TO: Biology Majors
FROM: H. Robert Horvitz, Professor of Biology

I am writing to inform you of an exciting course offering from the Department of Biology for the 2010-2011 academic year: a set of 18 very current seminar courses, 7.34x, Advanced Undergraduate Seminars. A complete list of the courses, instructors, and brief course descriptions are enclosed. The topics are highly varied and encompass areas of genetics, biochemistry, molecular biology, cell biology, cancer biology, stem cells, regenerative medicine, neurobiology, aging, systems biology, protein engineering, biotechnology, drug discovery, biofuels, and human disease.

A student can take any number of these courses. The courses, which generally involve four to eight students, are for 6 units, graded pass/fail, and meet two hours each week. The focus is on reading and discussing the primary research literature. Most courses have two short written assignments. Some include field trips to MIT research laboratories or to commercial sites using technologies discussed in the courses. The level of each course will be tailored to the students who enroll. Because of the small size of these courses, we expect students not to drop these courses once they have begun.

These courses offer a number of special features: small class size, a high degree of personal contact with the instructor, a focus on the primary research literature, and an opportunity to discuss current problems in biology interactively. I believe these courses greatly enrich an undergraduate's experience. There are limited alternative opportunities available to undergraduates to interact closely with instructors who are experienced full-time researchers; to learn to read, understand, and analyze primary research papers; and to engage in the type of stimulating discussions and debates that characterize how science is really done. Most advanced MIT undergraduates (generally juniors and seniors) have been sufficiently exposed to the basics of biology to be able to read the primary literature and appreciate both methodologies and cutting-edge advances. These courses have two goals: first, to expose students to the kind of thinking that is central to contemporary biological research; and second, to impart specific knowledge in particular areas of biology. These courses are designed to be intellectually stimulating and also to provide excellent preparation for a variety of future careers that require an understanding both of what modern biology is and of how it is done. Students who have taken Advanced Undergraduate Seminars in the past (different specific courses, same general design) have been enormously enthusiastic about their experiences.

I am writing to you before Registration Day to encourage you to consider enrolling in one of these seminar courses. Please feel free to contact any of the instructors to learn more about their courses.

To learn more about the Advanced Undergraduate Seminars to be offered during both the Fall 2010 and Spring 2011 semesters, please check our website (http://mit.edu/biology/www/undergrad/adv-ugsem.html) and/or contact the instructors.

Advanced Undergraduate Seminars
2010-2011

Fall 2010

7.340 Molecular Mechanisms of Learning and Memory

Instructor: Sven Loebrich (loebrich@mit.edu, 8-5241; laboratory of Elly Nedivi)
Fall 2010. Mondays, 1 – 3 pm. (Class time is flexible.) Room 68-151.

The mammalian brain significantly outperforms any man-made supercomputer with respect to computing time and process complexity. The brain adapts and changes constantly in response to external stimuli. Most importantly, the brain enables us to continuously learn and remember new things. A single experience, such as touching a hot plate, witnessing a tragedy, or experiencing the shocking taste of durian fruit can be remembered for life. What are the molecular mechanisms that lead to learning and memory? How do nerve cells, inter-neural connections (synapses) and brain circuits change over time to store information? Electrical activity in the nervous system controls the expression of genes that can affect neuronal function. What are the cellular roles that activity-regulated gene products play to implement changes in the brain? We will discuss the molecular mechanisms of such neuronal plasticity at the synaptic, neuronal and circuit levels. We will consider fundamental neurobiological processes, such as (1) synapse formation, (2) synaptic growth and stabilization, (3) synaptic transmission, (4) axonal and dendritic outgrowth, and (5) circuit formation, with some focus on the visual system. We will learn about the roles of some activity-regulated genes in these processes, and we will study their functions in various experimental systems, such as dissociated neuronal cultures, cultured brain slices, and the living brain. In addition, we will learn about the tools and techniques employed in modern neuroscience research. Our goal will be to understand molecular mechanisms the brain employs to bring about the complex phenomena of learning and memory.

