## Syllabus

<table>
<thead>
<tr>
<th>Feature</th>
<th>Considerations</th>
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<td><strong>Instructor &amp; TA Information</strong>&lt;br&gt;(for each Faculty and TA)</td>
<td>• Craig L. Hanis&lt;br&gt;• <a href="mailto:Craig.L.Hanis@uth.tmc.edu">Craig.L.Hanis@uth.tmc.edu</a>&lt;br&gt;• 713-500-9807&lt;br&gt;• RAS E423&lt;br&gt;• By Appointment</td>
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<td><strong>Course Description</strong></td>
<td>• GS11 1013, Genetics and Human Disease&lt;br&gt;• Fall 2020&lt;br&gt;• 3&lt;br&gt;• Face to Face/Zoom&lt;ref&gt;<strong>Course Description</strong>&lt;br&gt;This course introduces principles and methods of human genetic analysis with special reference to the contribution of genes to the burden of disease. Although molecular, biochemical and morphogenic processes controlled by genes will be briefly surveyed, the aim of the course is to describe the analytical processes whereby genetic mechanisms are inferred and genes on chromosomes are located.&lt;/ref&gt;</td>
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<td><strong>Textbook and Materials</strong></td>
<td>• None&lt;ref&gt;<strong>Textbook and Materials</strong>&lt;br&gt;• None&lt;/ref&gt;</td>
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<td><strong>Course Expectations</strong></td>
<td>• Students are expected to attend class and participate in discussions.&lt;br&gt;• Homework will be provided, but not graded. Even so, students are expected to complete the homework on a schedule that keeps pace with the lectures.&lt;br&gt;• Students are expected to interact with the instructors informally and in scheduled help sessions to discuss the homework and solutions.&lt;br&gt;• The adequacy of meeting course expectations will be determined based on performance on two midterms and a comprehensive final.&lt;ref&gt;<strong>Course Expectations</strong>&lt;br&gt;• Students are expected to attend class and participate in discussions.&lt;br&gt;• Homework will be provided, but not graded. Even so, students are expected to complete the homework on a schedule that keeps pace with the lectures.&lt;br&gt;• Students are expected to interact with the instructors informally and in scheduled help sessions to discuss the homework and solutions.&lt;br&gt;• The adequacy of meeting course expectations will be determined based on performance on two midterms and a comprehensive final.&lt;/ref&gt;</td>
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<td><strong>Course Learning Objectives</strong></td>
<td>1. Understand the basic properties of genetic variation determined by frequency and scale effects.&lt;br&gt;2. Understand the maintenance of genetic variation and equilibrium frequencies and testing for departures from equilibrium.&lt;ref&gt;<strong>Course Learning Objectives</strong>&lt;br&gt;1. Understand the basic properties of genetic variation determined by frequency and scale effects.&lt;br&gt;2. Understand the maintenance of genetic variation and equilibrium frequencies and testing for departures from equilibrium.&lt;/ref&gt;</td>
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3. Understand the concepts of heritability as associated with single genes and multiple genes for continuously measured traits as well as for discontinuous traits using concepts of liability.
4. Understand the statistical detection of segregation of alleles in pedigrees and the impact of ascertainment.
5. Understand the principles involved in the localization of genes via parametric and non-parametric linkage approaches.
6. Understand the application of fine-mapping and linkage disequilibrium mapping for identifying loci/haplotypes contributing to disease susceptibility.
7. Exposure to the multiple testing issues that attend large scale genomic approaches involving 100’s of thousands and millions of SNPs.
8. Ability to incorporate prior information into risk prediction using Bayes theorem.
9. Ability to critically evaluate the literature related to mapping and association studies associated with the common complex diseases.
10. Understand the current state of Next Generation Sequencing (whole exome and whole genome) and its potential in the context of Mendelian and complex disease.

List of Topics
- Patterns of Inheritance
- Hardy-Weinberg Equilibrium
- Meiosis, Chromosomes and Disease
- Heterozygosity and types of variation
- Genetic Markers
- Pedigree Analysis
- Recurrence Risk and Bayes Theorem
- Classic Linkage – three point test crosses
- LOD score based linkage
- Non-Parametric Linkage
- Genomics and Genome Organization
- Inbreeding and Identity
- Continuously Distributed Traits and Measured Genes
- Continuously Distributed Traits and Unmeasured Genes – Heritability
- Liability Methods
- Molecular Evolution
- Heterogeneity
- Linkage Disequilibrium and Disease Association
- Genome-wide Approaches
- Meta-analysis
- Next Generation Sequencing and Analysis
- Mendelian Randomization
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<th>Learning Activities</th>
<th>Lectures, homework, interactions with faculty and examinations</th>
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| Student Assessment And Grading Criteria | 2 Midterms each worth 100 points and a comprehensive final worth 150 points  
Typically, the following point totals must be achieved, though there may be slight modifications based on the performance for a given term.  
A: 290 out of the total 350 Points.  
B: 230 – 289 points  
C: 190 – 229 points  
F: < 190 points |
| PhD and Master’s Students | In addition to the assessments above, PhD students will be given two additional take home problem sets requiring additional synthesis of related concepts.  
Each of these will be worth 25 points each.  
Grading criteria for PhD students will typically require the following point totals, though there may be slight modifications based on the performance for a given term:  
A: 330 out of the total 400 Points.  
B: 265 – 329 points  
C: 220 – 264 points  
F: < 220 points |
| Prerequisites and/or Technical Requirements | General genetics and statistics |
| Policies and Procedures | It is expected that students will complete homework, but it will not be turned in and graded. Students are also expected to participate in class discussions.  
Only in unusual circumstances will a student be given an incomplete. Incompletes cannot be used to circumvent receiving a failing or other low grade. The only way to make up for an incomplete grade is to retake the class when next offered and demonstrate satisfactory completion of ALL midterms and the final |
• **Academic Integrity**

