

Ya-Chi Ho, MD, PhD

Associate Professor (tenured), Department of Microbial Pathogenesis (primary) and
Division of Infectious Diseases, Department of Medicine (secondary)
Director of Graduate Studies (DGS), Yale Microbiology PhD Program
Yale University School of Medicine

Education and training

1995-2002 MD, National Cheng Kung University College of Medicine, Tainan, Taiwan
**Phi Tau Phi*, graduated as 1st of class; Dean's award, Best Intern Award

2002-2005 Resident, Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan
*Best resident award in 3 out of 3 years

2005-2007 Infectious disease fellow, National Taiwan University Hospital, Taipei, Taiwan
MS, Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan
*Elected as Best Teaching Resident by interns and residents

2007-2008 Board-certified infectious disease attending physician, National Taiwan University Hospital, Yun-Lin Branch

2008-2013 PhD, Robert F. Siliciano Lab, Johns Hopkins University School of Medicine, Baltimore, MD
*HHMI International Student Research Fellowship
*Michael Shanoff Johns Hopkins Young Investigator Award, *Phi Beta Kappa*

2013-2014 Postdoc, Robert F. Siliciano Lab, Johns Hopkins School of Medicine

2014-2015 Research Associate, Johns Hopkins University School of Medicine
*NIH R21 awarded 1 year after PhD

2016-2017 Instructor, Department of Medicine, Johns Hopkins University School of Medicine
WW Smith Family Award, Johns Hopkins CFAR Young Investigator Award

2017 Assistant Professor, Department of Medicine, Johns Hopkins University School of Medicine

2017-2021 Assistant Professor, Department of Microbial Pathogenesis, Yale University School of Medicine
*R01 awarded within 1 year starting the lab

2021-present Associate Professor, Department of Microbial Pathogenesis, Yale University School of Medicine

Honors and awards

2017 Lois E. and Franklin H. Top, Jr. Yale Scholar

2018 Rudolf J. Anderson Fellowship

2018 Gilead Sciences Research Scholar in HIV, Gilead Sciences

2018 Andy Kaplan Prize, Cold Spring Harbor Laboratory Meetings on Retroviruses

2022 Thomas A. and Joyce E. Pearson Endowed Lecture and Keynote Speaker, Medical Scientist Research Symposium, University of Rochester

2022 Keynote speaker, The Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine

2023 Elected member, American Society for Clinical investigation (ASCI)

2023 Plenary speaker, International AIDS Society Annual Meeting

2023 Plenary Speaker, Nordic HIV & Virology Conference

Current funding

PI:

R01 AI141009 Role of clonal expansion in HIV-1 persistence (this is a renewal of my first R01)
R01 AI183430 Understanding HIV-1 persistence and HIV-1-induced inflammation in tissues
R01 AI174863 Understanding HIV-1 persistence in cytotoxic CD4+ T lymphocytes at the single cell level

MPI:

U01 DA053628 M-SCORCH: Methamphetamine use disorder data generation center for Single Cell Opioid Responses in the Context of HIV
P01 AI169768 High-Definition Characterization of the Persistence and Perturbation of the HIV Reservoir

Site PI:

U54 AI170856 CHEETAH Center for the Structural Biology of HIV Infection, Restriction, and Viral Dynamics
UM1 AI164570 BEAT-HIV: Delaney Collaboratory to Cure HIV-1 Infection by Combination Immunotherapy
UM1 AI164565 REACH: Research Enterprise to Advance a Cure for HIV

(Co-Investigator role on other collaborating awards not listed)

Services

- 2016- Reviewer for 22 NIH study sections (U01, P01, R01, F30/F31, and small business grants), American Foundation for AIDS Research (amfAR), European Research Council, European Science Foundation, The Netherlands Organisation for Scientific Research, Czech Science Foundation Study section, Millennium Science initiative Study section
- 2022 NIH/NIAID/DAIDS Subject Matter Expert (SME) on single-cell profiling
- 2023- Program committee, Conferences on Retroviruses and Opportunistic Infection
- 2025- Standing member, NIH HIVD study section

