Advanced Undergraduate Seminars
2016-2017

2016-2017

Fall 2016

7.341 Host Hacking: Parasitic Manipulations from a Micro- to a Macroscopic Scale
Instructors: Clare Harding (harding@wi.mit.edu, 617-324-5869, laboratory of Sebastian Lourido)
Diego Huet (dhuet@wi.mit.edu, 617-324-5869, laboratory of Sebastian Lourido)
Fall 2016. Tuesdays, 11 am - 1 pm. (Class day and time are flexible.) Room 68-150.

Parasites require a hospitable organism to reproduce and spread and have evolved multiple strategies to subvert their hosts. Parasites scavenge nutrients directly from host cells, evade the host immune system and even modify host behavior to increase their transmission. This course will explore the strategies used by a ubiquitous and harmful class of parasites to hijack the biology of their host cells. This class includes pathogens such as *Plasmodium* and *Toxoplasma,* responsible for some of the deadliest and most ubiquitous infectious diseases on the planet. Malaria is caused by several *Plasmodium* species and causes more than half a million deaths a year, mostly of children under five. After being transmitted through a mosquito bite, *Plasmodium* invades the liver and red blood cells. One of the most important manifestations of malaria is the modification of red blood cells by the parasite, causing them to stick to the walls of small blood vessels. Vessel blockage in the brain causes cerebral malaria, the most fatal form of the disease. As a pathogen of humans for the past 100,000 years, *Plasmodium* has evolved elegant strategies to survive and ensure its transmission, for example by hiding from the human immune system; it has been suggested that *Plasmodium* alters the behavior of infected mosquitos by making them more likely to seek hosts and to feed more often, thereby increasing the transmission of the parasite. *Toxoplasma gondii* might be the world's most successful pathogen, infecting up to half the human population. Although its sexual cycle only takes place within cats, *Toxoplasma* is able to survive within almost all warm-blooded animals. In humans, *Toxoplasma gondii* causes a chronic and asymptomatic infection in immuno-competent subjects. However, in immuno-compromised patients, *Toxoplasma* can cause fatal brain inflammation. *Toxoplasma* infection of otherwise healthy pregnant women can cause miscarriage, and *Toxoplasma* variants are a leading cause of eye disease in otherwise healthy people in South America. Intriguingly, chronic *Toxoplasma* infection has been linked to interesting behavioral alterations; for example, infected mice lose their fear of cats, increasing their chance of being eaten and so completing the parasite's lifecycle. In humans, *Toxoplasma* infection has been linked to risk-taking behavior and might be involved in schizophrenia. By exploring how these pathogens invade a host cell and replicate while evading the immune system, students will gain a broad understanding of basic cell biology, biochemistry and immunology, as well as learn techniques commonly used in cell biology. A major goal of the course is to teach students to critically analyze the primary research literature. Students will be challenged to think creatively and flexibly to understand, critique, interpret, and design scientific experiments in the field of host-pathogen interactions. This course will include a field trip to an academic laboratory focused on host-pathogen interactions, where students will learn about the use of several cutting-edge techniques for the study of the biology of *Toxoplasma* and the impact that these tools are having on the field of molecular parasitology

7.342 The RNA Revolution: At the Frontiers of Cell Biology and Molecular Medicine
Instructors: Salil Garg (salilg@mit.edu, 3-6457, laboratory of Phillip Sharp)
Amanda Ward (ajward@mit.edu, 3-6457, laboratory of Phillip Sharp)
Fall 2016. Tuesdays, 1 pm – 3 pm. (Class day and time are flexible.) Room 68-150.

