Human Genetics Ph.D. Program Guidelines

Rationale

Genetics is the study of variations in and transmission of hereditary material from generation to generation and how this information is translated into biological function. Genetics utilizes many techniques ranging from molecular to population genetics techniques. Because of the pervasive impact of genetic variation on biological function, genetics has become a significant unifying theme for research in the biological and biomedical sciences and can serve as a focus for the study of virtually all biological processes and systems. Genetics plays an ever increasing role in the elucidation of the cellular and molecular mechanisms of human disease and birth defects, and in their prevention, diagnosis and therapy. In addition to using genetics to study biomedical questions posed by other fields, genetics encompasses an important set of questions as to how the information content of a set of relatively simple molecules can be translated into complex systems and organisms, how variation at the molecular level can cause phenotypic differences among individuals, and how this variation within and among populations can be used to explain differences in disease prevalence.

In recent years, human genetics, as a major subfield of genetics, has contributed significantly to our understanding of disease processes. This explosive growth in our knowledge is an outcome of genetic analysis and the rapid technological advances fostered by the Human Genome Project, and will continue to increase over the foreseeable future. The Ph.D. Program in Human Genetics has already enabled Vanderbilt University to become a key player in this explosion of knowledge, both nationally and internationally, by attracting and training the best students interested in human genetic research and serving as a focus for the recruitment of new faculty interested in training students in genetics.

The goal of the Ph.D. Program in Human Genetics is to encourage the training of students to explore the questions motivated by genetic research in general and particularly as they apply to human disease. This curriculum will also teach students both within the program and in other disciplines how to use the tools of genetics to answer a variety of important biological questions. The program provides a cohesive program that unifies human genetic research at Vanderbilt and provides common direction and vision for investigators interested in training graduate students in genetics.

Training Objectives

The overall goal of the Human Genetics Ph.D. degree program is to provide students with a solid foundation for a career in human genetics research and teaching. Training is available in genetic analysis of humans and model systems that contribute to our understanding of human disease. The training combines a prescribed set of basic courses intended to ground students in the fundamentals of genetic analyses, the basics of human genetics, a set of elective courses designed to meet individual needs, and a rigorous research experience that will contribute to the field of genetics. Students completing the requirements of the Ph.D. program in Human Genetics will have demonstrated mastery of

knowledge in genetics and contributed substantial and original scientific knowledge to the field.

The specific objectives are:

1. To provide graduate training and research on the genetic basis of human disease;
2. To provide students with an integrated and comprehensive academic curriculum designed for a concentrated program of study in Human Genetics;
3. To ensure that the existing critical mass of faculty in genetic analysis will interact synergistically in their efforts to provide students with firsthand knowledge of emerging concepts and "state of the art" technology in the rapidly evolving field of Human Genetics.

The Ph.D. program will provide students with options for the study of human genetics from several perspectives, ranging from population genetics and genetic epidemiology to molecular genetics/genomics of model organisms and disease states, and will build on the training that students receive in the admitting programs including the Interdisciplinary Graduate Program in the Biomedical Sciences (IGP), the Chemical and Physical Biology Program (CPB), and the Medical Scientist Training Program (MSTP).

It is important to note that the intent of the training program is not to train students who only use one or a few techniques of genetics to address a wide variety of biological questions, but to train students who address questions fundamental to the discipline of Human Genetics. These areas include: 1) the characterization and implications of genetic variation; 2) the transmission of genetic information within and across populations; 3) genomic structure and function; 4) how genetic variation is translated into phenotypes; and 5) the genetic basis of human disease.

Relationship to the Interdisciplinary Graduate Program in the Biomedical Sciences (IGP) and Other Admitting Programs

Students may enter the Human Genetics Ph.D. Program from the IGP, CPB, and Medical Scientist Training Program (MSTP) programs. All graduate students entering these programs are admitted uncommitted to a specific department or Ph.D. program. Each program has its own initial course requirements, all of which are acceptable to the Human Genetics Ph.D. Program. Students will enter the Human Genetics Ph.D. Program at the end of the first year of the IGP or CPB programs. MSTP students will enter the Human Genetics Ph.D. Program at an equivalent time in their training.

