GENETICS

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http://medicine.yale.edu/genetics
M.S., M.Phil., Ph.D.

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Assistant Professors Grace Chen (*Immunobiology*), Maurizio Chioccioli (*Comparative Medicine*), Nada Derar, Teodoro Jerves Serrano, Nicole Lake, Monkol Lek, Deqiong Ma, Diyendo Massilani, Steven Reilly, Jason Sheltzer (*Surgery/Oncology*), Zachary Smith, Trevor Sorrells, Berna Sozen, Kaelyn Sumigray, Jia Di Wen, Frederick Wilson (*Internal Medicine/Oncology*), Chen Zhao

FIELDS OF STUDY

Cancer genetics: oncogenesis and tumor suppression, tumor progression, and metastasis. Cellular and developmental genetics: the genetic basis of germline development, skin development, internal organ development, stem cell development, genetic control and the role of the cilium, cytoskeleton, cell fate determination, cell cycle progression, cell migration, cell signaling, growth control and cell death during development, homeostasis and aging. Genomics: genome mapping, genome modification, high-throughput technology, evolutionary genetics, and functional genomics. Human genetics: genetic basis of human disease, chromosome rearrangements, population and quantitative genetics. Molecular genetics: chromosome

structure and function, genetic recombination, mosaic genetics, viral genetics, DNA damage repair, ribosome biogenesis, protein folding, neurodegenerative diseases, non-coding RNA function, and the regulation of gene expression. Model Organism Genetics: forward genetic screens and targeted genetic manipulations in *Drosophila*, *C. elegans*, zebrafish, frogs, mouse, organoids, and stem-cell-based embryo models.

To enter the Ph.D. program, students apply to the Molecular Cell Biology, Genetics, and Development (MCGD) track within the interdepartmental graduate program in Biological and Biomedical Sciences (BBS), https://medicine.yale.edu/bbs.

REQUIREMENTS FOR THE PH.D. DEGREE

The Ph.D. program in genetics is designed to provide the student with a broad background in general genetics and the opportunity to conduct original research in a specific area of genetics. The student is expected to acquire a broad understanding of genetics, spanning knowledge of at least three basic areas of genetics, which include molecular, cellular, organismal genetics and genomics. Normally this requirement is accomplished through the satisfactory completion of formal courses, many of which cover more than one of these areas. Advanced graduate study becomes increasingly focused on the successful completion of original research and the preparation of a written dissertation under the direct supervision of a faculty adviser along with the guidance of a thesis committee.

Laboratory Rotations and Choosing a Thesis Adviser Students must complete rotations in at least three laboratories in their first year in the MCGD program before selecting a thesis adviser. The student's dissertation adviser must hold a primary or secondary appointment in Genetics in order for the student to join the department.

Courses Students typically take two to three courses each term and three research rotations (GENE 911, GENE 912, GENE 913) during the first year and are required to pass at least five graduate level courses that are taken for a grade. The required Graduate Student Seminar course (GENE 675/GENE 676, two terms, graded Satisfactory/Unsatisfactory) is taken in the second year. In addition to all other requirements, students must successfully complete GENE 900 and GENE 901, Research Skills and Ethics I and II, prior to the end of their first year of study. In their fourth year of study, all students must successfully complete MCDB 504, RCR Refresher for Senior BBS Students. Students must meet the Graduate School's Honors requirement by the end of the fourth term of full-time study. Students must also maintain a High Pass average as required by the graduate school.

Qualifying Exam The qualifying exam (informally, QE or Quals) is an essential step in graduate-student training. The overarching goal is to provide a launching pad for the student to embark on a successful thesis project. The qualifying exam typically spans eight weeks and must be completed by December 15 in the student's second year. The exam consists of three parts:

1. A five-week reading period during which the student discusses a selection of primary research articles with each of three Qualifying Committee faculty readers. The adviser will not be a member of the Qualifying Committee and will not participate in the oral defense.

2. A two-week writing period during which the student writes an original research proposal modeled on the NIH F31 NRSA application and focused on the student's planned thesis work.
3. A one-week presentation period during which the student prepares an oral defense of the research proposal. The exam culminates in a two-hour oral defense of the research proposal, during which the committee provides feedback on the student's oral and written presentations and evaluates the readiness of the student to proceed with their proposed research.