The molecular biology revolution firmly established the role of DNA as the primary carrier of genetic information and proteins as the primary effector molecules of the cell. The intermediate between DNA and proteins is RNA, which initially was regarded as the "molecule in the middle" of the central dogma. This view has been transformed over the past two decades, as RNA has become recognized as a critical regulator of cellular processes. In this course, we will investigate the diverse types and functions of different RNA species, with a

focus on "non-coding RNAs," i.e. those that do not directly encode proteins. The course will convey both the exciting discoveries in and frontiers of RNA research that are propelling our understanding of cell biology as well as the intellectual and experimental approaches responsible. To achieve these goals, we will first discuss studies of long-described classes of RNAs, such as ribosomal RNA, transfer RNA and catalytic RNA, and then debate more controversial findings concerning less-characterized classes of RNAs, such as circular RNA and long non-coding RNA. After reading about the Nobel Prize winning discovery of small interfering RNA (RNAi), we will visit a local RNA therapeutics company that has translated this discovery into a novel class of disease treatments. We will consider new aspects of gene regulation revealed through the discovery of microRNAs and debate whether microRNAs should be considered to be simply endogenous small interfering RNAs. We also will investigate very current topics, such as RNAs that function in the CRISPR/Cas9 host defense systems. In this system, a guide RNA directs the Cas9 enzyme to cut DNA at a specific place, leading to the exciting potential for CRISPr/Cas9 approaches to gene therapy in the clinic and novel experimental approaches in the laboratory. Throughout the course, we will learn about the techniques employed in the discovery of various classes of RNAs, ranging from traditional genetic and biochemical approaches to the more recent application of next generation DNA and RNA sequencing approaches. Class sessions will be highly interactive and will focus on critical discussion of the primary research literature. Our broad goal will be to equip students with the tools to read and critique cutting-edge primary research articles, design properly controlled experiments to answer a given biological question, and understand how basic scientific discoveries are translated into novel therapies for disease.

7.343 Unraveling the Molecular Mechanisms of Aging and Age-Related Diseases
Instructor: Caitlin Ondracek (ondracek@mit.edu, 3-0809, laboratory of Leonard Guarente)
Fall 2016. Tuesdays, 3 pm – 5 pm. (Class day and time are flexible.) Room 68-150.

Biological aging is associated with a time-dependent decline in function. While everyone is familiar with the aging process, the mechanisms responsible for aging and age-related disease have yet to be fully elucidated. Did you know that Bama, a remote village in China, has the most active Centenarians (people at least 100 years old) living today? Why does Japan have the longest average lifespan expectancies in the world? Why does the average lifespan vary from species to species? Why do some breeds of dogs have lifespans of over 15 years, while others have lifespans of about seven years? Why do naked mole rats outlive other rodent species by more than 20 years? Why are older people more likely to experience diseases like cancer, stroke, and Alzheimer's disease? By studying the aging process, scientists hope to gain a mechanistic understanding of aging. In this course, we will explore the scientific discoveries that have led to revelations about the molecular and cellular biology of aging. We will discuss how different model organisms -- including yeast, the nematode *C. elegans*, naked mole rats and dwarf mice -- are used to study aging. Several cutting-edge technologies frequently used in the field of the biology of aging will be explored, including gene microarrays, nucleic acid sequencing, and computer modeling. We will address key questions in this field, such as: Is aging a result of or the cause of disease? Can we intervene to stop or reduce the aging process? We will discuss the connection between aging and several diseases, such as cancer and neurodegenerative disorders, including Alzheimer's and Huntington's diseases. Studies in the field of aging have led scientists to speculate that an "elixir of life" might prolong health span. During our discussion of potential pharmacological therapeutics with anti-aging properties, we will learn about two compounds – one found in red wine, called resveratrol, and another originally identified as an anti-fungal medication, rapamycin. We will also discuss how lifestyle and dietary regimens, such as calorie-restriction and exercise, can intervene in aging and age-related diseases. We will explore how new interventions might be designed to target the processes involved in aging. The class will attend a meeting of the Boston Area Aging Data Club, where we will meet the authors of some of the research papers that will be discussed in class; there we will hear presentations by scientists actively working on exciting and novel topics in the field of aging. The learning objectives of this class focus on students' developing the ability to read, critique and effectively interpret primary scientific literature. By the end of this course, while learning about important techniques and breakthroughs in the field of aging, students should be able to identify experimentally tractable interesting biological problems and design experimental approaches.

7.344 Metabolism and Human Disease

Instructors: Allison Lau (anlau@mit.edu, 5-4523; laboratory of Matthew Vander Heiden)
Alexander Muir (amuir@mit.edu, 5-4523; laboratory of Matthew Vander Heiden)
Fall 2016. Wednesdays, 11 am- 1 pm. (Class day and time are flexible.) Room 68-150.

