SPECIAL TOPICS IN MOLECULAR PATHOGENESIS (M&IM 8334)

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Overview

This Ph.D. level course is to provide graduate students in biomedical fields with the opportunity to study topics of specific relevance to their thesis research and/or enhance their broad perspective of biomedical research. Class time will be devoted to lectures and discussions with peers and faculty preceptors who have specific interests in the topics. In consultation with the course director and mentors, students shall select from the following menu of two-week modules to create a personalized course syllabus. Modules will be offered based on the number of students interested in the course. As a result, not all modules listed may be offered. A meeting will be held prior to the selection of modules so that students can discuss their interest as well as suggest any new ideas for course modules.

Module Descriptions

Bacterial Biofilms *(Dr. Maria Hadjifrangiskou)*
This short course will cover the basics of bacterial biofilm development (adherence, maturation, dissemination); information on how metabolic requirements are fulfilled in the biofilm; how evolution is shaped in biofilms and will end with examples of bacterial pathogens that form biofilms on diverse niches.

Preparing Figures Using Adobe Illustrator *(Dr. Chris Aiken)*
In this module, students will learn the basics of how to use Adobe Illustrator to prepare figures for publications and for grant applications. The sessions will include lectures, in-class exercises and discussions, and assignments. Students must have access to the software prior to the first class meeting.

Basic Fluorescence and Confocal Microscopy *(Dr. Jay Jerome)*
Fluorescence microscopy, and particularly confocal microscopy, has become a basic tool for biomedical research. However, they are often misused, or the data generated misinterpreted. Some background information on the principles behind the techniques and their applications will be provided. In addition, there will be time to discuss students' own microscopy needs and to allow hands-on microscope operation.

Organs-on-Chips *(Dr. John Wikswo)*
Introduction to Organs-on-Chips: Neither animal models nor in vitro assays with monocultures of immortalized or primary cells grown on flat plastic can adequately predict for humans the efficacy, pharmacodynamics, or toxicity of drugs. Microphysiological systems use organs-on-chips or organoids to create two- and three-dimensional in vitro models of functional organ tissues, typically supporting the coculture of multiple cell types. Microfluidics enables perfusion at physiologically realistic rates, organ-organ interactions, and multi-omic analysis. This module will discuss the strengths and weaknesses of these models and their potential applications to physiology, pharmacology, medicine, and toxicology.

Introduction to Practical Histology *(Dr. Jay Jerome)*
A key to understanding changes occurring in tissue due to pathology or experimental manipulation is a grasp of basic tissue structure and organization. This module will review the microscopic appearance of normal tissues (epithelium, connective tissue, blood, muscle, nerve, etc.) and their assembly into organs. We will also discuss some of the major changes that are observed in pathologic conditions.

Introduction to the Cloning Workshop *(Dr. Maria Hadjifrangiskou)*
Everyone should know how to clone, especially microbiologists! We will go over the fundamentals of good cloning strategies; cover the basics and the logic behind each strategy used; unpack how/why some kits work (or not) and we will work (hands-on!) on a construct assignment selected by each participating student (i.e. bring your cloning problems to class!)

Extracellular Vesicles in the Immune System *(Dr. Heather Pua)*
In this course, we will explore emerging data on the composition, cargo, and function of extracellular vesicles in the immune system. After a brief introduction to the topic by the instructor, the class will discuss a series of current papers that have led to our first glimpse of the critical roles these tiny mediators of cellular communication may play in physiologic and pathologic inflammatory responses.

Introduction to Genomic Analysis in the R Computing Environment *(Dr. Tom Stricker)*
In this module, we will explore the R computing environment, and learn how to analyze an RNA sequencing experiment. Topics will include installing and setting up R, loading packages, how to load and access data, data structures, generalized linear models and experimental design, visualization and heatmaps, pathway analysis, and use of RMarkdown and RNotebooks for reproducibility. This module will focus on the analysis of a single dataset; however, lessons will be generalizable to other types of analyses. Access to a laptop for in-class work is necessary, as there will be both in-class and out-of-class analyses.

