

Division of Epidemiology
Department of Environmental Health
University of Cincinnati College of Medicine

Molecular Epidemiology (BE-9073/PH-9073)

Spring term, 2020

2 Credit hours

Day/time: Mondays 10:00 AM - 11:50 PM

Room: Kettering 121

Instructor: Scott Langevin, PhD, MHA, CT(ASCP)
Associate Professor of Epidemiology
Office: 243 Kettering
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Office hours: By appointment

Prerequisites: *Introduction to Epidemiology (BE-7076)*

Text: No text is required for this course. Readings will be based on assigned journal articles listed in the course outline of the syllabus.

Course Description: This course is intended for graduate-level students interested in epidemiology, clinical research, or related fields. The course covers both the major theoretical concepts and practical issues involved in conducting research that involves biomarkers in human populations from an epidemiology perspective. Recent advances in basic science and biotechnology are revolutionizing the field of epidemiology, creating vast opportunities for studying the relationship between variations at the molecular or cellular level and early detection, etiology, or prognosis of health related states. Course topics will include: the theoretical advantage of biomarkers; criteria for evaluating potential biomarkers; sample collection and storage; quality control considerations; issues in epidemiologic study design and analysis; ethical/legal concerns; tools available for molecular epidemiology research, including an introduction to “omics” technologies; and a practical hands-on laboratory experience.

Course Objectives: Students completing this course will develop an understanding of the major theoretical and practical issues involved in conducting research that integrates laboratory and epidemiology techniques. Core competencies that should be gained from this course include:

- I. *Comprehension of basic principles of molecular biology from an epidemiologists perspective*
 - A. Upon completion of this course, students should gain a working understanding of genetics, epigenetics, immunology and cellular biology that is necessary for conduct of molecular epidemiologic research

- II. *Study design*
 - A. After completion of this course, students should have a working comprehension of potential study design nuances specific to molecular epidemiologic research.
 - B. Students should be aware of issues involved in specimen collection, storage and quality control measures that may arise in molecular epidemiologic research.
 - C. Students should be able to apply these principles to epidemiologic research.

- III. *Tools available for molecular epidemiologic research*
 - A. This course should introduce the student to potential laboratory tools that can be applied to molecular epidemiology research to address health-related research questions in human populations.
 - B. Students will gain a practical introductory experience in a molecular epidemiology laboratory that provides them with a basic understanding of what goes into sample preparation for molecular epidemiology studies.

Course Requirements:

Blackboard: Blackboard will be used to share and discuss progress on the literature review, send course announcements, and post speaker slides, readings, and student presentations.

Readings: For each lecture, there will be selected readings to support and complement the lecture material, as listed on the course outline of the syllabus. Students are expected to read the material for each lecture ahead of time to enhance the learning experience.

Grading Outline:

15%	Attendance and participation (including reading of assigned manuscripts prior to class)
15%	Homework assignments
35%	Exam (Units I and II)
35%	Functional annotation project
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100%	Total

Homework Assignments:

Unless otherwise stated, homework assignments will be due at the start of class on the respective due date listed on the course outline in this syllabus. Late assignments will be docked 10 percentage points per week late.

1. UC lab safety, environmental, and blood-borne pathogen training module

Due: 02/03

Go to: <http://www.ehs.uc.edu/itc/compliance.asp>

Click on the link for Web Based Compliance Training then sign in using your UC 6+2 username and password. Complete the modules for Bloodborne Pathogens, Hazard Communication, and Hazardous Waste by clicking on the links in the left margin (under Topics). Print out a copy of the certificate of completion for each module to turn in. Please note: you may take each module as many times as necessary to achieve a passing score.

2. Identification of Publicly Available Datasets

Due: 2/10

You will each be assigned a disease and “omic” modality of interest: e.g. DNA methylation, gene expression, genome-wide SNP (GWAS), or somatic mutation (whole-exome sequencing). Using either GEO or dbGAP, please identify a publicly available dataset, provide a brief description of the study (2-4 sentences), list the GEO or dbGAP accession number, platform (assay) used, and number of cases and (if applicable) controls available in the dataset. Briefly describe why you chose your dataset and what, if any, are the limitations.

