



CURRICULUM VITAE

Name: Zhinan Yin, M.D., Ph.D.

Born: October 1, 1964

Citizenship: Chinese

Current Position: Professor and Dean (National Changjian Scholar)
 The Biomedical Translational Research Institute
 Jinan University, Guangzhou, China;
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Education:	1984 M.D.	Hubei Medical University (Wuhan University School of Medicine)
	1988 M.S.	Shanghai Second Medical University (Shanghai Jiao tong University School of Medicine)
	1997 Ph.D.	Free University Berlin, Germany

Career:	1984-1985	Teaching Assistant, Department of Microbiology and Immunology, Yun Yan Medical College, Tong Ji Medical University, Yun Yan, People's Republic of China
	1988-1992	Assistant Professor, Department of Microbiology and Immunology, Guangzhou Medical College, Guangzhou, People's Republic of China
	1992-1994	Research Fellow, Division for Experimental Oncology, Reference Center for Oncology, Aviano (PN), Italy
	1994-1997	Ph.D Candidate, Klinikum Benjamin Franklin, Free Univ. Berlin (Degree received 9/97)
	1997-1999	Postdoctoral Fellow, Section of Rheumatology,

1999-2001	Yale School of Medicine Associate Research Scientist, Section of Rheumatology, Yale School of Medicine
2001-2006	Assistant Professor, Section of Rheumatology, Yale School of Medicine
2006-2007	Associate Professor, Section of Rheumatology, Yale School of Medicine
2007-2011	Dean and Professor, College of Life Sciences, Nankai University
2007-2013	Professor, College of Life Sciences, Nankai University, China, P.R.C Associate Professor (Adjunct), Section of Rheumatology, Yale School of Medicine
2013-Present	Professor and Dean (National Changjian Scholar) The Biomedical Translational Research Institute Jinan University, Guangzhou, China
2019-Present	Chief Academic Advisor Zhuhai People's Hospital (Jinan University Teaching Hospital)

Professional Honors:

1. National or Regional Awards:

- First Prize for Outstanding Master's Thesis in 1988 (Chinese Society for Microbiology) for the paper titled " β -D-galactosidase/anti- β -D-galactosidase monoclonal antibody complexes (GAG) and their applications in ELISA and immunohistochemistry."
- Young Investigator Award from the National Rheumatology Foundation in 2000.
- Membership of the Yale Cancer Center in 2000.
- Membership of the American College of Rheumatology (ACR) in 2000.
- Membership of the American Association of Immunologists (AAI) in 2002.
- Membership of the American Association for Cancer Research (AAC) in 2002.
- Young Professor Conference Award from the American Association of Immunologists (AAI) in 2004.
- National Science Fund for Distinguished Young Scholars in 2007.
- "Changjiang Scholar" Distinguished Professor appointed by the Ministry of Education of China in 2007.
- Tianjin "Entrepreneurial Leader" in 2009.
- "High-level Overseas Study Returnee Entrepreneurial Talent" by the Ministry of Human Resources and Social Security of China in 2010.
- "Outstanding Young Expert with Outstanding Contributions" in the New "Hundred, Thousand, and Ten Thousand Talents Project" by the Ministry of Human Resources and Social Security of China in 2013.

- Leader of the Fourth Batch of Innovative Entrepreneurial Teams introduced in Guangdong Province in 2013.
- Fifth China Overseas Chinese (Innovation Talent) Contribution Award in 2014.
- 14th Guangdong Province Ding Ying Science and Technology Award in 2018.
- Second Prize of China Overseas Chinese Federation Contribution Award in 2018.
- First Prize of Guangdong Province Science and Technology Progress Award in 2020 (fifth completion).
- Important Medical Advances in China (basic medicine and biology) in 2021: Discovery of new mechanisms of IL-27 signaling in the regulation of obesity and type 2 diabetes.

2. Institutional Awards:

- Brown Core Scholarship from Yale School of Medicine.
- Cancer Research Award from the Yale Cancer Center in 2001.
- Research Achievement Award from the Department of Internal Medicine at Yale School of Medicine in 2006.
- Advanced Individual Award for Foreign Affairs Work and Significant Scientific Research Achievement from Jinan University in 2019.