Cancer and diabetes are the 2nd and 7th leading causes of death in the United States, with diabetes also being a major risk factor for other deadly conditions, such as cardiovascular disease. The incidence rates for both diabetes and cancer are increasing, and together cancer and diabetes will kill more than half a million U.S. residents this year. It is pressing to understand, prevent and treat these increasingly prevalent diseases. Underpinning both cancer and diabetes are dramatic changes in metabolism, the basic energy and mass-producing biochemical reactions of the cell. In this course, we will explore how metabolic alterations drive cancer and diabetes. We will ask questions such as: Why do tumors consume more sugar than normal cells? Why does a drug used to treat diabetes also decrease cancer incidence and death? How does the liver store excess sugar after a meal, and how do metabolic changes in diabetics alter liver function? How do fat cells know when to store or burn fuels? We will read, discuss and critically evaluate primary scientific papers about these topics to learn how scientists experimentally approach fundamental issues in biology and medicine. We will see that recent findings have challenged the traditional textbook understanding of metabolism and given us new insight into cancer and diabetes. For example, we will discuss the surprising finding that isocitrate dehydrogenase (IDH), a well characterized metabolic enzyme previously thought to simply function in the energy-producing TCA cycle, can become mutated to become a potent oncogene by producing a novel cancer-causing metabolite. Students will have the opportunity to visit a local pharmaceutical company that is developing therapeutics to target cancer metabolism, including inhibitors of mutant IDH proteins, in an effort to revolutionize cancer therapy.

7.345 Reproductive Medicine: From Bench to Bedside and Bedside to Bench

Instructors: Michelle Carmell (michelle.carmell@gmail.com, 617-258-5174; laboratory of David Page)
Peter Nicholls (nicholls@wi.mit.edu, 617-258-5164; laboratory of David Page)
Fall 2016. Wednesdays, 1 - 3 pm. (Class day and time are flexible.) Room 68-150.

In the western world, approximately 10-15% of couples suffer from subfertility. Over 5 million babies have been born thanks to assisted reproductive technologies, and more than half of those have been born in the past six years. In some countries, 3-5% of births are achieved with assisted reproductive technologies, and this number is projected to grow as societies become increasingly interested in beating the biological clock. This class will introduce the basic biology behind fertility and explore the etiology and diagnosis of infertility. A major goal of the class is to teach students to read and critically evaluate the primary research literature. We will cover the latest developments in reproductive science and consider the clinical challenges of translating research findings into medical treatments. We will discuss recent studies of gonadal stem cells and their use for rejuvenation of fertility, oocyte and embryo cryopreservation, and key mouse models with abnormal reproductive phenotypes. This class will highlight open questions in reproductive biology, familiarize students with both tried-and-true and emerging reproductive technologies, and explore the advantages and pitfalls of each. Students will have the opportunity to visit a Boston-area IVF (*in vitro* fertilization) clinic and speak with researchers who are on the front lines of reproductive technologies.

7.346 Hunting for the Genes that Cause Brain Disorders and Aging

Instructors**:** Christin Glorioso, MD PhD (glorioso@mit.edu; 412-596-9587; laboratory of Leonard Guarente)
Zara Herskovits, MD PhD (aherskov@mit.edu; 3-4140; laboratory of Dr. Leonard Guarente)
Fall, 2016. Wednesdays, 3 - 5 pm. (Class day and time are flexible.) Room 68-150.

