Advanced Undergraduate Seminars
2020-2021

Fall 2020

7.341 The Microbiome and Drug Delivery: Cross-species Communication in Health and Disease
Instructor: Miguel Jimenez (jmiguelj@mit.edu, 949-285-0318, laboratory of Robert Langer)
Fall 2020. Tuesdays, 9:30 am – 11:30 am. (Class day and time are flexible.) Remote.

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? Through small group discussions, we will explore the primary scientific literature to find the answers to these questions and to learn how 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 how researchers discover and characterize these key interactions through the use of cutting-edge technologies, such as next-generation sequencing, microfluidics, mass spectrometry-based metabolomics and the use of germ-free ("gnotobiotic") mice. Together these mechanistic insights and emerging tools are transforming microbiome research and likely leading to novel types of therapeutics and methods of drug delivery for improving human health. This course will feature a virtual tour of Synlogic Therapeutics, a leading microbial therapeutics company founded out of MIT as well as guest discussions with scientists from Vedanta Biosciences (a microbiome biotechnology.

7.342 The Seeds and the Soil: Roles of Tumor Heterogeneity and the Tumor Microenvironment in Cancer Metastasis
Instructors: Yun Zhang (y.zhang@wi.mit.edu, 919-600-8633, laboratory of Bob Weinberg)
Arthur Lambert (alambert@wi.mit.edu, 603-978-2866, laboratory of Bob Weinberg)
Fall 2020. Thursdays, 1 pm – 3 pm. (Class day and time are flexible.) Remote.

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. 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? Accumulating evidence suggests that epigenetic changes, which are not driven by particular mutations but instead are somehow 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 and 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 a primary tumor to distant anatomical sites. Next, we will turn our attention on two critical factors that influence cancer metastasis: heterogeneity of and plasticity among neoplastic cells in the tumor (the seeds) and components of the tumor and tissue microenvironment (the soil). We will explore these frontiers through analysis and discussion of relevant primary research articles, with an emphasis on mechanisms of metastasis that can be applied across different cancer types. Students will gain a

broad understanding of the field of cancer metastasis, including state-of-the-art techniques that are being used to address pressing questions in the field. There will also be an opportunity for a remote "field trip," where students will virtually visit with cancer scientists working a local biotech and pharmaceutical companies. 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.

7.343 Microbial Megaproducers: Discovery, Biosynthesis, Engineering and Applications of Natural Products

Instructors: Kenton Hetrick (khetrick@mit.edu, 617-571-4580, laboratory of Ron Raines)
Emily Ulrich (eulrich@mit.edu, 608-215-6892, laboratory of Cathy Drennan)
Fall 2020. Wednesdays, 1 pm – 3 pm. (Class day and time are flexible.) Remote.

The natural world is a mega-factory of small molecules, peptides, fatty acids, phospholipids, and a host of other compounds. These compounds, or natural products (NPs), are immensely diverse in structure and function. The intricate chemical architectures of NPs arise from a fascinating interplay of simple starting materials and biosynthetic enzymes to create the varied structures that enable a wide array of biological functions. Indeed, NPs have strongly influenced how we treat infectious disease, cancer, pain, and a host of other conditions. Roughly half of the drugs that have been approved in the past 30 years are NPs, derivatives of NPs or NP-inspired. Where do these NPs come from? What organisms produce these NPs and for what reasons? How are these compounds biosynthesized? Can we discover new compounds or modify the structure and function of existing compounds to inspire new therapeutics? Decades of work to answer these questions have yielded immense progress. Furthermore, the explosion of genomic data over the past 15 years has revolutionized NP research and allowed researchers to explore the wealth of NPs using novel, high-throughput approaches. In this discussion-based course, we will delve into research on discovering NPs from producing organisms, investigating the biochemistry of NP production, and using synthetic biology to create NP derivatives — all with a particular emphasis on how genomic data guides and informs all these studies. Our class will primarily focus on bacterial producers of two types of NPs: **ri**bosomally synthesized and **p**ost-translationally modified **p**eptides (RiPPs) and **n**on-**r**ibosomal **p**eptide–polyketide (NRP–PKS) hybrids, drawing on papers from laboratories in chemistry, chemical engineering, biological engineering, and biology. We will conclude with a discussion of NPs produced by plants and NPs of the human microbiome. Students will hone their skills reading and critiquing primary research articles and become familiar with common chemical and biological techniques used by NP researchers. This class will also provide students with the opportunity to examine a NP paper of their choice and develop their critical writing and speaking skills through a short written assignment and oral presentation to the class. In addition, students will have the opportunity to engage with a career panel of scientists and professionals with experience in NP research.

