IMMUNOBIOLOGY

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

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FIELDS OF STUDY

The Immunobiology graduate program is designed to prepare students for independent careers in research and teaching in immunology or related disciplines. The educational program emphasizes interdisciplinary training and collaborative and interactive research, an approach based on the idea that solving difficult problems requires the integration of individuals with common goals but differing expertise. Graduate students are diverse in their interests and ethnic backgrounds, and more than 50 percent are women.

RESEARCH AREAS

Research focuses on the molecular, cellular, and genetic underpinnings of immune system function and development, on host-pathogen interactions, and on human and translational immunology, with a particular interest in a variety of autoimmune disorders. These research interests break down into six major themes, spanning almost all aspects of the immune system and its role in disease prevention.

Lymphocyte development A central focus of research is to understand the molecular events underlying the development of B and T lymphocytes. Areas of major interest include the receptors and signals that control lymphocyte lineage commitment, cell maturation, cell proliferation, and cell death; the establishment of the proper environments for lymphocyte development; mechanisms that regulate the state of chromatin during lymphocyte development; and the mechanisms by which antibody and T cell receptor genes are assembled and diversified.

Mounting an immune response An effective immune response requires the coordinated action of numerous cell types. A critical first step is the activation of cells of the innate immune system, including monocytes, macrophages, dendritic cells, and neutrophils; and the receptors and signaling molecules that control this process are under intensive study. The mechanism by which cells take up, process, and present antigen is a major interest, as is the recognition of this antigen by T cell receptors on T lymphocytes. Cytoplasmic signal transduction molecules, nuclear transcription factors, and mechanisms controlling gene expression are all under study.

Regulating the immune response The immune response is tightly regulated through the interaction of cell surface receptors with secreted cytokines and with one another, and the mechanisms by which these interactions exert their regulatory influences are studied in several laboratories. Another major interest is in learning how specialized cells or anatomic locations, such as vascular endothelial cells or the epidermis, regulate and direct the immune response.

Consequences of an immune response Apart from the obvious consequence of the elimination of an invading organism, an appropriate immune response results in immunological memory and large numbers of activated lymphocytes, which must be eliminated. The mechanisms controlling immunological memory, tolerance, and apoptosis, as well as those leading to autoimmunity, are a major interest of many faculty. Diabetes, multiple sclerosis, lupus, and rheumatoid arthritis are just some of the autoimmune diseases under study. Much of this work takes place in the context of the Section of Human and Translational Immunology.

Infectious disease and the host-pathogen interaction A major interest is the study of infectious organisms – bacterial, viral, and parasitic – and the immune response to them. A great deal of effort is directed toward understanding the strategies used by infectious agents to avoid the immune system. HIV, HBV (hepatitis B virus), herpes simplex virus, parvoviruses, Candida albicans, Borrelia burgdorferi (the causative agent of Lyme disease), Leishmania, Streptococcus pneumoniae, and Legionella pneumophila are all under study.
**Structural analysis of immune system receptors and effectors** There is a growing interest in using structural approaches to understand the function of key molecules of the immune response. For example, a major effort is devoted toward understanding how the Toll-like receptors, despite their similarity in extracellular-ligand recognition regions, are able to specifically recognize such a wide variety of pathogen-associated molecular patterns (PAMPS). Another effort is aimed at understanding the mechanism of APOBEC enzymes in controlling viruses such as HIV.

**FACILITIES**

More than thirty laboratories are actively involved in research in immunology. Many share immediately adjoining or nearby laboratory space on the top three floors of the Anlyan Center (TAC), 10 Amistad Street, and 300 George Street, and three faculty are funded by the Howard Hughes Medical Institute. The Department of Immunobiology provides one of the largest, highest-ranked training programs in immunology in the country, led by a faculty with a reputation for excellence in research. The Department of Immunobiology maintains a wide variety of major equipment, and Dr. Richard Flavell oversees a very active transgenic mouse/ES cell/knockout facility to which members of the department have access.

**PROGRAM ENTRY**

Most students enter the Immunobiology graduate program through the Immunology track of the interdepartmental graduate program in Biological and Biomedical Sciences (BBS), http://bbs.yale.edu. Other types of students enter from the M.D./Ph.D. program (see below), the MRSP (see below), or another BBS track, with approval of the Immunobiology director of graduate studies (DGS) and the faculty adviser.

The faculty and students of the BBS program are organized into interest-based tracks. Immunology, being one of eight tracks, encourages individualized attention to maximize scientific interactions. There is complete freedom to work with any of the 350 faculty members affiliated within any of the tracks and to take courses offered by any of the BBS departments or programs. Students are encouraged to supplement core courses in molecular and cellular immunology with additional courses selected from the wide range available in cell biology, molecular biology, developmental biology, biochemistry, genetics, pharmacology, molecular medicine, neuroscience, and bioinformatics. Research seminars and informal interactions with other graduate students, postdoctoral fellows, and faculty also form an important part of graduate education.