Funded Projects:

- 1) "Mechanisms and Functions of $\gamma\delta$ T Cell Differentiation," NIH grant project, grant number: 1 R01 AI56219-01, January 15, 2004 - December 31, 2008, total funding: \$1,430,600.
- 2) "Regulation and Functions of $\gamma\delta$ T Cell Differentiation," NIH grant project, grant number: 1 K01 AR02188-05, March 1, 2004 - February 28, 2006, total funding: \$685,700.
- 3) "Regulation and Functions of $\gamma\delta$ T Cell Differentiation," National Rheumatology Foundation grant project, research grant, July 1, 2004 - June 30, 2006, total funding: \$405,000.
- 4) "Mechanisms and Functions of $\gamma\delta$ T Cell Differentiation," NIH grant project, grant number: 1 R21 AI 56219-01, July 15, 2003 - July 14, 2004, total funding: \$327,000.
- 5) "Role of $\gamma\delta$ T Cells in Sarcoma Fibrosis," NIH grant project, grant number: 5P30 AR041942-090024, April 1, 2002 - March 31, 2003, total funding: \$32,700.
- 6) "Molecular Mechanisms and Functions of $\gamma\delta$ T Cells," American College of Rheumatology Postdoctoral Fellowship, July 1, 2000 - June 30, 2001, total funding: \$32,700.
- 7) "Functions of $\gamma\delta$ T Cells in Cancer Immunity," Yale Cancer Center, Cancer Research Award, July 1, 2000 - June 30, 2001, total funding: \$25,000.
- 8) "Role of $\gamma\delta$ T Cells in Systemic Lupus Erythematosus," Brown Core Postdoctoral Research Fellowship, July 1, 1998 - June 30, 1999, total funding: \$28,000.
- 9) "Protein Function in the Interaction between Tumors and Immune Cells," Minister of Science and Technology 973 Project, funding: CNY 25 million (CNY 8.96 million), July 2007 - July 2011
- 10) "Mechanisms of Autoimmune Recognition and Response," National Natural Science Foundation of China, Major Project, Subproject, funding: CNY 2.8 million, January 2009 - December 2012, project number: 30890143.
- 11) " $\gamma\delta$ T Cell Differentiation and its Role in Tumor Immunity," National Natural Science Foundation of China, National Distinguished Young Scholar Grant, funding: CNY 2 million, January 2008 - December 2011, project number: 30725015.

- 12) "Development of Breast Cancer Vaccines," Tianjin Science and Technology Support Program, Key Project, funding: CNY 500,000, October 2007 - October 2009.
- 13) "Immunological Mechanisms and Intervention Strategies in Rheumatoid Arthritis," National Key Research and Development Program by the Ministry of Science and Technology, January 2010 - August 2014, funding: CNY 23 million (CNY 8.96 million), project number: 2010CB529100.
- 14) "International Collaboration on Rheumatoid Arthritis Molecular Mechanisms," International Science and Technology Cooperation Program by the Ministry of Science and Technology, funding: CNY 2.9 million, January 2011 - December 2013, project number: 2010DFB34000.
- 15) "Role of $\gamma\delta$ T Cells in Natural Immune Responses in the Liver," Key Project of National Natural Science Foundation of China, funding: CNY 3.25 million, January 2013 - December 2017, project number: 31230025.
- 16) "Development of Clinical Diagnostic Reagents for Major Diseases," Guangdong Province Key Project for Innovative Entrepreneurial Teams, funding: CNY 10 million, January 2013.
- 17) "Regulation and Molecular Mechanisms of Mutual Regulation between Gut Microbiota and $\gamma\delta$ T Cells," Major International Cooperation Project of National Natural Science Foundation of China, funding: CNY 2.89 million, January 2014.
- 18) "Role and Molecular Mechanism of $\gamma\delta$ T Cells and IL-27 in Fatty Liver Disease," Major Cultivation Project of Natural Science Foundation of Guangdong Province, funding: CNY 1 million, July 2014.
- 19) "Development of Humanized Animal Models with Human Hematopoietic and Immune Systems and Their Translational Applications," 863 Program by the Ministry of Science and Technology, funding: CNY 7.5 million, January 2014 - June 2016.
- 20) "Innovative Diagnosis and Treatment of Tuberculosis and Tuberculosis Complicated with Chronic Viral Infections," Key Project of Guangzhou Science and Technology Support Program, funding: CNY 6.5 million, July 2016 - June 2019, project number: 201510201011371.
- 21) "Innovation Introduction Base for Molecular Mechanisms of Immunoregulation," National Foreign Experts Bureau and Ministry of Education "111" Innovative Introduction Base, funding: CNY 9 million, January 2016 - December 2020.
- 22) "Molecular Mechanisms of $\gamma\delta$ T Cell Differentiation and Their Role in Tumor Immunity," Key Project of National Natural Science Foundation of China, project number: 31830021, funding: CNY 2.82 million, September 2019 - December 2023.
- 23) "PhD Training Program in Translational Medicine for the Greater Bay Area," National Scholarship Council, "Double First Class" Project for Top Universities, 2020-2022.
- 24) "Major Basic Research Program on Mechanisms of Immune Regulation and Differentiation of Lymphocytes," National Key Research and Development Program by the Ministry of Science and Technology, project number: 32030036, funding: CNY 3.04 million, September 2020 - October 2021.
- 25) "Mechanisms of Immunoregulation in Intestinal Cell Development, Differentiation, and Function," National Natural Science Foundation of China, Key Project, project number: 31420103901, funding: CNY 2.89 million, November 2020 - October 2025.