7.341 RNAi: A Revolution in Biology and Therapeutics

Instructors: Allan Gurtan (gurtan@mit.edu, 3-6458; laboratory of Phillip Sharp)
Michael Goldberg (michaelg@mit.edu, 3-6457; laboratory of Phillip Sharp)
Fall 2010. Tuesdays, 1 pm – 3 pm. (Class time is flexible.) Room 68-151.

The goal of medicine is to prevent, ameliorate or cure disease. Despite centuries of effort, modern medicine struggles against the same obstacles today as it did in its early days: identifying the cause of disease and treating it specifically without inducing side effects. While significant advances in medicinal chemistry have been made over many decades, traditional small molecule therapeutics remain unpredictable, often because of a lack of specificity. Similarly, the recent advent of recombinant DNA technology, though ushering in an era of protein-based therapeutics, has achieved only limited success owing to difficulties posed by the large sizes and instabilities of these macromolecules. What,

then, is the next therapeutic frontier? The answer might lie in RNA interference (RNAi), a fundamental biological process discovered only a dozen years ago and recognized soon afterwards with the 2006 Nobel Prize in Physiology or Medicine. RNAi is mediated by small interfering RNAs (siRNAs), which direct the efficient degradation of specific messenger RNAs, thereby inhibiting protein synthesis. Since its discovery, RNAi has revolutionized basic science research by allowing the dissection of cellular processes with unprecedented specificity, thus providing an invaluable tool to identify the bases of disease. More importantly, the race is now on to develop siRNAs as therapeutic agents and to achieve a level of success in patients that has eluded medicine thus far. In this course, we will discuss in detail the therapeutic potential of RNAi. More generally, we will discuss its discovery, functions in normal biological processes, utility as an experimental tool, potential for therapeutic use, and pursuit by the biotechnology industry.

7.342 Systems and Synthetic Biology: How the Cell Solves Problems

Instructor: Hyun Youk (hyouk@mit.edu, 68-365, laboratory of Alexander van Oudenaarden)

Fall 2010. Wednesdays, 11 am – 1 pm. (Class time is flexible.) Rm 68-151.

A millennial challenge in biology is to decipher how vast arrays of molecular interactions inside the cell work in concert to produce a cellular function. Systems biology, a new interdisciplinary field of science, brings together biologists and physicists to tackle this grand challenge through quantitative experiments and models. Molecular biology has provided us with a detailed understanding of the components that make up a cell – including the wealth of genes, RNAs, proteins and other macromolecules – as well as specific intracellular biochemical interactions. The diversity among species of specific cellular components in the context of broadly conserved chemical classes is one aspect of the beauty and elegance of biology. Systems biology is now revealing another elegant aspect of biology: when all these cellular components are integrated into a network of interactions, we find that there are common themes across a wide spectrum of organisms. There seems to be unifying principles that all organisms use to perform cellular functions. In this course, we will discuss what these principles are. We will begin by considering several early papers in systems biology that identified key challenges faced by a cell in both single and multi-cellular organisms. One such challenge is that many intracellular processes, such as production of specific proteins and RNA molecules, are stochastic in nature. In other words, even within a population of cells that are genetically identical and live in the same environment, there can be significant variation from one cell to another in the level of individual gene products. This cell-to-cell variability can lead to stark phenotypic variation within a genetically and environmentally homogeneous population of cells. We will discuss how the network of genes in a cell is wired to control for the amount of noise and even take advantage of cell-to-cell variability for survival. Another challenge that a cell has to meet is reliably measuring how many key molecules are present in its surrounding environment so that it can respond appropriately. We will discuss papers that revealed that there is an ultimate limit to how accurately cells can ”count” the number of extracellular molecules. We will then discuss how cells, from

those in a bacterium to those in the embryo of a fruit fly, meet this challenge. Finally, we will discuss how researchers in the field of synthetic biology are using the new knowledge gained from studying naturally-occurring biological systems to create artificial gene networks capable of performing new functions.