Dissertation Prospectus and Admission to Candidacy By January 15 of their third year, each student must prepare a written summary of the proposed nature and scope of the thesis research, together with a provisional title for the dissertation, following the format described in the *Genetics Department Handbook*. This document should be written in clear, plain English with minimal jargon, abbreviations, or colloquialisms. The student's adviser must review the prospectus and indicate their approval in writing via an email to the DGS. The student then sends the prospectus and the adviser's approval to their DGS, who may require additional changes, for review. Once the DGS has approved the prospectus, the student sends the prospectus and approval emails to the Genetics registrar for their file and so it may be noted on their transcript. Students will not be admitted to candidacy nor will they be allowed to register for their fourth year of study without an approved prospectus.

In order to be admitted to candidacy, the student must fulfill (1) all course requirements, (2) the Honors requirement, (3) the qualifying examination, (4) the dissertation prospectus, and (5) the holding a satisfactory Thesis Committee meeting, at the conclusion of which, the committee will give their assent for the student to be admitted to candidacy. Upon completion of these requirements, final approval for admission to candidacy is granted during a subsequent faculty meeting—usually in late spring of the third year of study.

Thesis Committee The Thesis Committee normally comprises three to four faculty members, including the student's adviser, and is assembled by the student in consultation with the thesis adviser. At least two members (including the adviser) must have primary or secondary appointments in the Department of Genetics. If a committee member outside of Yale is included, the committee should consist of: the advisor, two Yale faculty members, and the outside committee member, making four members in total. Names of committee members should be submitted to the DGS for approval, with the Genetics registrar copied, within the first month of the spring semester of the student's second year. Students in years two and three at are required to meet with their committee at least once per year, while students in year four and beyond are required to meet with their committee every six months.

Teaching and Departmental Presentations An important aspect of graduate training in genetics is the acquisition of communication and teaching skills. Students participate in departmental presentation seminars and two terms (or the equivalent) of teaching. Teaching activities are drawn from a diverse menu of lecture, laboratory, and seminar courses given at the undergraduate, graduate, and medical school levels. Students are not expected to teach until they pass their qualifying exam. Students are also expected to present in the departmental Research in Progress seminar.

M.D.-PH.D. STUDENTS

M.D.-Ph.D. students affiliate with the Department of Genetics graduate program via a different route than other incoming graduate students in the department, resulting in some modification of the academic requirements for the Ph.D. portion of the M.D.-Ph.D. degree. Typically, one or more research rotations are done during the first two years of medical school (in many cases, the first rotation is done during the summer between years one and two). No set number of research rotations is required. M.D.-Ph.D. students officially affiliate with the Department of Genetics after selecting a thesis adviser and consulting with the director of graduate studies (DGS). M.D.-Ph.D. students interested in Genetics are required to consult with the DGS prior to formal affiliation to determine an appropriate set of courses tailored to the student's background and interests.

The courses, rotations, and teaching requirements for M.D.-Ph.D. students entering the Genetics graduate program (see below) are modified from the normal requirements for Ph.D. students. Besides the modifications in these three requirements, M.D.-Ph.D. students in the Department of Genetics are subject to all of the same requirements as the other graduate students in the department.

Laboratory Rotations and Choosing a Thesis Advisor One or more rotations are necessary to identify a thesis adviser. No set number of research rotations is required. The student's dissertation adviser must hold a primary or secondary appointment in Genetics in order for the student to join the department.

Courses Four graduate-level courses taken for a grade are required. (Yale graduate-level courses taken for a grade during medical school may be counted toward this requirement at the discretion of the DGS.) Coursework is aimed at providing a firm basis in genetics and in cellular molecular mechanisms, with graduate-level proficiency in genetics, cell biology, and biochemistry.

Required courses: In addition to the four graduate-level courses, all M.D.-Ph.D. students must take: Graduate Student Seminar (GENE 675 and GENE 676, two terms, graded Satisfactory/Unsatisfactory); Responsible Conduct of Research (B&BS 501, graded Satisfactory/Unsatisfactory); and, in their fifth year of study, RCR Refresher for Senior BBS Students (MCDB 504).

Electives: Other courses may be taken in a wide variety of fields relevant to the biological and biomedical sciences.

Qualifying Exam M.D.-Ph.D. students take their qualifying exam in the second year in the Ph.D. program. The structure of the qualifying exam is identical to that for other Ph.D. students in genetics as described above.