The Section of Human and Translational Immunology (HTI) is a component of the Immunobiology department and is located at 10 Amistad Street and 300 George Street. Its mission is to accelerate the application of new developments in the field of immunology to the treatment of human diseases. HTI faculty study the immunologic aspects of a very broad range of human diseases, encompassing investigations in the fields of cancer; transplantation of solid organs and stem cells; autoimmune diseases; and neurologic disease.

The Medical Research Scholars Program (MRSP) is open to students who have already been accepted into the BBS program. A separate application is also required, and is to be submitted to the BBS. A total of eight students each year (four first-years and four second-years) will be enrolled as Medical Research Scholars. They remain in their BBS tracks or departments but participate in the additional MRSP curriculum. The program bridges barriers between traditional predoctoral and medical training by providing Yale Ph.D. students with both medically oriented course work and a mentored clinical experience. This combination of medical knowledge and face-to-face interaction with patients and their doctors provides a new perspective to Ph.D. students and enhances the rigorous training in basic science already provided.

**Admission requirements** In addition to meeting general BBS requirements, applicants are expected to have a firm foundation in the biological and physical sciences. It is preferred that students have taken courses in biology, organic chemistry, biochemistry, genetics, cell biology, physics, and mathematics. Actual course requirements, however, are not fixed, and students with outstanding records in any area of the biological sciences may qualify for admission. There are no specific grade requirements for prior course work, but a strong performance in basic science courses is of great importance for admission. In special cases, the Medical College Admission Test (MCAT) scores may substitute for scores on the general GRE.

**SPECIAL REQUIREMENTS FOR THE PH.D. DEGREE**

Students are required to take six courses for a grade in the Yale Graduate School.

Required graded courses for first- and second-year students are:

1. IBIO 530, Biology of the Immune System (Students have the option of passing out of IBIO 530 by taking the final exam from the previous year.)
2. IBIO 531, Advanced Immunology
3. Two Immunobiology seminar courses taken from this series: IBIO 536, IBIO 537, IBIO 538, IBIO 539 (The second seminar course can be audited if a student has grades in six other science courses and has already taken one seminar course for credit.)

Required credit-only, nongraded courses for first-year students are:

1. IBIO 600, Introduction to Research
2. IBIO 611, IBIO 612, IBIO 613, Research Rotations (short research projects are taken under the guidance of three Yale professors)
3. IBIO 601, Fundamentals of Research: Responsible Conduct of Research
Fourth-year students are required to take IBIO 503, a refresher training course in the responsible conduct of research.

Additional courses are determined based on the individual needs of the student, and include courses in biochemistry, cell biology, genetics, molecular biology of prokaryotes, molecular biology of eukaryotes, animal viruses, the structure of nucleic acids and proteins, microbiology, and disease mechanisms. Students choose courses after consulting the DGS and the thesis adviser.

Honors The Graduate School uses grades of Honors, High Pass, Pass, or Fail. Students are required to earn a grade of Honors in at least two courses in the first two years, and are expected to maintain a High Pass average. There is no foreign language requirement.

Teaching Students are required to serve as a science TA (teaching assistant) for two terms before the end of their sixth term. Teaching protocol and rules are as follows:

1. Teaching two term-long science courses is required as a fulfillment of the Ph.D.;
2. First-year students do not teach;
3. Teaching opportunities are first given to students who need teaching credit;
4. Teaching for additional income is available when openings exist after those selected for credit are hired; approval signatures from the adviser and DGS are required.
5. The maximum teaching allowed is one course per term.

A Yale McDougall Center one-day seminar entitled “Teaching at Yale” is offered each year. Attending this seminar is recommended prior to teaching.

Prospectus and qualifying exam Early in the fourth term (or in certain circumstances, in the third term), students make a thirty-minute presentation to the department of their proposed research and initial results. Thereafter, they meet with their prospectus committee, which assigns four or five broad areas of biology and immunology that are of particular relevance to the proposed research and on which the student will be examined in the qualifying exam. During the next several weeks, students prepare a formal research proposal (in NIH grant format) concerning the proposed thesis research and study for the exam. The exam is held within three months. It is an oral exam covering all aspects of immunology generally, with a focus on the assigned areas mentioned above. The student is questioned on aspects of the thesis proposal.

Admission to candidacy Requirements for admission to candidacy, which usually takes place after six terms of residence, are: completion of course requirements, one of the two teaching requirements, the qualifying exam, and the third-year committee meeting—at the one-year anniversary of the qualifying exam—with a signed certification form from the adviser and committee members verifying that the student has made good progress.

Progress in thesis research in the third and later years is monitored carefully by the student’s thesis committee (composed of the adviser and three or four other faculty). See below.