7.343 Vascular Development in Life, Disease and Cancer Medicine
Instructor: Alexandra Naba (anaba@mit.edu, 2-2769; laboratory of Richard Hynes)
Christopher Turner (turnercj@mit.edu, 3-6409; laboratory of Richard Hynes)
Fall 2010. Wednesdays, 1-3 pm. (Class time flexible.) Room 68-151.

The growth of blood vessels, a process known as angiogenesis, is one of the earliest events in mammalian development and is regulated by a sensitive interplay of growth factors and other molecules. Abnormal or excessive angiogenesis occurs in diseases that include cancer, diabetes and atherosclerosis, whereas insufficient angiogenesis or vessel regression can lead to Alzheimer's disease, ischemic heart disease and impaired wound healing. For this reason, more than $4 billion dollars has been invested in research and development to identify medicines that either promote or reduce the growth of new blood vessels, making angiogenesis one of the most exciting and heavily funded research areas in biomedicine today. In this course, we will discuss the key molecular regulators of blood vessel development as well as the techniques and experimental systems that have been utilized by vascular biologists. Emphasis will be given to the recent progress made in the microscopic visualization of blood vessels and live cell and intravital imaging used for diagnosis in the clinic. We will also examine the success of several anti-angiogenic treatments that inhibit the pro-angiogenic vascular endothelial growth factor VEGF, that have been approved by the Food and Drug Administration (FDA), and that are now being used to treat age-related macular degeneration. Finally, we will explore how during the course of cancer progression, establishment of a blood supply into a tumor can lead to the growth and spread of cancer cells to secondary sites. We will discuss the caveats and potential pitfalls of targeting tumor blood vessels to starve cancer cells and prevent the spread of cancer, which remains one of the leading causes of death in the U.S.A.

7.344 *p53:* How the Guardian of our Genome Prevents Cancer
Instructor: Wen Xue (wxue@mit.edu; 617-452-3821; laboratory of Tyler Jacks)
Fall 2010. Wednesday 3 - 5 pm. (Class time is flexible.) Room 68-151.

Cancer is a leading cause of death worldwide. Cancer involves uncontrolled cell growth, resistance to cell death, failure to differentiate into a particular cell type and increased cellular motility. A family of gate-keeper genes, known as tumor suppressor genes, plays important roles in preventing the initiation and progression of cancer. Among these, p53 is the most famous. More than 50% of human cancers harbor mutations in or deletion of p53. p53 is induced by upstream signals, such as DNA damage and hyperactive cell-growth signals. The p53 protein, functioning as a transcription factor, binds to the promoters of many target genes involved in the cell cycle, programmed cell death (apoptosis) and DNA repair. Because of its essential role in maintaining genomic

integrity, p53 is often called the guardian of the genome. During this course, we will study how p53 serves as a pivotal tumor suppressor gene in preventing cancer. We will examine the discovery of the p53 protein, the spectrum of p53 mutations in human cancer and the role of p53 as a transcription factor. The function of p53 in DNA damage, cell death, cell cycle regulation and genome integrity will be discussed. We will also consider some recent studies of p53 mutant mouse models and the regulation by p53 of small RNA expression. We will discuss how future cancer treatments might be achieved by therapies that restore p53 function to tumor cells.

7.345 Survival in Extreme Conditions: The Bacterial Stress Response

Instructor: Celeste Peterson (cnpeterso@gmail.com, 8-8684; laboratory of Michael Laub)

Fall 2010. Thursdays, 11 am - 1 pm. (Class time is flexible.) Room 68-151.