7.344 How Parasites Hijack Their Hosts: Mechanisms of Host-Pathogen Interactions

Instructors: Elizabeth Boydston (liz@wi.mit.edu, 617-324-5869, laboratory of Sebastian Lourido)
Jon McGinn (mcginn@mit.edu, 617-258-6455, laboratory of Rebecca Lamason)
Fall 2020. Tuesdays, 2 pm-4 pm. (Class day and time are flexible.) Remote.

Pathogens 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 these pathogens and the diverse mechanisms they employ to exploit and manipulate their hosts. Specifically, we will examine the strategies that intracellular pathogens use to invade host cells, establish an intracellular niche, avoid host immune detection, and disseminate through host organisms and populations. For example, the SARS-CoV-2 virus, the causative agent of the COVID-19 pandemic that has led to over 500,000 deaths, has evolved multiple strategies that enable it to efficiently infect, replicate, and spread in humans. 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. Eukaryotic parasites like *Plasmodium falciparum*, which causes malaria, have evolved specialized mechanisms to spread throughout populations, including by altering the feeding behavior of infected mosquitos. In less complex systems, some bacteriophages 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 viral, prokaryotic, and eukaryotic intracellular pathogens, 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 hear from a guest scientist who has been working on the front lines of COVID-19 research to hear how cutting-edge technologies are being used to gain a mechanistic understanding of this novel virus to enable the development of novel treatments to address this unprecedented pandemic.

7.346 Chemical Biology: Using Chemicals and Chemistry to Probe Biological Mechanisms and Identify Therapeutic Targets

Instructor: Boyuan Wang (boyuanw@mit.edu, 917-855-1293, laboratory of Michael Laub)
Fall 2020. Thursdays, 10 am – noon. (Class day and time are flexible.) Remote.

Chemical biology is an interdisciplinary field that has contributed numerous convenient and sometimes exclusive solutions to biological problems. Chemical biology derives from three major areas of biomedicine: genetics, medicinal chemistry and synthetic biology. In the pre-genomics era, small-molecule drugs were mostly identified ahead of their targets, and target identification was a long, arduous and costly process. After spending their early careers synthesizing and analyzing such drugs, a few chemists realized that a drug can be used directly to identify its binding protein(s) and likely functional target(s) and, more generally, to relate these targets to the cellular processes affected by the drug. Hence chemical drugs could be used to identify biologically relevant proteins and pathways in the same way that mutations can be used to identify biologically relevant proteins and pathways via mutagenesis screens in genetics. This approach was named "chemical genetics." Early discoveries in the field of chemical genetics include calcineurin (which controls T-cell activation) and mTOR (target of rapamycin; a protein kinase that senses nutrients and regulates cell growth). More recently, phenotypic screens using large chemical libraries, analogous to mutagenesis screens in genetics, have powered the discovery of many small-molecule drugs, including Remdesivir, the anti-Ebola drug recently repurposed to treat COVID-19. In medicinal chemistry, chemists synthesize natural products and related compounds to systematically modify their structures and define structure-function relationships. Similarly, modified proteins are synthesized for the mechanistic elucidation of protein functions. For example, in the first potassium channel structure, four short α-helices adjacent to the channel pore align their electrostatic dipole moment towards a K^+ outside the channel. To test the functional role of this dipole-cation interaction, the dipole moments were disrupted by changing a peptide bond in the backbone of α-helices into an ester bond, which was achieved by a remarkable effort of chemical synthesis. Medicinal chemistry also uses the structure of substrates to guide the design of enzyme inhibitors. Chemical biologists extended this idea to design inhibitors that covalently react with the catalytic nucleophile of hydrolases, which use water molecules to cleave specific covalent bonds. These inhibitors were applied to capture, identify and quantify hydrolase activities from living cells. Comparisons of hydrolase-activity profiles between healthy and disease cells allows dissection of the role of individual hydrolases in the disease. In addition to genetics and medicinal chemistry, synthetic biology has provided a foundation of the field chemical biology. To develop chemical reactions as efficient and specific as those catalyzed by enzymes, chemists re-purpose, engineer or evolve naturally occurring proteins. By iteratively mutagenizing and selecting for the desired reactivity, chemical biologists evolved the P450 oxygenase that our bodies use to detoxify toxins to instead perform site- and stereo-specific oxidation reactions for the synthesis of drugs, including taxol (cancer), artemisinin (malaria) and pravastatin (heart disease). They also engineered fluorescent proteins to fluoresce in all colors of the rainbow to enable multi-wavelength imaging and the simultaneous illumination of multiple facets of the world of cell biology. We will read, discuss and critique papers from the primary research literature, focusing on experimental design and methods, such as quantitative mass spectrometry and the chemistry used to synthesize or label biomolecules. Students will identify a research area that was recognized by a Nobel Prize since 1960 and will write a brief proposal describing how they would use modern approaches of chemical biology to address the same problem or extend the earlier findings. Students will also prepare an oral critique of a research paper in the field of chemical biology. We will visit (most likely virtually) a research group at Merck that develops strategies to chemically label surface proteins in B cells in spatial proximity to the programed-death ligand 1 (PD-L1), an

