Advanced Undergraduate Seminars
Spring 2019

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7.341 How DNA's Sister Does All the Work: The Central Roles of RNA in Gene Expression

Instructors: Ana Fiszbein (anafisz@mit.edu, 617-749-8096, laboratory of Chris Burge)
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Spring 2019. Wednesdays, 11 am -1 pm. (Class day and time flexible.) Room 68-150.

While most cells in the body have exactly the same DNA, cells differ drastically in how they use their DNA. RNA, which is transcribed from DNA, is front and center of this specificity of expression and regulation of genetic information. This course will explore the frontiers of the world of RNA biology using primary research papers to trace how the original odd detail sometimes led to major discoveries. We will discuss exciting discoveries about the unexpected diversity of RNA classes and the mechanisms by which they are generated and exert their function. For example, while DNA base-pairing is mainly used to replicate genetic information, RNAs employ base-pairing for a wider array of functions, including specific binding to other RNAs. We will first review and update our knowledge about the historically best characterized RNAs: messenger RNA (mRNA), transfer RNA and ribosomal RNA, which together employ base-pairing to read the genetic code and synthesize proteins. In many organisms mRNAs undergo a processing step called splicing, which allows for many alternative variant messages to be made from the same gene and explains how the human body can make over 100.000 proteins from only 20.000 genes. Splicing defects are involved in a broad variety of human disorders. We will then turn to more recently discovered small non-coding RNAs, such as microRNAs, siRNAs, and piRNAs, which regulate the functions of other genes and can change cell fates during development. Finally, we will discuss RNA species about which we still know very little, such as long non-coding RNAs and circular RNAs. Some long non-coding RNAs associate with chromatin, thereby altering the expression of other genes or bringing together different chromosomes in the nucleus. Circular RNAs are unexpected products of splicing that have no ends and are therefore very stable compared to other RNAs. Many circular RNAs might simply be by-products, but some exist in surprisingly large quantities and can alter regulation by microRNAs or RNA-binding proteins, in one case with very specific consequences on behavior. Also, some circular RNAs have the capacity to be translated and make small proteins, adding to the already vast protein diversity enabled by alternative splicing. As we discuss the exciting diversity of RNA functions and marvel at the wonders of RNA, we will critically analyze both landmark and very recent primary research papers. We will visit the biotechnology company Moderna Therapeutics, which develops artificial mRNAs that can be administered to patients as a drug to substitute missing mRNAs or activate genetic programs that are needed for recovery from injuries.

7.342 Cellular Organelles in Health and Disease

Instructors: Nora Kory (617-840-5206, nkory@wi.mit.edu, laboratory of David Sabatini)
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Spring 2019. Wednesdays 1 pm- 3 pm. (Day and class time are flexible.) Room 68-180.

The cell is the basic functional unit of life. Cells perform their diverse functions through a versatile series of biochemical reactions that require different chemical and physical environments. In eukaryotic cells, a complex compartmentalized system consisting of membrane-bound organelles allows these reactions to occur under optimal conditions and prevents accumulation of harmful metabolic intermediates in the wrong places. Additionally, these organelles are sites of signaling and metabolic regulation that enables cells to survive and perform their specialized functions in the body. In this course, we will explore the primary scientific literature to learn about different organelles, including the nucleus, endoplasmic reticulum, mitochondrion, lysosome, peroxisome and the Golgi, in addition to the new emerging field of phase-separated compartments. We will study the biogenesis, biology, and specialized functions of organelles in different organs and tissues, like the function of mitochondria in powering muscle function in some types of muscle but not in others. We will also learn about human diseases that are caused by organelle dysfunction, e.g., storage diseases caused by mutations in lysosomal genes and congenital metabolic disorders in children with mitochondrial gene mutations. We will learn about the biochemical, molecular and cell biological techniques that scientists (including ourselves) use to study cellular organelles. While discussing these multiple aspects of organelle biology, we will learn about scientific reading

skills and how to critically think about the scientific literature, identify open questions in the field, and articulate ideas in a research plan. We will visit a research laboratory that studies cellular organelles to see how experiments we discuss in class are performed in the laboratory.

7.343 The Microbiome and Drug Delivery: Cross-species Communication in Health and Disease
Instructor: Miguel Jimenez (jmiguelj@mit.edu, 949-285-0318, laboratory of Robert Langer)
Spring 2019. Thursdays, 11 pm – 1 pm. (Class day and time are flexible.) Room 68-150.

Are humans superorganisms? There are more microbes permanently living in our gut than there are human cells in our bodies. This rich community of bacteria, fungi and viruses, called the microbiome, plays a central role in human health and disease. Recent research has linked this passenger community to nutrition, circadian rhythms, infectious disease, inflammatory disease, cancer, diabetes, arthritis and even immune system and nervous system development. The connections seem to be so far-reaching that some scientists are starting to consider this human-microbiome system as a "holobiont" or "superorganism." Why are we realizing this situation only now? Are microbes actually interacting with us so fundamentally? What are the mechanisms by which effects of the microbiome are mediated? Could we survive without our microbiome? How can we analyze such a complex system? Can we exploit the microbiome to improve human health? Can interactions with microbes be harnessed for drug delivery? In this course, we will explore the primary scientific literature to find answers to these questions and to learn to critically assess observational and experimental data and distinguish between correlation and causality. We will discuss several of the key signaling molecules that mediate the interactions between humans and their microbiomes, such as human-produced antimicrobial peptides, microbial pheromones, bacterial peptide toxins and neuroactive microbial metabolites. We will learn about recent methods that make possible the analysis of these interactions. We will learn about such cutting-edge technologies as next-generation DNA and RNA sequencing and the use of germ-free mice. In addition, we will discuss how a large reduction in the cost of DNA synthesis is enabling the development of synthetic microbes that can be used to interrogate and manipulate the microbiome. Together these mechanistic insights and emerging tools are transforming microbiome research and might lead to new types of therapeutics and drug delivery for improving human health.