M.D./Ph.D. Students Majoring in Immunobiology

Required Six courses for a grade. Out of the six courses the following are mandatory:

1. IBIO 530, Biology of the Immune System (Students have the option of passing out of IBIO 530 by taking the final exam from the previous year.)
2. IBIO 531, Advanced Immunology
3. Two Immunobiology seminar courses taken from this series: IBIO 536, IBIO 537, IBIO 538, IBIO 539 (The second seminar course can be audited if a student has grades in six other courses and has already taken one seminar course for credit.)

Also required Two grades of Honors: Yale University graduate courses taken for a grade at the School of Medicine may be counted toward the Honors fulfillment and the six total required courses. Verification must be provided to the DGS. One term of teaching: Previously taught courses in the School of Medicine may count toward this requirement. To request credit for previous teaching experience, a note from the course director describing the teaching experience (duration of the teaching experience, frequency of class meetings, number of students taught, materials covered, dates, and for whom) should be provided to the Immunobiology DGS. Responsible Conduct of Research, Refresher Course: Fourth-year students are required to take a refresher training course in the responsible conduct of research. M.D./Ph.D. students can fulfill this NIH requirement through Immunobiology (IBIO 503) or through the M.D./Ph.D. program.

M.D./Ph.D. students are not required to take:

1. IBIO 600, Introduction to Research
2. IBIO 611, IBIO 612, IBIO 613, Research Rotations
3. IBIO 601, Fundamentals of Research: Responsible Conduct of Research. A note from the DGS of the M.D./Ph.D. program must be forwarded to the Immunobiology DGS stating that the student has taken a course in Research Conduct and Ethics, or its equivalent in the School of Medicine. Include dates, titles, and faculty. If the student has not taken this course, then registration in this class is required.
Annual thesis committee meetings Each student is required to have a thesis committee meeting at least every twelve months, and more frequently if the student or committee feels that it would be appropriate or helpful. The thesis supervisor (the student’s PI) then submits a thesis committee report form to the DGS summarizing the student’s progress.

MASTER’S DEGREES

M.Phil. A student is entitled to the M.Phil. degree once all academic and prospectus requirements, and one of the two teaching requirements, have been met. Also required is a third-year committee meeting at which the members sign an approval form stating that the student is making good progress toward the student’s research.

M.S. (en route to the Ph.D.) Students who complete at least one year of resident graduate study at Yale with the quality of work judged satisfactory by the Department of Immunobiology faculty and who have satisfied ten courses with an average grade point average of High Pass (graded) may petition for the award of the M.S. degree. Students must petition through the Registrar’s Office of the Graduate School in early October for the December award of the M.S. and by the middle of March for the May award. Students who are eligible for or who have already received the M.Phil. will not be awarded the M.S.

For additional information on the Program in Biological and Biomedical Sciences see http://bbs.yale.edu.

COURSES

For a complete listing of immunology-related courses, see http://bbs.yale.edu.

IBIO 503b, Responsible Conduct of Research, Refresher Course Staff
The NIH requires that students receive training in the responsible conduct of research every four years. This course meets that requirement for fourth-year students. The course has two components: (1) one large-group session is held for all fourth-year students through the BBS; the main topics are scientific misconduct and authorship; (2) two Immunobiology faculty facilitate discussions based on RCR topics, gathered in advance from the students; anonymous or hypothetical stories are selected by the faculty and discussed in a workshop environment in which students are then asked to analyze each case and suggest courses of actions.

IBIO 530a / MBIO 530a / MCDB 530a, Biology of the Immune System Eric Meffre and Staff
The development of the immune system. Cellular and molecular mechanisms of immune recognition. Effector responses against pathogens. Immune memory and vaccines. Human diseases including allergy, autoimmunity, cancer, immunodeficiency, HIV/AIDS.

IBIO 531b, Advanced Immunology Staff
The historical development and central paradigms of key areas in immunology. The course attempts to develop a clear understanding of how these paradigms were established experimentally. Landmark studies are discussed to determine how the conclusions were obtained and why they were important at the time they were done. Lecture and discussion format; readings of primary research papers and review articles. Prerequisite: IBIO 530 or equivalent. Enrollment limited to fifteen.

IBIO 532b, Inflammation Ruslan Medzhitov
This course covers fundamentals of inflammation from a broad biological perspective, with a focus on both physiological and pathological aspects of inflammation.

IBIO 536a, Immunobiology Seminar: Neuroimmunology Staff
This course explores the diverse array of interactions between the immune and nervous systems, both in homeostasis and disease settings, including but not limited to neurodegenerative, vascular, and malignant diseases.