Professional Association Positions:

- Member of the Yale Cancer Center since 2000.
- Member of the American College of Rheumatology (ACR) since 2002.
- Member of the American Association of Immunologists (AAI) since 2002.
- Member of the American Association for Cancer Research (AAC) since 2002.
- Editorial Board Member of Cellular & Molecular Immunology since 2007.
- Editorial Board Member of the Chinese Journal of Microbiology and Immunology.
- Deputy Editor-in-Chief of the Journal of Reproductive Immunology (China).
- Council Member of the Chinese Society of Immunology since 2010.
- Review expert for the Immunology Department of the National Natural Science Foundation of China.
- Secretary-General of the Guangdong Society of Immunology since 2013.
- Chairman of the Guangdong Province Society of Immunology since 2019.
- Chairman of the Immunology Cell Subcommittee of the Chinese Society for Cell Biology since 2019.

Research Summary

Professor Yin has been engaged in basic and translational research in immunology for nearly 30 years. He is a pioneer in the study of $\gamma\delta$ T cell anti-tumor function globally and has served as the chairman of the 9th International $\gamma\delta$ T Cell Symposium. He was the first to confirm the safety of allogeneic $\gamma\delta$ T cells for tumor immunotherapy, and the product has entered the stage of industrial transformation, driving the development of this treatment technology worldwide. In recent years, he has focused on the role of the immune system in the development of metabolic diseases. He was the first to discover the beneficial effects of IL-27 on obesity and type 2 diabetes, which was published in Nature (2021) and has attracted high attention from the academic and industry communities. IL-27, as a cytokine, is also regarded as one of the important drug targets in the field of obesity treatment in 2021. He has served as the chief scientist for several major projects, including the 973 Program and the Key Program of the National Natural Science Foundation of China. He has published a total of 192 papers, including 79 papers as corresponding/co-corresponding author in authoritative journals such as Nature (2 papers) and Nature Immunology, with more than 6,000 citations. He has been listed as a highly cited researcher in China by Elsevier from 2014 to 2020. He has received honors such as the "Changjiang Scholar" Distinguished Professor by the Ministry of Education, the National Distinguished Youth Science Fund, and the 14th Ding Ying Science and Technology Award of Guangdong Province. His research achievements have been selected as "China's Important Medical Advances in 2021" and have won the First Prize of Guangdong Province Science and Technology Progress Award, the First Prize of the Chinese Anti-Cancer Association, and the Special Prize of Zhuhai City.

Dr. Yin's representative research achievements are as follows:

1. Firstly discovered a novel immune cell therapy - allogeneic $\gamma\delta$ T cells, and elucidated the new mechanism of $\gamma\delta$ T cell functional differentiation.

Compared with traditional $\alpha\beta$ T cells, $\gamma\delta$ T cells have inherent immune characteristics such as MHC-independent antigen recognition and no sensitization pre-activation. However, little is known about the physiological or pathological functions of $\gamma\delta$ T cells in the body. Dr. Yin is the discoverer of early IFN- γ production by $\gamma\delta$ T cells in anti-tumor immunity and elucidated the regulatory mechanism of $\gamma\delta$ T cells in local anti-tumor immunity (Ref 11, 1st part). Furthermore, He systematically analyzed the new mechanisms by which cytokines, transcription factors, epigenetic modifications, ion channels, vitamins, and cellular metabolism regulate the anti-tumor immune function of $\gamma\delta$ T cells (Ref 8,10,16,18,19,21,24,33,44,46, 1st part).

