MOLECULAR BASIS OF MEDICINE

The MBM Foundation is designed to: (1) allow medical students to explore diverse areas of basic science and (2) maximize the time available for original research at the laboratory bench. Through these activities, MBM Scholars will strengthen their understanding of the molecular mechanisms that underlie human health and disease. They will also be well-positioned to pursue basic biomedical research at subsequent stages of their careers and to apply new scientific advances to their clinical practices.

Due to its emphasis on laboratory research, the MBM Foundation typically requires a significant commitment on the part of the medical student. The majority of MBM Scholars will complete the equivalent of a year of full-time research and will therefore pursue a five-year graduation plan. Some students elect to continue their research by entering a PhD program. MBM Scholars are also encouraged to affiliate with Stanford departments, interdepartmental programs (IDPs), or institutes, allowing them to benefit from administrative resources for training and mentoring graduate students. These structures will also help MBM Scholars connect with faculty and students working in related fields.

Medical students can pursue the MBM Foundation alone or in combination with any of the Scholarly Concentration Applications. In the latter case, the students will design a curriculum that spans both Foundation and Application areas.

Program Requirements

Courses:

MBM Scholars are required to complete 12 course units when enrolled in the Foundation alone. If the MBM Foundation is combined with a Scholarly Concentration Application, 6 MBM course units are required. All courses for the MBM curriculum are taken as electives, and they should emphasize basic science. Coursework options include both didactic classes and independent research. Students are encouraged to devise a course plan to present to the Director.

Research:

MBM Scholars will identify a research project and mentor that focuses on basic science. Total MBM research time typically spans at least one year, and financial support for time spent in the lab may be obtained by applying to the MedScholars Program. Students are also encouraged to seek funding from outside sources. In certain circumstances, students can obtain MBM course credit for their research activities, according to the guidelines outlined in the MBM Coursework section.

It is anticipated that a portion of MBM Scholars will achieve research results worthy of an MS degree. Such students may petition to meet the MS requirements in the degree-granting program most closely aligned with their area of study. MBM Scholars interested in the possibility of achieving an MS degree should familiarize themselves early on with the coursework, research, and thesis requirements for the appropriate degree-granting program, as they may exceed those of the MBM Foundation.

Presentation of Research:

All students are expected to present their research at least once in an approved forum. This may a national or international meeting, the annual Medical Student Research Symposium, or another venue approved by the Director.

Written Report of Research:

Students are expected to produce a written report of their research results. This will typically be in the form of a manuscript to be submitted for publication (or if already published, a copy of the published paper). If a publication is not expected, the final written report should take the form of a manuscript for publication.

Annual Meeting with the Director:

Students will meet with the Director to devise their MBM curriculum and at least annually to review progress. A final meeting will certify that all MBM requirements have been completed.

MBM COURSEWORK

Course Requirements

12 units are required without an Application, 6 units are required with an Application

All courses for the MBM curriculum are taken as electives, and coursework options include both didactic classes and independent, graduate-level research in the basic sciences. Students are encouraged to devise a course plan to present to the MBM Director, and if appropriate, to the Director of their Application Area.

Coursework Description

Each MBM Scholar will pursue graduate-level studies tailored to fit his/her scientific background and interests. The individualized curriculum will be developed in consultation with the Director, enabling each student to receive rigorous basic science training. This experience will help MBM Scholars formulate and undertake a significant basic science project for their scholarly research. In addition, their participation in these activities will foster interactions with PhD students, enriching the training of both groups. MBM Scholars will bring a valuable medical perspective to discussions with their PhD program peers, while learning basic science approaches, modes of inquiry, and critical evaluation skills.

Graduate courses taken to fulfill the MBM Foundation requirements should emphasize basic science concepts and/or experimental approaches. The subject matter will be typically taught from the primary literature rather than textbooks, and course activities will involve lectures, rigorous student discussions of original scientific papers, and/or the development of an original research proposal. Representative courses are listed in the following sections, and other classes may be taken with permission of the MBM Director. Courses that focus on research seminars and/or journal clubs (e.g., CBIO 280, IMMUNOL 223, INDE 217, STEMREM 250, STEMREM 280, etc.) can count toward the MBM course requirements; however, there is a 3-unit cap for including such classes as part of the MBM curriculum.

