

Introduction to Molecular Epidemiology (173:156)
Fall 2007
1155 MERF

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Course Description

This course will serve as an introduction to the use of the basic techniques of molecular biology (DNA, RNA, and protein techniques) in various aspects of epidemiological research, including diagnosis of disease and biomarker discovery and validation.

Course Objectives

Techniques of molecular biology have become increasingly important in their application to epidemiological studies. This course aims to familiarize the student with these techniques, their applications, and their limitations. After completion of this course, the student should be able to:

1. Discuss strengths and weaknesses of current molecular methods for epidemiologic applications.
2. Design a validation and reliability study
3. Demonstrate knowledge of web-based resources for molecular epidemiology
4. Design an appropriate experiment and/or study to answer a research question

Prerequisites

Pre- or co-requisite: 173:140 Principles of Epidemiology

Teaching Methods

The course is comprised of didactic lectures; journal club format, student-led discussions; and student oral presentations at the course end.

Evaluation of Student Performance

Students will be graded based on their performance on a written examination (30%), class participation (20%), homework assignments (10%), and a final project consisting of a grant proposal and oral presentation (40%).

Instructional Material

There is no text for this course. Readings will consist of original literature and review articles.

Class Lectures and Topics

This represents a likely topic schedule for fall 2007; modifications to the schedule and/or readings will be announced in advance.

	Instructor	Topic	Activities	Readings and Assignments
8/29	Smith	What is molecular epidemiology? Introduction to molecular epidemiology	Lecture/ discussion	Foxman and Riley, "Molecular Epidemiology: focus on infection," Shpilberg <i>et al.</i> , "The next stage: molecular epidemiology," Schulte, "A conceptual and historical framework for molecular epidemiology." (Molecular Epidemiology: Principles and practices, chapter 1)
8/31	Smith	Introduction/review of molecular biology. DNA methods.	Lecture/ discussion	Peltonen and McKusick, "Dissecting human disease in the post-genomic era," Couzin, "To what extent are genetic variation and personal health linked?," Olson and Varki, "Sequencing the chimpanzee genome: insights into human evolution and disease."
9/5	Smith	Introduction/review of molecular biology. DNA methods continued.	Lecture/ discussion	Jansen, "Studying complex biological systems using multifactorial perturbation."
9/7	Smith	Introduction/review of molecular biology. RNA methods.	Lecture/ discussion	Smith, "Getting down to details," Benvenuti <i>et al.</i> , "Identification of cancer genes by mutational profiling of tumor genomes."
9/10	Smith	Introduction/review of molecular biology. RNA methods continued.	Lecture/ discussion	Wilhelm and Pingoud, "Real-time polymerase chain reaction," Dale and von Schantz, "Analysis of gene expression," chapter 13 in "From genes to genomes."
9/12	Smith	Introduction/review of molecular biology. Protein methods.	Lecture/ discussion	Hess <i>et al.</i> , "Immunoproteomics." Dunne, "Immunity is the best biomarker." Rodland, "Proteomics and cancer diagnosis: the potential of mass spectrometry," Gao <i>et al.</i> , "Biomarker discovery in biological fluids," Zhu <i>et al.</i> , "Proteomics," Hanash, "Disease proteomics."