Dr. Yin also discovered severe functional impairment of $\gamma\delta$ T cells in tumor patients (Ref 75,1st part) and traditional autologous immune cell therapy has not achieved satisfactory clinical efficacy. The application of allogeneic $\gamma\delta$ T cells from healthy individuals for anti-tumor immunotherapy in cancer patients and the mass expansion of allogeneic $\gamma\delta$ T cells are two major international challenges in this field. The patent formulation developed by Dr. Yin can massively expand peripheral blood $\gamma\delta$ T cells while enhancing their tumor-killing function; moreover, the innovative application of allogeneic $\gamma\delta$ T cells in the treatment of advanced liver cancer, lung cancer, and other malignant tumors worldwide has confirmed the safety and efficacy of allogeneic $\gamma\delta$ T cell therapy. This breakthrough has changed the international landscape of $\gamma\delta$ T cell applications, and since then, many biopharmaceutical companies worldwide have regarded allogeneic $\gamma\delta$ T cells as immune cell therapies. The representative paper (Ref 66, 1st part) was recently recognized as the best paper of the past 10 years by the journal *Cellular and Molecular Immunology*. The applicant also conducted the first clinical trial of allogeneic $\gamma\delta$ T cell therapy for multidrug-resistant tuberculosis worldwide (Ref 67, 1st part) and found that allogeneic $\gamma\delta$ T cells significantly improved cavity and lesion absorption, opening up new possibilities for the treatment of acute infectious diseases using allogeneic $\gamma\delta$ T cells.

In addition, Dr. Yin also discovered the protective or pathogenic roles of $\gamma\delta$ T cells in various diseases such as acute/chronic hepatitis, liver fibrosis, acute spinal cord injury, cerebral hemorrhage, coronary artery disease, psoriasis, recurrent miscarriage, and thoroughly analyzed their roles and regulatory mechanisms (Ref 61,62,64,65,74,75, 1st part), providing new theoretical basis and treatment directions for the diagnosis and treatment of related diseases. The applicant also constructed the $\gamma\delta$ T single-cell transcriptome and single-cell chromatin accessibility atlas, systematically elucidating the heterogeneity of $\gamma\delta$ T cell subsets, and discovered a new $\gamma\delta$ T cell subset - GZMA⁺ $\gamma\delta$ T cells (Ref 77, 1st part), which played an important role in the study of thymic development, differentiation, heterogeneity, and new functions of $\gamma\delta$ T cell subsets.

2. Revealing a novel mechanism of immune system regulation of metabolism : the regulatory function of Interleukin-27 (IL-27) on tissue cells

The immune system plays an important regulatory role in the progression of chronic metabolic diseases such as obesity and type 2 diabetes, but the underlying mechanisms are not clear. Using various conditional gene-engineered mice and cellular and molecular biology techniques, Dr. Yin first discovered that IL-27 improves obesity and insulin resistance by regulating the thermogenic effect mediated by UCP1. The main target cells of IL-27 are adipocytes rather than immune cells.

Injection of IL-27 significantly reduces body weight and increases insulin sensitivity, demonstrating for the first time the therapeutic effects of IL-27 in alleviating obesity and improving type 2 diabetes. This research was published in *Nature* (Ref 67, 1st part) and received widespread attention from the scientific community and industry. The achievement was recognized by the Chinese Academy of Medical Sciences as one of the "Important Medical Advances in China in 2021", and IL-27 has become an important target in the field of obesity and metabolic diseases. The applicant's patent on the use of IL-27 to improve obesity and other metabolic diseases through UCP1 has been granted, and innovative drugs targeting obesity and metabolic diseases are being developed.

The applicant also discovered the protective effects of IL-27 on acute hepatitis and anti-tumor immunity. They found that IL-27 derived from DC cells improved acute liver injury induced by Concanavalin A (Ref 34, 1st part). IL-27 can also promote anti-tumor immunity by recruiting NK/NKT cells, providing new theoretical basis for drug development for related diseases such as acute hepatitis and tumors (Ref 32, 1st part).