Bacteria survive in almost all environments on Earth, including some considered extremely harsh. From the steaming hot springs of Yellowstone to the frozen tundra of the arctic to the barren deserts of Chile, microbes have been found, often thriving. Their tenacity to survive in such extreme and varied conditions allows them to play fundamental roles in global nutrient cycling. Microbes also cause a wide range of human diseases and can survive inhospitable conditions found in the human body. In this course, we will examine the molecular systems that bacteria use to adapt to changes in their environment. What types of signal transduction pathways do bacteria use to monitor their surroundings? How do they activate the appropriate cellular response? Model systems such as the bacteria *E. coli* and *B. subtilis* have been the tools for discovering many key concepts, and the first part of the course will address how these organisms execute their responses to changes in their environment. We will consider stresses typically encountered, such as starvation, oxidative stress and heat shock, with some focus on how the adaptive responses affect the evolution of the bacteria. We will also examine how different signals integrate into signal transduction pathways to determine whether the bacteria will deal with one specific stress or enter a more general dormant state and "batten down the hatches" until conditions improve. The second portion of the course will address the far-reaching clinical and industrial applications of the stress responses of environmentally and medically relevant organisms. How do bacteria cope with toxic metal stresses caused by pollution? How does mounting a general stress response affect antimicrobial drug activity? How is the course of virulence in human disease affected by the stress response? We will gain an appreciation of the power of bacterial genetics and how our detailed understanding of the microbial stress response is key to our ability to control bacteria in the wild and in disease.

7.346 Stem Cells: A cure or disease?

Instructors: Grant Welstead (welstead@wi.mit.edu, 8-5205; laboratory of Rudolf Jaenisch)
Steve Bilodeau (bilodeau@wi.mit.edu , 8-5236; laboratory of Richard Young)

Fall 2010, Thursdays, 1-3 pm. (Class day and time is flexible.) Room 68-151.

Have you ever considered going to a pharmacy to order some new cardiomyocytes (heart muscle cells) for your ailing heart? It might sound crazy, but recent developments in stem cell science have made this concept not so futuristic. In this course, we will explore the underlying biology behind the idea of using stem cells to treat disease, specifically analyzing the mechanisms that enable a single genome to encode multiple cell states ranging from neurons to fibroblasts to T cells. We will study new developments in the area of cellular reprogramming and transdifferentiation and highlight how we have gained the power to control cell states in a Petri dish. Specifically, this course will not only introduce important biological concepts like pluripotency and epigenetics but also focus on key technologies that are used to study them, such as genome-wide sequencing and transcription-mediated reprogramming. We will also consider the potential consequences and limitations of stem cell therapy, particularly the connection between stem cells and cancer. Overall, we hope to provide a comprehensive overview of this exciting new field of research and its clinical relevance.

7.347 Biological Networks: What Can Networks Teach Us about Biology?

Instructors: Igor Ulitsky (ulitskyi@gmail.com, 8-5990; laboratory of David Bartel)
Muhammed Yildirim (yildirim@gmail.com, 4-1651; laboratory of David Bartel)

Fall 2010. Thursdays, 3 pm – 5 pm. (Class time is flexible.) Room 68-151.

What do Facebook, the human brain, the electricity grid and transcriptional regulation in the cell have in common? One simple answer is that they can all be represented as networks. In fact, studying the structures and features of these networks can help us understand the principles of all of these complex systems. Although networks from entirely different domains share surprising similarities, biological networks also have their own unique characteristics. Analysis of these networks involves using established techniques from statistics, physics and computer science as well as methods developed specifically for studying systems biology. In this course we will introduce biological networks and how they are studied in the context of general network theory. In addition, we will discover how network-based approaches are advancing various areas of biomedical research. We will begin by presenting the basic principles of network structures. We will then cover many of the basic molecular interaction networks studied in biology, including those of protein-protein interactions, transcriptional regulation, microRNA targeting, genetic interactions, drug-target interactions and others. We will see how these networks are constructed from data, what kinds of models are used to study them and what such models can teach us about the organizational principles of biological systems. Furthermore, we will discuss specific questions that can be answered by understanding networks: what is the best way to perturb a biological network to escape from a disease? what does the position of a gene in a network tell us about its function? how can we use networks to identify drugs that share a mode of action? The course will not require any expert knowledge in biology, computer science or statistics and is open to students from any relevant department.

