Genetics for Epidemiologists
Application of Human Genomics to Population Sciences

Course Overview:

Genetics for Epidemiologists (GFE) is a short course for investigators and trainees in the field of epidemiology and related population-based sciences. The overall goal of GFE is to familiarize these researches with recent developments in the theory and methods of human genetics that might be applied to the study of the distribution, natural history, and etiology of diseases in populations. This course intends to focus on the interface between genetics and epidemiology with an emphasis on the application of modern human genome analysis methodologies to studies of human populations through the design, conduct, analysis, and interpretation of studies which effectively answer the epidemiologic question of interest.

Course Objectives:

In order to achieve these goals, Genetics For Epidemiologists has the following learning objectives:

1. To review the structure and function of the human genome as it is relevant for testing epidemiologic hypotheses.
2. To understand methods used to identify and measure genetic variation and to be able to locate descriptions of these gene variants in current databases.
3. To appreciate the assumptions, advantages, and disadvantages of various designs used in gene association studies.
4. To understand the application of newer genome technologies to the testing of genetic hypotheses.
5. To describe the methods of statistical analyses used to identify and quantify genomic risk.
6. To describe biases that can occur in gene association studies and the strategies to correct for them.
7. To understand the role of replication studies and functional studies in support of gene studies' results and interpretations.
8. To be able to apply the information derived from gene association studies to genetic testing, pharmacogenetic aspects of clinical trials, and other uses.

At the end of the course, the participant should be able to design an epidemiologic study with appropriate methods of collection, analysis, and interpretation of data which measures variants of the human genome as possible causes of the disease under investigation.

Instructors:

Thomas A. Pearson, MD, PhD

Professor, University of Rochester School of Medicine

Visiting Scientist, NHGRI (9/1/07 – 5/30/08)

Teri Manolio, MD, PhD

Director, Office of Population Genomics

NHGRI

Genetics for Epidemiologists:
Applications of Human Genomics to Population Sciences

Tuesday, May 13

Lecture 1
12:30-1:30 pm

Genetics for Epidemiologists: T. Pearson
- A. Course Overview and Introduction
- B. The Biologic Basis for Analysis of Genetic Variants
  1. Review of relevant gene structure and function
  2. Paradigms for Genetic Causation of Disease
     - a. Mendelian Disorder Paradigm
     - b. Common Gene-Common Disease Paradigm
  3. Developing models of disease with genetic causes

Lecture 2
1:30 – 2:30 pm

Measurement of Genetic Exposure: T. Manolio
- A. Methods to Measure Genetic Variation
  1. Family History
  2. Candidate Genes
  3. Whole Genome Approaches
- B. Methods to Identify Gene Variants
  1. Genbark
  2. Entrez
  3. NCBI/dbGaP
  4. OMIM
- C. Quality Control of Genetic Analyses

Break
(2:30-3:00))

Lecture 3
(3:00-4:00)

Study Designs: Family-based Studies: T. Pearson
- A. Twin Studies
- B. Linkage Analysis
- C. Trios, TDT
- D. Other family-based designs

Lecture 4
(4:00-5:00 pm)

Study Designs: Genetic Association Studies: T. Manolio
- A. Case-Control
  1. Candidate Genes
  2. Genome-wide Association
- B. Prospective (Cohort) Studies
- C. Randomized/Experiential Designs

Wrap-up
(5:00)

Questions and Answers

Wednesday, May 14

Lecture 5
(8:30-9:30 am)

Analysis of Genetic Association Studies: T. Manolio
- A. Quantitative Traits

B. Measures of Association
   1. Correction for False Positives
   2. Statistical Tests (Pearson, Fisher Chi Square)
   3. Q-Q Plots, Chromosomal Mapping
   4. Odds Ratios
      a. Allelic
      b. Genomic
   5. Models of Genetic Transmission
      b. Dominant/Recessive
      c. Gene-gene Interaction
      d. Gene-environment Interaction

Lecture 6 (9:30-10:30) — Bias in Human Genomic Studies: T. Pearson

A. Subject Selection
   1. Representativeness of cases and controls
   2. Super Cases/Super Controls
   3. Latent Cases
   4. Population Stratification
B. Genome Analysis Errors (Differential)
C. Outcome Misclassification
D. Analysis and Interpretation (The winner's curse)
E. Strategies to Prevent or Minimize Bias

Break (10:30-11:00)

Lecture 7 (11:00-12:00) — Replication and Functional Studies: T. Manolio

A. Replication of GWAS
   1. Criteria (Chanock & Manolio)
   2. Designs
   3. Reasons for inability to replicate findings
B. Functional Studies
   1. Genes in neighboring regions
   2. Fine sequencing
   3. Gene expression
   4. Invivo Studies/Knock-in vs. Knock-out
   5. Other

Lecture 8 (12:00-1:00) — Applications of Genetic Tools to Clinical and Translational Research: T. Pearson

A. Inference on causation from genetic studies
B. Genetic Screening
   1. Types of Genetic Screening
   2. Association vs. Prediction
C. Pharmogenomics
D. Use of Genetic Data in Randomized Trials
E. Data Sharing Policy for NIH-funded GWA studies

Course Wrap-Up (1:00-1:30) — Course Evaluation (T. Manolio & T. Pearson)