Neurological diseases are one of the most important medical challenges facing society today. One in four people will have an episode of major depression in their lifetimes, and almost half of people over 85 years old have Alzheimer's disease. The burden on patients and their families and the cost to society are enormous. The brain is complex, and identifying and understanding the functions of genes involved in brain diseases has been a challenge. This course will walk through how the first genes for monogenic neurodegenerative diseases, such as

amyotrophic lateral sclerosis and Huntington's disease, were discovered using classical approaches. We will continue through current studies, from which the genetic architecture of complex diseases such as schizophrenia are just being uncovered. We will discuss how an individual's risk of developing a disease can be assessed based both on small genetic changes in nucleotide sequence and on larger structural variations that affect entire regions of a chromosome. We will read papers from the primary scientific literature to understand how genetics is informing the treatment of patients with neurological disorders. Genomic analysis has spurred the development of new treatment strategies, such as antisense oligonucleotide therapies for diseases such as spinal muscular atrophy and amyotrophic lateral sclerosis. We will debate social, legal and ethical aspects of genetic testing. The course will combine discussions of primary scientific research papers with hands-on data analysis and small group presentations. A major goal of the class is to teach students to read and critically evaluate the primary research literature. We will take a field trip to a local pharmaceutical company to learn about how new treatments for devastating neurological conditions are being developed.

Spring 2017

7.341 Peptides as Biological Signaling Molecules and Novel Drugs
Instructor: Mohammed Shabab (shabab@mit.edu, 617-253-3745, laboratory of Graham Walker)
Spring 2017. Wednesdays, 11 am - 1pm. (Class day and time are flexible.) Room 68-150.

All living cells possess the machinery for peptide synthesis, secretion, and posttranslational modifications, which together generate enormous structural and functional peptide diversity. Peptides are broadly used as signal molecules for intercellular communication in prokaryotes, plants, fungi, and animals. Peptide signals in animals include vast numbers of peptide hormones, growth factors and neuropeptides. Some of the best known examples are enkephalins (which help us sense pain), somatotropin (which helps us grow), and insulin and glucagon (both of which regulate our blood glucose levels). In plants, peptide signals such as CLAVATA3 play important roles in development. Peptides are also used as components of host defense systems. What determines the functional specificity of each peptide? How do these small polymers of amino acids survive hostile protein-digesting enzymes? How are peptides able to communicate with specific peptide receptors or interacting proteins for proper function? In this course, we will learn about the molecular bases of peptide signaling. In addition, peptides are promising novel therapeutic agents. For example, antimicrobial peptides (AMPs) have broad spectrum antimicrobial activity against bacteria, viruses, and fungi and are found among all classes of life. The ability of these natural molecules to kill multidrug-resistant microorganisms has gained considerable attention and clinical interest, since multidrug-resistant microorganisms have developed resistance to multiple antimicrobial agents and are difficult to treat with available antibiotics. One of the most notorious multidrug-resistant microorganisms are MRSA, deadly strains of methicillin-resistant *Staphylococcus aureus*. Infections with these pathogenic bacteria are untreatable with known antibiotics like gentamicin, streptomycin and kanamycin**.** Some antimicrobial peptides can kill methicillin-resistant *S. aureus* strains, making these peptides promising future drugs. In this class, we will discuss AMPs, their biological functions, mechanisms of action, and applicability as therapeutic agents. Students will learn about various human defense peptides, such as defensins, and about plant peptides involved in symbiosis, such as nodule-specific cysteine-rich peptides. We will consider techniques to detect, quantify and modify peptides. We will also discuss experimental methods such as high-performance liquid chromatography (HPLC) and liquid chromatography coupled with mass spectroscopy (LC-MS) used for quantification of peptides and other small molecules. We will focus on the primary research literature, and students will learn how to read and critique research papers. Additionally, we will visit Cubist Pharmaceuticals, a pharmaceutical company based in Lexington, MA, which is developing peptides as drugs for various pathological conditions, such as complicated urinary tract infections.

7.342 Translesion Synthesis DNA Polymerases: The Next-generation of Cancer Targets?
Instructor: Kinrin Yamanaka (kinrin@mit.edu 617-253-3745; laboratory of Graham Walker)
Spring 2017. Wednesdays, 1 pm – 3 pm. (Class day and time are flexible.) Room 68-150.

