PHARMACOLOGY

Sterling Hall of Medicine B316, 203.785.7469
http://medicine.yale.edu/pharm
M.S., M.Phil., Ph.D.

Chair
Mark Lemmon (SHM B 203/WC ABC-301B, mark.lemmon@yale.edu)

Directors of Graduate Studies
David Calderwood (SHM B 395C, 203.737.2311, david.calderwood@yale.edu)
Kathryn Ferguson (WC ABC-305C/SHM B 226C, kathryn.ferguson@yale.edu)

Professors Karen Anderson, Anton Bennett, David Calderwood, Yung-Chi Cheng, Joseph Contessa (*Therapeutic Radiology*), Craig Crews (*Mollecular, Cellular, and Developmental Biology*), Barbara Ehrlich, Jonathan Ellman, Seth Herzon (*Chemistry*), Leonard Kaczmarek, Irit Lax, Mark Lemmon, Elias Lolis, Kathleen Martin (*Cardiovascular Medicine*), Angus Nairn (*Psychiatry*), Joseph Schlessinger, Dianqing Wu

Associate Professors Titus Boggon, Jason Cai (*Radiology and Biomedical Imaging*), Kathryn Ferguson, Daryl Klein, Yansheng Liu, Ya Ha, Faye Rogers (*Therapeutic Radiology*), Benjamin Turk

Assistant Professors Claudio Alarcón, Assaf Alon, Moitrayee Bhattacharyya, Joel Butterwick, Sangwon Lee, Ken Loh (*Comparative Medicine*), Wei Mi

FIELDS OF STUDY

Major emphases in the Pharmacology Graduate Program are in the areas of molecular pharmacology, mechanisms of drug action, signal transduction, structural biology, infectious diseases, neuropharmacology, and chemotherapy.

To enter the Ph.D. program, students should apply to the interdepartmental graduate program in Biological and Biomedical Sciences (BBS), https://medicine.yale.edu/bbs, and select one of the interest-based tracks. Most students interested in a Ph.D. in pharmacology select the Translational Molecular Medicine, Pharmacology, and Physiology (TMMPP) or the Biochemistry, Quantitative Biology, Biophysics, and Structural Biology (BQBS) tracks.

SPECIAL REQUIREMENTS FOR THE PH.D. DEGREE

The field of pharmacology encompasses many disciplines. Flexibility in the Pharmacology Graduate Program permits students to concentrate in the areas of their particular interest. Students are required to take at least five courses. Students must take both terms of the graduate seminar course (PHAR 501 and PHAR 502) or equivalent courses from another program. The other three required courses are selected based on the interest of each student, but must include at least one of the following core courses: PHAR 504, PHAR 528, PHAR 529, MB&B 720, MB&B 752, or other DGS-approved BBS courses. Students are also required to do three laboratory rotations in their first year (PHAR 506). The graduate school requires a grade of Honors for a minimum of two courses. Honors for rotations cannot be used toward this requirement and only one Honors grade from PHAR 501/PHAR 502 can count toward

this requirement. Students must meet this Honors requirement prior to being admitted to candidacy and must maintain an overall High Pass average. A grade of Honors or High Pass is required for the selected core courses. Student progress toward these goals is reviewed at the end of the second and subsequent terms.

Prior to registering for a second year of study, students must successfully complete PHAR 580, The Responsible Conduct of Research, or the equivalent from another department. In addition, B&BS 503, RCR Refresher for Senior BBS Students, must be completed by the end of the fourth year. PHAR 580 and B&BS 503 do not count towards the five required courses.

Students are required to pass the qualifying examination by the end of their fourth term. In preparation for this, Pharmacology Graduate Program students must take PHAR 540, Developing and Writing a Scientific Research Proposal, in the spring term of their second year (this does not count toward the five-course requirement). Before the end of the third year, a thesis prospectus must be submitted and accepted for admission to candidacy. Once a student's original doctoral dissertation research is largely complete, they give an oral presentation to the Pharmacology faculty (pre-defense) for approval. Within six months of passing the pre-defense, the student must submit a preliminary written thesis to the thesis committee and an outside reader. A public Ph.D. dissertation seminar will then be scheduled, followed by a closed examination by the student's thesis committee and the outside examiner. Once the draft of the written thesis is approved by the thesis committee, it is submitted to the Graduate School. One first-author manuscript is required from the thesis research. The Pharmacology Graduate Program faculty recognizes that some types of thesis-related work can take a long time. If deemed necessary, with agreement across the faculty that the student has made substantial progress in a project of this sort, the faculty can exempt a student from the one first-author paper requirement.

An important aspect of graduate training in pharmacology is the acquisition of teaching skills through participation in teaching courses related to the student's scientific interests. These opportunities can be drawn from a diverse menu of lecture, laboratory, and seminar courses given at the undergraduate, graduate, and medical school levels. Ph.D. students are required to participate in two terms (or the equivalent) of teaching. Students are not expected to teach during their first year.

