Advanced Undergraduate Seminars

Spring 2025

7.341. Implications of Cellular Stress Responses for Cancer: A Matter of Life or Death
Instructors: Michaela Bartusel (bartusel@mit.edu, 617-870-8290, laboratory of Eliezer Calo) and Jennifer Chu (jennchu@mit.edu, 857-269-4531, laboratory of Chris Burge)
Spring 2025. Tuesdays, 11 am – 1 pm. (Class day and time are flexible.)

Are you feeling stressed? So are your cells! Species across all kingdoms of life have developed strategies that help them deal with the diversity of organismal and cellular stresses they experience. For decades, scientists have explored the complex mechanisms that govern cellular stress response pathways to better understand how cells in a multicellular organism decide when it might be advantageous to the organisms for those cells to promote their own deaths. While these pathways are important for organismal health and fitness, if inappropriately regulated, they can be detrimental and even tumor-promoting. In this course, we will explore how stress signaling is tumor-suppressing in certain contexts but tumor-promoting in others. Questions we will address include: (1) What are the key molecular changes that occur when cells are exposed to stress? (2) How do different types of cellular stresses (e.g. DNA damage, oxidative stress, nutrient deprivation) contribute to cancer, e.g., by evading cell death, reprogramming metabolism, and/or promoting uncontrolled cellular proliferation? (3) How do the stress responses of malignant cells differ from those of cells in normal tissue? (4) What are the types of stresses that cancer cells face, and how do these stresses affect cancer cell growth and ability to spread throughout the body? (5) What are examples of current standard-of-care treatments that trigger cellular stress responses to combat cancer, and how do these treatments work? (6) What strategies do cancer cells employ to evade chemotherapy? Addressing these questions will help us understand how key signal transduction pathways influence cellular fate decisions, like autophagy (cellular self-digestion and recycling) and apoptosis (programmed cell death). This course will be discussion-based and focus on the critical reading of the primary literature relevant to cellular stresses, cancer biology, and therapeutic resistance. Students will develop skills for evaluating scientific journal articles, interpreting experimental data, and designing rigorous experiments with appropriate controls. We will delve into the varied experimental methods used in the field of cellular stress and cancer. We will also discuss how companies have translated discoveries from basic research into therapeutics that target stress-response pathways
for cancer therapy. We will take a field trip to Cellarity, a Cambridge-based startup that utilizes single-cell technologies and machine learning to develop new cellular stress response-triggering therapeutics to treat a variety of diseases, including myelofibrosis, a type of bone marrow cancer. As part of the class, students will also practice both scientific writing and the oral critiquing of scientific data. By the end of the course, students will be equipped with the basic knowledge of the field and critical thinking skills necessary to evaluate the primary research literature.

7.342. B cells and their Antibodies: Paving the Road for the Next Vaccine
Instructor: Raphael Reyes (rreyes13@mgh.harvard.edu, 818-961-6894, laboratory of Facundo Batista)
Spring 2025. Wednesdays, 1 pm – 3 pm. (Class day and time are flexible)

The human immune system is able to generate antibodies against millions of diverse antigens and thereby protect us against disease-causing pathogens. To ensure that we have appropriately protective antibodies before we encounter a pathogen, we can use vaccines to educate our immune system in preparation for potential exposure. How can we design a vaccine to recognize a novel pathogen, and how can we predict how effective such a vaccine will be at protecting us once we are exposed? In this course we will critically discuss the primary research literature to understand how scientists learn from humans naturally infected with pathogens to identify the key targets of protective immunity and how scientists can use preclinical animal models to test the efficacy and durability of protection of newly developed vaccines. We will discuss fundamental aspects of molecular immunology, in particular about B cell and antibody responses against difficult to tackle diseases like malaria and HIV, in addition to pathogens for which we already have effective vaccines, such as SARS-CoV-2 and flu. Students will learn to

critically assess and extract information from the primary research literature, to understand and interpret data presented using the latest immunological methodologies, and to independently think about how basic research findings can translate into the treatment of human disease and lead to future research directions. Students will improve their scientific communication skills, first by writing a short grant proposal outlining one or a few experiments that would help contribute to the design of a vaccine for unknown disease X and second by a final oral presentation leading a peer-review critique about an unpublished preprint relevant to novel vaccine design. This course will include a field trip to the newly built Moderna research and development facilities in Kendall Square, where current research is aimed at developing vaccines against infectious diseases using the mRNA delivery platform that was highly successful for Moderna's COVID-19 vaccine. During this visit students will also get the opportunity to speak with a panel of Moderna scientist to learn about careers outside of the traditional academic path, gain insight about their experiences navigating from their undergraduate training to their current position, and discover the opportunities offered by Moderna for undergraduates interested in research. Students with no prior immunology or research experience are welcome to this course.

