

2023-24

MICROBIOLOGY & IMMUNOLOGY

Degree Offered: Doctor of Philosophy



Program Description

The Graduate Program in Microbiology & Immunology (M&I) seeks to teach and train the next generation of research scientists in the molecular and cellular biology of bacterial pathogens, virus/host interactions, the innate and adaptive immune responses, animal and cellular model systems of infection and immunity, the microbiome, and the molecular mechanisms of gene expression, signal transduction, cell proliferation and cancer biology. It is the goal of the faculty and students to utilize classic and cutting-edge methodologies and technologies to conduct interdisciplinary research that will solve problems that are of significant biomedical importance.

Through participation in a variety of departmental activities, M&I graduate students receive a broad education and training base that encompasses various aspects of biomedical science including those centered in the fields of bacteriology, immunology, virology, molecular biology, microbe-host interactions, genetics/gene expression and cancer biology. Our students develop essential technical skills and/or capabilities that allow them to conduct independent research, and effectively communicate scientific accomplishments in both written and oral forms. In general, M&I faculty seek to promote accomplishment of these objectives by providing a stimulating work and learning environment in which scientific curiosity is encouraged, scientific questions of significance are investigated, rigorous experimental approaches to problems are designed and executed, data is critically interpreted, and sound and cogent concepts are developed. The M&I Graduate Program assesses accomplishment of these objectives through several mechanisms including didactic course requirements, required annual research in progress (RIP) scientific presentations, semi-annual meetings with dissertation committee members coupled with submission of committee report forms, and dissertation-specific qualifying and defense examinations. The ultimate goal of the M&I Graduate Program is to produce well-rounded scientists that possess the necessary maturity, experience, and knowledge base to become independent leaders in the biomedical sciences within academia, industry, government, or other health-related career venues. These goals are consistent with the mission of the MCW Graduate School and of the Medical College of Wisconsin as a whole.

Admission Requirements

In addition to the general [Graduate School admission requirements](#), this program has additional specific requirements.

Students enter the graduate program in the Department of Microbiology and Immunology through the [Interdisciplinary Program in Biomedical Sciences \(IDP\)](#), the [Neuroscience Doctoral Program \(NDP\)](#), the [Medical Scientist Training Program \(MSTP\)](#), or by [direct entry into the department](#). Students who choose a mentor in the Department of Microbiology and Immunology will enter the department upon satisfactory completion of a written and oral qualifying examination.

Fields of Study

The following areas of research in the Department of Microbiology and Immunology offer excellent opportunities for graduate dissertation projects:

Molecular Biology of Bacterial Pathogenesis

- Characterization of the molecular properties of bacterial exotoxins, with the goals of defining their mode of action and how toxins modify host cell physiology
- Identification of host and bacterial proteins involved in attachment of *Borrelia burgdorferi* and *Leptospira interrogans* to human cells, and the consequences of these interactions for the host
- Investigation of the secretion and function of bacterial virulence factors encoded by *Pseudomonas aeruginosa* and other opportunistic infections
- Investigation of genetic, biochemical, and signaling pathways required for antimicrobial resistance and gut colonization by enterococci
- Studies of the phasevarion regulatory system in the pathogenesis of *Haemophilus influenzae*, *Moraxella catharrhalis*, *Helicobacter pylori* and *Neisseria* species
- Investigation of host defenses in the cytosol and how professional cytosolic pathogens like *Listeria monocytogenes* evade them

The Microbiome

- Role of xenobiotics in disrupting gut microbiota and consequences on metabolism
- Importance of bacteriophage in regulating composition of gut microbiota
- Role of xenobiotics in disrupting the gut microbiota/metabolism, two-component signaling, and predatory-prey interactions
- Role of the mosquito microbiome in shaping immune responses to malaria infection

Molecular Genetics of Human Viruses

- Investigation of the molecular mechanisms employed by human herpesviruses to escape detection by the immune system
- Characterization of interactions between cancer-associated gammaherpesviruses and host systems that either promote or restrict lytic and chronic gammaherpesvirus infection, with a particular interest in lipid metabolism
- Investigation of proteins involved in establishing a permissive environment for herpesvirus replication using mass spectrometry