M.D.-PH.D. STUDENTS

M.D.-Ph.D. students must satisfy all of the above requirements for the Ph.D. with the following modifications: (1) only two of three laboratory rotations are required; (2) some medical-school courses (except pharmacology) can qualify as graduate-school courses as long as the M.D.-Ph.D. student registers for them in OCS (Online Course Selection); and (3) only one term of teaching is required. Current graduate-school courses cannot be used to fulfill any medical-school course requirements.

MASTER'S DEGREES

M.Phil. See Degree Requirements under Policies and Regulations.

M.S. Students who withdraw from the Ph.D. program may be eligible to receive the M.S. degree if they have met the requirements and have not already received the

M.Phil. degree. For the M.S., students must successfully complete the first three terms of the Ph.D. program. This includes one year of lab rotations and course requirements.

Program materials are available upon request to the Director of Graduate Studies, Department of Pharmacology, Yale University, PO Box 208066, New Haven CT 06520-8066.

COURSES

PHAR 501a and PHAR 502b / C&MP 629a and C&MP 630b / PATH 679a and PATH 680b / PTB 629a and PTB 630b, Seminar in Molecular Medicine, Pharmacology, and Physiology Staff

Readings and discussion on a diverse range of current topics in molecular medicine, pharmacology, and physiology. The class emphasizes analysis of primary research literature and development of presentation and writing skills. Contemporary articles are assigned on a related topic every week, and a student leads discussions with input from faculty who are experts in the topic area. The overall goal is to cover a specific topic of medical relevance (e.g., cancer, neurodegeneration) from the perspective of three primary disciplines (i.e., physiology: normal function; pathology: abnormal function; and pharmacology: intervention). Required of and open only to Ph.D. and M.D./Ph.D. students in the Molecular Medicine, Pharmacology, and Physiology track.

PHAR 504a / PTB 504a, Molecular Mechanisms of Drug Actions Elias Lolis

This course provides fundamental background in core principles of pharmacology, molecular mechanisms of drug action, and important research areas in contemporary pharmacology. Material covered includes quantitative topics in pharmacology such as drug-receptor theory, multiple equilibria and kinetics, pharmacokinetics, therapeutic drug monitoring, and drug metabolism. Specific content on the mechanisms of drug action includes autonomics; ion channel blockers; endocrine agents (hormones); cardiovascular drugs (ACE inhibitors, organic nitrates, β-blockers, acetylsalicylic acid); antimicrobials (anti-bacterials, fungals, and virals); anti-cancer, anti-inflammatory, anti-asthma, and anti-allergy drugs; and immunosuppressants. Students learn how to model drug-receptor interaction parameters and how to analyze steady-state enzyme kinetics and inhibition data. Senior students serving as teaching assistants lead discussion groups covering problem sets, review topics or assigned manuscripts. The course includes a self-study component consisting of video modules produced in collaboration with Yale faculty and Merck that explore the preclinical and clinical phases of drug development.

PHAR 506a / C&MP 506a / PATH 620a / PTB 620a, Lab Rotations Staff

Students work in laboratories of faculty of their choice. The schedule for each rotation is announced at the beginning of the fall term.

PHAR 528b, Principles of Signal Transduction Anton Bennett

The regulation of intracellular signaling is of fundamental importance to the understanding of cell function and regulation. This course introduces the broad principles of intracellular signal transduction. More detailed lectures on specific intracellular signaling pathways are given in which students learn both the basic and most recent and cutting-edge concepts of intracellular signaling. Topics include regulation of signaling by protein phosphorylation, small G proteins, G-protein-coupled receptors, hormones, phospholipids, adhesion, and gasses.

PHAR 529b / MB&B 529b, Structural Biology and Drug Discovery Titus Boggon and Ya Ha

A comprehensive introduction to the concepts and practical uses of structural biology and structural biology-related techniques in drug discovery. The first half of the course focuses on techniques used to discover and optimize small and macromolecule drugs. Students are introduced to topics such as small molecule lead discovery, X-ray crystallography, cryo-electron microscopy, and biophysical techniques. The first half of the course also includes a practical component where students conduct hands-on structural biology experiments and learn about biophysical techniques in a laboratory setting. The second half of the course focuses on drug discovery, particularly for protein kinases. It includes a field trip to the Yale Center for Drug Discovery, where the students are introduced to the in-house Yale screening facilities for small molecule drug discovery. Two half-credit courses—PHAR 530 and PHAR 531—are also offered for the two halves of PHAR 529.

PHAR 530b, Targeted Use of Structural Biology in Drug Discovery Titus Boggon and Ya Ha

This 0.5-credit course, the second half of PHAR 529, begins in February. The goal of the course is to show students how concepts of structural biology are applied to areas of great importance in pharmacology such as protein kinases, proteases, cell surface receptors, integrins and other membrane-bound enzymes, and transporters and channels, and how these concepts facilitate drug development. ½ Course cr

PHAR 531b, Concepts of Structural Pharmacology Titus Boggon and Ya Ha

This 0.5-credit course, the first half of PHAR 529, introduces students to the concepts of structural biology and provides the background for how these concepts are applied to areas of great importance in pharmacology and how they facilitate drug development. ½ Course cr

PHAR 537a, Systems Pharmacology and Integrated Therapeutics Kathryn Ferguson

This course provides an in-depth, "hands-on" experience in drug design, drug discovery, high-throughput screening, state-of-the-art proteomics, and target validation.