MBM Scholars can also receive course credit for independent research in a basic science laboratory, according to the following guidelines:

- Students must first complete 1 full-time equivalent quarter (FTEQ) of MedScholars research to be eligible for research-based MBM course credit (399level coursework). For example, this requirement can be fulfilled by completing 1 FTEQ of MedScholars research during the first-year summer quarter.
- Students can earn 3 units of MBM course credit for every 0.25 FTEQ of laboratory research (10 hours/week). Course credit is awarded in multiples of 0.25 FTEQs, and prorated units for less research time is not permitted.

- Students cannot receive both MedScholars funding and MBM course credit for the same research time. For example, full-time MedScholars-supported research during the summer cannot be applied toward the MBM coursework requirement.
- Students pursuing independent research for MBM course credit must provide the MBM Director with the following documents by the end of the corresponding quarter: (1) a two-page summary of his/her research progress; and (2) a mentor letter evaluating the student's performance. If MedScholars and MBM curriculum-related research are pursued concurrently (e.g., 0.25 FTEQ each), both documents must explain how the research activities were additive rather than overlapping.

Examples of Foundational Courses

BIO 214/BIOC 224/MCP 221: Advanced Cell Biology

Taught from the current literature on cell structure, function, and dynamics. Topics include complex cell phenomena such as cell division, apoptosis, signaling, compartmentalization, transport and trafficking, motility and adhesion, and differentiation. Weekly reading of current papers from the primary literature. Preparation of an original research proposal. Prerequisite for advanced undergraduates: <u>BIO 129A or 160</u>, and consent of instructor.

Term: Win | Units: 4 | Grading: Medical Option (Med-Ltr-CR/NC)

BIOC 241/BIOPHYS 241/SBIO 241: Biological Macromolecules

The physical and chemical basis of macromolecular function. Topics include: forces that stabilize macromolecular structure and their complexes; thermodynamics and statistical mechanics of macromolecular folding, binding, and allostery; diffusional processes; kinetics of enzymatic processes; the relationship of these principles to practical application in experimental design and interpretation. The class emphasizes interactive learning, and is divided equally among lectures, in-class group problem solving, and discussion of current and classical literature. Enrollment limited to 40. Prerequisites: Background in biochemistry and physical chemistry recommended but material available for those with deficiency in these areas; undergraduates with consent of instructor only.

Term: Aut | Units: 3-5 | Grading: Medical Option (Med-Ltr-CR/NC)

GENE 205: Advanced Genetics

Emphasis on developing the ability to solve problems using genetic ideas and methods, to understand the nature and reliability of genetic inference, and to apply genetic reasoning to biological research. Weekly paper discussions based on original research papers that define or illustrate the ideas and techniques covered in the lecture.

Term: Win | Units: 3 | Grading: Medical Option (Med-Ltr-CR/NC)

Examples of Specialty-Area Courses

BIO 152/CSB 222/MCP 222: Imaging: Biological Light Microscopy

This intensive laboratory and discussion course will provide participants with the theoretical and practical knowledge to utilize emerging imaging technologies based on light microscopy. Topics include microscope optics, resolution limits, Köhler illumination, confocal fluorescence, two-photon, TIRF, FRET, photobleaching, super-resolution (SIM, STED, STORM/PALM), tissue clearing/CLARITY/light-sheet microscopy, and live-cell imaging. Applications include using fluorescent probes to analyze subcellular localization and live cell-translocation dynamics. We will be using a flipped classroom for the course in that students will watch iBiology lectures before class, and class time will be used for engaging in extensive discussion. Lab portion involves extensive in-class use of microscopes in the CSIF and NMS core microscopy facilities.

Terms: Aut, Win | Units: 3 | Grading: Medical Option (Med-Ltr-CR/NC)

BIOE 214/BIOMEDIN 214/CS 214/GENE 214: Representations and Algorithms for Computational Molecular Biology

Topics: introduction to bioinformatics and computational biology, algorithms for alignment of biological sequences and structures, computing with strings, phylogenetic tree construction, hidden Markov models, basic structural computations on proteins, protein structure prediction, protein threading techniques, homology modeling, molecular dynamics and energy minimization, statistical analysis of 3D biological data, integration of data sources, knowledge representation and controlled terminologies for molecular biology, microarray analysis, machine learning (clustering and classification), and natural language text processing. Prerequisite: CS 106B; recommended: CS161; consent of instructor for 3 units.