Cellular and Molecular Analysis of the Immune Response

- Autoimmunity. Investigation into roles of T cells and B cells and mechanisms of central and peripheral tolerance in autoimmune disorders including type 1 diabetes, multiple sclerosis, arthritis, and colitis
- Oncology. Investigation of tumor microenvironment and immune response against solid and liquid tumors; mechanistic studies of immunity, anti-tumor evasion and tolerance in anti-tumor response
- Cellular therapy. Allogeneic hematopoietic cell transplantation (Allo-HCT), studies of allogeneic T- and B-cell mediated graft-versus-host (GVH) and graft-versus-leukemia/lymphoma (GVL) responses. Adoptive T-cell Therapy (ACT) including chimeric antigen receptor (CAR) T-cell therapy. Investigations of T-cell activation, differentiation, persistence, and migration immunotherapy against cancer
- Inflammation. Basic mechanisms of immune regulation and inflammation; structure-function studies of adhesion molecules and integrins; immunobiology investigations of

- chemokines and cytokines and their receptors
- Host Defense. Studies of MHC, antigen presentation, innate and adaptive immune responses to bacterial and viral infections, autoimmune diseases, and cancer
 - Immune Metabolism and Molecular Immunology. Seahorse energy metabolism, metabolomic, proteomic, single cell sequencing, and ATAC sequencing analyses of immune system in health and disease

Molecular Mechanisms of Gene Expression

- Studies of the mechanisms and consequences of signal transduction: endothelin-mediated signaling through small GTPases, cyclooxygenase-2, and the prevention of apoptosis.
- Study of two-component signal transduction networks in bacteria
- Studies of mosquito non-coding genetic variation in transcriptional enhancers and differential malaria susceptibility

Credits Required to Graduate

60 credits minimum

Program Credit Requirements

Students entering from the IDP and NDP, or who are direct admits into the department, are required to take 9 credits of advance coursework as a minimum. MSTP students are required to take 6 credits of advanced coursework at a minimum.

All students must also complete 16242 Techniques in Molecular and Cellular Biology, and 25300 Seminar for 2 semesters (1 semester if the student receives an "A" or "A-"). Furthermore, students entering from the IDP or NDP need to complete 16270 Integrated Microbiology and Immunology, 16292 Writing a Scientific Paper, and 16293 Writing an Individual Fellowship which are all from the IDP.

Required Courses

10222 Ethics and Integrity in Science. 1 credit.

This course provides the basis for understanding the ethical issues related to basic scientific and medical research, including animal and human subject research, fraud, and misconduct, and governmental, institutional, and researcher responsibilities. Bioethics 10222 is offered during the spring and summer terms only.

10444 Research Ethics Discussion Series. 1 credit.

Prerequisite: 10222 Ethics and Integrity in Science.

The course is directed by members of the Bioethics Faculty and provides facilitated discussions of a series of topics in research ethics. Discussions are led by members of the Basic Science faculty and are focused on ethical issues that commonly come up in biomedical research. The course is meant to not only reinforce the basic ethics taught in the online course Ethics and Integrity in Science, which is a prerequisite, but also to explore the gray areas of the individual topics. The intent is to offer students illustrative examples of ethical issues that might arise in their careers, to emphasize the

ethical principles that apply in such situations, and the provide practical guidance on how these types of situations should be correctly handled. This course is offered as a discussion series. Students are expected to attend and participate in the discussion. Bioethics 10444 is offered during the spring terms only.

16242 Techniques in Molecular and Cellular Biology. 2 credits.

The primary objective for this course is to provide information and conceptual knowledge of a number of the most common techniques required for biomedical research. The information presented in this course should facilitate comprehension of the scientific literature and introduce procedures that students will commonly use in their research projects. The lecture materials will present the theory behind each technique, the practical limitations of each technique and the questions that each technique addresses. Additional lectures will assist the student in use bioinformatics and biostatistics methods and in preparing results for publication.