immunity checkpoint protein produced by cancer cells and a major target for cancer therapeutics. By the end of this course, students should be able to critically read research papers, be familiar with the field of chemical biology, and understand how to design research experiments using tools from the field of chemical biology.

Spring 2021

7.341 CRISPR-Cas, from Bacterial Defense to Genome Engineering and Therapeutics
Instructor: Alireza Edraki (edraki@wi.mit.edu, 774-232-6805, laboratory of David Bartel)
Spring 2021. Tuesdays, 10 am – noon. (Class day and time are flexible.) Possibly remote.

You may have heard of CRISPR-Cas9, with headlines claiming that CRISPR is the answer to all questions in biology, medicine and agriculture. But where do these "Clustered Regularly Interspaced Short Palindromic Repeats" come from? Is Cas9 synonymous with CRISPR? What exactly is a guide RNA? As is the case with most revolutions in biomedical sciences, CRISPR was discovered when scientists were examining aspects of biology seemingly unrelated to the vast array of the applications envisioned today. In short, CRISPR emerged from studies of bacteria, studies that were focused on improving the production of yogurt and cheese. Research in the CRISPR field has resulted in widespread use of CRISPR today with even broader applications envisioned for the future. The aim of this course is to explore the primary research literature to equip you both with the skills needed to critically read research papers and with a basic knowledge of CRISPR biology as well as of other new genome editing tools. The first part of the course will cover the prokaryotic origins of CRISPR. Specifically, we will discuss key papers that demonstrated CRISPR is an anti-bacteriophage bacterial defense pathway and elucidated its mechanism of action. We will discuss the different types of CRISPR systems and compare and contrast their phage inhibitory mechanisms. You will learn that CRISPR systems with Cas9 are in the minority, and that other types of CRISPR systems implement very diverse pathways to defend against phages. We will then discuss advances in genome editing brought about by the CRISPR revolution. We will consider different CRISPR nucleases, such as Cas9, Cas12 and Cas13, and how Cas9 emerged as the one so far best suited for genome editing. We will look at the potential pitfalls and challenges of CRISPR genome editing, such as off-target effects and issues concerning the delivery of CRISPR to the desired target tissues and cells, and how such issues might be overcome. We will delve into new CRISPR-based molecular tools, including base editing and prime editing. Such tools take advantage of the programmability of Cas9 to deliver specific enzymes to a genomic site of interest for precise editing without DNA cleavage. We will discuss the use of CRISPR in agriculture to improve crop yield and quality to address the ever-growing need for food. Finally, we will consider emerging therapeutics based on CRISPR, and the promise they hold for patients with genetic diseases. We are planning for a field trip to a Cambridge-based CRISPR company to hear about the latest developments in CRISPR therapeutics. We will debate the ethics of CRISPR use and examine several controversies that CRISPR genome editing has generated (e.g. embryo editing). By the end of this course, you will know the origins, methods and applications of CRISPR and be well prepared to apply this knowledge both in your future career and as a responsible member of your broader community.

