**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  
Karen Mohlke, mohlke@med.unc.edu, 966-2913, 5096 Genetic Medicine

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.

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