The course emphasizes the following core competencies: biomedical knowledge of a variety of commonly used research techniques, research skills through understanding published literature and experimental design, critical and creative thinking through the ability to judge information in the literature related to the techniques covered, interpersonal and communication skills through class participation and discussion and written exams, professionalism by interacting respectfully with others in the class, arriving to class on time and being prepared to participate, and lifelong learning by developing new learning and independent thinking skills.

16270 Integrated Microbiology and Immunology. 3 credits.

The purpose of this course is to introduce basic and integrated concepts in immunology and cellular microbiology through lectures, readings from texts and current journals. The course is geared toward first year students matriculating into the Microbiology and Immunology (MI) Graduate Program as well as any student interested in contemporary concepts of cellular microbiology, immunology, and host-pathogen interactions. The course has been designed to integrate fundamental concepts in immunology and microbiology with the goal of students being able to understand and critically evaluate the complex nature of host-pathogen interactions and immune dysfunction regardless of their specific research focus. Students learn fundamental concepts in immunology and gain an appreciation of the basic properties of bacteria and virus structure, replication, and pathogenesis. In the final block of the course, students integrate their knowledge of pathogens and the immune system. Required for IDP and NDP students.

16292 Writing a Scientific Paper. 1 credit.

This course will present a step-by-step approach to putting together a scientific paper. Students will be divided into groups of 3, and these groups will stay together for the duration of the course. Each group will be given an identical set of data with which to compose a manuscript. Each week, a different aspect of paper writing will be discussed, and students will be given a take home assignment to write that particular component of the paper within the small groups. In the final week of the class, the finished papers will be peer reviewed by 2 other groups and a member of the faculty. The course will be graded on attendance, successful and timely completion of the assignments and evaluation of the final manuscript.

16293 Writing an Individual Fellowship. 2 credits.

Prerequisite: 16292 Writing a Scientific Paper

This course provides a systematic approach towards writing a F31-like individual research fellowship. Topics include the organization of the NIH, how the NIH invites investigators to submit applications to support their doctoral studies, how PhD trainees and their mentors respond to these invitations, and how the NIH reviews a fellowship application. A weekly didactic session will be presented to the entire group of students who will have weekly individual writing assignments to complete and will have a weekly small group session to share their progress towards the completion of their writing assignments. Each student will identify a mentor-approved research topic that will be developed into a fellowship proposal, emphasizing the writing of a Summary, Specific Aims Page, and Research Plan as outlined in PA-19-195 and SF-424(F).

25295 Reading and Research. 1-9 credit(s).

The course of study for Reading and Research is designed by each student with his/her advisor to focus on readings in literature in the student's field, to build bibliographic resources for the dissertation, and to conduct supervised, independent research.

25300 Seminar. 1 credit.

In this course, students are trained to organize and present a scientific seminar. Students identify an area of interest and select one to several reports from the literature on which to base the seminar. Students are instructed how to develop an effective introduction, how to progress through the description of scientific questions, the presentation of data figures and conclusions, and how to logically tie the data and conclusions together into a coherent and compelling story. Students are required to meet periodically with the course directors prior to their seminar to decide on the seminar topic, to discuss PowerPoint slides, and to conduct practice seminars. Students must also meet with course directors following the seminar to discuss audience comments and recommendations for improvement. Students in the Department of Microbiology and Immunology are required to enroll and complete the seminar course twice as part of their departmental core curriculum.

25399 Doctoral Dissertation. 9 credits.

This course is required for the completion of the PhD degree. The PhD candidate must submit a dissertation based on original research of a high scholarly standard that makes a significant contribution to knowledge in their chosen field.

Required Courses as Needed

25002 Master's Thesis Continuation. 0 credits.

Prerequisite: 25299 Master's Thesis

This is a form of registration available to students who have completed all of the required coursework, including thesis credits but have not yet completed the writing of the Thesis. Continuation status is limited to three consecutive terms following the completion of Thesis credits.

