August 19, 2008

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 2008-2009 academic year: a set of seven very current seminar courses, 7.341-7.347, 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, systems biology, neurobiology, aging, biotechnology, protein engineering 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 2008 and Spring 2000 semesters, please check our website (http://mit.edu/biology/www/undergrad/adv-ugsem.html) and/or contact the instructors.

Advanced Undergraduate Seminars
2008-2009

Fall 2008

7.341 New Ammunition for the War Against Cancer: Personalized Therapeutic Regimens based on Defective DNA Damage Signaling in Tumors

Instructor: C. Reinhardt (reinharc@mit.edu, 2-2443; Labs of M. Yaffe and T. Jacks)
Fall 2008. Wednesdays, 3 pm - 5 pm. (Class time is flexible.) Room 68-151.

Prerequisites:
The prerequisites for this course are 7.03, 7.05, 7.06, or 7.28. Grading: Pass/Fail.

Course summary:
In 1971, President Nixon declared the "War on Cancer". Over recent years we have seen the development of new armament for this war - treatment strategies that are based on unique characteristics of tumor cells. Increased mutation propensity is a hallmark of cancer and an increasing number of genes involved in the DNA damage response and DNA repair have been found mutated or inactivated in human cancers, thus underlining the importance of an intact DNA damage response as a critical anti-cancer barrier. Cellular responses to DNA damage constitute one of the most important fields in cancer biology. Exciting work in this area has taught us important lessons, such as: DNA damage can cause cancer; paradoxically, the induction of DNA damage is also the mechanism of action of many currently used anti-cancer therapeutics, such as radiation and chemotherapy; and DNA damage of normal tissues is responsible for most of the side effects of cancer therapy, such as hair loss. In this class we will analyze classical and recent papers from the primary research literature to gain a profound understanding of cell cycle regulation and DNA damage checkpoints that act to prevent cancer. We will consider basic principles of cell proliferation and molecular details of the DNA damage response, and we will discuss the methods and model organisms typically used in this field. Building on this foundation we will address new concepts in the treatment of cancer and discuss how these concepts are based on and exploit characteristic differences in the DNA damage response between normal cells and cancer cells. While mutations in genes involved in cell cycle control and the DNA damage response allow the runaway proliferation of incipient cancer cells, such genetic defects can also be seen as the "Achilles heel" of cancer. We will consider the emergence of therapeutic regimens that are guided by a spectrum of characteristic mutations that differ among individual patients – paving the way for personalized anti-cancer therapy. This course will not stop at discussing the literature. We will go one step further by gathering and analyzing real data in an MIT Cancer Biology laboratory. Refreshments will be provided.

7.342 Systems Biology: Stochastic Processes and Biological Robustness
Instructors: Jeff Gore (gore@mit.edu; 68-365; laboratory of Alex van Oudenaarden)
Arjun Raj (arjunraj@mit.edu; 68-365; laboratory of Alex van Oudenaarden)
Fall 2008. Thursdays, 1 pm – 3 pm. (Class time is flexible.) Room 68-151.

Molecular biology has been extremely successful in deciphering the details of specific cellular biochemical interactions, such as those that control inter- and intracellular signaling and gene expression. However, a full understanding of cellular function will require an understanding of how all of these interactions work together in a network to perform particular tasks. Such an understanding is the goal of the new field of systems biology. In this seminar, we will discuss some of the main themes that have arisen in this field, including the concepts of robustness, stochastic cell-to-cell variability and the evolution of molecular interactions within complex networks. Robustness is a property of many natural biological networks whereby the behavior of the network is insensitive to variations in the numbers of inputs and the strengths of interactions. One classic example is bacterial chemotaxis, in which the bacterial food sensing mechanism is insensitive to perturbations in the levels of key proteins. This insensitivity to variations is particularly important given recent work demonstrating that gene expression has a strongly random component, leading to large variations from cell to cell even in genetically identical populations. In certain networks, this "gene expression noise" can lead to intrinsically random divergence in developmental fates. We will also discuss networks in a more global context, considering the structure and evolutionary dynamics of networks in whole organisms. Finally, we will study how researchers in the field of synthetic biology are using such new knowledge about biological networks to create artificial gene networks capable of performing new functions. Examples range from simple genetic switches and oscillators to the transplantation of entire networks capable of producing drugs, biofuels, and synthetic materials.

7.343 Molecular Biology of Aging and Age-related Diseases
Instructors: Sergiy Libert (libert@mit.edu, 3-4786; laboratory of Leonard Guarente)
Gizem Donmez (gdonmez@mit.edu; 3-0809; laboratory of Leonard Guarente)
Fall 2008. Thursdays, 11 am – 1 pm. (Class time is flexible.) Room 68-151.

Over time, most organisms deteriorate and die in the process called biological aging. The desire of humanity to conquer this process and slow down or reverse aging is depicted in the oldest manuscripts available. The biological basis of aging is now being attacked using modern biological knowledge and sophisticated genetic and molecular tools. It is widely recognized that longevity is genetically controlled. Mouse lifespan is slightly longer than 2 years, the dog has a lifespan of about 15 years, humans about 80 years and some whales can easily reach the 200-year mark. There are also substantial variations within species. Some people look "very old" at the age of 50, while others are still quite energetic and youthful after 85. Scientists have generated a number of mutant and transgenic animals that have extended or shortened lifespans. Many genes that modify lifespan have been identified, and genetic pathways that govern longevity had been defined. What genes control aging, and how do these genes and their products work? In this course, we will discuss the advances that have been made in the field of the biology of aging. We will cover what is known about molecular genetic pathways that govern the rate of aging and longevity. We also will analyze interventions proposed to slow aging or at least delay the onset and severity of age-related diseases.