7.342 How Cells Perform Amazing Functions and Evolve to Overcome Challenging Environments
Instructor: Idan Frumkin (frumkini@mit.edu, 617-335-4294, laboratory of Michael Laub)
Spring 2021. Wednesdays, 10 am-12 pm. (Class day and time are flexible.) Possibly remote.

Cells must perform an enormous number of complex functions to survive ever-changing environments. To what degree can cells be considered to be optimized? Why do mechanisms of cell biology sometimes seem arbitrary and overly complicated? How could evolution have ever produced something as complex as a eukaryotic cell? Although the cell is commonly referred to as "the most basic unit of life," it is actually so complex that despite over 350 years of research we are still far from fully understanding its structural, functional and evolutionary workings. Bringing together the fields of cell biology and evolution into an integrated field of "evolutionary cell biology" provides a powerful perspective for studying mechanisms that produce cellular functions. This field offers insight into the evolutionary bases behind variations in cellular functions, significantly advancing our

understanding of the fundamental principles governing cellular systems. An early example of evolutionary cell biology is the endosymbiotic theory of how mitochondria arose, a concept that revolutionized our understanding of the origins and structure of eukaryotic cells. In this course, we will discuss biological principles that have driven the adaptation of cellular functions, pathways, and structures. Questions we will explore include: How can cells optimize their gene expression patterns? How do core cellular machineries adapt to changing physiological and environmental needs? How do they expand their signaling capacity within already complex networks? How can phenotypic plasticity facilitate the evolution of novel cellular functions? How can comparative biology reveal novel functions for both well-studied and uncharacterized proteins? Are all observed cellular phenotypes functional, or can we detect the work of neutral evolution? How do new genes and new cellular functions emerge in evolution? Does cellular evolution help reduce the frequency of genetic diseases? By reading and critiquing the primary scientific literature, we will answer these questions and also learn how to (i) identify an important biological problem to study, (ii) rigorously design experiments, (iii) critically assess experimental data, and (iv) learn what challenges face biologists today. Students not only will gain insights concerning cutting-edge biological questions in cellular evolution but will also acquire essential soft skills for the modern biologist.

7.343 Food for Thought: How Metabolism Controls Cancer Cell Biology

Instructors: Alicia Darnell (adarnell@mit.edu, 5-4523; laboratory of Matthew Vander Heiden)
Evan Lien (elien@mit.edu, 5-4523; laboratory of Matthew Vander Heiden)
Spring 2021. Tuesdays, 12 pm - 2 pm. (Day and class time are flexible.) Possibly remote.

Metabolism is a process carried out by thousands of chemical reactions through which cells break down nutrients like sugars to generate energy and use this energy to synthesize complex molecules like proteins, lipids, and nucleic acids. Though the key pathways in metabolism were discovered more than 50 years ago, it is far from the passive reaction map sometimes depicted on wall charts – metabolism is fascinatingly unique in different cell types, and is rapidly adaptable to both external and internal stresses. Once viewed as the simple end product of enzyme expression and regulation, metabolite levels in fact can control many cellular processes, including gene expression itself. These new insights into the active role of metabolism in cell biology have also illuminated its fundamental contributions to the pathology of human disease. Cancer provides a striking example of a disease driven by alterations in metabolism – cancer cells depend on changes to nutrient utilization to support their survival, growth, and uncontrolled proliferation. In this course, we will examine how the role of metabolism in cancer and ask: Why do tumors consume more sugar than normal tissues? How do the genetic mutations that lead to cancer re-wire cellular metabolism? What determines the nutrients available to cancer cells, and how does this local nutrient environment shape their metabolic strategies for proliferation? How does metabolism control more complex disease phenotypes like metastasis and drug resistance? And finally, can we target the idiosyncratic and essential metabolic traits of cancer to improve disease therapy and outcomes? As we explore these topics, students will learn (1) how to digest, discuss, and critically evaluate the primary research literature, (2) both time-tested and cutting-edge experimental methods to tackle questions about metabolism in biology and medicine, and (3) how recent findings in cancer biology have challenged the traditional textbook understanding of metabolism. During each class, we will discuss two primary research papers with a focus on the logic, experimental methods, and rigor of the interpretations. In addition to weekly active participation in these discussions, students will complete a written assignment mid-semester and an oral presentation at the end of the semester. We will discuss with a panel of experts how they have applied recent discoveries about metabolism to their careers in research, medicine, and drug discovery. We also will take a (likely) remote field trip to a local laboratory to learn more about the techniques and equipment used in cancer metabolism research.