3. GeneCards

Due: 02/17

You will each be assigned a gene. Use GeneCards (<http://www.genecards.org/>) to find the following information:

- a) List the first 5 aliases listed for your gene and/or corresponding protein
- b) Provide a (brief) description of your gene
- c) Provide the chromosomal location of your gene (i.e. chromosome and band)
- d) Where does it primarily localize in relation to the cell? (Confidence ≥ 4)
- e) List the first 5 Gene Ontology (GO) biological process terms displayed for your gene (if fewer than 5 are shown, list all that are displayed)
- f) List the top 3 associated diseases/disorders inferred by MalaCards

Please turn in a typed list of your answers on the due date listed above.

Functional Annotation Project: Each student will select a single nucleotide polymorphism (SNP) that has been associated with a health-related state, exposure, or outcome in the peer-reviewed literature. The length of your report should be between 2-5 pages (not including the bibliography) and should include relevant citations. Please be sure to include the following elements in your report:

1. Identify and describe the gene or sequence in which the SNP is situated, including chromosomal location, range of genomic coordinates, (GRCh38), and gene function.
2. Describe the SNP, including (but not limited to) the refseq id (rs number), sequence change and corresponding amino acid change (if applicable); and whether or not there is a functional impact of the polymorphism and, if so, what it is.
3. Provide the population frequency(s) of the polymorphism (browser.1000genomes.org)
4. Using the genomic coordinates of the (GRCh38), provide the sequence +/- 100 bases.
5. Describe the sequence context (e.g. 5'UTR, promoter, exon, intron, 3'UTR, intergenic).
6. Is the SNP situated in a CpG island?
7. List any proximal (1kb) DNase I hypersensitivity sites (ENCODE)
8. Summarize the relationship between the SNP and health-related state in humans, as described in the scientific literature, including conflicting results or the findings from meta-analyses (if available).

Functional annotation reports must be submitted electronically via email no later than 11:59 PM on Monday, April 27, 2020.

Attendance: Attendance will constitute a portion of your final grade. Legitimate absences can be made up at the discretion of the instructor by writing a 200- to 250-word synopsis of the lecture slides (posted on Blackboard) and for each reading for that week.

Academic Ethics: The Faculty of the Department of Environmental Health believe that the conduct of a student taking a course in the Department should be consistent with that of a professional individual. All students in this course will be expected to conduct themselves with complete integrity. All work by the student will be the work of that student, unless otherwise referenced.

Counseling Services: Students have access to counseling and mental health care through the University Health Services (UHS), which can provide both psychotherapy and psychiatric services. In addition, Counseling and Psychological Services (CAPS) can provide professional counseling upon request; students may receive five free counseling sessions through CAPS without insurance. Students are encouraged to seek assistance for anxiety, depression, trauma/assault, adjustment to college life, interpersonal/relational difficulty, sexuality, family conflict, grief and loss, disordered eating and body image, alcohol and substance abuse, anger management, identity development and issues related to diversity, concerns associated with sexual orientation and spirituality concerns, as well as any other issue of concerns. After hours, students may call UHS at 513-556-2564 or CAPS Cares at 513-556-0648. For urgent physician consultation after-hours students may call 513-584-7777.

Title IX: Title IX is a federal civil rights law that prohibits discrimination on the basis of your actual or perceived sex, gender, gender identity, gender expression, or sexual orientation. Title IX also covers sexual violence, dating or domestic violence, and stalking. If you disclose a Title IX issue to me, I am required forward that information to the Title IX Office. They will follow up with you about how the University can take steps to address the impact on you and the community and make you aware of your rights and resources. Their priority is to make sure you are safe and successful here. You are not required to talk with the Title IX Office. If you would like to make a report of sex or gender-based discrimination, harassment or violence, or if you would like to know more about your rights and resources on campus, you can consult the website www.uc.edu/titleix or contact the office at 556-3349.