7.348 Biology of Aging and Age-Related Diseases

Instructors: Michael S. Bonkowski (mbonkows@mit.edu, 3-4768, laboratory of Lenny Guarente)
Sergiy Libert (libert@mit.edu, 3-4768, laboratory of Lenny Guarente)

Fall 2010. Fridays, 11 am – 1 pm. (Class time is flexible.) Room 68-151.

Aging is a familiar yet mysterious aspect of human biology. Why are older people so much more likely to experience diseases like osteoporosis, stroke, and neurodegenerative disorders? Is aging itself a disease? What changes happen at the molecular and cellular levels to cause the changes that we associate with old age? Can changing the nutrient balance of the human diet extend lifespan and diminish negative features of the aging process? The specific molecular causes of aging remain poorly defined. Common laboratory organisms such as yeast, the roundworm *C. elegans*, and mice undergo aging, and scientists have studied these organisms to try to unlock the mysteries of the aging process. For all of these organisms, mutations have been identified that slow aging, allowing the organism to live up to ten times as long as normal. The finding that aging can be controlled by individual genes has led to the exciting idea that drugs might be developed to intervene with the actions of such genes, slow the aging process and delay the onset of the diseases of aging in humans. In this course, we will explore the scientific discoveries that have led to various theories of the molecular basis of aging. We will study the shared genetic pathways that control lifespan in organisms as different from each other as yeast and mice. We will also discuss the first tests of drugs such as resveratrol, a small molecule found in red wine, which might target aging pathways in mammals. We will participate in a field trip to a meeting of the Boston Area Aging Data Club, where we will meet the authors of some of the papers that we have covered in class and hear a presentation by a researcher actively working on a hot topic in the aging field.

Spring 2011

7.340 Antibiotics, Toxins, and Protein Engineering: Science at the Interface of Biology, Chemistry, Bioengineering, and Medicine

Instructor: Caroline Koehrer (koehrer@mit.edu, 3-1870; laboratory of Uttam L. RajBhandary)

Spring 2011. Monday, 1 – 3 pm. (Day and time are flexible.) Room 68-151.

The discovery of penicillin in the 1930s ushered in a new era in modern medicine and paved the way for the development of various antibiotics against disease-causing microbes. After decades of widespread use, however, many antibiotics are not as effective as they used to be. Resistance to commonly used antibiotics and the surfacing of multidrug-resistant microbes – so called *superbugs* – have become major clinical problems. Today, the Centers for Disease Control and Prevention call antibiotic resistance "one of the world's most pressing public health problems." Did you know that many of the commonly used antibiotics – such as tetracyclines, aminoglycosides and

macrolides – specifically target the cell's translational apparatus and disrupt protein synthesis? In this course, we will discuss the structure and function of the ribosome and look into the most basic concepts of protein synthesis. We will explore the mechanisms of action of antibiotics and toxins targeting the translational machinery, their roles in everyday medicine, and the emergence and spread of drug resistance. We will also discuss the identification of new drug targets and how we can manipulate the cell's protein synthesis machinery to provide powerful tools for protein engineering and potential new treatments for patients with devastating diseases, such as cystic fibrosis and muscular dystrophy.

7.341 Bench to Bedside: Molecularly Targeted Therapies in Blood Disorders and Malignancy

Instructors: Bill Wong (pwong@wi.mit.edu, 650-799-8364; laboratory of Harvey Lodish)

Spring 2011. Wednesdays, 3 – 5 pm. (Class time is flexible.) Room 68-151.

How are new drugs and treatments discovered? This course will take you from the discoveries of basic research to the customized design of drugs for treating patients with specific deadly blood disorders. Students will experience the scientific journey from the rationale of the scientists who started basic research projects to the clinicians who designed the trials to test the safety and efficacy of prospective drugs. We will consider the scientific discoveries that led to development of Gleevec, which is often referred as a miracle drug or silver bullet for a specific leukemia, chronic myelogenous leukemiz. Gleevec was developed based on the principle of molecularly targeting an aberrant kinase activity encoded by an oncogene and in this way killing leukemia cells while leaving normal cells alone. The following topics will be discussed: (1) identification of a bcr-abl chromosomal translocation and demonstration that this translocation generates an abnormal kinase activity that causes leukemia, (2) drug design and efficacy and toxicity testing in mice and humans, (3) mechanisms of drug resistance and finally, (4) uses of Gleevec in other diseases that also abnormally express the oncogenic abl kinase. We will also discuss other topics that demonstrate the process from "bench to bedside," such as stem cell and gene therapy, the design of drugs based on RNA interference, and the reprogramming of somatic cells into stem cells for regenerative medicine.