Invited speaker

International conferences: Keystone Symposia/HIV and Co-infections (Whistler, Canada), Keystone Symposia/HIV Cure: Antiretroviral Therapy-Free Control of HIV Infection (Durban, South Africa), AIDS Clinical Trial Group (ACTG) Annual Meeting, Conference on Cell & Gene Therapy for HIV Cure, The International AIDS Annual Meeting (Amsterdam, Mexico City, Melbourne), Conferences on Retroviruses and Opportunistic infections, The Japanese Society for AIDS Research (Kumamoto, Japan), Palm Springs Symposium on HIV/AIDS, International AIDS Vaccine initiative (IAVI), The Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine, HIV Cure and Reservoir Symposium (Ghent, Belgium), SPP1923 international Meeting (Heidelberg, Germany), AC41 Annual international Symposium on HIV Reservoirs at Institut Pasteur (Paris, France), Nordic HIV & Virology Conference (Stockholm, Sweden)

Non-HIV meetings: The international Meeting of the institute of Human Virology (Baltimore, MD), AACR Special Conference on Cancer: Dormancy and Residual Disease (Montreal, Canada), Nebraska Center for Virology (NCV) Symposium (Lincoln, NE), Chromatin Control of Viral Infection Workshop (NIH, Bethesda)

Invited workshops: American Foundation for AIDS Research Think Tank, National institutes of Health and Bill & Melinda Gates Foundation Joint Workshop

Academic institutions: University College London (UK), Ulm University (Germany), Seattle Children's Research institute, George Washington University, Memorial Sloan Kettering Cancer Center/Weill Cornell Medicine

Center for AIDS Research seminars: Penn CFAR, University of Washington/Fred Hutchinson CFAR, Miami CFAR, Emory University CFAR

Contribution to Science

As a physician-scientist and an elected member of American Society of Clinical Investigation, my research program aims to dissect the heterogeneity in immune responses and identify the rare cells causing disease, such as HIV latent reservoir and cancer. I started my career to investigate mechanisms of HIV persistence, particularly characterizing the rare HIV latent reservoir, i.e. the one-in-a-million CD4+ T cells that harbor infectious HIV that prevents a cure. During my PhD at Dr. Rober Siliciano's lab at Johns Hopkins University, I developed the first HIV full-length single-genome sequencing method that became the standard measurement of the size of the HIV latent reservoir (*Cell* 2013). As a postdoc, I identified how cytotoxic T lymphocytes (CTLs) shape the landscape of intact and defective HIV proviruses (corresponding author, *Cell Host Microbe* 2017).

After starting my lab at Yale University in September 2017, I developed HIV SortSeq and identified the rare HIV-infected cells for single-cell RNAseq. I found that HIV drives cancer gene expression through HIV-to-host aberrant RNA splicing as a novel mechanism of HIV-1 persistence (*Science Translational Medicine* 2020). I developed a dual-reporter drug screen and identified JAK inhibitor filgotinib which can suppress HIV-induced cancer gene expression (*JCI* 2020). I developed a genome-wide CRISPR-inhibition screen and identified HIV silencing factors – the chromatin and transcription modulator SAFB family proteins and RNA processing NEXT and PAXT complexes (*JVI* 2022). I developed HIV-4C and examined HIV-host 3D genome interactions using HiC and HiChIP. We found that HIV interacts with human chromatin in cis (*Genome Research* 2023).

My HIV program studies mechanisms of HIV persistence, HIV-induced immune dysfunction, and clonal expansion dynamics of HIV-infected cells using single-cell multi-omic methods (using *Immunity* 2022, *Immunity* 2023, *Cell Reports Medicine* 2025, *Immunity* 2025). We identified preferential persistence of HIV in cytotoxic CD4+ T cells. We found that a transcription factor *IKZF3* (Aiolos) promotes the proliferation of HIV-infected cells and a granzyme B inhibitor Serpin B9 helps HIV-infected CD4+ T cells evade immune clearance. We found that transcription factor *BACH2* promotes HIV persistence in the gut in a mechanism distinct from that in the blood by promoting long-lived memory and restraining effector function. We are currently developing spatial transcriptomics tools to dissect HIV infection in tissues and tumor microenvironment.

We are expanding our research program beyond HIV into T cell fate decisions in the context of diet, cancer, CAR-T cell immunotherapy, and aging.