25003 Doctoral Dissertation Continuation. 0 credits.

Prerequisite: 25399 Doctoral Dissertation

This is a form of registration available to students who have completed all of the required coursework, including dissertation credits but have not yet completed the writing of the Dissertation. Continuation status is limited to three consecutive terms

following the completion of Dissertation credits.

25299 Master's Thesis. *6-9 credits.*

Students in the Ph.D. degree program who cannot or elect not to complete that program may be allowed to transfer to the Master's program. This transfer must be approved by the student's advisor, the Program Director, the Chair, and the Graduate School. To transfer to the Master's Program, the student must be in good academic standing according to regulations established by the Graduate School.

Elective Courses

16217 Foundations in Biomedical Sciences III. *3 credits.*

Module III builds on the cell biology fundamentals introduced in the latter part of Modules I and II. This course starts with three lectures on cell signaling and a discussion of a primary research article on the topic. This forms the basis of Exam 1. The second part focuses on proteins specialized for ion flux and transport. Themes are exemplified by case studies on several diseases that affect either epithelial transport or excitable cells. Exam 2 captures this material. The third and last part of the course focuses on DNA homeostasis, genetic principals, the basis of stem cells and cancer. Exam 3 closes out the Fall semester.

25230 Current Topics in Microbiology and Immunology. *2 credits.*

This advanced course consists of introductory lectures on a selected topic followed by in-depth discussions of original research articles on topics such as bacterial invasion, virulence factors, immune evasion, virus-host interactions, T-cell functions, and viral regulatory proteins.

25251 Advanced Molecular Genetics. *3 credits.*

Specific topics in molecular genetics are explored through a combination of lectures and sessions in which research papers are presented and critically evaluated. Emphasis is placed on developing the ability to critically read and evaluate experimental results from original research papers. Specific topics for this course, which vary from one year to the next, include: cancer genetics, gene therapy, meiotic recombination, and DNA repair.

25259 Mucosal Immunity. *1 credit.*

Prerequisites: 16270 Integrated Microbiology and Immunology.

This focused immunology course on the mucosal immune system introduces students to advanced concepts and biomedical research relevant to human health and disease at the mucosal surface.

25260 Mucosal Pathogenesis. *1 credit.*

Prerequisites: 16270 Integrated Microbiology and Immunology.

Mucosal Pathogenesis is an upper-level, one-credit hour Microbiology course that focuses on the interactions of microbial pathogens with cells of the mucosal epithelium. Students gain a detailed and comprehensive understanding of specific infectious microbial pathogens, and the mechanisms utilized by the microorganisms to associate, invade, and/or cause disease at the mucosal surface. Microorganisms to be discussed include those that target the respiratory tract, the gastrointestinal tract, and the genital/urinary tract.

25261 Bacterial Toxin-Mucosal Cell Interactions. *1 credit.*

Prerequisites: 16270 Integrated Microbiology and Immunology.

Bacterial Toxin-Mucosal Cell Interactions is a one-credit hour upper-level Microbiology course that addresses the interactions between bacterial toxins and mucosal cells. The goal of this course is to provide students an appreciation of how bacterial toxins that target mucosal cells function as virulence factors and are utilized as vaccines and for clinical therapies. The course format includes formal lectures and paper discussions.

25262 Tumor Immunology. 1 credit.

Prerequisites: 16270 Integrated Microbiology and Immunology.

Tumor Immunology is an upper-level, 1-credit hour Microbiology/immunology course that will focus on the interactions of tumor cells with various components of the immune system. These interactions are complex, and immune-based strategies for treating cancer have had limited success in the clinic. This course will examine the following: (a) how the immune recognizes tumor cells as foreign, (b) immune strategies for targeting cancer, (c) barriers to achieving effective tumor immunity, (d) monitoring the immune response to cancer, and (e) use of animal models to study the interactions between tumor cells and the immune system.

