The Pillai laboratory asks questions about the biology of the immune system and susceptibility to disease. Some of these questions are 1) can we manipulate the immune system to treat autoimmunity and cancer and to increase immunological memory? 2) can we understand how genetics and the environment affect lymphoid clones to drive common diseases? and 3) can this latter information be used to better understand and develop new therapies for chronic inflammatory human diseases such as lupus, systemic sclerosis and IgG4-related disease? Our discovery of the role of an enzyme called Btk in the activation of B cells has contributed to the generation of Btk inhibitors that are effective in B cell malignancies and in trials of autoimmunity. One of the pathways we are currently studying suggests new approaches for the treatment of autoimmune disorders. We are also exploring novel ways to strengthen immune responses and enhance helper T cell memory that provide hope for developing more effective personalized immune-system based treatments for cancer.

A novel human T cell subset that drives fibrosis (NIAID Autoimmune Center of Excellence at MGH)

In studies on the immunology of IgG4 related disease and scleroderma, performed in collaboration with John Stone (MGH Rheumatology) and Dinesh Khanna, (U. of Michigan, Rheumatology), we have identified an unusual, clonally expanded and potentially “fibrogenic” human CD4+ effector T cell subset in affected tissues. The differentiation and protective role of these CD4+ CTLs in cancer and chronic viral infections are currently being investigated using chromatin accessibility mapping, DNA methylation studies and single cell RNA-seq approaches.

Studies on murine and human B cell development and activation

We are using a number of single cell transcriptomic, epigenetic and genetic approaches to examine the heterogeneity and development of murine and human B cells, as well as the molecular bases of the processes of T-B collaboration and germinal center formation.

DNA methylation, B cell self-renewal and chronic lymphocytic leukemia

We have long been interested in cell fate decisions in B cell development and in the development of self-renewing B cell subsets. The roles of DNMT3a in B-1a B cell self-renewal and of specific methylation events in chronic lymphocytic leukemia are being investigated.

Dock2 regulates T cell memory and T-B collaboration

We have identified Dock2 as a regulator of the strength of the immune response and the generation of CD8+ and CD4+ T cell memory. This gene also contributes the strength of the germinal center response. The inactivation of
A model for the evolution of CLL.

Epigenetic changes in B-1a B cells

Polyclonal B-1 cell expansion

Monoclonal B lymphocytosis

CLL

Selected Publications:


this gene leads to the clearance of intracellular pathogens and may enhance anti-tumor immunity.