7.344 Polymer Biology – Engineering Microbes To Make and Break Plastics

Instructor: Jan-Georg Rosenboom (jgr@mit.edu, 857-928-9496, laboratory of Bob Langer)
Spring 2021. Wednesdays, 2 pm - 4 pm. (Class day and time are flexible.) Possibly remote.

Bioplastics, biofuels and bio-economy. Biotech, bio-drugs and biocompatible medication. Are you somewhat excited but also confused about the uses of “bio” in these terms? In this course, we will define these terms and, more generally, discuss the tremendous positive impact on both sustainability and health that can be derived by

combining biology and polymer science. Our world is facing a variety of pressing challenges, including the pollution of our environment by plastics and the mortality caused by newly emerging infectious diseases. Both challenges can be addressed using breakthroughs in biology and polymer science. Do you want to change the world to make it a better place by helping develop and apply such breakthrough technologies? This course will provide you with a fundamental understanding of the field of polymer biology. We will discuss exciting frontier topics and consider questions such as: How can we use microorganisms to convert biological wastes into polymer precursors, ideally at low cost? Why and how do some bacterial species, fungi and even algae store plastics as an energy source in their bodies? Is genetic engineering of plastic-eating microbes a plausible solution for sustainable recycling? Why do biopolymers offer exciting prospects as materials to carry drugs safely and targeted specifically to tumors? The answers to these questions are key to the development and application of future successful technologies. Particularly given the geopolitical climate of today, to succeed in such efforts it will be crucial to understand which interpretations of scientific data make sense, and which do not. We will compare and contrast complementary and contrary findings and attempt to develop novel technological ideas based on the conceptual framework defined through our readings and discussion. This course will be interactive and discussion-based, with a focus on critiquing both classic and current papers in the primary research literature. We will see science in action by visiting a local research laboratory or biotechnology company with a focus on polymer biology. From this course you will learn both about fascinating technologies in biopolymer science and more generally about how science works – how to critically read research papers, evaluate primary data, design meaningful experiments with the crucial controls, and define creative yet realistic next steps and visions for the future.

7.345 Peptides and Nucleosides: Structures, Synthesis and Therapeutic Strategies

Instructors: Christine Arbour (arbour@mit.edu, 617-253-0206, laboratory of Barbara Imperiali)
Leah Seebald (lseebald@mit.edu, 617-253-0206, laboratory of Barbara Imperiali)

Spring 2021. Thursdays, 11 am – 1 pm. (Class day and time are flexible.) Possibly remote.

Peptides and nucleosides are ubiquitous building blocks in biology. These biomolecules have been an inspiration for modern pharmaceutical development, playing important roles as drug scaffolds and as tools for drug delivery modalities. In this course, we will discuss broad aspects of peptide and nucleoside chemistry and biology. We will emphasize how the structures of and synthetic approaches to these biomolecules influence the trajectory of therapeutic development and applications. The main challenge to assembling these biomolecules chemically is the available synthetic toolbox, which lacks sophisticated peptide and nucleoside methodology. This problem has led to developments of new "greener" synthetic strategies, i.e. aqueous based as opposed to using excessive amounts of chemicals that have poor atom efficiency for transformations. (Poor atom efficiency means that the chemical components of reagents are not incorporated into the final desired compound, resulting in excessive chemical waste.). These greener strategies will both facilitate scaling to an industrial pharmaceutical setting and have a positive environmental impact. Examples of peptides important to pharmaceutical development include cell-penetrating peptides, cyclic peptides used as immunosuppressants, and post-translationally modified peptides that alter peptide pharmacokinetics. Examples of post-translational modifications include glycosylated peptides, amino acids that contain functionalized sugars through *O*, *S*, and *N*-atom linkages, and disulfide-bonds (which involve the oxidization of and linkage between two cysteines residues within a peptide sequence or between two peptide fragments). Posttranslational modifications are integral in the production of an important peptide hormone, insulin, the major treatment for diabetes. Similarly, nucleosides are the precursors of natural products that possess a variety of biological activities -- including antibacterial, antiviral, and antitumor properties -- and serve as important scaffolds for drug development. We will discuss how nucleosides are incorporated as building blocks into natural nucleic acids, e.g., DNA and RNA. We will then compare the structures and syntheses of artificial nucleic acids. We will consider locked nucleic acids (LNAs) that have a ribose-bridging methylene between the 2' oxygen and 4' carbon, and peptide nucleic acids (PNAs) that have an amino acid-nucleoside hybrid structure substituting the phosphate backbone. These modifications can enhance the chemical stability and delivery of nucleic acids, which makes these biomolecules important scaffolds for current and developing therapeutics, such as anticancer agents and in vaccine development. Nucleic acid-based vaccines are a new generation of vaccines that carry the instructions to express a viral antigen protein that can train the body to elicit an immune response. Currently nucleic acid-based vaccines, such as mRNA vaccines, are the front runners for