PHAR 538a, Pharmacokinetics and Pharmacodynamics in Neuropharmacology Jason Cai

This course is designed to give a historic account of drug discovery and development for brain diseases, introduce methods to understand the pharmacological mechanisms of drugs working on neurological systems, and inspire young generations to join the endeavor of drug discovery and development for brain diseases. It is designed for advanced graduate students, postdocs, and residents with basic knowledge in chemistry, pharmacology, and neuroscience. The lecturers and guest lecturers are leading experts in the field of PET and MR imaging, and industry leaders in pharmaceutical science. This course also introduces the applications of advanced imaging technologies (PET, MRI) in the study of pharmacokinetics and pharmacodynamics of CNS drugs in humans and its implications to our understanding of neurodegenerative and neuropsychiatric disorders. Each class constitutes a forty-five-minute didactic lecture and a thirty-minute interactive discussion section. The classroom activities are expected to prepare students for their future endeavor in the field of neuropharmacology. Open to students second-year and up.

PHAR 540b, Qualifying Exam Prep Class for Pharmacology Mark Lemmon, Titus Boggon, and Moitrayee Bhattacharyya

The goal of this class is to teach students to conceive, write, and defend a grant proposal. The timing of this half-term course is aligned with the pharmacology qualifying exam in the spring term, for which a written research proposal is required. This course takes students through the steps of proposal writing, guiding them in defining a problem of their own and training them in the mechanics of writing. Additional support is given as needed to students with more limited writing experience. By taking the "guesswork" out of the writing process, students can focus on the development of their research proposal without the added anxiety associated with an unfamiliar process. Students learn about the structure and components of fellowship and grant proposals. They engage in "mock study sections", providing written critiques and participating in discussion of sample proposals assigned by the instructors. Students give oral presentations of their specific aims followed by classroom discussion. At the end of the course, students will have made substantial progress toward completing the written portion of their qualifying exam and gained a set of competencies central to this program. Open to graduate students only. Priority is given to pharmacology students.

PHAR 550a / C&MP 550a / ENAS 550a / MCDB 550a / PTB 550a, Physiological Systems W. Mark Saltzman and Stuart Campbell

The course develops a foundation in human physiology by examining the homeostasis of vital parameters within the body, and the biophysical properties of cells, tissues, and organs. Basic concepts in cell and membrane physiology are synthesized through exploring the function of skeletal, smooth, and cardiac muscle. The physical basis of blood flow, mechanisms of vascular exchange, cardiac performance, and regulation of overall circulatory function are discussed. Respiratory physiology explores the mechanics of ventilation, gas diffusion, and acid-base balance. Renal physiology examines the formation and composition of urine and the regulation of electrolyte, fluid, and acid-base balance. Organs of the digestive system are discussed from the perspective of substrate metabolism and energy balance. Hormonal regulation is applied to metabolic control and to calcium, water, and electrolyte balance. The biology of nerve cells is addressed with emphasis on synaptic transmission and simple neuronal circuits within the central nervous system. The special senses are considered in the framework of sensory transduction. Weekly discussion sections provide a forum for in-depth exploration of topics. Graduate students evaluate research findings through literature review and weekly meetings with the instructor.

PHAR 560b / C&MP 560b / ENAS 570b / MCDB 560b, Cellular and Molecular Physiology: Molecular Machines in Human Disease Emile Boulpaep and Peter Takizawa

The course focuses on understanding the processes that transfer molecules across membranes at the cellular, molecular, biophysical, and physiological levels. Students learn about the different classes of molecular machines that mediate membrane transport, generate electrical currents, or perform mechanical displacement. Emphasis is placed on the relationship between the molecular structures of membrane proteins and their individual functions. The interactions among transport proteins in determining the physiological behaviors of cells and tissues are also stressed. Molecular motors are introduced and their mechanical relationship to cell function is explored.

Students read papers from the scientific literature that establish the connections between mutations in genes encoding membrane proteins and a wide variety of human genetic diseases.

PHAR 580b / C&MP 650b / PATH 660b / PTB 650b, The Responsible Conduct of Research Staff

Organized to foster discussion, the course is taught by faculty in the Pharmacology, Pathology, and Physiology departments and two or three senior graduate students. Each session is based on case studies from primary literature, reviews, and two texts: Francis Macrina's *Scientific Integrity* and Kathy Barker's *At the Bench*. Each week, students are required to submit a reaction paper discussing the reading assignment. Students take turns leading the class discussion; a final short paper on a hot topic in bioethics is required.