7.343. How to Build an Organism: Principles and Mechanisms of Complex Biological Systems
Instructors: Arjuna Rajakumar (arajak@wi.mit.edu, 857-313-1267) & Christoph Gäbelein (chrisgae@wi.mit.edu, 857-829-1678) (both in the laboratory of Ruth Lehmann).
Spring 2025. Thursdays 10 am -12 pm. (Class Day and time are flexible.)

On Earth, complex life-forms have evolved through a series of major transitions over the course of the last 3.7 billion years. These transitions involved a wide range of evolutionary innovations, resulting in the strikingly diverse forms of life today. Two of the key transitions were: (1) the evolution of eukaryotic cells from bacterial ancestors through endosymbiosis, and (2) the evolution of multicellular organisms from single cells. Researchers have learned about these processes and the mechanisms involved first by simple observations and comparisons and later through experimental interventions, driven most recently by a variety of technological innovations (e.g., next-generation sequencing, microfluidics, gene editing, induced pluripotent stem cells). Interdisciplinary research in bioengineering, experimental evolution, and developmental biology has enabled major advances that have challenged some long-existing paradigms about the origins of complex life and led to new hypotheses from studies that have engineered cells in fundamentally novel ways. Our course will be journal-club style – reading and critiquing the primary research literature – with each week focusing on a major topic and exploring how current concepts have been shaped and evolved. We will compare and contrast historically significant and state- of-the-art studies across disciplines. For example, drawing from the concepts of endosymbiotic theory as pioneered by Lynn Margulis, we will discuss how obligate endosymbionts are now being engineered to fight malaria and dengue. Similarly, inspired by concepts in self-organization and tissue morphogenesis, we will consider how the advent of organoids – tiny, stem cell derived, three-dimensional tissue cultures – and synthetic embryos are continuing to drive medical breakthroughs concerning autoimmune and neurological diseases as well as extend our fundamental understanding of human biology. After examining the course evolution took on earth, we will go a step further and explore the field of the search for life across the universe. To learn about some of the current approaches to seeking life in the universe, we will go on a field trip to the laboratory of Professor Sara Seager at MIT. She is pioneering the study of exoplanets – from the technical difficulties of discovering them to the study their atmospheres and their potential for hosting life. Students will have the opportunity to propose a set of experiments to investigate how complex biological life might be propagated extraterritorially or to characterize primordial life from distant galaxies. This course will equip students with critical skills for their future careers: (1) analyzing and discussing the primary research literature, (2) developing novel hypotheses, (3) designing experiments to test these hypotheses and (4) orally presenting a critique of a research paper to peers.

7.344. Bacterial Chromosomal Architecture and Its Impact on Gene Expression and Human Infections
Instructor: Roberto Jareth Vazquez Nunez (robertvn@mit.edu, 775-340-3480, laboratory of Seychelle Vos)
Spring 2025. Tuesdays, 10 am - 12 pm. (Class Day and time are flexible.)

Bacterial chromosomes are remarkably compact, stretching 1.5 mm long, yet fitting into a cell only 1.5 μm in length. This 1,000-fold compaction is akin to squeezing a rope from the MIT Dome to the Stata Center into a soccer ball! Bacteria face the challenge of not only packing their DNA tightly but also replicating, segregating, and expressing genes in a highly coordinated and flexible way in this cramped space. To manage these tasks, bacteria use nucleoid-associated proteins, which act as "traffic officers," ensuring smooth operations despite the crowding. Researchers have unveiled multiple mechanisms bacteria employ to achieve DNA compaction and efficient gene expression, shedding light on their role in pathogenicity and antibiotic resistance. For instance, the nucleoid-associated protein H-NS present in gram-negative bacteria such as E. coli compacts DNA and silences genes transferred from one bacteria species to another (horizontal gene transfer), typically associated with adaptation to the host immune response and antibiotic resistance. In this course, students will delve into primary research literature to understand how bacterial chromosomes compact functionally. During the first half of the course, we will discuss the principles of biochemical, biophysical, and genomic techniques used to study chromosome conformation, such as enzymatic assays, single-molecule kinetics, and high-throughput sequencing, all in the context of how these varied methods have been applied. During the second half, students will explore gene-regulation mechanisms dependent on chromosome structure and topology and their roles in human pathogens. We will consider mechanisms employed by uropathogenic *E. coli* to invade the urinary tract, by *S. enterica* to evade the immune system and establish gut infections, and by *Pneumococcus* to counteract antibiotics during respiratory infections. Throughout the course, students will learn how both to understand experimental design to test and explore scientific hypotheses and to critically analyze the scientific literature. Assignments will include a written future-directions proposal of a research article related to chromosome architecture and a final oral presentation about a research paper focused on a gene-regulatory mechanism that involves genome organization. This course will feature a field trip to the Broad Institute to a laboratory that develops new antibiotics, offering a practical glimpse into the importance of studying fundamental processes related to bacterial gene expression and applying such knowledge to the current global health issue of the widespread emergence of antibiotic resistance.