OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: wang, ying

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0001-7958-8182

Position Title: Supervisor, Research Assistant Member

Organization and Location: Hackensack Meridian Health, Center for Discovery and Innovation, Nutley, NJ, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Temple University, Philadelphia, Pennsylvania, United States	Postdoctoral Fellow	09/2011	08/2016	Neurodegenerative diseases
Shanghai Institute of Materia and Medica, Chinese Academy of Sciences, Shanghai, Shanghai, China	DOCTOR OF PHILOSOPHY	09/2006	07/2011	Neuropharmacology
Tianjin University, Tianjin, Tianjin, China	BACHELOR OF ENGINEERING	09/2001	07/2005	Pharmaceutical Engineering

Appointments and Positions

2021 - present Supervisor, Research Assistant Member, Hackensack Meridian Health, Center for Discovery and Innovation, Nutley, NJ, United States

2016 - 2021 Associate Scientist, Temple University, Philadelphia, PA, United States

Products

Products Closely Related to the Proposed Project

1. Wang Y, He S, Calendo G, Bui T, Tian Y, Lee CY, Zhou Y, Zhao X, Abraham C, Mo W, Chen M, Sanders-Braggs R, Madzo J, Issa JP, Hexner EO, Wiest DL, Reshef R, Xue HH, Zhang Y. Tissue-infiltrating alloreactive T cells require Id3 to deflect PD-1-mediated immune suppression during GVHD. Blood. 2024 Jan 11;143(2):166-177. PubMed Central PMCID: PMC10797551.
2. Wang Y, Bui T, Zhang Y. The pleiotropic roles of EZH2 in T-cell immunity and immunotherapy. Int J Hematol. 2022 Dec;116(6):837-845. PubMed Central PMCID: PMC12975279.
3. He S, Liu Y, Meng L, Sun H, Wang Y, Ji Y, Purushe J, Chen P, Li C, Madzo J, Issa JP, Soboloff J, Reshef R, Moore B, Gattinoni L, Zhang Y. Ezh2 phosphorylation state determines its capacity to maintain CD8(+) T memory precursors for antitumor immunity. Nat Commun. 2017 Dec 14;8(1):2125. PubMed Central PMCID: PMC5730609.
4. Wang Y. Pharmacological targeting EZH2 to modulate chronic graft-versus-host disease. Blood Sci. 2022 Jul;4(3):177-178. PubMed Central PMCID: PMC9742112.
5. WANG Y, HUANG Q, ZHOU Y, HOOPER R, Sanders-Braggs R, CHEN M, TIAN Y, KENT T, POMERANTZ R, CLANDO G, Chung W, Issa JJ, Soboloff J, Zhang Y. EZH2 and intracellular Ca2+ signals interdependently coordinate alloreactive and CAR T cell responses. Cellular and molecular immunology. Forthcoming.

Certification:

I certify that the information provided is current, accurate, and complete. This includes but is not limited to information related to domestic and foreign appointments and positions.

I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§ 287, 1001, 1031 and 31 U.S.C. §§ 3729-3733 and 3802.

Certified by wang, ying in SciENcv on 2026-03-31 15:45:11

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: wang, ying

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0001-7958-8182

Position Title: Supervisor, Research Assistant Member

Organization and Location: Hackensack Meridian Health, Center for Discovery and Innovation, Nutley, NJ, United States

Personal Statement

My research focuses on defining how epigenetic and calcium channels integrate to confer transcriptional alterations and direct T cell differentiation trajectories, and on applying these insights to immune-mediated diseases and cancer. I am particularly interested in how dysregulated T cell programs underlie graft-versus-host disease (GVHD), relapse after hematopoietic stem cell transplantation, and the limited durability of current CAR-T therapies.
My studies have been centered on uncovering the molecular regulatory network of T cell persistence and functional differentiation. My early studies identified EZH2 as a central chromatin regulator of effector and memory T cell formation, demonstrating how its loss disrupted key transcriptional networks and abolished durable responses. Building on this, I discovered that Id3, an EZH2-regulated transcription factor, maintains progenitor-like alloreactive T cells in GVHD target tissues, thereby sustaining pathogenic persistence. These findings advanced the concept that transcriptional control of stemness is a major determinant of T cell–driven alloimmunity and revealed Id3 as a potential therapeutic node, as Id3-deficient human CAR-T cells preserved antitumor capacity without inducing GVHD.
More recently, my study has uncovered that EZH2 and calcium signaling interdependently shape T cell activation, survival, and differentiation. EZH2 serves as a brake on calcium influx, while calcium signals reciprocally constrain EZH2-driven gene programs. This inter-regulatory mechanism balances T cell survival vs terminal differentiation and fine-tunes CAR-T activity. This work then led me to explore the role of another intracellular calcium store-mitochondria, in T cell alloimmunity and antitumor potency. I started with the sole mitochondrial calcium uptake channel, mitochondrial calcium uniporter (MCU) complex. Our studies identify MCU as a rheostat of T cell stemness programs, manipulation of which ablates GVHD while preserves anti-leukemia potency. This work positions MCU as a novel point of therapeutic intervention.
Taken together, my work has defined calcium signaling-epigenetic crosstalk as a central regulatory mechanism of T cell pathogenicity and protective activity. My long-term vision is to translate these mechanistic insights into challenging clinical settings such as acute myeloid leukemia and post-transplant relapse, while continuing to uncover new molecular mechanisms that may inform the next generation of durable T cell–based immunotherapies.