Terms: Aut | Units: 3-4 | Grading: Medical Option (Med-Ltr-CR/NC)

CBIO 240: Molecular and Genetic Basis of Cancer

Focus is on fundamental concepts in the molecular biology of cancer, including oncogenes, tumor suppressor genes, and cellular signaling pathways. Emphasis will be given to seminal discoveries and key experiments in the field of cancer molecular biology. Course consists of two 1-hour lectures and one 2-hour discussion per week. Enrollment of undergraduates requires consent of the course director.

Terms: Aut | Units: 4 | Grading: Medical Option (Med-Ltr-CR/NC)

CSB 250: The Biology of Chromatin Templated Processes

Topics include mechanisms of DNA replication; gene expressions regulation; DNA damage sensing and DNA repair; chromatin structure and function; and epigenetics and nuclear reprogramming. Prerequisite: working knowledge of molecular biology, biochemistry and genetics, or instructor consent.

Terms: Spr | Units: 3 | Grading: Medical Option (Med-Ltr-CR/NC)

DBIO 210: Developmental Biology

Current areas of research in developmental biology. How organismic complexity is generated during embryonic and post-embryonic development. The roles of genetic networks, gene regulation, organogenesis, tissue patterning, cell lineage, maternal inheritance, cell-cell

communication, signaling, and regeneration in developmental processes in well- studied organisms such as vertebrates, insects, and nematodes. Team-taught. Students meet with faculty to discuss current papers from the literature. Prerequisite: graduate standing, consent of instructor. Recommended: familiarity with basic techniques and experimental rationales of molecular biology, biochemistry, and genetics.

Term: Spr | Units: 4 | Grading: Medical Option (Med-Ltr-CR/NC)

GENE 211: Genomics

The goal of this course is to explore different genomic approaches and technologies, to learn how they work from a molecular biology viewpoint, and to understand how they can be applied to understanding biological systems. In addition, we teach material on how the data generated from these approaches can be analyzed, from an algorithmic perspective. The papers that are discussed are a mixture of algorithmic papers and technological papers. Finally, the course has a strong programming component, with Python being the language that we teach. All of our problem sets require Python programming - while beginning programmers succeed in our course, it is a steep learning curve, and the problem sets can require a significant time investment.

Terms: Win | Units: 3 | Grading: Medical Option (Med-Ltr-CR/NC)

MI 210: Advanced Pathogenesis of Bacteria, Viruses, and Eukaryotic Parasites

The molecular mechanisms by which microorganisms invade animal and human hosts, express their genomes, interact with macromolecular pathways in the infected host, and induce disease. Current literature. Undergraduate students interested in taking this class must meet with the instructor to obtain approval before enrolling.

Terms: Aut | Units: 4 | Grading: Medical Option (Med-Ltr-CR/NC)

STEMREM 201A: Stem Cells and Human Development: From Embryo to Cell Lineage Determination

Prepares students for the future of regenerative medicine by exploring central concepts in stem cell biology and the actual experiments that led to these concepts. Provides educational foundation for future physician-scientists to understand mechanisms underlying regenerative therapies. The latest advances in stem cell research will be discussed, including tissue regeneration; how stem cells are discovered by lineage tracing or transplantation; how stem cells differentiate and form organized tissues; stem cell niches; signaling centers and extracellular signals; chromatin and cellular reprogramming; organoids; and cancer stem cells, with emphasis on unresolved issues in the field.

Terms: Aut | Units: 1-3 | Grading: Medical Option (Med-Ltr-CR/NC)

MBM STEERING AND REVIEW COMMITTEE

The following faculty serve as the MBM Steering Committee and Research Review Committee:

Director

James Chen, PhD Professor and Chair, Department of Chemical and Systems Biology jameschen@stanford.edu

Committee

Jeffrey Axelrod, MD, PhD Professor, Department of Pathology

Jonathan Long, PhD Assistant Professor, Department of Pathology

James Ferrell, MD, PhD Professor, Department of Chemical and Systems Biology

Faculty in the Basic Biomedical Sciences at the School of Medicine and in the Department of Biological Sciences at the School of Humanities and Sciences are potential research mentors for MBM Scholars. Faculty from other departments throughout the university can also petition the MBM Steering Committee to serve as mentors.