9/14	Smith	Introduction/review of molecular biology. Protein methods continued.	Lecture/discussion	Cesareni <i>et al.</i> , “Comparative interactomics,” McCook, “The Human Interactome falls into place,” Sellers and Yates, “Review of proteomics with applications to genetic epidemiology,” Rhodius <i>et al.</i> , “Impact of genomic technologies on studies of bacterial gene expression,” MacBeath, “Protein microarrays and proteomics,” Zhang <i>et al.</i> , “Library on a slide for bacterial comparative genomics,” Russo, “Chip Critics Countered,” Hunter, “Microarray data analysis: separating the curd from the whey.”
9/17	Smith	Microarrays	Lecture/discussion	Kaminski, “Bioinformatics: a user’s perspective,” Elkin, “Primer on medical genomics. Part V: bioinformatics.”
9/19	Smith	Bioinformatics and online molecular epidemiology resources	Lecture/discussion	
9/21		Group assignment 1 due—discussion in class		
9/24	Smith	Validity, variability	Lecture/discussion	Vineis <i>et al.</i> , “Technical variability in laboratory data.” Schulte and Perera, “Validation.”
9/26	Smith	Quality control	Lecture/discussion	
9/28	Smith	Choosing the right tool	Lecture/discussion	
10/1		Group assignment 2 due—discussion in class, review for exam		
10/3		Exam		
10/5	Smith	Bringing it together—theory and application	Lecture/discussion	Cox <i>et al.</i> , “Integrating gene and protein expression data: pattern analysis and profile mining,”
10/8	Smith	Human evolution and disease	Lecture/discussion	Kotb, “Genetics of susceptibility to infectious diseases.” Background reading: Engels and O’Brien, “Epidemiological methods for studies of genetic factors that influence infectious diseases.” (Molecular Epidemiology, chapter 1)
10/10		Elaine Smith	Lecture/discussion	
10/12		Margaret Chorzay	Lecture/discussion	
		Case Studies		
10/15	Smith	Forensic molecular epidemiology— <i>Y. pestis</i>	Paper presentation/discussion	Drancourt <i>et al.</i> , “Detection of 400-year-old <i>Yersinia pestis</i> in human dental pulp: an approach to the diagnosis of ancient septicemia.” Raoult <i>et al.</i> , “Molecular

				identification by “suicide PCR” of <i>Yersinia pestis</i> as the agent of Medieval Black Death.”
				Background: Drancourt and Raoult, “Molecular insights into the history of plague.”
10/17	Smith	Influence of infectious agents on the human genome--what role has disease played in shaping our genomes, and vice-versa; and how does it relate to molecular epi?	Paper presentation/discussion	Galvani and Slatkin, “Evaluating plague and smallpox as historical selective pressures for the <i>CCR5-Δ32</i> HIV-resistance allele.” Background reading: Galvani and Novembre, “The evolutionary history of the <i>CCR5-Δ32</i> HIV-resistance mutation.”
10/19	Smith	Using molecular epidemiology of pathogens to look backward into history	Paper presentation/discussion	Ghose <i>et al.</i> , “East Asian genotypes of <i>Helicobacter pylori</i> strains in Amerindians provide evidence for its ancient human carriage,” Falush <i>et al.</i> , “Traces of human migrations in <i>Helicobacter pylori</i> populations.” Background reading: Spratt, “Stomachs out of Africa,” Suerbaum and Achtman, “ <i>Helicobacter pylori</i> : recombination, population structure and human migrations,” Zimmer, “Genetic trees reveal disease origins.”
10/22	Smith	Using serology to determine the epidemiology of pathogens: example of Ebola.	Paper presentation/discussion	Gonzalez <i>et al.</i> , “Ebola and Marburg virus antibody prevalence in selected populations of the Central African Republic.” Background reading: Feldman <i>et al.</i> , “Ebola virus ecology: a continuing mystery,”
10/24	Smith	1918 influenza—DNA sequence analysis	Paper presentation/discussion	Reid <i>et al.</i> , “Origin and evolution of the 1918 “Spanish” influenza virus hemagglutinin gene.” Background reading: Taubenberger <i>et al.</i> , “Capturing a killer flu virus,” Hughes <i>et al.</i> , “Evolutionary analysis of molecular sequence data” (Molecular Epidemiology, chapter 8).
10/26	Smith	PFGE and outbreak epidemiology	Paper presentation/discussion	Jones <i>et al.</i> , “ <i>Salmonella enterica</i> serotype Uganda infection in New York City and Chicago,” Nevas <i>et al.</i> , “Infant botulism acquired from household dust presenting as sudden infant death syndrome.” Background reading: Lukinmaa <i>et al.</i> , “Application of molecular genetic methods in diagnostics and epidemiology of food-borne bacterial pathogens.”
10/29	Smith	Mass spectrometry and	Paper	Petricoin <i>et al.</i> , “Use of proteomic patterns

