

GNET 647: Human Genetics and Genomics

Spring 2019

February 14 – March 26, 2019 (no classes during spring break March 11-15)

Lectures Tuesdays and Thursdays 12:30-1:45 PM, 2004 Marsico Hall

Recitation Fridays 1:30-2:30 pm 2004 Marsico Hall

Handouts, readings, and assignments will be posted on Sakai at <https://sakai.unc.edu>.

Instructors: Samir Kelada, samir_kelada@med.unc.edu, 962-2148, 5072 Genetic Medicine
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Additional faculty: Jonathan Berg, jsberg@med.unc.edu, 5092 Genetic Medicine

TA Clark Cunningham clark_cunningham@med.unc.edu; office hours by appointment

This 1-credit module covers principles and modern approaches of human genetics and genomics, including human genetic variation, genome-wide association analysis, sequencing in monogenic and complex diseases, epigenomics, regulatory variation, gene-environment interactions, causality of variants, and clinical genetics. Readings include landmark papers and the current literature and should be read before class to facilitate discussion in class and recitation.

The course is targeted to graduate students in the biomedical sciences, and previous advanced coursework in genetics is expected. Others may attend for credit, audit, or participate informally with prior permission from a 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 will include interpretation of required readings. During the course, student pairs/groups will briefly present an example of a course topic from a recent paper. Grades (H, P, L, F) will be based on the exam (75%) and presentation/participation (25%). The exam is a take-home to be completed by the student alone without discussion with classmates, colleagues, faculty etc. The Honor Code applies.

Schedule of topics and readings, subject to change. Required readings are listed and subject to exam questions. Readings to be discussed during the indicated class are marked with an asterisk (*). Additional optional readings are provided on the Sakai site.

Date	Topic	Readings	Assignments
Feb 14 (Thurs)	1. Human genetic variation in individuals and populations – Karen Mohlke Content of the human genome; Variants in individuals and populations; Linkage disequilibrium	*Erlich Science 18 1K Genomes Nature 15	
Feb 15 (Fri)	Recitation – human genome web resources: LD, genome browser, variant interpretation – Hannah Perrin and Chelsea Raulerson		
Feb 19 (Tue)	2. Genome-wide association studies of common and low frequency variants – Karen Mohlke GWAS goals and study design, association analysis, meta-analysis, interpretation of results	*Hysi NatGen 18 Visscher AJHG 17	Problem Set 1 distributed (topics 1-3)

Feb 21 (Thurs)	3. Sequencing for variant discovery in monogenic and complex diseases – Karen Mohlke Sequencing exomes, genomes, targeted regions; Monogenic disease gene identification; Tests of association using aggregated variants	*UK10K Nature 15 Bamshad NatRevGn 11	Presentation assignment distributed
Feb 22	Recitation – Clark Cunningham Discussion of Problem Set 1		
Feb 26 (Tue)	4. Functional variants and causality – Discussion - Karen Mohlke Molecular mechanisms, allelic and genetic heterogeneity; Burden of proof	*MacArthur Nature 14 *Platzer AJHG 18	
Feb 28 (Thurs)	5. Medical genetics – Jonathan Berg Use of genetics in the clinic across the lifespan; Direct-to-consumer genotyping	Strande AnnRevGHG 16	
Mar 1 (Fri)	Recitation – Data display in human genetics and genomics – Samir Kelada		
Mar 5 (Tue)	6. Revisiting GWAS, and effect modification – Samir Kelada Calculation of odds ratios in GWAS; polygenic risk scores; and effect modification by exposure (gene-environment interaction)	*Nan JAMA 15 Kaufman JACI 12	Problem Set 2 distributed (topics 4-7)
Mar 7 (Thurs)	7. Regulatory variation – Samir Kelada Genetic variants associated with gene expression level; Expression QTLs; Allelic expression imbalance; Tissue specificity	*Musunuru Nature 10 Albert NatRevGen 15	
Mar 8 (Fri)	Recitation – Clark Cunningham Discussion of Problem Set 2		Selection of presentation paper due
	Spring break March 11-15		
Mar 19 (Tue)	8. Epigenomics – Samir Kelada Regulatory elements, the ENCODE and Roadmap Epigenomics projects; chromatin interactions; other ‘omics data	*Alasoo NatGen 18 Furey Science 13 Furey NatRvGen 12	
Mar 21 (Thurs)	9. Genome editing – Clark Cunningham & Student presentations (Group 1) – two student presentations from a recent paper on a course topic	*TBD	Presentation due group 1
Mar 22 (Fri)	Recitation – Review and Q&A – Samir Kelada, Karen Mohlke, Clark Cunningham		
Mar 26 (Tue)	10. Student presentations (Group 2) – four student presentations from a recent paper on a course topic	*TBD	Presentation due group 2; Final Exam Distributed

The exam will be distributed by March 26th by 4:30 pm and will be due April 2nd at 4:30 pm