17</td>
<td>Familial Hypercholesterolemia (FH) - Clinical features of heterozygous and homozygous FH, population distribution of heterozygous FH</td>
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<td>9/22</td>
<td>Role of the LDL-receptor gene in Familial Hypercholesterolemia, structure of the LDL-receptor protein, classification of LDL-receptor mutations: A brief description of other monogenic disorders that affect plasma LDL cholesterol and the risk of CAD</td>
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<td>9/24</td>
<td>Role of apolipoprotein E in lipoprotein metabolism and risk of CAD</td>
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<td>9/29</td>
<td>Genetic variation in the apolipoprotein E gene and its role in affecting plasma cholesterol levels and the risk of CAD, and Type III hyperlipoproteinemia</td>
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10/1  Overview of pharmacokinetics/pharmacodynamics and a genetic basis for variability in drug response (Dr. Empey)
10/6  Application of pharmacogenomics in clinical practice (Dr. Empey)
10/8  Alzheimer’s disease - Epidemiology, pathological features and risk factors
10/13  Genetics of Alzheimer’s disease
10/15  Possible treatments for Alzheimer’s disease
10/20  **Fall Break – No Class**
10/22  **Mid-Term Examination**
10/27  **Due date for the written paper**
10/27  Introduction to Epigenetics: Etymology, definitions and molecular basis of epigenetics (Dr. Koldamova)
10/29  Mechanisms of epigenetics: DNA methylation and chromatin remodeling (Dr. Koldamova)
11/3   Mechanisms of epigenetics: RNA interference and microRNA (Dr. Koldamova)
11/5   Schizophrenia and bipolar disorder– Epidemiology, risk factors and biological mechanisms (Dr. Nimgoankar)
11/10  Genetics of Schizophrenia and bipolar disorder (Dr. Nimgoankar)
11/12  The Immune System – Part 1
11/17  The Immune System – Part 2
11/19  Eye diseases
11/24  Age-related macular degeneration (AMD) – Epidemiology, risk factors, and clinical features
11/26  **Thanksgiving Holiday – No Class**
12/1   Genetics of age-related macular degeneration
12/3   Autoimmune diseases
12/8   Systemic lupus erythematosus (SLE) - Epidemiology, risk factors, and clinical features
12/10  Genetics of systemic lupus erythematosus
12/15  **Final Examination**