Advanced Undergraduate Seminars

Spring 2026

7.341. Programming Immunity: Bioengineering T Cells to Fight Cancer and Autoimmune Disorders
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Spring 2026. Thursdays, 1 pm – 3 pm. (class day and time are flexible and will be defined based on availability of students and instructor)

How does your body's immune system distinguish friend from foe? What happens when this system errs? How are scientists "reprogramming" cells of the immune system to fight cancer and autoimmune disorders? In this class, we will explore the immune system with particular emphasis on T cells. T cells and B cells are two classes of lymphocytes, white blood cells in the vertebrate immune system. Unlike B cells, which generate antibodies that recognize pathogens in extracellular spaces, T cells specialize in recognizing fragments of foreign proteins presented on the surface of infected or abnormal cells—an ability that allows them to detect threats such as viruses and cancer. This unique function is matched by the extraordinary diversity of T cell receptors (TCRs): through V(D)J recombination – a random gene rearrangement process that occurs in the thymus – T cells can theoretically generate up to 10^{15} unique TCRs, vastly exceeding the total number of T cells in the human body. This intricate developmental process equips the T cell repertoire to recognize a wide array of peptides presented by major histocompatibility complex (MHC) molecules – specialized proteins found on the surface of all nucleated cells and that present internal cellular contents for immune surveillance. We will explore the molecular mechanisms underlying T cell antigen recognition, including the structural basis of TCR-peptide-MHC interactions and the cellular processes governing antigen presentation on the surface of both professional antigen-presenting (APCs) cells and all other nucleated cells. While all nucleated cells can display internal proteins using certain types of MHC molecules, professional APCs – such as dendritic cells, macrophages, and B cells – play a specialized role in initiating immune responses by presenting a broader range of antigens and delivering essential activation signals to T cells. We will explore both classical and emerging methodologies for discovering which antigens T cells recognize. Techniques such as peptide–MHC tetramer staining (used to detect antigen-specific T cells) and genetic library screening using cDNA expression systems will be discussed, along with newer high-throughput approaches. These approaches include genome-wide antigen discovery using barcoded peptide libraries, high-throughput T cell receptor (TCR) sequencing to map the diversity of T cell responses, and machine learning-based computational tools to predict antigens from protein sequence data. We will also explore how the principles of T cell biology can be applied to develop novel clinical approaches. We will discuss recent advances in bioengineering that are enabling researchers to harness and redirect T cell specificity for therapeutic applications in oncology and autoimmune disease. One striking example of a clinical approach involves cancer immunotherapy—treatments that redirect the immune system to eliminate tumors. Among these, chimeric antigen receptor (CAR)-engineered T cell therapies have shown remarkable success. For instance, CAR T cells targeting CD19, a molecule expressed on B cell malignancies, have led to the disappearance of all signs of cancer in up to 90% of pediatric patients with relapsed acute lymphoblastic leukemia (ALL)—a disease once considered nearly untreatable. We will also examine how failures in T cell tolerance—the mechanisms that prevent T cells from attacking the body's own tissues—can lead to autoimmune disease. For example, in Type 1 diabetes, T cells target insulin-producing pancreatic β-cells, leading to their destruction. In multiple sclerosis, T cells mount pathogenic responses against central nervous system (CNS) proteins such as myelin basic protein (MBP), contributing to demyelination and neurodegeneration. Understanding these breakdowns in tolerance provides insight into therapeutic strategies, such as regulatory T cell therapy, which aims to restore immune balance by enhancing the function or number of T cells that suppress inappropriate immune responses. By the end of this course, students will have a foundational understanding of T cell biology, antigen discovery, and immunotherapy development. The course will be discussion-based and center on learning to critically read, evaluate, and debate findings from the primary research literature in immunology and biomedical science more broadly. To connect these insights to real-world applications, we will also examine how companies have translated discoveries from basic research – particularly those involving T cell biology and antigen recognition – into cellular therapeutics for cancer treatment. In this context, we will visit a biotechnology company developing immune-based therapies, to see how research moves from the academic laboratory to drug development and ultimately to the clinic. We will also learn from company scientists about their own career paths and opportunities in the biotechnology and pharmaceutical company world