MOLECULAR MEDICINE PROGRAM

Lerner Research Institute, ND-46
http://www.lerner.ccf.org/molecmed/phd/
Phone: 216.445.9417
Jonathan Smith, PhD, Program Director

The Molecular Medicine PhD Program is a unique collaborative graduate training opportunity that integrates medical knowledge into graduate training. The goal of this program is to produce scientists trained in translational research: basic or applied research relevant to human health and disease that can lead to new understanding of disease, clinical and diagnostic tools, medications, and therapies.

Students train rigorously to apply basic science discoveries to human health and to the causes and treatments of human disease. The mastery of competencies necessary to translate scientific observations from the research bench to clinical care is the focus of this PhD program. Graduates will be well prepared to collaborate with physicians and for the challenge of using molecular and cellular biology to advance human health.

PhD in Molecular Medicine

Admission into the Molecular Medicine PhD program is obtained through application directly to the program. Graduate students complete didactic coursework, independent research, and other doctoral requirements to earn the PhD. First-year students complete two to four laboratory rotations among the laboratories of training faculty and are exposed to trainer research projects during the Frontiers of Molecular Medicine seminars. The first year begins mid-July. Students from all years present their research and received feedback in the Student Seminar Series. During subsequent years, students will devote the majority of their time to thesis research while attending advanced graduate courses, and seminars. Advanced elective courses may be chosen from any department or program on campus with the approval of the graduate program director and the student's thesis committee over the first two years. Students must take a total of 36 semester hours of courses and pre-candidacy thesis research, including 24 graded credit hours, and maintain a B average.

The qualifying exam will be comprised of preparing and defending a grant application in the NIH format. The topic of the grant is the area of the student's thesis research. At least one aim of this proposal will consist of a specific translational or clinical aim.

All efforts should be made to complete the PhD within five years from the date of matriculation. All students are expected to submit two or more first-authored primary research publications in peer-reviewed scientific journals. At least one manuscript must be accepted for publication prior to the thesis defense.

PRISM Program (Physicians Researchers Innovating in Science and Medicine)

NIH recognizes the need for physician on-ramps into research training, including the option for obtaining a PhD during residency / fellowship. The Molecular Medicine PhD Program offers a track for Cleveland Clinic physician trainees in GME accredited programs, who wish to pursue a PhD in laboratory-based research in the Molecular Medicine PhD Program, a program completely housed and administered at the Cleveland Clinic. If you are a Cleveland Clinic physician trainee and have questions about this opportunity, please email molmedphd@ccf.org.

PhD Program Requirements

Coursework

Students begin in July by taking MMED 402 Tools for Research and MMED 410 Introduction to Human Physiology and Disease. The student will follow a progressive curriculum including Cell Biology; Metabolism and Pharmacology; Nucleic Acids, Gene Expression and Gene Regulation; Mammalian Genetics; and Infection and Immunity. In the second summer, students take Principles of Clinical and Translational Research. During year two, students are required to take MMED 521 Molecular aspects of the diagnosis, pathology, and treatment of selected human diseases, focusing on molecular mechanisms of human disease, and an independent study mentored MMED 612 Clinical Experience.

Research Rotations

The research rotations allow the student to sample areas of research and become familiar with faculty members and their laboratories. The main purpose of these rotations is to aid the student in selecting a laboratory for the thesis work. Students will begin their rotations in July. At least two rotations are highly recommended prior to choosing the thesis advisor.

Choosing a Thesis Advisor

During or after the second semester of the first year, students select an advisor for their dissertation research. The emphasis of the PhD work is on research, culminating in the completion of an original, independent research thesis.

Plan of Study

Please also see Graduate Studies Academic Requirements for Doctoral Degrees (http://bulletin.case.edu/schoolofgraduatestudies/academicrequirements).

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<th>First Year</th>
<th>Units</th>
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<th>Spring</th>
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<tr>
<td>Research Rotations (MMED 400)*</td>
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<td>Tools for Research (MMED 402)</td>
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<tr>
<td>Introduction to Human Physiology and Disease (MMED 410)*</td>
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<tr>
<td>Cell Biology (MMED 415)</td>
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<tr>
<td>Student Seminar Series (MMED 504)</td>
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<tr>
<td>Research Rotations (MMED 400)</td>
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<tr>
<td>Metabolism and Introduction to Principles of Pharmacology (MMED 412)</td>
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<td>Nucleic Acids, Gene Expression, and Gene Regulation (MMED 413)</td>
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<td>Mammalian Genetics (MMED 414)</td>
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<td>Host Defense: Infection and Immunity (MMED 416)</td>
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<td>Student Seminar Series (MMED 504)</td>
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<tr>
<td>Molecular aspects of the diagnosis, pathology, and treatment of selected human diseases (MMED 521)</td>
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Dissertation Research (MMED 601)* | 2
Clinical Experience (MMED 612) | 2
Advanced Electives (approved by program director)** | varies
Dissertation Research (MMED 601)* | 7
Year Total: | 9

