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Course time: Monday, 9:00 am – 12.00 noon

Classroom: Health Sciences Building, Room 3233

Office hours: Flexible, but by appointment

Prerequisites: Epidemiological Methods (EPI 5340)

Background and Objectives

Recent advances in genotyping technology have enabled data on potential genetic risk factors to be incorporated into epidemiological studies. This has been a very exciting development as genetic factors are likely to affect the occurrence of numerous common diseases, and therefore identifying and characterizing the associated risk (or protection) will be important in improving the understanding of etiology and potentially for developing interventions based on genetic information. Family-based study designs and modifications of “classical” epidemiological study (that is, cross-sectional, case-control, and cohort) designs have been developed for the purposes of gene discovery, to address the potential problem of population stratification (confounding by ethnic origin) and gene-environment and gene-gene interaction. However, the most common design in use for the past decade or so has been the case-control study, which investigates genetic associations - more than 34 000 articles were published between 2001 and 2008. Despite many similarities between genetic association studies and “classical” observational epidemiologic studies of lifestyle and environmental factors, genetic association studies present several specific challenges including an unprecedented volume of new data and the likelihood of very small individual effects. Therefore, there is an increasing need for epidemiologists to understand the genetic basis of disease, read and interpret genetic studies, incorporate the collection and analysis of genetic information into studies of disease etiology, and evaluate interventions based on genetic information.

The objectives of this course are to provide epidemiologists with an understanding of: (1) basic genetics; (2) study designs and approaches used by geneticists and genetic epidemiologists; (3)

the integration of genetic data into “classical” epidemiological study designs; and (4) issues in the evaluation of interventions based on genetic information. After completing this course, students will be able to read and interpret genetic epidemiological studies, and evaluations of interventions based on genetic information. In addition, they will be able to contribute to the design, conduct and analysis of epidemiological studies that incorporate collection of data on genetic factors.

Course Design

The main format of the session will be short lectures followed by critical appraisal of relevant literature. Students are expected to have read papers in advance of the session, and will be expected to contribute actively to the discussion. Students will be assessed on journal club presentations and participation.

In addition, students will be expected to prepare a review of a genetic association of their choice following HuGENet guidelines.

Textbook

Genetic epidemiology is a fast moving field so the few textbooks tend to be out of date as soon as they are published! For this reason, there is no required textbook. However, students may find it useful to refer to:

Khoury, M.J., Beaty, T.H., Cohen, B.H. *Fundamentals of Genetic Epidemiology*, Oxford University Press, New York , 1993.

Khoury, M.J., Little, J., Burke, W. *Human Genome Epidemiology*, New York: Oxford University Press, 2004. [a new edition is to be published in 2009]

Some of the chapters in this book are available through the following link
<http://www.cdc.gov/genomics/training/books/huge/Preface.htm>

Thomas, D.C. *Statistical Methods in Genetic Epidemiology*. New York: Oxford University Press, 2004.

Ziegler, A. Konig, I.R. *A Statistical Approach to Genetic Epidemiology: Concepts and Applications*. Weinheim: Wiley-VCH, 2006. [a new edition is to be published in 2009]

Genetic Epidemiology, 2009
Schedule and Contents of Sessions

Session	Date	Topic
1	Jan 12	<p>Introduction</p> <p>(a) Basic scope of genetic epidemiology,</p> <p>(b) overview of types of human genetic variation: chromosomal anomalies, CNVs, SNPs,</p> <p>(c) overview of population genetics: mutation, selection, random genetic drift and gene flow</p> <p>(d) common gene-common variant and heterogeneity hypotheses</p>
2	Jan 19	<p>Gene discovery</p> <p>(a) Epidemiological evidence pointing to genetic factors</p> <p>(b) Is there familial aggregation? Assessment of effect of family history on disease risk</p> <p>(c) Heritability, segregation analysis and linkage</p>
3	Jan 26	<p>Genetic association studies - 1</p> <p>(a) Reminder of “classical” epidemiological designs</p> <p>(b) Measurement of genetic variation: candidate gene studies; genome-wide association studies</p> <p>(c) Pattern of accumulation of knowledge on genetic associations; replication</p> <p>(d) Assessment of risk of bias: genotyping errors; population stratification (is there a problem?)</p>
4	Feb 2	<p>Genetic association studies – 2</p> <p>(a) Assessment of risk of bias: population stratification, contd. (design and analysis approaches); departure from Hardy-Weinberg equilibrium; other diagnostics in genome-wide association studies</p> <p>(b) Modelling haplotype variation</p> <p>(c) Imputation of genotypes by linkage disequilibrium</p> <p>(d) Multiple testing</p>
5	Feb 9	<p>Gene-environment and gene-gene interaction -1</p> <p>(a) Concepts (biological and statistical)</p> <p>(b) Statistical power</p> <p>(c) Design approaches: nested case-control; case-cohort;</p> <p>(d) Analytic approaches</p>
	Feb 16	Family Day holiday – no class

6	Feb 23	<p>Gene-environment and gene-gene interaction - 2</p> <p>(a) Design approaches, contd.: family based: case-only (b) Analytic approaches</p> <p>Mendelian randomization</p>
7	Mar 2	<p>Evaluation of potential value of genetic information in screening (e.g. newborn screening), family history tools and genetic testing.</p>