

**Advanced Undergraduate Seminars  
2019-2020**

**Fall 2019**

**7.341 The Microbiome and Drug Delivery: Cross-species Communication in Health and Disease**

Instructors: [Miguel Jimenez](#) (laboratory of Robert Langer)

Wednesdays, 11 p.m. – 1 p.m.

Are humans superorganisms? There are more microbes permanently living in our gut than there are cells in the human body. This rich community of bacteria, fungi and viruses, called the microbiome, plays a central role in human health and disease. Recent research has linked this passenger community to nutrition, circadian rhythms, infectious disease, inflammatory disease, cancer, diabetes, arthritis and even immune system and nervous system development. The connections seem to be so far-reaching that some scientists are starting to consider the human-microbiome system as a “holobiont” or “superorganism.” Why are we realizing this situation only now? Are microbes actually interacting with us so fundamentally? What are the mechanisms by which effects of the microbiome are mediated? Can we survive without our microbiome? How can we analyze such a complex system? Can we exploit the microbiome to improve human health? Can interactions with microbes be harnessed for drug delivery? In this course, we will explore the primary scientific literature to find the answers to these questions and learn to critically assess observational and experimental data and to distinguish between correlation and causality. We will discuss several of the key signaling molecules that mediate the interactions between humans and their microbiomes, such as human-produced antimicrobial peptides, microbial pheromones, bacterial peptide toxins, microbial carbohydrates and neuroactive microbial metabolites. We will learn about recent methods that make possible the analysis of these interactions. We will learn about cutting-edge technologies, such as next-generation DNA and RNA sequencing and the use of germ-free mice. Finally, we will discuss how a large reduction in the cost of DNA synthesis is enabling the design and development of synthetic microbes that can be used to interrogate and manipulate the microbiome. Together these mechanistic insights and emerging tools are transforming microbiome research and might lead to new types of therapeutics and drug delivery for improving human health.

**7.342 Stem Cell Regulation in Physiology, Regeneration, and Disease**

Instructors: [Miyeko Mana](#) and [Heaji Shin](#) (laboratory of Omer Yilmaz)

Thursdays, 3 p.m. - 5 p.m.

Stem cells have a remarkable ability to self-renew and differentiate into multiple cell types. The balance between self-renewal and differentiation is tightly controlled during development and regeneration to ensure tissue homeostasis, and mis-regulation of this balance can give rise to disease. For example, cancers can arise from the over-proliferation of stem cells, and

neurodegenerative diseases can arise from the decline of stem cell function during aging. Therefore, understanding how stem cell self-renewal is controlled promises not only new basic biological insights but also therapeutic strategies for pathologies as diverse as colorectal cancer and possibly Alzheimer's disease. In this course, we will explore key concepts of stem cell biology to understand how stem cell function is acquired and regulated at the molecular level. We will begin our discussion by defining principles that govern stem cell biology and learning about diverse mechanisms that maintain the stem cell state. We will focus on stem cell models, such as embryonic stem cells and tissue-resident adult stem cells in both invertebrates and vertebrates, to examine strategies of stem cell self-renewal throughout multiple tissues and under various physiological states. We will discuss asymmetric cell divisions that are typical of fruit fly germ cells to understand how the orientation of cell division can give rise to different fates. We will examine how planaria and amphibians regenerate body parts after amputation, something most mammals cannot do. We will examine how stem cell self-renewal is controlled by the neighboring microenvironment, called the stem cell niche, and learn about various niches, such as the endothelial niche for hematopoietic stem cells. In addition, we will discuss how key cellular pathways driving self-renewal can be misregulated in a disease context, such as in carcinomas and leukemia. Example topics will include: (1) definitions of stem cell self-renewal capacity defined by potency: what are the functional differences of toti-, pluri- and multi-potency? (2) cell cycle and cellular signaling pathways that maintain stem cell states: how do stem cells and their niches talk to each other? (3) tissue-specific stem cell maintenance: what are the similarities and differences among different tissues in maintaining the stem cell state? (4) molecular mechanisms of regeneration: how have diverse organisms evolved a natural capacity to regenerate themselves? (5) lineage choice and plasticity: how can differentiated cells return to the naïve, stem cell-like state, and what are molecular triggers? (6) what are the roles of the stem cell niche: how do we identify and analyze such niches? (7) technological advances in stem cell therapy: how can insights from stem cell biology be translated into therapeutic applications? The class will be didactic and discussion-based. As we explore these topics by reading and analyzing the primary research literature, students will develop the ability to critically read papers, interpret scientific data, and understand and develop experimental designs. Students will also be encouraged to bring their creativity to ask new questions that build upon the concepts presented in the literature. By the end of the course, students should be able to evaluate the validity of methods used, identify key experimental controls, interpret figures, and draw their own conclusions on the importance of a manuscript. Students will also learn how scientists approach fundamental questions in stem cell biology and will have opportunities to visit an academic laboratory at MIT and/or a local biotechnology company to observe an actual stem cell research environment.