Funding:
New Jersey Health Foundation # PC 227-25. 2025-2026.
Role: PI.
Manipulating T cell mitochondrial calcium uniporter to suppress graft-versus-host disease

Honors

2025	ASH member, American Society of Hematology
2024	poster awards, Annual Symposium on Applied Immunological Research
2020	poster award, Annual Symposium on Epigenetics, Immunity and Cancer
2015	poster award, Neurological disorder summit
2011	3A student, Chinese Academy of Science

Contributions to Science

1. Since 2016, my research has focused on investigating epigenetic regulatory mechanisms during T cell immune response, with the goal of curbing aberrant T cell alloimmunity following allogeneic hematopoietic stem cell transplantation (allo-HSCT) and boosting long-term T cell anti-tumor potency.
   I studied the role of EZH2 in T cell anti-tumor potency and identified its critical function in effector T cell persistence, memory formation, and recall response. EZH2 regulates the expression of master transcription factors (Id3, Tbx21, Eomes, Blimp1), which determine T cell fate and control T cell anti-tumor capacity. This work established the critical role of EZH2 in T cell

anti-tumor potency.
My subsequent research identified hyperactive calcium signaling in T cells lacking Ezh2, leading me to propose that EZH2 functions as a brake for calcium signaling during T cell immune response. To test this hypothesis, I conducted a study to identify the calcium channel(s) that mediate the regulatory function of EZH2. Through the generation of transgenic mice with Ezh2 and Stim1 or Itpr2 deletion specifically in T cells, I discovered that Stim1 or Itpr2 deletion restored T cell dysfunction caused by Ezh2 deficiency, and identified the overlapped transcriptional regulation by EZH2 and STIM1, as well as that by EZH2 and IP3R2. This work uncovers the transcriptional orchestration between EZH2 and calcium signaling that can be manipulated to curtail aberrant immune response following allo-HSCT. This work also demonstrates priming CAR-T cells with calcium signaling inhibitors can retain EZH2 function, thereby improving CAR-T cell tumor control capacity, a potentially novel approach that can be translated for clinical application.

2. Based on the findings in EZH2 work, I investigated the role of Id3, a master transcription factor directly regulated by EZH2 transcriptionally, in T cell alloimmunity. My work identified Id3 deficiency abolished GVHD while preserving anti-tumor potency using both Id3-ablated murine T cells and human CAR-T cells. Mechanistically, I found Id3 deflected the suppressive PD1 signaling in alloreactive T cells through epigenetically regulating Pdcd1 expression and maintaining the survival of PD1+ alloreactive T cells. Id3 also preserved the less differentiated alloreactive T cell pool in GVHD target organs to sustain T cell alloresponse. Additionally, we also identified EZH2-Id3 might contribute to the development of GVHD in Vitamin D-deficient patients. These studies highlighted Id3 as a promising target to curtail GVHD progression.

3. My recent research identified another molecule, mitochondrial calcium uniporter (MCU) as a biphasic regulator of T cell alloimmunity. Using allo-HSCT model, I found MCU governs the durability of CD8+ T cell stemness under chronic alloantigen exposure, thereby dictating T cell exhaustion development and long-term persistence upon repeated antigen stimulation. My work demonstrated MCU as a potential novel target, the manipulation of which could effectively suppress pathogenic while retaining protective T cell immunity. I also found a pharmacological approach that suppresses T cell aberrant responses by altering MCU activity. Ongoing study is focusing on manipulating MCU to boost T cell antitumor activity and mechanistic investigation.

4. During my PhD and postdoctoral training, I investigated mechanisms of neurocognitive disorders and explored novel treatment approaches.
   My PhD research focused on identifying compounds with neuroprotective properties which could potentially be translated to treat ischemic stroke and Alzheimer's Disease (AD). I discovered that a compound T33, previously identified to protect against type II diabetes in rodent models, had potent anti-inflammatory activity against brain damage from ischemic stroke. My work showed T33 inhibited the inflammatory cascades in astrocytes and microglial cells, the hyperactivities of which underlies a broad range of neurological disorders. My other project uncovered a novel neuroprotective mechanism of the drug Huperzine A (HupA), used to treat mild AD in China. Using transgenic mice exhibiting AD pathology, I found HupA significantly improves the density of the dendritic spines, the critical structure for neuronal communication, associated with reducing the toxic amyloid beta (Abeta) in the brain. HupA reduces Abeta generation by increasing the expression of alpha-secretase while inhibiting the membrane transport of beta-secretase, diverting from beta- to alpha-cleavage of its precursor protein.
   My postdoc research uncovered the HIV Viral Protein R (VPR) inhibits mitochondria axonal transport in neurons, promoting neuronal senescence and impairing their function, which contributes to HIV-associated neurological disorders (HAND). I found VPR directly interacts with adenine nucleotide translocator, inhibits ATP production, disrupts microtubule and reduces the expression of mitochondria motor protein Miro-1. Importantly, I found VPR increases SNCA expression, which is neurotoxic. My subsequent work demonstrated VPR regulates SNCA expression by altering the DNA methylation status at SNCA antisense promoter. All these findings were recapitulated in aged mice, supporting VPR ages brain.

5. Complete List of Published Work in MyBibliography:

   https://www.ncbi.nlm.nih.gov/myncbi/collections/mybibliography/

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