The goals of the course will be to gain an in-depth understanding of the complex interactions between tumor cells and the immune system, and to learn how animal models can be used to better understand these interactions. While the course will be heavily weighted towards the discussion of important papers in the field of Tumor Immunology, it will also involve didactic lectures. Students will be evaluated through attendance and participation (30% of final grade) and a final exam (70% of final grade). The course will meet twice a week for a total of 6 weeks.

25263 Signaling in the Immune System. 1 credit.

Prerequisites: 16270 Integrated Microbiology and Immunology.

Signaling in the Immune System is an upper-level, 1-credit hour Microbiology course that focuses on how cell signaling processes shape and determine the activity of the immune system. Topics to be discussed include how cell signaling modulates cell development, antigen recognition, cell activation and migration. The course will consist of formal lectures by instructor and group discussions from scientific papers. Students will be evaluated by a single closed-book exam (60% of final grade). The final 40% of the student's grade is determined by attendance and active participation in group discussions.

25265 Immunological Tolerance. 1 credit.

Prerequisites: 16270 Integrated Microbiology and Immunology.

Immunological Tolerance is an upper-level 1 credit hour Microbiology & Molecular Genetics course that focuses on the multiple mechanisms responsible for maintaining self-tolerance. Failure of self-tolerance results in autoimmune diseases that can affect every organ system of the human body. Conversely, the induction of self-tolerance may also be exploited for therapeutic purposes. In this mini course, we will consider the general features and mechanisms of self-tolerance in T cells and B cells. These mechanisms include (1) anergy, (2) deletion by apoptosis, and (3) suppression by regulatory T cells. In addition, this course will consider select models of autoimmunity that have proven to be effective tools in our effort to understand tolerance as a complex biological process. In addition to formal lectures by the instructors, the course will feature group discussions of seminal papers that have shaped current thinking in the field. Students will be evaluated by their participation during group discussion and by a single take-home final examination. Each component will contribute equally to the final grade. The course will meet twice weekly for 6 weeks.

25266 Clinical Immunology. 1 credit.

Prerequisites: 16270 Integrated Microbiology and Immunology.

Clinical Immunology is an upper-level, one-credit hour Microbiology course that will provide advanced information and conceptual knowledge regarding the human immune system in health and disease. Specific topics will include primary and secondary immunodeficiencies, autoimmune diseases (systemic autoimmune diseases and autoimmune diseases of the skin and gastrointestinal tract), atopic diseases, HLA and bone marrow transplantation. The course will comprise a combination of formal lectures by instructors, and group discussions of scientific papers from the recent literature.

25267 Bacterial Diversity and the Microbiome.**25269 Advanced Bacterial Physiology. 1 credit.**

Prerequisites: 16270 Integrated Microbiology and Immunology.

Advanced Bacterial Physiology is a 1 credit hour Microbiology course that focuses on fundamental and diverse aspects of bacterial physiology. Students will gain an understanding of the mechanism's bacteria use to execute, coordinate and control basic cellular processes such as macromolecular synthesis, nutrient utilization and metabolism, signal transduction, and stress responses. The course focuses on critical evaluation and discussion of papers from the primary literature. These discussions will be augmented by short didactic presentations of background material by the course director to place the paper's topic and findings in context.

25271 Membranes and Organelles. 1 credit.

Prerequisites: 16216 Foundations in Biomedical Sciences II.

Membranes and Organelles is an upper-level, one-credit hour Cell Biology course that focuses on the topics of membrane protein trafficking and membrane biogenesis. Students will gain a detailed understanding of organelles and membrane protein trafficking and degradation, membrane vesicle fusion, secretion, and membrane biogenesis. The course will consist in part of readings of seminal papers describing the genetic screens for sec and vps mutants, as well as the Rothman in vitro vesicle fusion experiments. These experiments provide the first description of the proteins we know today to be involved in membrane protein fusion, secretion, and trafficking. After gaining grounding in the design and outcome of these historic screens, the class will focus on what is known today about the initial proteins identified in the original ground-breaking screens. The newer areas of membrane biology will follow similar format, examining the discovery of paradigm, and delving into what is known today. Students will be evaluated by participation in paper discussion (40%) and an in-class paper presentation (60%).

