Dr. Donna Farber

Immune responses occur in diverse anatomical sites, including protective responses to pathogens and dysregulated immune responses in autoimmune and inflammatory diseases. Mechanisms for the control of immune responses in vivo have been identified predominantly in mouse models, while our knowledge of human immune responses derives almost exclusively from studies of peripheral blood. This research program takes a new approach to address key deficiencies in our understanding of human immune responses, by focusing on immunity in human tissue sites. We have established a unique tissue resource involving the acquisition of multiple tissues from organ donors, through a collaboration with the New York Organ Donor Network (NYODN), giving us unprecedented access to all research-consented organ donors in the NY metropolitan area. The quality and quantity ofthe tissues, and our results showing reproducibility of data from diverse donors, has revealed an unprecedented potential of using this unique resource for groundbreaking studies in human immunology. The major goal ofthis research program is to take a novel, whole body approach to define how cells of the lymphoid lineage, are organized, function and adapted to tissue sites in steady state conditions and during an in situ response in intestinal transplantation. We have assembled an outstanding team of top immunologists together with experts in bioinformatics and computational biology to use this unique tissue resource in conjunction with tissues from transplant recipients and employ multiple state-of-the-art approaches to investigate the cells, molecules and pathways involved in targeting immune responses to tissue sites. Project 1 (PI: D.L. Farber) will investigate the generation, diversity and homeostasis of T cell subsets throughout the body; Project 2 (PI: M.J. Shiomchik) will focus on B cell distribution, diversity and selection in tissues; Project 3 (PI: D. Artis) will analyze human innate lymphoid cells and regulation of tissue homeostasis; and Project 4 (P.I.: M. Sykes) will address lymphocyte reconstitution and responses in intestinal transplantation. All projects will obtain tissues and samples from a central human tissues core, and will be supported by an administrative/database management core and a bioinformatics core. The bioinformatics core will be essential for interpreting and coordinating the results from proposed analysis of immune diversity throughout the body, and gene expression analysis of tissue-resident subsets. Results from this research program will provide fundamental insights into human immunity in vivo and alter the way in which we interpret, treat and monitor disease.