Acceptance into the Human Genetics Ph.D. program depends on satisfactory performance (B or better in all classes) in the admitting program. Acceptance will also depend on the recommendation of a thesis advisor who is part of the Human Genetics program faculty.

Academic Curriculum for the Genetics PhD

Ph.D. students in Human Genetics are required to complete a minimum of 29 credit hours of formal coursework (combined credits from required and elective courses). One of the required courses will be a statistics course to be chosen from the many currently available

on campus and approved by the Human Genetics Ph.D. Program Oversight Committee. Students will take a minimum of 6 hours of didactic classes per semester during their first two years of study. It is expected that during the second year at least one semester will exceed this minimum to complete the required courses prior to year 3 of study. The electives will come from an approved list of advanced genetics courses (see below). In individual cases, other courses approved by the Director of Graduate Studies and a student's committee can serve as electives. The choice of these courses will be based on the individual student's research interests. Other specific needs of students can be met with the electives, or in very rare cases students with the support of their mentors can petition to replace **one** required course with another one suited to their research needs.

Courses summaries are included in this document (Appendix I).

All Students (Example for IGP students)

Required Courses - Fall, Year 1

IGP: *Bioregulation I* (8)

Required Courses - Spring, Year 1

IGP: *Bioregulation II modules* (5)

Required Courses for All Students

Genetics Interest Group (HGEN 8335) (1)
Human Genetics I (HGEN 8340) (3)
Tutorials in Human Genetics I (HGEN 8370) (1)
Human Genetics II (HGEN 8341) (3)
Tutorials in Human Genetics II (HGEN 8371) (1)
Fundamentals of Genetic Analysis (HGEN 8385) (1)
One statistics class

Advanced Genetics Course Electives

BioVU Study Design (HGEN 8391) (3)
Introduction to the Vanderbilt Center for Undiagnosed Diseases (HGEN 8393) (2)
Analytic Techniques for Genetic Epidemiology (EPD 8333) (3)

Introduction to Statistical Computing (BIOS 6301)
Principles of Modern Biostatistics (BIOS 6311)
Modern Regression Analysis (BIOS 6312)

Courses from other relevant programs (for example, Molecular Physiology & Biophysics, Biomedical Informatics, Biostatistics, and Epidemiology) may be taken for credit towards the HGEN PhD program with permission of the HGEN DGS and the course instructor.

Academic Performance

All students must maintain an overall B (3.0) grade point average (GPA) in their didactic coursework. Student progress will be monitored by the Director of Graduate Studies (DGS), who will meet with each student at least once per semester. If a student's GPA drops below 3.0, he/she will be placed on academic probation. If the GPA remains below 3.0 after a second semester, the Oversight Committee will evaluate the student's overall performance and may recommend either further remedial action or dismissal from the program. If the GPA remains below 3.0 for a third semester, the student will likely be dismissed from the program unless there are extraordinary circumstances. Continuation in the program would then require the unanimous decision of the oversight committee.

Any financial support received from training grants or the Ph.D. program is contingent upon maintaining an overall GPA of 3.0 and taking a full course load each semester.

Ph.D. Qualifying Examination

To qualify for candidacy, a student must complete all of the required first and second year courses with an average GPA ≥3.0 in the required Human Genetics I and II courses (HGEN 8340 & 8341), must be in good academic standing (GPA ≥3.0), and must pass a two-part oral candidacy examination. The qualifying examination will be taken by the beginning of the third year of graduate school for those entering from the IGP or CPB programs, and the fourth year for MSTP students. The student's supervisor will not be present during either Phase I or II of the Qualifying Exam.

Examination Phase I:

The first part of the candidacy process is a ninety minute oral examination testing general knowledge in the field of genetics and related topics. It is assumed that all students will have a general understanding of a broad array of topics in genetics. This examination will be administered by the Human Genetics Ph.D. program Oversight Committee or representatives appointed by the committee. At least 3 out of 5 members of the examining committee must be members of the Oversight Committee. The remaining members may be chosen from the Human Genetics training faculty. The Director of Graduate Studies and/or his/her representative (*ex officio*) must be present for all exams. If a student taking the Qualifying Examination is in the laboratory of a member of the Oversight Committee, that member will be excused from duties in administering the examination for his/her student, and will be replaced with another member of the Human Genetics Ph.D. Program faculty.