Dissertation Prospectus and Admission to Candidacy M.D.-Ph.D. students submit their prospectus in their second year in the Ph.D. program once their qualifying exam has been completed, but no later than April 30 following their exam. Each student must prepare a written summary of the proposed nature and scope of the thesis research, together with a provisional title for the dissertation, following the format described in the *Genetics Department Handbook*. This document should be written in clear, plain English with minimal jargon, abbreviations, or colloquialisms. The student's adviser must review the prospectus and indicate their approval in writing via an email to

the DGS. The student then sends the prospectus and the adviser's approval to their DGS, who may require additional changes, for review. Once the DGS has approved the prospectus, the student sends the prospectus and approval emails to the Genetics registrar for their file and so it may be noted on their transcript. Students will not be admitted to candidacy nor will they be allowed to register for their fourth year of study without an approved prospectus.

In order to be admitted to candidacy, the student must fulfill (1) all course requirements, (2) the Honors requirement, (3) the qualifying examination, (4) the dissertation prospectus, and (5) the holding of a satisfactory Thesis Committee meeting, at the conclusion of which meeting the committee will give their assent for the student to be admitted to candidacy. Upon completion of these requirements, final approval for admission to candidacy is granted during a subsequent faculty meeting.

Thesis Committee The composition of the Thesis Committee for M.D.-Ph.D. is the same as for Ph.D. students as described above. M.D-Ph.D. students are required to have one Thesis Committee meeting per year, beginning the term after passing their qualifying exam, and two meetings per year beginning in the fourth year in the Ph.D. program.

Teaching and Departmental Presentations One term of teaching is required. Previous teaching while enrolled at the Yale School of Medicine may count toward this requirement at the discretion of the DGS. Students are also expected to present in the departmental Research in Progress seminar.

MASTER'S DEGREES

M.Phil. Students are not admitted for this degree. The M.Phil. is awarded only to students who are continuing for the Ph.D. Students must have completed all of their course requirements, their qualifying exam, and have been admitted to candidacy as described above to be awarded this degree. Students will be automatically petitioned by the university for a M.Phil. after successful completion of the requirements at the end of the third year. No additional action is required on the part of the student.

M.S. Students are not admitted for this degree. They may receive this recognition if they leave Yale without completing the qualifying exam but have satisfied the course requirements as described above, as well as the Graduate School's Honors requirement. Students who are eligible for or who have already received the M.Phil. will not be awarded the M.S.

Prospective applicants are encouraged to visit the BBS website (https://medicine.yale.edu/bbs), MCGD Track.

COURSES

GENE 625a / MB&B 625a / MCDB 625a, Basic Concepts of Genetic Analysis Jun Lu
The universal principles of genetic analysis in eukaryotes are discussed in lectures. Students also read a small selection of primary papers illustrating the very best of genetic analysis and dissect them in detail in the discussion sections. While other Yale graduate molecular genetics courses emphasize molecular biology, this course focuses on the concepts and logic underlying modern genetic analysis.

GENE 645a / CB&B 647a, Statistical Methods in Human Genetics Hongyu Zhao
Probability modeling and statistical methodology for the analysis of human genetics data are presented. Topics include population genetics, single locus and polygenic inheritance, linkage analysis, quantitative trait analysis, association analysis, haplotype analysis, population structure, whole genome genotyping platforms, copy number variation, pathway analysis, and genetic risk prediction models. Offered every other year. Prerequisites: genetics; BIS 505; S&DS 541 or equivalent; or permission of the instructor.

GENE 655a / CBIO 655a, Stem Cells: Biology and Application In-Hyun Park
This course is designed for first-year or second-year students to learn the fundamentals of stem cell biology and to gain familiarity with current research in the field. The course is presented in a lecture and discussion format based on primary literature. Topics include stem cell concepts, methodologies for stem cell research, embryonic stem cells, adult stem cells, cloning and stem cell reprogramming, and clinical applications of stem cell research. Prerequisites: undergraduate-level cell biology, molecular biology, and genetics.

GENE 663b / AMTH 552b / CB&B 663b / CPSC 552b, Deep Learning Theory and Applications Smita Krishnaswamy
Deep neural networks have gained immense popularity within the past decade due to their success in many important machine-learning tasks such as image recognition, speech recognition, and natural language processing. This course provides a principled and hands-on approach to deep learning with neural networks. Students master the principles and practices underlying neural networks, including modern methods of deep learning, and apply deep learning methods to real-world problems including image recognition, natural language processing, and biomedical applications. Course work includes homework, a final exam, and a final project—either group or individual, depending on enrollment—with both a written and oral (i.e., presentation) component. The course assumes basic prior knowledge in linear algebra and probability. Prerequisites: CPSC 202 and knowledge of Python programming.