Spring 2009

7.344 Directed Evolution: Engineering Biocatalysts
Instructor: Kerry Love (kerryluv@mit.edu; 4-0727; Laboratory of Hidde Ploegh)
Spring 2009. Thursdays, 11 am – 1 pm. (Class time is flexible.) Room 68-151.

Enzymes, nature's catalysts, are remarkable biomolecules capable of extraordinary specificity and selectivity. These characteristics have made enzymes particularly attractive as an alternative to conventional catalysts in numerous industrial processes. Oftentimes, however, the properties of an enzyme do not meet the criteria of the application of interest. While biological evolution of an enzyme's properties can take several million years, directed evolution in the laboratory is a powerful and rapid alternative for tailoring enzymes for a particular purpose. Directed evolution has been used to produce enzymes with many unique properties, including altered substrate specificity, thermal stability, organic solvent resistance and enantioselectivity – selectivity of one stereoisomer over another. One example is the improvement of the catalytic efficiency of glutaryl acylase, an important enzyme in the manufacturing of semi-synthetic penicillin and cephalosporin. The technique of directed evolution comprises two essential steps: mutagenesis of the gene encoding the enzyme to produce a library of variants, and selection of a particular variant based on its desirable catalytic properties. In this course, we will examine what kinds of enzymes are worth evolving and the strategies used for library generation and enzyme selection. We will focus on those enzymes that are used in the synthesis of drugs and in biotechnological applications.

7.345 Antibiotics, Toxins, and Protein Engineering
Instructors: Caroline Koehrer (koehrer@mit.edu, 3-1870; laboratory of Uttam RajBhandary)
Mandana Sassanfar (mandana@mit.edu, 452-4371; Education Office)
Spring 2009. Thursday, 1 – 3 pm. (Class time is flexible.) Room 68-151.

The lethal poison Ricin, best known as a weapon of bioterrorism; *Diphtheria* toxin, the causative agent of a highly contagious bacterial disease; and the widely used antibiotic tetracycline have one thing in common: they all specifically target the cell's translational apparatus and disrupt protein synthesis. In this course, we will explore the mechanisms of action of toxins and antibiotics, 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 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.

7.346 Cancer Development, Progression and Metastasis – Is There a Cure in Sight?
Instructors: Christine Chaffer (chaffer@wi.mit.edu, 8-5715; Laboratory of Bob Weinberg)
Christina Scheel (scheel@wi.mit.edu, 8-5176; Laboratory of Bob Weinberg)
Spring 2009. Tuesdays, 3-5 pm. (Class time is flexible.) Room 68-151.

Despite decades of concentrated research effort, cancer remains one of the leading causes of death in the Western world. Generic agents, such as chemotherapeutics that target and kill proliferating cells, are still the most effective treatment for cancer patients. In the case of relapse, however, cancer cells usually become resistant to chemotherapy. To date, even with new targeted therapeutic approaches, advanced forms of the disease are generally incurable. Is there a cure in sight? Why does successful cancer therapy remain elusive? The answers lie, in part, in the remarkable complexity and diversity of the disease.
In this course, while learning to critically evaluate the primary research literature, we will discuss the fundamentals and latest discoveries in cancer research to gain an understanding of the hallmarks of cancer development and progression. We will explore the diversity in biological properties between and within cancer subtypes. We will discover that multiple mechanisms are involved in the transition from early-stage disease, usually consisting of discrete tumors, to late-stage disease in which the cancer cells have spread to distant organs. The course will provide an overview of the current field of cancer biology, with analyses of the latest experimental techniques and disease models, and will introduce some of the most exciting and promising research areas of the field.

7.347 From Molecules to Behavior: Cell Biology of the Synapse
Instructors: Alex Chubykin (chubykin@mit.edu; 46-3301; laboratory of Mark Bear)
Jason Shepherd (jshephe@mit.edu; 46-3301; laboratory of Mark Bear)
Spring 2009. Wednesdays, 1 pm - 3 pm. (Class time is flexible.) Room 68-151.

The brain has an amazing capacity to store, retrieve and use information about past experiences. Understanding the mechanisms that underlie information storage in the brain spans many disciplines in neuroscience, from molecules to behavior. Neurons and their connections, known as synapses, are the fundamental units of information storage and processing in the brain. This course will introduce students to current cutting-edge research concerning the cell biology of neurons and synapses. The course will span many aspects of synaptic transmission, development and plasticity. Specific topics will include: (1) the molecular mechanisms of synapse formation during development and how abnormalities in synapse formation can result in cognitive disorders, such as autism and mental retardation; (2) the molecular mechanisms that regulate the functions of neurotransmitter receptors; (3) the physiology of synaptic transmission, including the generation and propagation of action potentials; (4) mechanisms of synaptic plasticity and the relationship of synaptic plasticity to learning and memory; and (5) how synaptic function is affected in neurological disorders, using Alzheimer's Disease as an example. We will discuss the latest tools that neuroscientists use to study synapses, including optical and genetic manipulations of synaptic transmission. The course will rely on reading and analyzing original research papers from the scientific literature and will involve small discussion groups. Students will learn how experiments are designed, how data are obtained and how scientists evaluate and interpret these data.