The general knowledge portion of the Qualifying Examination must be passed prior to proceeding to the second part of the Examination.

Examination Phase II:

The second part of the candidacy examination is a ninety minute oral defense of the student's likely thesis proposal. The proposal defense will be in front of a faculty

committee that has expertise on the thesis topic and can adequately judge the student's knowledge of the topic and his/her ability to carry out the project.

The examining committee will be chosen by the DGS after consultation with the Oversight Committee. It will consist of four members of the Human Genetics training faculty, one faculty from outside the training program, and the DGS and/or his representative (*ex officio*). One of the Human Genetics Ph.D. Program faculty will be chosen by the DGS to serve as the chair of the examining committee. The student's supervisor will not be included in the examining committee, nor will they be present during the examination.

The proposal will be written by the student in the format of a Research Plan of an NIH F31 grant proposal, Predoctoral Individual National Research Service Awards. The written proposal will be limited to 7 pages (Arial 11 point, 0.5 inch margins, single spaced) of narrative text including all figures and tables. (References are not counted in the page limit, but there should, in general, not be more than 40). The organizational style should be similar to an NIH grant proposal, and students are encouraged to further develop their proposal into a grant proposal to be submitted to NIH. The guidelines for the proposal are:

Abstract: A summary of the project including a brief description of the problem, specific aims, and research design to be employed. (no more than 30 lines of text, ~400 words, on a separate page not counted in the 7 page limit)

Specific Aims (no more than 1 page, on a separate page): State concisely the goals of the proposed research, list the specific objectives, and summarize the expected outcome(s).

Significance (~1/2 page):*:* The importance of the problem and how the proposed project will improve scientific knowledge and/or technical capability.

Innovation (~1/2 page)*:* How the application challenges and seeks to shift current research or clinical practice paradigms.

Approach (~5 pages): Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims. Include how the data will be collected, analyzed, and interpreted. Discuss potential problems, alternative strategies, and benchmarks for success.

The student will prepare this document, but may seek advice on specifics of the proposal from anyone they choose and should seek advice and input from their faculty supervisor. It is essential that the document be written by the student, in his/her own words and not extracted from previously existing documents. To assure that this is the case, the chair of the examining committee may request to see pre-existing grant proposals or papers from the student's mentor. Access to existing proposals allows the student the opportunity to read grant applications from their laboratory or mentor, as this can be a valuable preparatory experience. However, it is essential that the student's written proposal be crafted in his/her own words. In preparing the written proposal the student is encouraged

to seek advice and guidance from any person who he/she feels will be helpful in improving the proposed research; this may include the student's mentor.

The abstract for the proposal will be due to the Program Coordinator (Roz Johnson) two weeks after the student completes their Phase 1 exam. The abstract should be limited to one page. The Program Coordinator will forward the abstract to the Oversight Committee members, who will communicate to the DGS within two weeks whether the abstract is appropriate and potentially defensible. The DGS will then communicate to the student if any substantial changes to the abstract are advised. Typically, at this stage the main concern is whether the scope and substance of the aims is appropriate and the questions to be addressed are clearly articulated.

The student must turn in the full, complete proposal to the examining committee at least two weeks prior to the student's exam date. All examining committee members will then provide a one-paragraph review of the proposal to the exam committee chair and they will also specifically indicate whether or not the proposal is sufficiently adequate (i.e. defensible) so that the oral exam can proceed. Written feedback summarizing these comments will be sent to the student within a week of their scheduled exam by the exam committee chair. This feedback is intended to give the student some indication of the proposal's perceived quality, strengths, and weaknesses before the oral exam takes place. If two or more examining committee members indicate that the proposal is inadequate to such an extent that the defense cannot proceed, then the student must revise the proposal and reschedule his or her exam at least one month later than originally scheduled.