Epigenetic Landscapes of Hematopoietic and Immune Cell Development *(Dr. Mary Philip)*
Genetically identical cells in multi-cellular organisms adopt a wide variety of stable fates with distinct phenotypes and functions. These heritable cell fates are determined by epigenetics. Understanding how epigenetics controls differentiation, and how cells can be reprogrammed from one cell fate to another, are fascinating and important scientific challenges. We will use hematopoiesis as a model to understand epigenetic regulation of stem cell differentiation to distinct cell fates, focusing on key papers to learn about epigenetics analysis methods used to study differentiation and cellular reprogramming.

The Beauty of B Cells *(Dr. Rachel Bonami)*
B cells promote protective immunity. Under the wrong conditions, they can drive autoimmunity. We will go over the mechanisms by which they contribute to protective or pathologic responses along with new technologies to investigate their biology.

RNA Modifications: Techniques and Emerging Roles in Virus Replication *(Drs. Chris Aiken, Manny Ascano, John Karijolich)*
Ribonucleic acid (RNA) is critical for life and is amazing stuff. In addition to mediating the transfer of information from DNA, RNA molecules fold into complex secondary and tertiary structures and can function as biological catalysts. In this module, we will explore the recently identified roles of chemical modifications of RNA in gene regulation and/or virus replication. The class meetings will consist of mini-lectures on the background and technical aspects of RNA modification together with selected readings of recent research articles. Grading will be based on student participation and a take-home exam based on the assigned readings.

Antibodies and Vaccines *(Drs. James Crowe and Ivelin Georgiev)*

Antibodies are an essential component of the human immune response to vaccination against many pathogens. This module will focus on recent conceptual and technological advances for the development of vaccines capable of eliciting effective antibody responses.

Role of the Gut Microbiota in Health and Disease *(Dr. Mariana Byndloss)*

One of the most striking recent advances in science is the discovery that the gut microbiota, the largest microbial community inhabiting our body, fulfills important functions for human health such as protection against infection, nutrition, and regulation of our immune system. Therefore, the imbalance in the intestinal microbial community (known as "dysbiosis") has emerged as a key player in the pathogenesis of a variety of diseases, ranging from cardiovascular disease and cancer to neuropathies and much more. This class will combine lectures and paper discussions to introduce the exciting field of the microbiome. We will cover the role of the gut microbiota in promoting human health, how gut dysbiosis occurs, and the implications of gut dysbiosis in infectious and non-infectious diseases.

Gene Expression Analysis in Health and Disease *(Dr. John Karijolich)*

The proper regulation of gene expression is central to maintaining an organism's homeostasis, and alterations in the control and coordination of gene expression regulation are etiological for many diseased states. Additionally, changes in gene expression underlie the response to many biological stimuli. Thus, the ability to evaluate gene expression dynamics qualitatively and quantitatively as well as identify the factors responsible is necessary for a complete understanding of health and disease. This methods-based module will cover techniques for purifying, quantifying, and determining the structure of nucleic acids. Students will become familiar with both sequencing and non- sequencing-based approaches for the analysis of transcription and/or decay rates, steady-state gene expression, as well as identifying and mapping transcript features such as transcription start and end sites. We will also discuss methods that facilitate an unbiased discovery of proteins that interact with either DNA or RNA. Lastly, we will discuss open-source software for the analysis of sequencing data that can be implemented by students and laboratories that have no bioinformatics expertise. This module will be lecture-based with examples drawn from the literature. Additionally, there will be time to address specific questions that students may have regarding the best approaches to take for analyzing or discovering gene expression regulatory proteins in their system.

Immunometabolism *(Drs. Jeff Rathmell and Alyssa Hasty)*

This module will discuss principles of cell and systems metabolism and how they influence disease from inflammation to cellular differentiation. Each class session will consist of a short introduction followed by discussions of current papers in the field. Key topics will include (1) how obesity leads to inflammation and diabetes, (2) how changes in cellular metabolism influence immune cell differentiation and immunological function, and (3) how the regulation of metabolism can dictate host-pathogen interactions on both the host and pathogen side.