reducing the spread of SARS-CoV-2 in the current pandemic. Nucleic-acid vaccines are faster to develop because they circumvent the need to produce pure viral proteins on an industrial scale, reducing the time it takes to scale for mass production. By studying how peptides and nucleosides serve as the foundations for many emerging biotechnologies, students will gain a broad understanding of the interrelated fields of chemical biology and organic synthesis as well as a deeper understanding of the pivotal technologies upon which many local biotechnology companies are founded. This class will be entirely discussion-based and will focus on select articles from the primary research literature to facilitate conversations about the synthesis, structure, and applications of the molecules being considered. A major goal will be to learn how to critically analyze the primary research literature. This class will include both written and oral assignments based on relevant literature, and students will have the opportunity to visit (likely virtually) a local biotechnology start-up, where we will discuss current cutting-edge techniques and discoveries in peptide and/or nucleoside development.

7.346 Plants at War: How Conflicts Shape Plant Genetics, Molecular Biology, and Development
Instructors: Satyaki Rajavasireddy (satyaki@wi.mit.edu, 781-819-4075, laboratory of Mary Gehring)
Rebecca Povilus (rpovilus@wi.mit.edu, 248-953-1498, laboratory of Mary Gehring)
Spring 2021. Thursdays, 1 pm – 3 pm. (Class day and time are flexible.) Possibly remote.

Plants might appear to be passive fixtures in the environment. However, these often over-looked organisms are constantly engaged in battles against a wide variety of assailants on scales small and large – from genomic to ecological. This course will take a plant's-eye-view of three main types of conflicts, and in doing so will explore core concepts across genetics and molecular and developmental biology. First, we will examine how plants deal with other organisms in the race for resources. We will discuss how parasitic plants hijack resources and genes of their hosts, how the plant immune system uses RNA-silencing to confront viral pathogens, how mutually-beneficial partnerships with bacteria that live inside roots are negotiated, and how plants use molecular signals to manipulate their environments to defend precious resources. Second, we will focus on conflicts during reproduction. We will explore the race among male gametes as they search for egg cells, as well as the struggle between parental genomes as each tries to maximize its own fitness while fighting over how maternal resources are invested into seeds. We will start with classic interploidy-cross experiments that uncovered this interparental conflict by altering parental genome dosage in the offspring, then look at more recent discoveries about how gene dosage, genetic imprinting, and epigenetic modifications are involved, and finally explore how this tug-of-war between mothers and fathers can lead to the creation of new species. Third, we will examine conflicts that occur within an individual plant, both during development and within the genome. We will discuss the molecular signals plants use while deciding to allocate resources to vegetative (leaves, branches) or reproductive (flowers, fruits) growth, and the resulting consequences for plant architecture and reproductive fitness. On a genomic scale, we will learn how selfish, self-replicating genetic elements known as transposons try to take over a plant's genome, and how some genes use a process called "meiotic drive" to manipulate the machinery behind chromosome segregation during meiosis to break the rules of Mendelian inheritance. We will focus on the primary research literature so that students will learn principles of experimental design and how to critically read a scientific paper. Students will analyze and prepare a written report about a paper of their own choosing, and then present and critique another paper to the class during an oral presentation. The course will include a field trip (in-person or virtual) to the Weld Hill plant biology research facility at Boston's Arnold Arboretum. Overall, this course will use plant biology not only as a context for learning about emerging topics in biology but also as an introduction to the dynamic, surprising, and often beautiful nature of plants.