Evaluation of Examinations:
The overall aim of the candidacy examination is to insure sufficient general knowledge in a specific area of genetics to allow the student to place his or her own research into proper perspective, and to determine if the student has the knowledge and comprehension of genetics to define important future areas of investigation. Part I of the examination is used to evaluate general knowledge. Part II of the examination is used to evaluate the student's knowledge in a specific area on which he/she is proposing to do thesis work. The student's performance on Part II of the examination will be evaluated by the examining committee on the basis of both the written document AND the student's ability to defend it orally. The examining committee will provide any additional written comments concerning the student's proposal within a week following the phase II exam, regardless of the outcome of the qualifying examination.

Part I and Part II of the candidacy examination will be graded separately, and students must pass both to advance to candidacy. For each part of the examination there will be three possible outcomes:

1) Pass;
2) Conditional Pass – Specific conditions and time requirements to meet the conditions will be determined by each committee with approval of the DGS; multiple serious deficiencies should be classed as a "Fail".
3) Fail.

At the end of the exam the examining committee will confer in private to reach consensus on the outcome. If consensus cannot be reached, a majority vote of the committee will decide the outcome.

In the case of failure, the student will be typically given no more than four months to retake the part(s) of the examination that was failed. The examining committee with approval of the DGS will determine the date of the second examination. Failure to pass a second examination will result in dismissal from the Ph.D. program. In this case, a plan for a terminal master's degree may be developed.

On satisfactory completion of both parts of the examination, the student will be admitted to candidacy.

Dissertation Committee

Once a student has achieved candidacy for the Ph.D. degree, he/she will select a dissertation advisory committee that will be chaired by a faculty member other than the research mentor. The committee will be chosen in consultation with the DGS and the student's advisor. The committee must include at least 2 members of the Human Genetics faculty other than the mentor and at least one faculty member from another discipline who is not a member of the Human Genetics program faculty. The chair of the committee must be a Human Genetics faculty member. The DGS will serve as an *ex officio* member of the committee if he/she is not an official member of the committee. Thus committees should include at least 5 faculty members, including the mentor. A committee may include a sixth member if deemed appropriate by the student, research mentor, and the DGS. The student should meet with his or her thesis committee as soon as practical but no later than four months after their phase 2 exam, and then approximately every six months thereafter until graduation. Dissertation committees will serve as a resource for direction and assistance.

The role of the Dissertation Committee is to serve as a resource for direction and assistance to the student as needed and to help guide the development of the student's research and career. However, the research mentor is primarily responsible for guidance of the student's research and training. The Dissertation Committee is responsible for administering the final Ph.D. examination and will determine whether the candidate has presented an acceptable thesis. Thesis committee members are also strongly encouraged to provide written comments on the student's thesis research proposal at the first committee meeting. A summary of all committee meetings will be written by the student and approved by the committee. Copies of the summary will be sent to all committee members and the DGS and become a part of each student's permanent record. The chair of the Dissertation Committee will inform the DGS in writing of the results of the final examination, including completion of any required revisions. If all other requirements are satisfied, the DGS will notify the Dean of the Graduate School that the student has completed the requirements for the Ph.D. degree.

Candidates for the Ph.D. degree in Human Genetics must present an acceptable dissertation that adds to or modifies what was previously known. The requirements of the Graduate School, as described in the Graduate School Bulletin, must be followed when preparing the thesis. Professional achievement must also be evident and should include the presentation of research work at a national meeting(s). Prior to the thesis defense the student should have at least one first authored publication (published or in press) in a peer reviewed scientific journal.

Applied Clinical Rotation

Each Ph.D. student is required to complete a minimum of one clinical genetics rotation. After the rotation the student will write a one page summary of his or her experiences to be kept in the student's file. The purpose of this experience is to expose the students to issues related to the utility of genetics for the diagnosis, treatment, and prevention of human diseases. The format of the clinical rotation will be decided by the student's faculty supervisor in consultation with the PhD committee. A typical clinical rotation will involve a clinical member of the PhD committee and will serve to allow the student to have a practical view of a subject involved in their thesis research. If that is not possible, a clinical rotation can be designed in consultation with the DGS.

Students entering the Human Genetics Program through the MSTP program will not be required to complete a clinical rotation. HGEN 8393 will also satisfy this requirement.