Course Outline by Week

Date	Topic	Reading
Unit I: Introduction to Molecular Epidemiology		
Week 1 01/13/20	Introduction to Molecular Epidemiology	<u>Homework #1</u> : Complete UC lab safety, environmental, and blood-borne pathogen training module (due 02/03)
01/20/20	MLK Day – NO CLASS	
Week 2 01/27/20	Molecular Epidemiology Study Design	<u>Readings</u> : Gallo et al. <i>Strengthening the Reporting of Observational studies in Epidemiology – Molecular Epidemiology (STROBE-ME): An extension of the STROBE statement</i> . Eur J Clin Invest 2012;42(1):1-16. Pepe et al. <i>Pivotal evaluation of the accuracy of a biomarkers used for classification or prediction: standards for study design</i> . J Natl Cancer Inst 2008;100:1432-8.
Week 3 02/03/20	Biobanking and Data Sharing	<u>Homework #2</u> : Identification of publicly available dataset assignment (due 02/10) <u>Reading</u> : Yong, Dry & Shabihkhani. <i>A practical approach to clinical and research biobanking</i> . Methods Mol Biol. 2014;1180:137-62 Lab safety, environmental, and blood-borne pathogen due
Week 4 02/10/20	Basics of Genetics & Epigenetics	<u>Homework #3</u> : GeneCards Assignment (due 02/17) <u>Readings</u> : Langevin SM and Kelsey KT. <i>Genetics and gene-environment interactions</i> (Ch. 2). In: Anttila SL, Boffetta P, and Straif K (eds). <i>Occupational Cancer</i> (1st edition). Springer. 2014, pp. 21-31. Mill & Heijmans. <i>From promises to practical strategies in epigenetic epidemiology</i> . 2013;14:585-94. Public dataset homework (#2) due
Unit II: Biospecimen Collection & Storage		
Week 5 02/17/20	Basics of Immunology, Hormones, & Receptors	<u>Readings</u> : Kravathas, Krause & Ruddle. <i>Organization and Cells of the Immune System</i> (Ch. 2). In: Krause PJ, Kavathas PB, and Ruddle NH (eds). <i>Immunoepidemiology</i> (1st edition). Springer. 2019, pp. 21-38. Helden et al. <i>Signals and Receptors</i> . Cold Spring Harb Perspect Biol. 2016;8(4): a005900. Genecards homework (#3) due

Week 6 02/24/20	Lecture: Nucleic Acid Storage & Extraction Lab I: DNA extraction	Virtual DNA Extraction link: http://learn.genetics.utah.edu/content/labs/extraction/
Week 7 03/02/20	Lecture: Measuring nucleic acid concentrations Lab II: Measuring DNA concentration	NanoDrop Video Links: https://www.youtube.com/watch?v=aUZD8sj5c4w https://www.youtube.com/watch?v=MxBRIuIq2Rs
Week 8 03/09/20	EXAM: Covering Units I and II	
03/16/20	Spring Break – NO CLASS	
Unit III: Techniques & Approaches		
Week 9 03/23/20	Molecular Epidemiology of Infectious Disease (Dr. Senu Apowokin, MD)	<u>Readings:</u> Quince et al. <i>Shotgun metagenomics, from sampling to analysis</i> . Nat Biotech. 2017;35(9):833-44. Gargis, Kalman & Lubin. <i>Assuring the Quality of Next-Generation Sequencing in Clinical Microbiology and Public Health Laboratories</i> . JCM. 2016;54(12):2857-65.
Week 10 03/30/20	Online Resources and Genome Browser Workshop (bring laptop to class)	<u>Readings:</u> Gallagher & Chen-Plotkin. <i>The Post-GWAS era: from association to function</i> . AJHG. 2018;102(5):717-30. Ecker et al. <i>Genomics: ENCODE explained</i> . Nature. 2012;489:52–5
Week 11 04/06/20	Polymerase Chain Reaction (PCR) Fluorescent In-Situ Hybridization (FISH)	<u>Readings & Multimedia:</u> Garibyan & Avashia. <i>Research techniques made simple: polymerase chain reaction (PCR)</i> . J Invest Dermatol. 2013;133(3):e6. Cui, Shu & Li. <i>Fluorescence in situ hybridization: cell-based genetic diagnostic and research applications</i> . Front Cell Dev Biol. 2016;4:89.
Week 12 04/13/20	DNA Adducts, Breaks, Proteins, & Small Molecules	<u>Readings:</u> Reddig et al. <i>DNA damage assessment and potential applications in laboratory diagnostics and precision medicine</i> . J Lab Precis Med. 2018;3:31. Langevin SM and Kelsey KT. <i>Mechanisms of Environmental and Occupational Carcinogenesis</i> (Ch. 3). In: Anttila SL, Boffetta P, and Straif K (eds). <i>Occupational Cancer</i> (1st edition). Springer. 2014, pp. 21-31.
Week 13 04/20/20	Introduction to “Omics” technologies	<u>Readings:</u> Aleksyev et al. <i>A Next-Generation Sequencing Primer—How Does It Work and What Can It Do?</i> Acad Pathol. 2018;5:1-11.
04/27/20	FUNCTIONAL ANNOTATION PROJECT DUE (no later than 11:59pm)	