## Spring 2020

### **7.341 How Parasites Hijack Their Hosts: Mechanistic Exploration of Host-Pathogen Interactions**

Instructors: [Elizabeth Costa](#) (laboratory of Sebastian Lourido) and [Jon McGinn](#) (laboratory of Becky Lamason)

Wednesdays, 11 a.m. - 1 p.m.

Parasites have evolved sophisticated mechanisms to hijack host cell biology to promote infection and survival. Obligate intracellular parasites are supremely adapted to life inside host cells and offer fascinating systems to study host-pathogen interactions. This course will explore the biology of parasites and examine the mechanisms employed by diverse obligate intracellular parasites to exploit and manipulate their hosts. Specifically, we will examine the strategies that intracellular pathogens employ to invade host cells, establish an intracellular niche, avoid host immune detection, and disseminate through host organisms and populations. For example, Plasmodium, which causes malaria leading to almost 500,000 deaths worldwide per year, has evolved a number of strategies to survive and promote transmission to humans, including altering the feeding behavior of infected mosquitos. Intracellular bacteria, such as the foodborne pathogen Listeria monocytogenes, can hijack host actin, which enables them to move freely in the host cytoplasm and spread to neighboring cells. Even in less complex systems, some bacteriophage have recently been shown to evade bacterial immune response systems (such as CRISPR-Cas) by creating a nucleus-like shell to protect their DNA from attack. By surveying bacteriophage, prokaryotic, and eukaryotic intracellular parasites, we will explore the commonalities and differences among the mechanisms evolved by diverse organisms to subvert their respective host cells. These topics will be covered through critical reading and discussion of both classic and modern primary research literature. Throughout this course, students will learn principles of experimental design, data analysis, and how to read and critique papers in the field of biomedicine. Students will also have the opportunity to visit a local biotechnology company or an academic laboratory to see how cutting-edge techniques are used to uncover novel biologies of intracellular parasites.

### **7.342 The Seeds and the Soil: Roles of Tumor Heterogeneity and the Tumor Microenvironment in Cancer Metastasis**

Instructors: [Yun Zhang](#) and [Arthur Lambert](#) (laboratory of Bob Weinberg)

Thursdays, 10 a.m. – 12 p.m.

Tumors grow and evolve over many years or decades, sometimes progressing to the lethal stage of metastasis, in which cancer cells that have left the primary tumor establish new growths in organs throughout the body. For example, in late-stage breast cancer patients, tumor cells frequently migrate to the bone, liver, lung or brain, forming tumor masses that impair the function of these vital organs. Metastatic disease is responsible for the vast majority of deaths associated with cancer and is considered incurable, yet our understanding of how metastases arise is still developing. The path from a normal cell to a primary tumor, driven by genetic mutations, has been extensively mapped over the past 40 years and is reasonably well

understood. But how do some primary tumors progress to the metastatic stage? And, when they do, what determines the location where metastases develop? Accumulating evidence suggests that epigenetic changes, which are not driven by particular mutations but are hijacked from latent developmental programs, play an essential role in enabling tumor cells to form metastases. These mechanisms change both the intrinsic characteristics of tumor cells as well as their interactions with surrounding “normal” cells, reshaping the microenvironment, at both the primary and metastatic sites, to favor tumor growth and escape from immune attacks. We will begin this course by introducing various concepts and models that have been proposed to explain how cancer cells disseminate from the primary tumor to distant anatomical sites. Then we will turn our attention to two critical factors that influence cancer metastasis. First, we will discuss how cancer cells of the same tumor (the seeds) are actually quite heterogeneous and plastic, and consider how these phenotypic differences impact metastatic spread. Next, we will examine how components of the tumor and tissue microenvironment (the soil) can support or resist metastatic colonization. We will explore these frontiers through analysis and discussion of relevant primary research articles, with an emphasis on mechanisms of metastasis that act across different cancer types. Students will gain a broad understanding of the field of cancer metastasis, including state-of-the-art techniques such as single-cell RNA sequencing, lineage-tracing, and CRISPR-based approaches that are being used to address pressing questions in the field. Most importantly, through these discussions students will develop the ability to critically analyze research papers and to logically design experiments to explore scientifically important questions. Students will also have the opportunity to tour a nearby company developing novel approaches to treat metastatic cancer.