Academic integrity is the pursuit of scholarly activity free from fraud and deception and is an educational objective of this institution. Academic dishonesty includes, but is not limited to, cheating, plagiarizing, fabricating information or citations, facilitating acts of academic dishonesty by others, having unauthorized possession of examinations, submitting work of another person or work previously used without informing the instructor, or tampering with the academic work of other students. Individuals found guilty of academic dishonesty may be dismissed from the degree program. It is a student’s responsibility to have a clear understanding of how to reference other individuals’ work, as well as having a clear understanding in general as to the various aspects of academic dishonesty. Any student accused of a specific act stated in the previous paragraph is subject to UTHealth School of Public Health academic policies and procedures pertaining to violations of the student code of conduct for academic integrity. Each student in this course is expected to abide by the UTHealth School of Public Health Honor Code signed at first matriculation. Any work submitted by a student in this course for academic credit will be the student's own work.

You are encouraged to study together and to discuss information and concepts covered in lecture and the sections with other students. You can give "consulting" help to or receive "consulting" help from such students. However, this permissible cooperation should never involve one student having possession of a copy of all or part of work done by someone else, in the form of an e-mail, an e-mail attachment file, a diskette, or a hard copy. During any quiz or exam you must do your own work. Talking or discussion is not permitted during a quiz or exam unless specifically stated, nor may you compare papers, copy from others, lend or borrow calculators, or electronic devices, or collaborate in any way unless specifically stated. Any collaborative behavior during a quiz or exam will result in failure, and may lead to failure of the course and UTHealth SPH disciplinary action. Should copying occur, both the student who copied work from another student and the student who gave material to be copied will both be held accountable.

Please remember that you signed the academic integrity policy at orientation. No academic dishonesty of any kind (including copying/plagiarism) will be tolerated. All suspected academic dishonesty (actual or attempted) or other violations of the student code of conduct will be immediately reported to the UTHealth SPH Associate Dean for Academic Affairs. You can review the
Student Conduct and Discipline Policy in the Handbook of Operating Procedures (HOOP) at [https://www.uth.edu/hoop/policy.htm?id=1448220](https://www.uth.edu/hoop/policy.htm?id=1448220).

- ADA Accommodation
- UT Policy on Accommodations for Disabilities: UTHealth is committed to providing equal opportunities for qualified employees, job applicants, and students with disabilities in accordance with state and federal law. Student applicants and enrolled students can obtain information concerning program-related accommodations in each school from the school’s Section 504 Coordinator (usually found in the Student Affairs office of each school). The Disability Coordinator (in Human Resources) and the Section 504 Coordinators can provide information and referrals regarding campus accessibility, disabled parking permits, transportation services, and other resources. The full policy can be found online in HOOP Policy Number 101, Disability Accommodation [http://www.uth.edu/hoop/policy.htm?id=1448050](http://www.uth.edu/hoop/policy.htm?id=1448050). If you believe you have a disability requiring an accommodation, whether new or existing, please contact Mary Ann Smith, Assistant Dean of Students and ADA Accommodation Coordinator for UTHealth School of Public Health at mary.a.smith@uth.tmc.edu or (713) 500-9236.

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<th>Course Calendar</th>
<th>SEPARATE DOCUMENT</th>
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For help with learning objectives, see [http://www.sph.uth.tmc.edu/oid/default.aspx?id=9224](http://www.sph.uth.tmc.edu/oid/default.aspx?id=9224)
GENETICS AND HUMAN DISEASE - FALL SEMESTER 2020

Instructors: Craig L. Hanis, Ph.D.  RAS E423: 713-500-9807  HOME:  713-515-9515
Email: Craig.L.Hanis@uth.tmc.edu

To Meet: Tuesdays and Thursdays: 11:30 AM - 12:50 PM in RAS E605 and ITV

Grading: Two midterms and a comprehensive final
Problem Sets: Will be given and are expected to be done, but are not graded
Assigned Literature: Will be expected to participate in discussions
Help Sections: Will prove helpful

Course Objective:

The purpose of the course is to provide students an introduction to the methods by which inferences regarding the contribution of genetic variation to disease susceptibility are made. This includes elements of population genetics, segregation analysis, linkage and association and analysis of whole exome and genome sequence data. Upon completion, students should be able to access and critically evaluate the literature with regard to the genetics of disease.