7.342 Powerhouse Rules: The Role of Mitochondria in Human Diseases

Instructor: Dan Ferullo (ferullo@mit.edu, 3-3745; laboratory of Graham Walker)

Spring 2011. Wednesdays, 11 am – 1 pm. (Class time flexible.) Room 68-151.

Exactly how important is the mitochondrion, the "power house" of the cell? Once a bacterial symbiote, the mitochondrion is an organelle that provides unique functions to nucleated eukaryotic cells. Specifically, mitochondria produce the majority of cellular ATP, support aerobic respiration, and are key players in apoptosis (programmed cell death). An interesting feature of a mitochondrion is that it contains its own DNA, a relic of its bacterial ancestor. The mitochondrial genome encodes some but not all of the

proteins crucial for mitochondrial functions. Defects in mitochondrial functions have been found to cause or be associated with a variety of human diseases, including neurodegenerative and neuromuscular disorders and cancer as well as with aging. Accordingly, mitochondria have become attractive targets for developing therapies for disease. In this course, we will discuss the biological roles of mitochondria and how mitochondria malfunction in human disease. We will learn about mitochondrial DNA (mtDNA) and how it is very easily damaged. As such, we will discuss mechanisms that cells use to repair damaged mtDNA. Importantly, we will examine how inadequate repair of mtDNA causes harmful mutations, compromises mitochondrial function, and is deleterious to the cell. We will examine how the problem of faulty mtDNA repair contributes to pathogenesis in disease. We will also discuss how mitochondria are key players in a normal process called "apoptosis" or "programmed cell death" designed to eliminate old or unhealthy cells in a controlled manner. However, mitochondrial defects can lead to improper apoptosis and in this way impact several diseases. Lastly, we will discuss how mitochondria produce reactive oxygen species (ROS), which are potentially damaging molecules that can cause cellular injury when produced at high levels. We will examine how elevated ROS production is caused by faulty mitochondria and is involved in disease and aging. By discussing studies using experimental systems ranging from yeast to human cancer cells, we will learn how defects in mitochondrial functions compromise cellular and organismic health.

7.343 Regenerative Medicine: from Bench to Bedside and Bedside to Bench
Instructor: Petra Simic (psimic@mit.edu, 3-0809; laboratory of Leonard Guarente)
Spring 2011. Wednesdays, 1 pm – 3 pm. (Class time is flexible.) Room 68-151.

Regenerative medicine involves the repair and regeneration of tissues for therapeutic purposes, such as replacing bone marrow in leukemia, cartilage in osteoarthritis or cells of the heart after a heart attack. Tissue regeneration has been of interest throughout history. There is even a Greek myth that describes liver regeneration: Prometheus was chained to a mountain, and his liver was eaten daily by an eagle, regenerated and then eaten again the next day. Today advances in basic and clinical research make tissue regeneration feasible. Tissue is normally generated during fetal development by the differentiation of embryonic stem cells or during postnatal life by a similar differentiation of adult stem cells. Regenerative medicine tries to mimic these processes. In this course, we will explore basic mechanisms of how cells differentiate into specific tissues in response to a variety of biologic signaling molecules. We will discuss the use of such factors for *in vitro* tissue production. For example, bone morphogenetic proteins can be used *in vitro* to drive the differentiation of adult stem cells towards bone and heart. We will also study the cellular mechanisms involved in the cloning of animals and how Scottish researchers produced the sheep Dolly using the nucleus of a mammary gland cell from an adult sheep. We will read papers describing organ production, such as the *in vitro* formation of beating heart cells. We will also consider the molecular bases of cellular and functional changes of different organs that occur in disease and treatments that cause tissue remodeling to correct these changes. We will discuss how studies of the developmental, cellular and molecular biology of regeneration have led to the discovery

of new drugs. We will visit the Massachusetts General Hospital to see the patients with regenerated tissues.

