GNET 647: Human Genetics and Genomics Spring 2014

March 25 – April 25, 2014
Lectures Tuesdays and Thursdays 12:30-1:45 PM, Michael Hooker Research Center 0003/0004
Recitation Fridays 1:30-2:30 pm in McGavran Greenberg 1305 (except April 18, UNC holiday)
Handouts, readings, and assignments will be posted on Sakai at https://sakai.unc.edu.

Lead Instructor: Karen Mohlke, mohlke@med.unc.edu, 966-2913, 5096 Genetic Medicine
Additional faculty: Samir Kelada, Kristy Richards and Jonathan Berg
TA: Gary Cantor, gcantor@email.unc.edu, NIEHS

This 1-credit module covers principles and modern approaches of human genetics and genomics, including human genetic variation, linkage, genome-wide association analysis, sequencing for variant discovery in monogenic and complex diseases, regulatory variation, the molecular basis of disease, functional validation of disease variants, gene-environment interactions, cancer genetics and clinical genetics. Readings include landmark papers and the current literature.

The course is targeted to graduate students in the biomedical sciences, and previous coursework in genetics is expected. Others may attend for credit, audit, or participate informally with prior permission from the lead instructor.

Problem sets will be assigned and discussed in recitation but not graded. Problem set questions have the same format as exam questions. Exam questions may include interpretation of required readings. Additional brief assignments will be used to help assess participation and understanding. Grades (H, P, L, F) will be based on the exam (70%), participation (25%), and completing the course evaluation (5%). The exam is a take-home to be completed by the student alone without discussion with classmates, colleagues, faculty etc. The Honor Code applies.

Expected schedule of topics, subject to change. Required readings are subject to exam questions. Optional readings are shown in parentheses. Schedule and readings subject to change.

Date	Topic	Readings	Assignments
Mar 25	**1. Human genetic variation in individuals and populations** Content of the human genome; Individual variation; the 1000 Genomes Project; Population variation; the HapMap Project; Linkage disequilibrium	1000Genomes Nature 10 HapMap Nature 05 (MacArthur Science 12) (Thorisson GenRes 05)	
Mar 27	**2. Inheritance patterns and linkage analysis: monogenic and complex** Simple and complex patterns of inheritance; Genetic architecture of disease; Linkage analysis for monogenic traits; Variable expressivity; Penetrance	Risch Science 96 (Arelin EJHG 12) (Lander Gen 88)	Paragraph about a linkage paper of your choice due April 1
Mar 28	Recitation –web resources – Gary Cantor		
Apr 1	**3. Genome-wide association studies of common and low frequency variants** GWAS goals and study design; Association analysis; Meta-analysis; Interpretation of results	McCarthy NatRevGn 08 Willer NatGen 13 (Raychaudhuri Cell 11) (Nelson TIG 12)	Problem Set 1 distributed (topics 1-3)

Apr 3	**4. Gene–environment interactions** – Samir Kelada	Manolio Nature 09 Cantor EHP 10 Wang ATVB 14	
Apr 4	Recitation		Problem Set 1
Apr 8	**5. Sequencing for variant discovery in monogenic and complex diseases** Sequencing exomes, genomes, targeted regions; Monogenic disease gene identification; Sequencing for complex traits; Burden tests	Bamshad NatRevGn 11 Peloso AJHG 14 (Purcell Nature 14)	Problem Set 2 distributed (topics 4-6)
Apr 10	**6. Regulatory variation in human disease –** Samir Kelada Expression QTLs; Allelic expression imbalance; Tissue specificity; MicroRNAs	Yan Science 02 Montgomery NRvGn 11 Luo PLoSGen 11	
Apr 11	Recitation		Problem Set 2
Apr 15	**7. Non-coding regulatory elements across the genome** ENCODE; Epigenomics Roadmap project; HaploReg	ENCODE Nature 12 GENCODE GenRes 12	Problem Set 3 distributed (topics 7-10)
Apr 17	**8. Cancer genetics and genomes** – Kristy Richards Somatic vs germline variation; Oncogenes and tumor suppressors; Mutational mechanisms; The Cancer Genome Atlas (TCGA)	Knudson PNAS 71 Tiacci NEJM 11 (Walter NEJM 12)	Paragraph about a cancer genome paper due April 22
Apr 18	No Recitation – UNC Holiday		
Apr 22	**9. Functional validation of disease variants** Molecular mechanisms, loss-of-function, gain-of-function; Allelic and genetic heterogeneity; Burden of proof; Annotation resources	Musunuru Nature 10 Bonnefond NatGen 12 (Freedman NatGen 11) (Kircher Nat Gen 14)	
Apr 24	**10. Medical genetics** - Jonathan Berg Use of genetics in the clinic; role of genotyping and sequencing across the lifespan; Direct-to-consumer genotyping	Gonzaga-Jauregui AnnRevMed 12 Manolio 13 GenMed	
Apr 25	Recitation		Problem Set 3

The exam will be distributed by 5 pm April 25 and will be due 5 pm May 1.