Training in the Responsible Conduct of Research (RCR)

It is essential that all scientific inquiry be performed in a responsible and ethical manner. To that end, all incoming graduate students to Vanderbilt are required to attend initial RCR training. To reinforce and enhance this training over the course of the Ph.D. investigations, the program both encourages and requires additional documented RCR training. No student will be allowed to graduate without documented exposure to RCR training at least twice per year. Such training may take many different forms. A partial listing includes:

Attendance at GIG, which will have RCR discussion at least once per semester

Documentation in the summary letter of RCR discussions during the thesis committee meetings

Attendance at the mini-retreat and the full retreat, where RCR issues will be discussed

Additional Requirements

Students in the Human Genetics Ph.D. degree program will be required to obtain one hour of credit for attending the Genetic Interest Group (GIG). The one hour of credit will be given at the end of two consecutive semesters of satisfactory attendance at GIG. No more than one unexcused absence will be permitted to obtain credit.

In addition to attending and participating in the discussions at GIG, all students who have been admitted to candidacy will be required to present their research progress at GIG

once each year. The presentation will consist of a 40-minute talk followed by questions from the audience. These experiences will serve to train in students in oral presentation of their research and to provide increased input from the Vanderbilt genetics community regarding the research project.

Participation in the HGEN journal club, and other journal clubs available on campus which relate to the student's research project, is strongly encouraged.

Trainees studying off campus

In rare circumstances it may be necessary for a student to spend extended periods of time off campus. This is acceptable but extra care must be taken to maintain a high level of exposure to appropriate training experiences. In such a circumstance, the trainee and mentor must write a brief but detailed (~ one page) request for off-campus training. Requests will only be considered for trainees who have completed their first year of HGEN required courses and passed their phase I qualify exam. The request should provide the following information:

- Reason for the request, including the location and length of time away from Vanderbilt.
- Proof of good standing in the HGEN program and the Graduate School
- Details of the opportunities available for formal and informal training and experiences that are equivalent to those available at Vanderbilt including:
    - Regular seminars/discussion groups/ journal clubs equivalent to GIG
    - Availability of other seminars and training opportunities
    - If necessary, arrangement for the clinical rotation
- Method of documentation that these training experiences are being fulfilled
- Procedures to ensure that all the Program requirements are being met (e.g. regular committee meetings, etc.)

The request must be approved by the DGS and Program Director before the trainee physically leaves Vanderbilt.

Length of Training

Students and advisors should aim for completion of graduate studies within a period of three years after passing their qualifying examinations. Most students will be able to meet this expectation. All students are expected to graduate within six years of matriculating as graduate students at Vanderbilt. If this time limit is unlikely to be met, the student will be required to submit a formal petition to the Oversight Committee to grant an extension. The petition must include an explanation for the inability to complete training within six years and a projected time for degree requirement completion. If an extension is recommended by the Oversight Committee, the DGS will petition the Dean of Graduate School for the extension.

Faculty

Faculty with primary appointments at Vanderbilt and with an appointment in the Graduate school are eligible for appointment to the Human Genetics Ph.D. program

faculty. Faculty are chosen on the basis of their area of research expertise and their willingness to train students in the prescribed program. The program Oversight Committee will review the Curriculum Vitae of all interested faculty and determine their eligibility based on criteria given below.

Additional training faculty may be added based on the following criteria:

1) Area of research interest;
2) An active research laboratory with peer-reviewed support, or start-up funds;
3) A track record in training graduate students. For young faculty, potential to train students effectively will be considered sufficient to become members of the training faculty, but these faculty will be periodically counseled on the responsibilities and duties of a thesis advisor;
4) Active participation in Ph.D. related courses, seminars or other program activities.

Administrative Structure

The Ph.D. Program will be administered by the Program Director and the DGS in close consultation with an Oversight Committee. They will be advised by an Oversight Committee. Additionally, the Oversight Committee will evaluate student progress based on reports from the Dissertation committees.

The DGS will have primary responsibility for overseeing all aspects of the Ph.D. program. He/she will do so with the help of the Oversight Committee. The Program Director and the DGS will be the official spokespersons for the Ph.D. program and will serve as its representatives in matters related to University policy and programs. The DGS will be responsible for the maintenance of high standards in the academic program, including the continuing evaluation of all required and elective courses in the program, the qualifications and diversity of the faculty. The DGS will initiate and coordinate recruitment activities and will be also responsible for identifying and applying for (or assisting others in applying for) internal and external support for graduate training in Human Genetics.