		biomarker discovery in cancers	presentation/discussion	in serum to identify ovarian cancer,” Zheng <i>et al.</i> , Prostate carcinoma tissue proteomics for biomarker discovery.” Background reading: Zhu and Snyder, “Protein chip technology,” Ong <i>et al.</i> , “Mass spectromic-based approaches in quantitative proteomics,” Wulfschuhle <i>et al.</i> , “Proteomic applications for the early detection of cancer.”
10/31	Smith	Use of FISH to determine biomarkers in metastatic breast cancer	Paper presentation/discussion	Tedesco <i>et al.</i> , “Docetaxel combined with trastuzumab is an active regimen in HER-2 3+ overexpressing and fluorescent in situ hybridization-positive metastatic breast cancer: a multi-institutional phase II trial.” Background reading: Hicks <i>et al.</i> , “Assessment of the <i>HER2</i> status in breast cancer by fluorescence in situ hybridization: a technical review with interpretive guidelines.”
11/2	Smith	HLA variation and genetic susceptibility to <i>Streptococcus pyogenes</i>	Paper presentation/discussion	Kotb <i>et al.</i> , “An immunogenetic and molecular basis for differences in outcomes of invasive group A streptococcal infections.” Background—Kotb and Norrby-Teglund, “Host-microbe interactions in the pathogenesis of invasive group A streptococcal infections,” Erlich and Trachtenberg, “PCR-based methods of HLA typing.” (Molecular Epidemiology, chapter 7).
11/5	Smith	SNPs and B19	Paper presentation/discussion	Kerr <i>et al.</i> “Single-nucleotide polymorphisms associated with symptomatic infection and differential human gene expression in healthy seropositive persons each implicate the cytoskeleton, integrin signaling, and oncosuppression in the pathogenesis of human Parvovirus B19 infection.” Background:
11/7	Smith	Biomarkers and heart disease	Paper presentation/discussion	Koenig, “Predicting risk and treatment benefit in atherosclerosis: the role of C-reactive protein.”
11/9	Smith	Assignment #3 due Biomarkers in liver disease	Paper presentation/discussion	Smela <i>et al.</i> , “The aflatoxin B1 formamidopyrimidine adduct plays a major role in causing the types of mutations observed in human hepatocellular

				carcinoma.” Background: Shuker, “The enemy at the gates? DNA adducts as biomarkers of exposure to exogenous and endogenous genotoxic agents,” Amacher, “A toxicologist’s guide to biomarkers of hepatic response.”
11/12	Smith	Subtractive hybridization as a method to determine disease-associated genes	Paper presentation/discussion	Pettigrew <i>et al.</i> , “Identification of the lipooligosaccharide biosynthesis gene <i>lic2B</i> as a putative virulence factor in strains of nontypeable <i>Haemophilus influenzae</i> that cause otitis media.” Background reading: Winstanley, “Spot the difference: applications of subtractive hybridization to the study of bacterial pathogens.”
11/14	Smith	Individual meetings to discuss assignment #4		
11/16	Smith	Molecular epidemiology of antibiotic resistance	Paper presentation/discussion	Reinert <i>et al.</i> , “Antimicrobial susceptibility of <i>Streptococcus pneumoniae</i> in eight European countries from 2001 to 2003.” Background: Klugman and Lonks, “Hidden epidemic of macrolide-resistant pneumococci.”
11/26	Smith	VNTR and class 1 diabetes	Paper presentation/discussion	Rani <i>et al.</i> “Molecular basis of predisposition to develop type 1 diabetes mellitus in North Indians.” Background: Knight, “Regulatory polymorphisms underlying complex disease traits.”
11/28		No class—meet with groups to work on presentations		
11/30	Smith	MLST	Paper presentation/discussion	Jones <i>et al.</i> , “Multilocus sequence typing system for group B streptococcus.” Background: Urwin and Maiden, “Multilocus sequence typing: a tool for global epidemiology.”
12/3	Smith	Application of molecular epidemiology to bioterrorism	Paper presentation/discussion	Read <i>et al.</i> , “Comparative genome sequencing for discovery of novel polymorphisms in <i>Bacillus anthracis</i> .” Background reading: Cummings and Relman, “Microbial forensics—cross-examining pathogens.”
12/5	Smith	Application of molecular epidemiology to vaccine development	Paper presentation/discussion	Moxon and Rappuoli, “Bacterial pathogen genomics and vaccines.”
12/7		Student presentations		
12/10		Student presentations		

12/12 Student presentations
12/14 Student presentations
Assignment #4 due