25273 Advanced Immunology. 1 credit.

Prerequisites: 16270 Integrated Microbiology and Immunology.

Immunology is currently enjoying a golden age, and breakthroughs in immunology research have transformed our understanding of many areas of biomedical science. This rapidly evolving landscape is also giving rise to novel immune-based therapeutic approaches to prevent and cure many diseases such as autoimmunity, cancer, and infectious diseases. This is an advanced course to explore the experimental basis of immunology through lectures, readings from texts, and current

immunological journals. Topics covered include the cellular basis of the immune response, antigens, antibodies, and molecular basis for generation of immunologic diversity, regulation of the immune response, innate and adaptive immunity, and diseases of the immune system.

The objective for this course is to provide a comprehensive understanding of the experimental basis of the fundamental principles of immunology. This course is designed for second year graduate students and is intended to enhance the interpretation of experimental data and experimental design in the field of immunology. Emphasis will be placed on current knowledge of the immune system and how to read and critically analyze the primary literature. Topics to be discussed include Innate Immunity and Antigen Recognition, Immune Signaling and Development, Immune Responses and Diseases of the Immune System.

25280 Classical Papers in Microbiology and Immunology. 1 credit.

Classical Papers in Microbiology and Immunology (M&I) is a course suitable for all students in the Microbiology and Immunology graduate program. Through this course, instructors and students will review, discuss, and critique notable papers from the last century that have made seminal contributions to the fields of molecular biology, bacteriology, virology, immunology, biochemistry, and/or genetics. The impact of these contributions in the present day will also be discussed. In addition to instructor-identified papers, students will also choose and formally present a recent paper for discussion that they feel has made a substantive contribution to the biomedical sciences. Papers to be discussed are expected to vary between semesters depending on topic of discussion and instructor(s) facilitating the discussion. Ultimately, this course is expected to provide students with an expanded knowledge base of seminal papers in the broad fields of microbiology and immunology.

25289 Career Internships in the Biomedical Sciences. 0 credits.

Career Internships in the Biomedical Sciences is a 0-credit training course that will provide students in the Graduate Program in Microbiology and Immunology with an opportunity to complete a semester-long internship in a biomedical science career outside the postdoc-faculty pathway. Currently, this new course is being developed with three internship modules (Teaching, Clinical Microbiology, and Research Core Management); however, it is expected that new internship opportunities will be developed in the future to address additional student interests. Each internship has been developed such that students will gain direct hands-on experience in the career opportunity. Each internship also includes extensive opportunity for one-on-one mentoring with individuals experienced in that career pathway (i.e., site directors, course directors, research core managers, etc.). As part of each internship, students are required to complete a "scholarly activity" that will employ the use of information and/or techniques that have been acquired during the training period. Finally, site directors and/or other participants active in the student's training during the internship will complete evaluations providing the student with feedback regarding their performance during the internship.

25298 Immunology Journal Club. 1 credit.

The purpose of this course is to learn, evaluate and present cutting edge immunological research topics from leading journals to gain knowledge of new immunological findings and to stay current with emerging technologies. Students will attend and present in a weekly independently organized immunology journal club. During the semester, students will be required to attend the journal club and write a short paragraph after each presentation regarding what they learned. This should

include: The knowledge gap being addressed, the hypothesis being tested, strengths and weaknesses of the study and resulting conclusions. If a journal club is not scheduled for a particular week, the students will be required to attend an independently organized immunology work-in-progress series. For the students' presentations, students will select a research paper of immunological focus from a list of preapproved journals. While the student can choose any topic of interest, the selection will require approval from the course director. The presentation will consist of a PowerPoint style presentation including the following information: Why the student selected the article, the knowledge gap being addressed, background information supporting the hypothesis, the hypothesis being tested, discussion of the approaches and experimental data, strengths and weaknesses of the study and conclusions including potential future directions. Ultimately, this course is expected to provide students with an expanded knowledge base of current topics in the broad field of immunology.

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