Mucosal Immunology *(Drs. Danyvid Olivarez-Villagomez & Holly Algood)*

Goal: To familiarize students with the fundamentals of the immune system associated with mucosal sites, primarily the gastrointestinal tract. Summary: This module will provide students with an understanding of the functional properties of the intestinal mucosal immune system both in steady-state and disease. The module will focus on describing the immune cell populations associated with the gastrointestinal mucosa, their immunological roles, and their relevance in infectious and autoimmune diseases.

Going with the Flow: Flow Cytometry in Biomedical Research *(Dr. Lan Wu)*

Flow cytometry is an essential tool for immunologists and is underutilized in other fields of

biomedical research. Hop onto the wagon to learn key practical aspects, commonly used techniques, and a touch of new advancements in flow cytometry. Depending on the COVID-19 situation, hands-on experience may be offered.

Introduction to Working with the Mouse *(Dr. Erin Yu)*
This module is intended as an introduction to working with the mouse as a research model. The learning environment will include both lecture and hands-on instruction. Lecture topics will include basic mouse biology, behavior, diseases, and breeding colony management. Hands-on instruction will include commonly utilized lab techniques such as dose administration by several routes, genotyping, blood collection methods, and euthanasia.

Recombinant Proteins (Part I): Intro to Expression & Purification *(Dr. Heather Kroh)*
Making a pure, functional protein sample seems simple enough, but where do you start? This module will provide students with the basics in recombinant protein expression, focusing on the workhorse of protein production, *Escherichia coli*. Techniques for construct design, affinity-tag selection, and purification optimization will be introduced through lectures and assigned readings. Situations, where other expression systems (yeast, insect, or mammalian) could be necessary, will also be covered.

Recombinant Proteins (Part II): Challenges in Expression & Isolation *(Dr. Heather Kroh)*
Some protein constructs just will not express in a soluble form through conventional techniques. What if your favorite protein has a transmembrane region that complicates purification? Or perhaps it misfolds during expression--or is even toxic to the cells! Students will learn different approaches to overcome these challenges, through discussion of real-life examples and hands-on application of computational protein structure tools to identify potential trouble spots.

Introduction to antimicrobial resistance – Mechanisms, Detection, and Prevalence *(Dr. Romney Humphries)*
This course will provide a review of antibiotic resistance, including top global antibiotic resistance threats. The methods behind defining clinically relevant antibiotic resistance, and laboratory test methods for detection of resistance will be explored. Major themes of antibiotic resistance mechanisms will be explored through the evaluation of key antibiotic-resistant threats. Patient cases will be described.

Prerequisites for STMP

For students in the MHI and MPI programs, successful completion of the required fall semester coursework is a pre-requisite for this course. Students in the MPI program must have taken the Fall Immunology or Pathophysiology course. MHI students must have completed Immunology or Current Topics in Virology. For students in other Ph.D. programs, completion of the first- year of Ph.D. coursework is required.

Expectations of Students

Students are expected to complete all class assignments, attend the class meetings, and participate in any required activities (e.g. discussions). Modules may also include additional evaluative components, such as homework and tests. Because this is an advanced Ph.D. level course, students are expected to be proactive in learning.

Planned and unplanned absences

If you have a professional obligation (conference attendance, presentation, recruiting event), please notify the module director in advance to make appropriate arrangements. In the event of an absence owing to personal reasons other than an illness or medical emergency, credit is not guaranteed, but the module preceptor may propose a mechanism to obtain credit for the missed class.

Exemptions from the course

STMP is a required course for all students in the MPI and MHI Ph.D. programs. However, if the student and mentor know of another course that would better serve the student's academic goals, a substitute course may be considered. Substitution of STMP with an alternative course will require a petition (form provided by the Course Directors) signed by the mentor and is subject to approval by the Graduate Education Committee of the student's Ph.D. program. The petition will consist of a written explanation of how the alternative course will better serve the student and the development of their intended thesis research/field of study. All petitions for substitution are due on Dec. 18, 2020.

Auditing

Graduate students from various departments, advanced undergraduates, and postdoctoral fellows may take or audit the course with permission from the director. Course credit can be given for the completion of at least two modules (one credit hour per module).