Genomic DNA is constantly under attack by a wide variety of DNA-damaging agents. Although cells possess multiple DNA repair mechanisms, DNA lesions can escape repair. As a consequence, DNA synthesis can be blocked. Translesion DNA synthesis (TLS) is a mechanism that helps cells tolerate unrepaired DNA lesions through replication of damaged DNA by TLS DNA polymerases. The outcome of the lesion bypass can be either accurate or mutagenic, depending on the identity of the TLS polymerase involved and the type of DNA lesion. Thus, on the one hand TLS polymerases can prevent cancer from being triggered by catalyzing accurate replication bypass of specific DNA lesions and performing DNA repair synthesis. For example, TLS polymerase η accurately bypasses thymine dimers, the major ultraviolet light-induced DNA lesions, and deficiency in this polymerase causes Xeroderma Pigmentosum Variant XP-V, a disorder associated with a high incidence of skin cancer in humans. However, on the other hand, TLS polymerases upon encountering different DNA substrates also can promote carcinogenesis and chemoresistance by introducing mutations in genes during error-prone TLS or performing TLS past DNA lesions induced by chemotherapeutic agents. In this scenario, TLS polymerase η can facilitate cellular resistance to commonly used chemotherapeutic agents, such as cisplatin by catalyzing replication bypass of cisplatin-induced lesions. In this course, we will learn about mechanistic basis of both cancer development and chemoresistance, specifically through the discussion of the functions of TLS polymerases and how defects in and/or dysregulation of the functions of TLS polymerases can promote tumorigenesis and chemoresistance. Additionally, we will learn about the emerging cancer therapies that target TLS pathways. Toward the end of the course, we will discuss the roles TLS polymerases play outside TLS and how these previously unknown functions of TLS polymerases link to tumorigenesis and chemoresistance. Our focus will be the primary research literature to help students learn how to read and critique research papers. We will visit a laboratory researching on TLS polymerases. This is an excellent opportunity for students to gain hands-on experience in the laboratory techniques they learn in class.

7.343 Pluripotent Stem Cells and Genome Engineering for Modeling Human Diseases

Instructors: Malkiel Cohen (malkiel@wi.mit.edu, 617-852-5860, laboratory of Rudolf Jaenisch)
Katherine Wert (wert@wi.mit.edu, 425-922-9055, laboratory of Rudolf Jaenisch)

Spring 2017. Wednesdays, 3 pm – 5 pm. (Class day and time are flexible.) Room 68-150.

One of the major priorities in biomedical research is understanding the molecular events that establish the complex processes involved in human development and the relationships of these processes to human disease and disease progression. The role of stem cells as a tool to help reveal these mechanisms has long been appreciated. Mario Capecchi, Martin Evans, and Oliver Smithies made ground-breaking discoveries using mouse embryonic stem cells for gene targeting in mammals. Their efforts made it possible to modify the DNA of specific genes within living and fertile mice, allowing scientists to determine the roles of individual genes in health and disease. This approach of genome engineering has produced numerous non-human vertebrate models of human disorders, including diabetes, cancer, cardiovascular and neurodegenerative diseases. For their discoveries, Capecchi, Evans, and Smithies shared the 2007 Nobel Prize in Physiology and Medicine. In 2012, the Nobel Prize in Physiology and Medicine was received by Shinya Yamanaka and John Gurdon for their discovery that cells of mature humans and other animals can be reprogrammed to an early embryonic stage, known as pluripotency, and then differentiate into various cell types of the adult body. This work and many other studies have stimulated the stem cell field into generating pluripotent stem cells from human patients, and these patient-specific stem cells have been used to better model human diseases by reflecting aspects of those disorders in a cell-culture system. Scientists can now cause such patient-specific stem cells to differentiate into cell types affected by the disease, allowing the study of the diseased cells and an understanding of the mechanisms underlying disease progression. Such cells can be further used to test potential treatment options. In this class, we will explore the field of stem cell biology and the way in which this field has developed and shaped our ability to study complex human disease. We will introduce the topics of stem cell biology and genome engineering through critical reading of both the classical and newest primary research literature. This course will focus on the methods behind the generation of embryonic and induced pluripotent stem cells, genome editing to create transgenic animal models of human diseases, regenerative medicine (such as the transplantation of stem cell-derived cell types to replace diseased tissues), and current hot topics in genome engineering such as CRISPR/cas9, a novel method that can be used to delete or insert genes of interest in cultured cells and intact organisms. In addition, we will discuss specific disease model systems and their benefits/limitations for understanding the disease and facilitating the

development of treatments for patients. Students will obtain a deep understanding of the main concepts and questions concerning stem cell biology, become familiar with current research techniques to model complex human diseases, and learn to critically evaluate the experimental design and claims in this field.

