Vorkas Laboratory Health Sciences Center 15-0601 Laboratory of Innate Lymphocyte Biology PI: Charles Kyriakos Vorkas, MD Physician-Scientist Assistant Professor of Medicine, Microbiology and Immunology, Division of Infectious Diseases, Department of Medicine https://renaissance.stonybrookmedicine.edu/medicine



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Increasingly difficult to treat infections due to multi-drug resistant organisms and lengthy antimicrobial regimens inspire our work to identify how innate lymphocytes can be targeted in novel approaches to immune therapies and vaccine design. Our lab employs human cohorts, murine models, and systems biology approaches in BSL2 and BSL3 settings to develop strategies to target innate lymphocytes against disease.

**Current members:**, Atul Pradhan, PhD (post-doc), Rimanpreet Kaur, PhD (post-doc), Arshia Arasappan (PhD student), Nezar Mehanna (medical student), Marquise Soto (medical student), Gulnihal Mualla Dalgin (undergraduate), Sagar Makavana (undergraduate)

## Selected projects:

- A. Innate lymphocyte responses to initial Mycobacterium tuberculosis (*Mtb*) infection. We study household TB contact cohorts in Port-au-Prince, Haiti to identify the peripheral blood immune responses of human mucosal-associated invariant T (MAIT), γδ T, and Natural Killer (NK) cell repertoire responding to initial *Mtb* infection. Our long-term goal is to identify targets that will inform novel approaches to TB immunotherapy/vaccines.
- **B.** Immunology of tick-borne diseases. We study the innate immunology of acute tick-borne infections in patients evaluated at SBU Hospital. Our objective is to understand how innate lymphocytes respond during acute infection with *Borrelia burgdorferi* and *Babesia microti* during monoinfection or co-infection. We also investigate immune mechanisms that may underlie post-treatment syndromes.
- C. MR1 ligand diversity across diverse microbial taxa. We have developed assays to identify small molecule vitamin intermediates presented by the highly evolutionary major histocompatibility complex I-related protein, MR1. While the canonical ligands of the riboflavin and folic acid biosynthesis pathways have been well-defined, the unique composition of these ligands derived from specific microbes that induce activation, immune evasion, or tolerance is unknown. Our long-term goal is to target microbial vitamin biosynthesis pathways in immunotherapeutics.
- **D.** Innate lymphocyte priming as vaccination. We have pioneered in vivo murine vaccination models of MAIT cells and NK cells as a strategy to prevent or attenuate infections, including *M. tuberculosis*, Multi-drug resistant *Klebsiella pneumoniae*, and tick-borne infections.
- E. Innate lymphocytes during hematologic malignancies. We define immune subsets responding during acute and convalescent blood cancers with specific focuses on B and T cell lymphomas.

## **Selected Publications:**

- a. Vorkas CK, Wipperman M, Li K, Aubé J, Fitzgerald D, and Glickman MS. Mucosal-associated invariant and γδ T cell subsets respond to initial Mycobocterium tuberculosis infection. JCI Insight. 2018. Oct 4;3(19). PMID: 30282828.
- b. Vorkas CK, Levy O, Skular M, Li K, Aubé J, Glickman MS. Efficient-5-OP-RU-induced enrichment of Mucosal-associated invariant T cells in the murine lung does not enhance control of Mycobacterium tuberculosis infection. Infect Immun. 2020. Oct 19:IAI.00524-20. 2020. PMID: 33077620.
- c. Vorkas CK, Krishna C, Li Kelin, Aubé J, Mazutis L, Leslie CS, Glickman MS. Single cell transcriptional profiling reveals helper, effector, and regulatory MAIT cell populations enriched during homeostasis and activation. J Immunol. 2022. Mar 1;208(5):1042-1056. PMID: 35149530.