

Shiv Pillai, MD, PhD



Pillai Laboratory

Hugues Allard-Chamard,
MD, PhD
Alice Bertocchi
Jocelyn Farmer, MD, PhD
Kelsey Finn*
Kirsty Hillier, MD
Naoki Kaneko, DDS, PhD
Marshall Karpel*
Jesper Kers MD, PhD
Hang Liu, MD
Vinay Mahajan, MD, PhD
Cory Perugino, DO
Shiv Pillai, MD, PhD
Na Sun
Thomas Xu*
Grace Yuen, PhD

* PhD Candidate

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 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.

Pathogenesis of fibrosis (NIAID Autoimmune Center of Excellence at MGH)

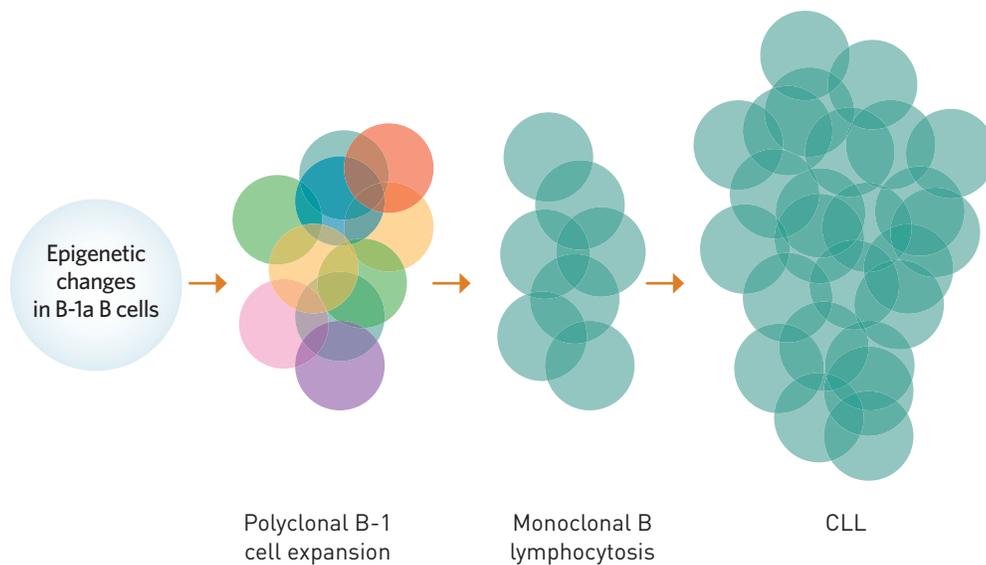
In studies on the immunology of IgG4 related disease and scleroderma, performed in collaboration with John Stone (MGH Rheumatology) and Dinesh Khanna, (U. of Michigan, Rheumatology), we have identified an unusual, clonally expanded and potentially “fibrogenic” human CD4+ effector T cell subset in affected 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. We have also discovered unusual B cell populations that are potentially fibrogenic both in the context of autoimmune fibrotic diseases and pancreatic cancer.

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. The contributions of DNA methylation and demethylation to the biology of CD4+ CTL and T_{FH} cells are also being investigated.



A model for the evolution of CLL.

Studies on Human *CTLA4* mutations and early B cell development

The underlying mechanism for the human B cell developmental defect in individuals with *CTLA4* mutations has been studied helping us to better understand how regulatory T cells can influence early B cell development and humoral autoimmunity.

Selected Publications:

Della-Torre E, Rigamonti E, Perugino C, Sain SB, Sun N, Maehara T, Kaneko N, Rovati L, Lanzillota M, Mahajan V, Mattoo H, Molineris I, Deshpande V, Stone JH, Falconi F, Manfredi AA and Pillai S. B lymphocytes directly contribute to fibrosis in IgG4-related disease. *Journal of Allergy and Clinical Immunology*. 2019 Jul 15. pii: S0091-6749(19)30936-4.

Perugino C, AlSalem SB, Mattoo H, Della-Torre E, Mahajan VS, Ganesh G, Allard-Chamard H, Wallace Z, Montesi MB, Kreuzer J, Haas W, Stone JH, Pillai S. Identification of Galectin-3 as an auto-antigen in IgG4 related-disease. *Journal of Allergy and Clinical Immunology* 2019 143, 736-745.

Maehara T, Mattoo H, Mahajan VS, Murphy SJH, Yuen GJ, Ishiguro N, Ohta M, Moriyama M, Saeki T, Yamamoto H, Yamauchi M, Dac-cache J, Kiyoshima T, Nakamura S, Stone JH and Pillai S. The expansion in lymphoid organs of IL-4+ BATF+ T follicular helper cells is linked to IgG4 class switching in vivo. *Life Science Alliance* 2019 Epub April 13.

Fraschilla I, Pillai S. Viewing Siglecs through the lens of tumor immunology. *Immunol Rev*. 2017 Mar; 276(1):178-191.