7.344 You Are More Than the Sum of Your Genes: Epigenetics in Health and Disease
Instructor: Ishara Azmi (ifazmi@mit.edu, 8-7352; laboratory of Steve Bell)
Spring 2017. Thursdays, 11 am – 1 pm. (Class day and time are flexible.) Room 68-150.

Hereditary information is primarily contained within the DNA sequence of cells. Such information has to be faithfully replicated in each cell cycle and transferred to daughter cells to maintain genomic stability, cellular viability and the continuity of life. The field of study of such hereditary information is known as genetics. Epigenetics, or "beyond genetics," encompasses processes that mediate inheritance of information not contained in the DNA sequence. In eukaryotic cells DNA is packaged into a condensed form known as chromatin, which is primarily composed of nucleosomes, each of which consists of about 147 base pairs of DNA wrapped around an octamer of histone proteins. The structure of heterochromatin (regions of compact chromatin that are suppressed in gene expression), histone modification (by phosphorylation, methylation or other processes) and DNA modification (by methylation) carry important epigenetic information from one generation to the next. Epigenetic information can be propagated to the next generation to maintain a functional state, such as whether specific genes are or are not expressed. Such epigenetic gene regulation is important during various stages of development to facilitate cellular differentiation and maintain genomic stability. In this class we will discuss the history of epigenetics, including classical epigenetic phenomena, such as position effect variegation (which results when genes are juxtaposed to heterochromatin, thereby decreasing their expression), polycomb silencing (which involves a group of protein complexes that repress gene activity through regulating chromatin state), dosage compensation (which enhances the transcription of most genes on the only X chromosome in males to match the level in XX females) and mechanisms of epigenetic memory transfer from one generation to another (DNA and histone modifications, heterochromatin formation). We also will discuss mechanisms of epigenetic inheritance during DNA replication and examples of how defects in epigenetic inheritance mechanisms contribute to human diseases. We will consider the experimental designs and techniques that have been employed to study epigenetics at the cellular and molecular levels. Finally, we will learn about cutting-edge research in the field of epigenetics, such as stem cell reprograming and epigenetic regulation by non-coding RNAs (which are transcribed but not translated into protein). Stem cell reprograming, which involves the generation of pluripotent stem cells from mature adult cells, is based on modifying the epigenetic control of gene expression. This technology has the potential to treat and cure a broad variety of human diseases. The major goal of this course is to help students learn to read, comprehend and critique the primary research literature. Students will visit the laboratory of Professor Mary Gehring at the Whitehead Institute. The Gehring laboratory studies epigenetic mechanisms in *Arabidopsis thaliana*, a popular model organism in plant biology. Students will visit the research facility and observe experimental approaches used to analyze how epigenetic mechanisms modulate plant growth and development.

7.345 Let's Talk About Sex (Chromosomes) and Human Genetics
Instructors: Adrianna San Roman (sanroman@wi.mit.edu, 617-258-5164, laboratory of David Page)
Maria Mikedis (mikedis@wi.mit.edu, 617-258-5164, laboratory of David Page)
Spring 2017. Thursdays, 1 pm - 3 pm. (Class day and time are flexible.) Room 68-150.

The many differences between males and females of mammalian species are driven by a simple disparity in sex chromosome content: males have one X and one Y chromosome, while females have two X chromosomes. Although this difference is widely appreciated, scientists are still learning how these sex chromosomes lead to distinctions between males and females at the cellular and organismic levels. As the only unequal pair of human chromosomes, X and Y have unique genetic properties that influence chromosome segregation, regulation of gene expression, and disease inheritance. During this course, we will take a multidisciplinary approach to delve into the many fascinating aspects of sex chromosome biology. First, we will discuss how the presence or absence of the Y chromosome in mammals determines whether testes or ovaries develop. We will address disorders of sexual