7.344 Taking Snapshots of Protein Complexes in Action

Instructor: Nozomi Ando (nando@mit.edu, 617-715-4891; laboratory of Catherine Drennan)
Edward Brignole (brignole@mit.edu, 617-715-4891; laboratory of Catherine Drennan)

Spring 2011. Wednesdays 3-5 pm. (Class time is flexible.) Room 68-151.

In 1958, John Kendrew and his co-workers used X-ray crystallography to solve the world's first structure of a protein at atomic resolution. This technological breakthrough was one of the defining moments in modern biology. Today, structure determination is an integral part of biology. More than 66,000 structures have been solved to date, allowing us to understand the chemistry, folding, and binding of proteins and other biomacromolecules. Inside a cell, however, many thousands of different proteins are working on a vast array of functions through their interactions with each other. So, now that we know what many proteins look like, how can we visualize them at work? Some protein complexes are too large and complicated to be easily crystallized, and some protein interactions are too weak or dynamic to be properly captured by crystallography. In this course, we will discuss the usage of two structural techniques, small-angle X-ray scattering (SAXS) and electron microscopy (EM), that help to fill the gap between atomic-level structure determination and cellular-level imaging. We will discuss the history of the now standard methods of biological structure determination, with emphasis on how SAXS and EM have been used to visualize complicated protein complexes such as viruses, DNA replication and repair machinery, and metabolic enzymes and how they have contributed to a dynamic view of the protein structure-function relationship. Students will learn about exciting protein structure-function research and current technologies used in this field.

7.345 Cancer and Its (Micro)environment – from Basic Science to Therapy

Instructors: Julia Rastelli (rastelli@wi.mit.edu, 8-5173; laboratory of Bob Weinberg)
Asaf Spiegel (spiegel@wi.mit.edu, 8-5173; laboratory of Bob Weinberg)

Spring 2011. Tuesdays, 2-4 pm. (Class time is flexible.) Room 68-151.

Despite major advances in cancer research, the treatment of most cancers remains insufficient, rendering the disease a leading cause of death in the western world. Tumors are complex tissues that consist not only of malignant cells but also of a variety of non-malignant stromal cells, such as blood vessel cells, immune cells, and fibroblasts. What is the role of stromal cells in the tumor, and what is the normal physiological role of such cells in the human body? Where do stromal cells come from, and what triggers their recruitment into tumors? How do stromal cells affect the fundamental steps of tumor progression, such as angiogenesis (blood vessel formation) and metastasis (spreading of tumor cells to distant tissues)? In this course we will discuss and critically evaluate

scientific papers that attempt to answer these questions in one of the most exciting and rapidly evolving fields in cancer research – the tumor (micro)environment. We will also discuss how non-malignant tumor cells might be used as new targets for cancer therapy as a complement to conventional therapy based on targeting only the malignant cells.

7.346 Metastasis: The Deadly Spread of Cancer

Instructors: John Lamar (lamarj@mit.edu, 452-2769; laboratory of Richard Hynes)
Amy McMahon (mcmahona@mit.edu, 452-2769; laboratory of Richard Hynes)

Spring 2011. Thursdays, 1-3 pm. (Class time is flexible.) Room 68-151.

Cancer is a devastating disease that kills millions of people every year. Greater then 90% of these deaths result from metastasis, the spread of cancerous cells from the initial tumor to other organs in the body. Metastasis is a complex cascade involving several essential cellular processes, including migration, invasion, intravasation and extravasation (entering and exiting the bloodstream, respectively), survival, and growth. It is still unclear what is occurring at the molecular level inside tumor cells to promote cancer progression, making metastasis an important area of research in cancer biology. In this course we will discuss current theories about how cancer cells gain the ability to metastasize as well as how several of the critical processes involved in metastatic dissemination are regulated at a cellular level. We will investigate how metastasis can be influenced by the interaction of tumor cells with other cells in the body, including non-malignant cells present in the tumor, the bloodstream, and distant organs to which tumor cells metastasize. We will learn about existing therapies that target metastatic dissemination and explore how new therapies could be designed to target the processes and interactions discussed throughout the course. We will visit a research facility and have the optional opportunity to attend research seminars presented by prominent scientists in the field.