SEPTEMBER

1  Pedigree Analysis by Inspection and Intro to Population Genetics  HANIS
   Pedigree nomenclature, Patterns of Inheritance
   Hardy-Weinberg Equilibrium, Random mating and union of gametes;
   Departures from Hardy Weinberg: selection, mutation, migration, drift

3  Population Genetics I  HANIS
   Hardy-Weinberg Equilibrium, Random mating and union of gametes;
   Departures from Hardy Weinberg: selection, mutation, migration, drift

8  Population Genetics II  HANIS
   Approach to Equilibrium: Sex-linkage
   Heterozygosity and Polymorphic Information Content (PIC)
   Hardy-Weinberg and Short Tandem Repeats
   2 Loci H-W

10 Genetic Markers.  HANIS
   ABO: One locus vs Two loci models
   ABO: Molecular basis and allele frequency estimation
   Bombay and Secretor
   Rh: Incompatibility and hemolytic disease and ABO protection

15 Meiosis, Chromosomes and Diseases of Repeats  BRESSLER
   The normal karyotype and nomenclature
   Errors in number: aneuploidy, polyploidy
   Establishing meiotic events

Revised July 2019
### Fragile X Diseases of Repeats – Anticipation

17 Recurrence Risks and Bayes’ Theorem HANIS
   Twin Zygosity & Paternity Testing
   Recurrence risks in genetic counseling/BRCA1 carrier status
   Conditional using Bayes Theorem
   Forensics

22 Introduction to Pedigree Analysis HANIS
   Ascertainment: complete, multiple, single
   Estimation of Segregation: Truncated Binomial Distribution
   Tests of Hypotheses: Poorness of Fit and Heterogeneity Chi-square
   Pitfalls and limitations

24 Inbreeding and Identity HANIS
   Identity by descent
   First Cousins
   Relative Risks
   Homozygosity Mapping

29 Linkage Analysis I - Review - Lessons from Flies and Corn HANIS
   Implications
   Coupling and repulsion
   Informative matings
   Three-point test cross

**OCTOBER**

1 Review Session 1 HANIS

6 **Midterm Exam I – written**

8 Linkage Analysis II - Affected Relative Pairs HANIS
   Identity by state
   Identity by descent
   Power

13 Linkage Analysis III HANIS
   LOD Score methods
   Exclusion analyses
   Maximum likelihood estimation

15 Continuously Distributed Traits and Measured Genes HANIS
   Red Cell Acid Phosphatase
   Frequency and Scale
   Average effects
   Genotype by Environment Interaction

20 Continuously Distributed Traits and Unmeasured Genes HANIS
   Heritability: Definition and Estimation

Revised July 2019
Experimental Design

22 Discontinuous Traits and Continuous Liability
   Explicit model
   Multiple Thresholds

27 Heterogeneity
   Genetic
   Phenocopies
   Multi-locus Models

29 Disequilibrium
   Definition
   Estimation and Examples
   Haplotype Tagging
   Haplotype Diversity

NOVEMBER

3 Genotype – Environment Interaction
   Cross Population
   Within Populations
   Interventions
   Pharmacogenetics

5 Review Session II

10 Midterm Examination II - Written

12 Disease Association
   Methods of detecting gene-disease association, potential pitfalls
   HLA and ankylosing spondylitis and IDDM
   RFLPs, Associations and continuous traits
   Transmission Disequilibrium Testing

17 Genome-Wide Association Studies
   Imputations
   Replication
   Meta-analysis
   SNPs, Genes or Pathways as the Units of Inference

19 GWAS and gene expression studies: Analytic issues
   It’s like drinking from a fire hose!
   Over-determination
   Multiple comparisons
   Experiment-wise error and False discovery rate

24 General Treatment of a single disease
   Segregation → Linkage → Mutations → Implications
   Cystic Fibrosis as an example

Revised July 2019
21 Whole Exome Sequencing
   Lab Methods
   Mendelian Disease Filtering
   Mutational Spectrum
   GWAS Approaches
   Burden Tests

26 THANKSGIVING - NO CLASS

DECEMBER

1 Whole Genome Sequencing
   Lab Methods
   Annotation, CNVs, Other Structures
   Conservation
   Population Genetics
   Disease Implications

3 Mendelian Randomization

8 Interacting Genomes – Genomics and the Microbiome

10 Review Session III

14-18 Final examination