IBIO 537b, Immunobiology Seminar: Translational Immunobiology Kevin O’Connor
This course is designed to introduce immunobiology Ph.D. students to translational research and medicine. Each weekly seminar focuses on a specific disease with a conspicuous immunological component. In-class periods consist of very interactive, didactic sections covering disease phenotype, underlying immunobiology and pathology, and mechanisms of treatment approaches, including limitations. Discussions are led by principal investigators who focus on human translational immunology and by clinician-scientists who see patients in associated clinics. Examples of topics include: T and B cell contributions to the underlying pathophysiology of multiple sclerosis, type 1 diabetes, systemic lupus erythematosus, myasthenia gravis, and other autoimmune diseases; immune responses to acute brain injury; inherited immune disorders; paradigms governing how antitumor immune responses are promoted or suppressed; and current approaches in immunotherapy-based clinical trials. Assignments challenge students to think creatively about solutions to problems that obstruct the progress toward understanding disease mechanisms and developing therapeutics. A term assignment, in the form of a research proposal, focuses on independent study of a translational immunobiology problem of each student’s choosing. Students are provided with elective opportunities for experiential learning through clinic visits with course faculty instructors. The combination of medical knowledge and interaction with translational and clinician-scientists provides a new perspective to immunobiology Ph.D. students that broadens their basic science training. The exposure to the practice of medicine enables them (and other graduate students) to work more confidently at the interface of research and medicine and facilitate collaborations with clinical investigators. Prerequisite: IBIO 531 or a similar course that provides a solid foundation in fundamental immunology; may be waived for highly motivated students.

IBIO 600a, Introduction to Research: Faculty Research Presentations Carla Rothlin
Introduction to the research interests of the faculty. Required of all first-year Immunology/BBS students. Pass/Fail.
IBIO 601b, Fundamentals of Research: Responsible Conduct of Research Carla Rothlin
A weekly seminar presented by faculty trainers on topics relating to proper conduct of research. Required of first-year Immunobiology students, first-year CB&B students, and training grant-funded postdocs. Pass/Fail.

IBIO 611a, Research Rotation 1 Carla Rothlin
Intensive experience in the design and execution of experiments in immunology or other areas of biology. Students design a focused research project in consultation with a faculty mentor and execute the designed experiments in the mentor’s laboratory. Students are expected to read relevant background papers from the literature, design and perform experiments, interpret the resulting data, and propose follow-up experiments. Students are also expected to attend the mentor’s weekly lab meeting(s) as well as weekly Immunobiology departmental seminars and Research in Progress seminars. The course concludes with the student giving a brief presentation of the work performed at Rotation Talks, attended by other first-year immunology-track graduate students. Evaluation is by the mentor; students also evaluate the rotation experience. Students must turn in a prioritized list of four possible mentors to Barbara Cotton in the office of the director of graduate studies at least one week prior to the beginning of the course. Mentors are assigned by the DGS. Graded Pass/Fail. 1 course credit; minimum of 20 hours/week. Required of all first-year Immunology/BBS students.

IBIO 612b, Research Rotation 2 Carla Rothlin
Intensive experience in the design and execution of experiments in immunology or other areas of biology. Students design a focused research project in consultation with a faculty mentor and execute the designed experiments in the mentor’s laboratory. Students are expected to read relevant background papers from the literature, design and perform experiments, interpret the resulting data, and propose follow-up experiments. Students are also expected to attend the mentor’s weekly lab meeting(s) as well as weekly Immunobiology departmental seminars and Research in Progress seminars. The course concludes with the student giving a brief presentation of the work performed at Rotation Talks, attended by other first-year immunology-track graduate students. Evaluation is by the mentor; students also evaluate the rotation experience. Students must turn in a prioritized list of four possible mentors to Barbara Cotton in the office of the director of graduate studies at least one week prior to the beginning of the course. Mentors are assigned by the DGS. Graded Pass/Fail. 1 course credit; minimum of 20 hours/week. Required of all first-year Immunology/BBS students.

IBIO 613b, Research Rotation 3 Carla Rothlin
Intensive experience in the design and execution of experiments in immunology or other areas of biology. Students design a focused research project in consultation with a faculty mentor and execute the designed experiments in the mentor’s laboratory. Students are expected to read relevant background papers from the literature, design and perform experiments, interpret the resulting data, and propose follow-up experiments. Students are also expected to attend the mentor’s weekly lab meeting(s) as well as weekly Immunobiology departmental seminars and Research in Progress seminars. The course concludes with the student giving a brief presentation of the work performed at Rotation Talks, attended by other first-year immunology-track graduate students. Evaluation is by the mentor; students also evaluate the rotation experience. Students must turn in a prioritized list of four possible mentors to Barbara Cotton in the office of the director of graduate studies at least one week prior to the beginning of the course. Mentors are assigned by the DGS. Graded Pass/Fail. 1 course credit; minimum of 20 hours/week. Required of all first-year Immunology/BBS students.