development in which the sex chromosomes do not match the physical appearance of the genitals. We will also investigate mechanisms of sex determination in non-mammalian organisms, such as flies, worms, birds, bees, and turtles, which have diverse means of generating phenotypic males or females. We will then read about reconstructing the evolution of the sex chromosomes, which will provide context for understanding current questions in sex chromosome biology. Concurrently, we will learn about the distinctive methods that were used to sequence the sex chromosomes as part of the Human Genome Project. Students will visit the laboratory of MIT Professor Dr. David Page to learn about DNA sequencing and other techniques used today to interrogate current questions concerning sex chromosome biology. Several unique properties of the sex chromosomes will be addressed, including inheritance of the Y chromosome and its relevance for reconstructing familial ancestry and understanding genetic predisposition to disease; the high proportion of repetitive DNA sequences in the Y chromosome that make it particularly susceptible to rearrangements that can lead to infertility; and the process of X-inactivation, which equalizes X chromosome gene expression between males and females and is key for understanding sex-biased manifestations of simple genetic diseases. Next, we will explore human genetic conditions related to abnormal numbers of whole sex chromosomes, such as Turner and Klinefelter syndrome. Finally, we will evaluate emerging evidence that sex chromosomes contribute to sex-specific molecular differences that might influence the pathogenesis of complex sex-biased diseases, such as multiple sclerosis, which is more prevalent in females, and autism, which is more prevalent in males. This course will introduce students to reading and critically evaluating the primary literature that has shaped key aspects of understanding sex chromosome biology**.**

7.346 Bacteria Fight Back – How Bacteria Evade Treatment and Novel Strategies to Outwit Them
Instructors: Julie Silverman (silverjm@mit.edu, 617-253-1834, laboratory of Barbara Imperiali)
Michele LeRoux (leroux_m@mit.edu , 617-253-3677, laboratory of Michael Laub)
Spring 2017. Thursdays, 3 pm - 5 pm. (Class day and time are flexible.) Room 68-150.

Bacteria and fungi have been producing antibiotics, small molecules that can kill or prevent growth of competing bacteria, since long before humans walked the earth. The discovery of antibiotics and the realization that they could cure bacterial infections radically changed modern medicine. The use of these molecules in the clinic has saved countless lives by eradicating infections that were previously impossible to treat, including syphilis, strep throat and tuberculosis. Although antibiotics were once referred to as the "wonder drugs" of modern medicine, an alarming number of drug-resistant bacteria have emerged since the beginning of the 20th century, compromising the effectiveness of these critical clinical tools. Antibiotic resistance has spread rapidly, leading to the emergence of multi-drug resistant bacteria and threatening the start of a post-antibiotic era. This phenomenon is in large part because bacteria can evolve rapidly to withstand antibiotics, and many species can transfer genes to one another. Research into antibiotic resistance has uncovered many unique mechanisms by which bacteria protect themselves from these threats to their survival, and has also uncovered many interesting aspects of bacterial physiology. Understanding how bacteria evolve to resist antibiotics will be fundamental for the future of medicine. During this course, we will discuss many aspects of antibiotics, including examples of how particular antibiotics were discovered, specific mechanisms of bacterial resistance, and how antibiotic resistance spreads among bacteria in the environment. For example, we will learn how penicillin was discovered, and then about the resistance mechanisms that arose following its widespread use. We will also discuss antibiotic-resistant bacteria more generally and delve into the molecular mechanisms underlying resistance and the spread of such resistance mechanisms, including point mutations, efflux pumps, and horizontal gene transfer. In addition, we will introduce students to fascinating bacterial behaviors, such as biofilm growth and dormancy, which allow bacteria to become temporarily tolerant of antibiotic treatment even in the absence of classical mutational changes that confer antibiotic resistance. The course will conclude with an examination of today's state concerning antibiotics and antibiotic resistance through a discussion of new pioneering work to treat infections with engineered antimicrobial peptides, bacteriophage therapies and microbiome replacement therapies such as fecal transplants. We will focus on the primary research literature, and we will learn practical laboratory techniques, experimental design and how to interpret data and critique the conclusions offered by authors. Students will have the opportunity to visit a local biotech company to learn about novel approaches to treating bacterial infections that go beyond the traditional small molecule antibiotic.