GENE 675a and GENE 676b, Graduate Student Seminar: Critical Analysis and Presentation of Scientific Literature Siyuan Wang and Trevor Sorrells
Students gain experience in preparing and delivering seminars and in discussing presentations by other students. A variety of topics in molecular, cellular, developmental, and population genetics are covered. Required of all second-year students in Genetics. Graded Satisfactory/Unsatisfactory.

GENE 734b / MB&B 734b / MBIO 734b, Molecular Biology of Animal Viruses Walther Mothes and Maudry Laurent-Rolle
Lecture course with emphasis on mechanisms of viral replication, oncogenic transformation, and virus-host cell interactions.

GENE 743b / MB&B 743b / MCDB 743b, Advanced Eukaryotic Molecular Biology Mark Hochstrasser, Matthew Simon, and Franziska Bleichert
Selected topics in transcriptional control, regulation of chromatin structure, mRNA processing including spliceosomal splicing, mRNA turnover, RNA interference, translational regulation, protein modification, and protein degradation. Emphasis is placed on how these processes are regulated and the experiments that led to

their discovery and understanding. Prerequisite: biochemistry or permission of the instructor.

GENE 760b, Genomic Methods for Genetic Analysis Bluma Lesch and Steven Reilly
Introduction to the analysis and interpretation of genomic datasets. The focus is on next-generation sequencing (NGS) applications including RNA-seq, ChIP-seq, and exome and whole genome sequencing. By the end of this time-intensive, practical problem-set based course, each student will be able to process and analyze large-scale NGS datasets and interpret the results. This course is intended only for graduate students who are interested in applying genomic approaches in their thesis research. A basic familiarity with working in a UNIX/Linux computing environment or prior experience with a programming language is *not* required but can be useful. Extra resources will be made available prior to the course starting for students without any programming experience. Prerequisite: permission of the instructor. Interested students must contact the instructor early in the fall term to discuss their prior experience and expectations for the course. Enrollment limited to approximately twenty-five students.

GENE 777b / MCDB 677b, Mechanisms of Development Kaelyn Sumigray and Zachary Smith
An advanced graduate seminar on animal development focusing on conserved mechanisms that govern germline development, embryogenesis, and somatic differentiation in molecular detail. The course runs in parallel to the Spring session of the Department of Genetics Seminar Series and is divided into two components: six Yale faculty-led lectures on core concepts in development and six combined journal club/student-led discussions with outside developmental biology speakers on their cutting-edge research. Over the course of the term, small student groups are responsible for presenting one journal club-formatted discussion on two papers selected from the outside speaker's lab, as well as emceeing a dedicated question and answer session between the class and the speaker. This course provides a rare opportunity for students to actively engage with world leaders on their work in developmental genetics, epigenetics, and cell biology, as well as learn essential skills in experimental thinking and scientific communication. The course grade is based on forty percent take-home problems, forty percent class participation and twenty percent student-led journal club / distinguished speaker question and answer session. There are no official prerequisites. However, some familiarity with concepts and techniques of modern biology is necessary to get the most out of the course.

GENE 900a / CBIO 900a / MCDB 900a, Research Skills and Ethics I Patrick Lusk
This course consists of a weekly seminar that covers ethics, writing, and research methods in cellular and molecular biology as well as student presentations ("rotation talks") of work completed in the first and second laboratory rotations.

GENE 901b / CBIO 901b / MCDB 901b, Research Skills and Ethics II Chenxiang Lin
This course consists of a weekly seminar that covers ethics, writing, and research methods in cellular and molecular biology as well as student presentations ("rotation talks") of work completed in the third laboratory rotation.

GENE 911a / CBIO 911a / MCDB 911a, First Laboratory Rotation Patrick Lusk
First laboratory rotation for Molecular Cell Biology, Genetics, and Development (MCGD) and Plant Molecular Biology (PMB) track students.

GENE 912a / CBIO 912a / MCDB 912a, Second Laboratory Rotation Patrick Lusk
Second laboratory rotation for Molecular Cell Biology, Genetics, and Development (MCGD) and Plant Molecular Biology (PMB) track students.

GENE 913b / CBIO 913b / MCDB 913b, Third Laboratory Rotation Patrick Lusk
Third laboratory rotation for Molecular Cell Biology, Genetics, and Development (MCGD) and Plant Molecular Biology (PMB) track students.