In addition, the DGS will be responsible for monitoring the progress of each student throughout his or her training. He/she will be responsible for explaining the program requirements to the students and monitoring their performance in course work. The DGS will also serve as a student advocate when personal problems arise and in cases of faculty irresponsibility or misconduct. Students will be encouraged to present issues regarding the program and/or courses directly to the DGS. However, they may also choose to do so through a representative of the Human Genetics Student Association (HGSA, described below). In cases where there is an issue with the DGS students should consult directly with the Program Director or a member of the Oversight Committee.

The Oversight Committee will also serve multiple roles. Included in its roles are:

1) An advisory committee on student-related issues, including monitoring student progress, performance, and welfare. However, it should be noted that the Committee will not provide the kind of individualized attention that the Dissertation Committee is required to do. The Committee's purpose instead is to make sure that the goals of the program are met in a more general sense.

2) A committee on policy changes for the program. This will include the addition of and removal of courses from the program and the addition of tracks to the program. Changes made to the program will not be retroactive and students who entered the program prior to changes will follow the requirements that were in place at the time of their admission. In some cases (at the discretion of the Program Director, the DGS and the Oversight committee) students may have the option of choosing to follow new or old guidelines. Prior to any changes input from the entire faculty of the program will generally be solicited;

3) Selection and evaluation of program faculty based on the criteria above.

The Oversight Committee will represent a broad spectrum of Ph.D. program faculty representing all of the areas of human genetics included in the training program and will be capable of advising the Program Director and the DGS on all program and research related topics pertinent to student training. There will be five voting members of the Oversight Committee, at least one of which will be a tenured Associate or Full Professor. The Program Director and the DGS will not be included in these five, but will serve as non-voting members and will coordinate meetings. In addition, a senior student (admitted to candidacy), appointed by the Genetics Graduate Student Association will serve as a non-voting member. The student member may be excused when discussions involve of issues of a confidential nature.

All members of the Oversight committee will be appointed to three year terms with the possibility of renewal. The graduate student member will serve for a one year term, but also may be re-appointed.

Human Genetics Student Association

The graduate students have formed a Human Genetics Student Association (HGSA). The HGSA serves to formalize student input for internal and external matters, to promote communication among students of the program, and to promote and welcome potential students to the graduate program. The HGSA adopts its own by-laws and elects its own officers following these by-laws. It also appoints a representative to the Oversight Committee.

In addition, the HGSA will be responsible for organizing a regular Student-to-Student discussion session. The purpose of this is to give students an opportunity to gain experience in presenting and defending their research orally. In addition, it will be used to help students develop mentoring skills. Attendance at these meetings will be expected for more junior students. The HGSA will, in consultation with each presenting student,

invite individuals outside of the program who may be helpful in terms of specific research expertise.

The HGSA is also responsible for inviting one outside speaker to Vanderbilt each year. They identify which individuals to invite and make all the arrangements for the visits with the help of the Program Coordinator.

Financial Support
Stipends and tuition allowances are awarded to students on the basis of academic merit. Stipend levels are set by the Biomedical Research and Training (BRET) office in consultation with the department chairs.

The first two semesters of support (while students are in the IGP) are provided by funds from the Graduate School. Following the first year, multiple avenues of support will be available. For United States citizens or permanent residents training grant slots may be available, in which case most of the tuition is covered by the training grant(s) and the remainder by tuition remission. For foreign students support will come from research grants with tuition remission. Alternative sources of support include faculty research grants for all students and individual fellowships from extramural sources. Financial support for senior students (years 4 and above) will be the responsibility of the thesis advisor. In some cases the Ph.D. program may have funds to support stipends or tuition for students not supported through other means. Requests for this support should be made to the Program Director and DGS. Financial support may be withdrawn from a student whose cumulative GPA is less than 3.0 at the end of two semesters or whose performance is deemed otherwise inadequate as described elsewhere in this document.

Appendix I.
Brief Course Descriptions: This information changes often and the information here may be out of date. Please check with the graduate school or the department for current information.