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<th>Third Year</th>
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<tr>
<td>Advanced Electives (if necessary)**</td>
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<tr>
<td>Dissertation Ph.D. (MMED 701)</td>
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<tr>
<td>Advanced Electives (if necessary)**</td>
<td>1-9</td>
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<tr>
<td>Year Total:</td>
<td>1-9</td>
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Total Units in Sequence: 38-54

* Starts in July
** Credits vary
+ Credits may vary to yield 9 credits per semester

Third Year and beyond: Complete elective coursework so total graded courses equal at least 24 credits; Research credits switch from MMED 601 Dissertation Research to MMED 701 Dissertation Ph.D. once passed into candidacy. Minimum of 1 credit of MMED 701 Dissertation Ph.D. is required each regular semester thereafter for a total of 18 credits to graduate.

Courses

**MMED 400. Research Rotations. 0 Unit.**
Research rotations are conducted to expose the student to several laboratory environments, a variety of research problems and numerous laboratory techniques as well as to assist them in the selection of their Research Advisor. Rotations will begin immediately upon enrollment and continue through the second semester of the first year. Usually rotations will last 12 weeks, however if a student decides that he/she is not interested in the assigned laboratory a shorter rotation is appropriate. The student is responsible for arranging each rotation with an approved trainer with the consultation of the Graduate Program Director. To assist in this endeavor, the Graduate Program Director will provide a list of approved trainers who have space, time and money to support a graduate student. During the rotation, students are expected to participate in all lab and departmental activities, e.g., lab meetings and seminars. At the completion of a rotation the student is required to submit a written Rotation Report including an outline of the problem being studied, a description of the experimental approaches, a discussion of the results of performed experiments as well as future directions.

**MMED 402. Tools for Research. 2 Units.**
The goal of this course is to provide a thorough and comprehensive review of current laboratory technology essential to research in molecular medicine, focusing on basic underlying principles, important controls and caveats. The students will clone a cytokine during a laboratory component of the course, which will involve designing appropriate primers, obtaining RNA from cytokine-expressing cells, performing RT/PCR, and ligating isolated, characterized fragments into cloning- and expression vectors, followed by transfection into mammalian cells. Additional bench work will include characterizing the cloned product using real time PCR, ELISA, western blot analysis, and immunohistochemistry. Seminars on commonly used molecular techniques will be given intermittently by guest lecturers with the relevant expertise. Evaluation will be based on the student’s lab techniques, class participation, and contribution to the group learning process.

**MMED 404. Journal Club / Frontiers in Molecular Medicine. 1 Unit.**
This course is a combination of a weekly discussion-based Journal Club with selected articles relevant to the core curriculum of the week and the Frontiers in Molecular Medicine Seminar series. The seminars are presented by Molecular Medicine faculty and guest lecturers to introduce first year students to the opportunities and issues in translational and clinical research.

**MMED 410. Introduction to Human Physiology and Disease. 4 Units.**
The purpose of this course is to give an introduction to the physiology of the major human organ systems, as well as selected associated pathophysiologies. The course will provide a physiological basis for subsequent study and research in Molecular Medicine. The integration of clinical faculty into the course will emphasize the importance of bringing scientific knowledge to bear on clinical problems, a theme which will be stressed throughout the Molecular Medicine curriculum. The course will also acquaint students with medical terminology.

**MMED 412. Metabolism and Introduction to Principles of Pharmacology. 2 Units.**
The course will include a combination of interactive lectures, research presentations, related journal club article, and group projects with presentations. Topics to be covered include: bioenergetics/oxidative phosphorylation, carbohydrate metabolism; lipid and lipoprotein metabolism, amino acid and nucleotide metabolism; integrative regulation of metabolism; and principals of pharmacology.

**MMED 413. Nucleic Acids, Gene Expression, and Gene Regulation. 2 Units.**
The course will include a combination of interactive lectures and problem-based learning. Each week will conclude with at least one clinical correlation where the weekly topic is presented in the context of a clinical problem. Topics to be covered include: DNA structure, chromosome structure, replication and repair; RNA synthesis and RNA processing, the organization of eukaryotic genes and the genetic code and translation; and gene regulation.

**MMED 414. Mammalian Genetics. 2 Units.**
The course focuses on genetics, genomics, and bioinformatics, and it will include a combination of interactive lectures, problem-based learning and a week-long group project. Topics to be covered include: genetic variation; linkage studies; association studies; complex traits, linkage disequilibrium, the Hap Map, pharmacogenetics; genome-wide expression studies, and mouse models of human disease, and bioinformatics.
MMED 415. Cell Biology. 2 Units.
The course will include a combination of interactive lectures and problem-based learning. Each week will conclude with at least one clinical correlation where the weekly topic is presented in the context of a clinical problem. Topics to be covered include: cell structure and organelles, prokaryotes/eukaryotes; intracellular compartments and protein sorting; receptors/endocytosis/rafts; the nucleus; cell communication; and mechanics of cell division.