7.347 Fueling Sustainability: Engineering Microbial Systems for Biofuel Production

Instructor: Michelle O'Malley (momalley@mit.edu, 3-9838; laboratory of Chris Kaiser)

Spring 2011. Thursdays, 3 pm – 5 pm. (Class time is flexible.) Room 68-151.

The need to identify sustainable forms of energy as an alternative to our dependence on depleting worldwide oil reserves is one of the grand challenges of our time. The energy from the sun converted into plant biomass is the most promising renewable resource available to humanity. Almost all of this energy is contained within cellulose, the natural yet difficult to digest polymer of sugars that make up plant cell walls. How can we unlock the energy within cellulose and convert it to more useful forms of energy? Fortunately, nature has evolved several enzymes that work together to break down cellulose. These enzymes are found within bacteria and fungi that thrive in cellulose-rich environments (*e.g.*, the digestive tracts of grazing animals, compost piles, and soil).

Sugars released from cellulose hydrolysis can later be fermented into biofuels like ethanol. We will examine each of the critical steps along the pathway towards the conversion of plant biomass into ethanol. We will focus on the biology behind enzymatic cellulose breakdown, the different types of enzymes required, and how these enzymes form complexes in nature that improve their catalytic performance. State-of-the-art methods currently in use to identify new cellulolytic enzymes with novel properties as well as metabolic engineering strategies to introduce these enzymes into yeast will be discussed. We will further examine issues associated with industrial-scale production and catalytic performance of cellulolytic enzymes; such issues have limited the economic feasibility of cellulosic biofuels. By the end of the course, students will have a broader knowledge regarding the biology behind cellulose breakdown, the challenges associated with industrial biofuel production, and new opportunities to further its development.

7.348 Bacterial Communities: Group Behavior through Chemical Signals

Instructors: Carla Bonilla (cbonilla@mit.edu, 3-6702; laboratory of Alan Grossman)
Houra Merrikh (merrikh@mit.edu, 3-6702; laboratory of Alan Grossman)

Spring 2011. Fridays ,11 - 1 pm. (Class time is flexible.) Room 68-151.

Bacteria are everywhere, living in the soil, the oceans and on and in our bodies. Bacteria help us stay healthy by aiding us in nutrient absorption and vitamin production as well as by guarding our bodies against virulent species. But bacteria can also threaten our health by causing deadly infections. Although they are single-celled organisms, much of what bacteria do, "good" or "bad," originates from their ability to perform complex communal behaviors that allow them to act as multicellular entities. How can such single-celled organisms function in multicellular communities? How do bacteria "talk" to each other? In this course, we will learn about conserved chemical languages that bacteria use to communicate with other bacteria of the same or different species. We will study group behaviors of bacteria, including the roles of such group behaviors in allowing bacteria to colonize a host, to defend themselves from predatory bacterial species or from antibiotics, and simply to live in harmony in large multicellular communities, such as in biofilms. We will learn about the chemical signals used by different bacteria, including certain pathogenic species, such as *Pseudomonas aeruginosa* and *Vibrio cholera*, and how these signals are sensed and interpreted through different genetic and molecular pathways. Understanding the language that bacteria use to communicate is important not only as a basic aspect of the extensive microbial world but also because of implications for developing new treatments for infections caused by pathogenic bacteria. Current antibiotics kill bacteria directly and consequently select for resistant individuals. With drugs designed to silence bacterial communication, on the other hand, there is no selective pressure to survive, and therefore such treatments might offer a way to circumvent the development of drug resistance, a major clinical problem today.