Advanced Undergraduate Seminars
2019-2020

Spring 2020

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

Instructors: Elizabeth Costa (liz@wi.mit.edu, 617-324-5869, laboratory of Sebastian Lourido)
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Spring 2020. Wednesdays, 11 am-1 pm. (Class day and time are flexible.) Room 68-150.

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

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Spring 2020. Thursdays, 10 am – noon. (Class day and time are flexible.) Room 68-150.

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.