HGEN 8340: **Human Genetics I**

This course focuses on the basic concepts of human genetics and of medical genetics. This course is divided into three modules of roughly equal length. The module subjects are:
(1) Introduction to the human genome

(2) Regulation, mutation, and molecular methods

(3) Human genetic diseases: from bench to clinic
Each module will be assessed separately and the final grade will be set by an average over the three module grades. FALL [3] Mortlock

HGEN 8341: **Human Genetics II**

This course introduces methods of statistical and population genetics with applications to complex disease. Students must have a strong understanding of

Mendelian genetics and basic biostatistics. As with HGEN I, this class will be split into three modules by subject.
(1) Human population genetics

(2) The genetic architecture of complex disease

(3) Computational genetic methods

Each module will be assessed separately and the final grade will be set by an average over the three module grades. SPRING [3] Davis

HGEN 8370. Tutorials in Human Genetics. A weekly seminar critically evaluating current and past scientific literature from many areas of genetic research. The focus will be on study methods and analysis. FALL. [1] Mortlock.

HGEN 8371. Tutorial in Statistical and Population Genetics. The class meets once weekly. Graduate students critically evaluate recent research publications in human genetics. There is an emphasis critical thinking about publications and on presentation of scientific results. SPRING. [1] Samuels.

HGEN 8385. Fundamentals of Genetic Analysis. This course is designed to accomplish three goals: (1) introduce students to critical topics of genetic research, (2) introduce students to important areas of genetic research not covered in first-year course work, and (3) promote an understanding of classical genetic analysis by learning genetics using the original literature. The approach will be to use classic literature that defined significant problems in genetic research. Specific topics will include: genetic analysis (segregation, independent assortment and locus mapping), human pedigree analysis and disease gene mapping, and population/quantitative genetics. SPRING. [1] Mortlock.

HGEN 8391 BioVU Study Design. This is a practical hands-on course on the design of research projects using the de-identified version of Vanderbilt's electronic medical record and the DNA bio-repository (BioVU). Students will go through the process of developing a BioVU project proposal. Topics covered will include : an overview of the clinical data available in the Synthetic Derivative (SD), techniques for defining phenotypes within the SD, proper control definition, limitation of BioVU for research, available genetic data, common problems with study design and how to address them, population stratification, IRB approval procedures and other RCR topics. The goal of this course is to guide the student through the process of developing a practical BioVU proposal to the point of application submission. [3] Samuels & Wells

HGEN 8393: **Introduction to the Vanderbilt Center for Undiagnosed Diseases.**

This course will introduce students directly to a powerful on-campus endeavor: The Vanderbilt Center for Undiagnosed Diseases (VCUD). VCUD is one of six sites added to the NIH sponsored Undiagnosed Diseases Network (UDN). The purpose of the UDN is to bring together clinical and research experts from across the United States to solve the most challenging medical mysteries using advanced

technologies. Interested patients apply to the network; if accepted, they undergo full phenotyping and if appropriate, whole exome- or whole genome-sequencing. The VCUD receives these data files and completes the analysis with a team of bioinformatics, biology, genetics, protein modeling, and clinical experts. The purpose of this course is to introduce students to the "needle in a haystack" problem of determining the causal genetic variants, out of the millions of variants carried by each individual, that underlie rare diseases. Students will attend two meetings per week in which new UDN cases will be discussed. For a final project, the student will present one of the cases at the Genomics Meeting at the end of the semester. The student will describe the findings from sequencing data after investigating the evidence associated with the variants, and make a case for which variants are diagnostic or which should continue to be pursued in the evaluation of the UDN participant. This will require the student to integrate the sequencing results, data from model organisms, and information in published literature with the presenting features of the participant. SPRING [2] Hamid

EPD 8333: Analytic Techniques for Genetic Epidemiology. This course takes an example-based approach to provide students with the skills necessary to conduct statistical association analysis of genetic data from human populations for genetic epidemiology studies. Topics will include quality control, statistical methods for association testing, common study design issues, future directions of genetic epidemiology and advanced topics. Course Instructors: Dr. Digna R. Velez Edwards and Dr. Todd L. Edwards [3]