MMED 416. Host Defense: Infection and Immunity. 2 Units.
The course will include a reading program, lectures, and weekly problem-based student-led presentations. Weeks 1 and 2 are dedicated to establishing the scope of the field and forming vocabulary. Week 3 and part of Week 4 will cover immune mechanisms. The remainder of the course will deal with clinical aspects of immunobiology. On a regular basis Clinical Correlations, relevant to weekly topics, are integrated into the material. Topics to be covered include: biology and molecular biology of infectious agents; fundamentals of immunology; innate and adaptive responses to infection, immune effector mechanisms; and clinical aspects of immunobiology.

MMED 501. Principles of Clinical and Translational Research. 4 Units.
To give an introduction to the ethical, statistical, methodologic and informatics basis of clinical and translational research. Topics will include the history of clinical and translational research, regulatory aspects of human subjects research, clinical trials study design, conflicts of interest, human subjects recruitment, research and publication ethics, technology transfer, biobank construction and utilization, and clinical and research database construction and utilization. In addition, students will be introduced to principles of biostatistics and clinical epidemiology relevant to clinical and translational research and gain expertise in statistical tool using problem based learning sets.

MMED 504. Student Seminar Series. 1 Unit.
This course is designed as a weekly seminar series that will include presentations by the MMED graduate students. The format will be as follows: seminar talks by students in years 3 and beyond to provide a research update presentations by second year students involving basic science-clinical case translation topics, and short presentations on lab rotation accomplishments by first year students. The primary goals of this series are to gain experience and improve oral presentation skills, to share results and thoughts with peers during research discussions, and to learn to take the lead in developing and asking questions during seminars.

MMED 521. Molecular aspects of the diagnosis, pathology, and treatment of selected human diseases. 3 Units.
The goal of this course is to integrate medical knowledge into PhD training. This team-taught seminar course focuses on a top down examination of selected human diseases starting with clinical presentations of the manifestations, diagnoses, and treatment of disease. This is followed by study of the pathology, cell biology, and molecular biology of the disease. This information forms the foundation of a final discussion of current treatment strategies and ongoing research to identify new strategies. Three to four separate disease areas will be discussed during each semester, such as diabetes, cancer, and cardiovascular diseases. The specific areas of discussion are selected to demonstrate the strength of an integrated team of clinical and basic scientists; and to provide a model for students to follow in future studies in their own area of expertise. Emphasis will be given to the basic scientific observations that formed the basis of successful clinical practice, and how this was utilized by integrated teams of basic and clinical investigators to provide better patient care. Students will prepare for discussions with close reading of the literature. Faculty will present an overview in a discussion format. It is anticipated that each disease area will be presented by an integrated team of clinical and basic scientists. The final weeks of the semester will be devoted to student preparation of a research proposal based upon the information discussed during the course. The specific topic of this proposal will be of the students choosing. Grading will be based both upon preparation for and participation in discussions, and upon the research proposal. Recommended Preparation: Introductory Graduate or Medical School courses in Cell Biology, Molecular Biology, and Physiology.

MMED 522. Grant Proposal Writing. 2 Units.
The goal of this course is to learn about the NIH institutes and grant proposal review and administration, how to compose the various sections of an NIH style grant proposal, and to gain practice in grant proposal writing skills. The course includes weekly writing assignments covering the different sections of an NIH style grant proposal. Upon completion of the grant proposal, students engage in a mock study section to review each other’s proposals. Grading will be based on grant writing assignments and participation in the mock study section.

MMED 601. Dissertation Research. 1 - 9 Units.
Research leading toward the Ph.D. dissertation in Molecular Medicine.

MMED 612. Clinical Experience. 2 Units.
Each student will be assigned a Clinical Mentor who will co-advice the student and serve on both the Qualifying Examination Committee and Thesis Committee. The Clinical Mentor will develop an individualized curriculum for the student in consultation with the Thesis Research Mentor and Program Director. The curriculum will be organized around the integrated, multidisciplinary disease groups at the Clinic. The students will attend and actively participate in the regularly scheduled multidisciplinary clinical conference organized by their disease group (most meet for one hour every week or every other week), usually involving a combination of case presentations and research presentations. At the conclusion of the semester the student will make a presentation to the group focused on a relevant translational research problem. The Clinical Mentor will also organize a series of supervised clinical experiences (with a Mentor) to various locations where students will observe clinician interactions with patients to better understand the disease from the patient perspective and to disease-related diagnostic and research laboratories.
MMED 701. Dissertation Ph.D. 1 - 9 Units.
Research leading toward the Ph.D. dissertation in Molecular Medicine.
Recommended preparation: Advancement to candidacy in MMED. Prereq:
Predoctoral research consent or advanced to Ph.D. candidacy milestone.