Hippocampal excitatory neurons (Vglut1+) play critical roles in learning and memory. Recent studies have revealed that the immune system has a significant impact on cognitive function, but the immune factors involved and the underlying mechanisms are largely unknown. Recently, Dr. Yin investigated the role of IL-27-IL-27R α signaling in enhancing the excitability of hippocampal neurons and protecting against age-related and neurodegenerative diseases-induced learning and memory deficiencies. Mechanistic studies showed that IL-27R α is selectively expressed in excitatory neurons of the dentate gyrus (DG) in the hippocampus, and IL-27 is produced by microglia. By directly targeting Vglut1+ neurons, IL-27 promotes neuronal excitability and enhances synaptic transmission. Furthermore, therapeutic intracranial injection of IL-27 into the DG significantly improved learning and memory in aged mice and 5XFAD transgenic mice. These findings suggest that IL-27 unexpectedly plays a protective role in regulating learning and memory in the central nervous system and may serve as a promising target for immunotherapy against cognitive dysfunction.

3. Revealing a new mechanism regulating T cell homeostasis and immune memory - RNA m6A methylation modification and the mTORC2 signaling pathway

The homeostatic proliferation of T cells is the basis for their clearance of pathogens and immune protective function, while T cell immune memory is crucial for specific recognition and clearance of pathogens upon secondary infection. However, the regulatory mechanisms underlying T cell immune homeostasis and immune memory are not well understood. Under the support of the "111" Project of the Ministry of Education, Dr. Yin collaborated with Professor Richard A. Flavell from Yale University and discovered that RNA m6A methylation modification affects the IL7-SOCS1/3-pSTAT5 signaling pathway, thereby maintaining T cell homeostatic proliferation and activation. This work represents the first exploration of the impact of RNA m6A methylation modification on specific cellular physiological and pathological functions in living mammals and was published in *Nature* in 2017 (Ref 49, 1st part), opening up the study of the role of RNA m6A methylation in T cell functional differentiation and homeostasis. Professor Yutaka Tagaya, an immunologist from the University of Maryland, commented on this research in F1000

Prime, stating that it "demonstrates, for the first time in vivo, the 'unexpected' connection between m6A RNA modification and peripheral T cell homeostasis and activation. Undoubtedly, this study has opened up a new field of research in immunology and cell biology".

In recent years, significant progress has been made in understanding the mechanisms underlying the establishment and maintenance of CD8⁺ T cell immune memory. However, there is still much unknown about memory CD4⁺ T cells. It is crucial to understand and explore the mechanisms of the establishment and long-term maintenance of CD4⁺ T cell immune memory. The applicant collaborated with Professor Lili Ye from the Army Medical University and Professor Jianqing Xu from Fudan University and revealed, for the first time, the role and mechanism of the mTORC2 pathway in the long-term maintenance of antigen-specific memory CD4⁺ T cells. This work was published in *Nature Immunology* (Ref 72, 1st part) and provides a new research foundation and perspective for the development of long-lasting vaccines and the treatment of autoimmune diseases. The paper was included as an important biomedical literature by Faculty Opinion.

4. Exploring the industrial transformation of academic achievements and contributing to society with remarkable achievements

Dr. Yin not only focuses on basic innovation but also attaches great importance to the transformation of research achievements and the promotion of socio-economic development. He led a team to develop a new method for ex vivo expansion of $\gamma\delta$ T cells and obtained an invention patent, which was transferred to Guangdong Jidekangmin Biotechnology Co., Ltd., dedicated to the research and development of $\gamma\delta$ T cell therapies. After seven years of research, Dr. Yin and his team discovered that IL-27 can act on adipocytes and promote fat burning through UCP1, making it one of the important "targets" in the field of obesity in 2021. The related patent has been specially approved and transferred to "Guangdong Jiantebio Biotechnology Co., Ltd.", focusing on the development of IL-27 protein and mRNA therapeutics. In addition, the applicant has been committed to precise immune function testing and serves as the Chief Scientist of Guangzhou PureBiotech Co., Ltd. Using large-sample, multi-parameter immune profiling combined with artificial intelligence technology, the applicant has calculated the "immune age" of the Chinese population, providing a new tool for health management of the general population and clinical diagnosis and treatment evaluation for patients with diseases.

Dr. Yin has a strong sense of social responsibility and maintains a high degree of political and ideological consistency with the Party Central Committee. They adhere to professional ethics, serve as a role model, and invest a lot of effort in nurturing graduate students and young researchers. He frequently disseminates scientific knowledge through various platforms and consistently gives lectures for graduate students on the Bilibili website, with over 3.8 million views. Leveraging their years of experience in overseas teaching, He actively promotes domestic and international academic exchanges and attracts outstanding young talents who have studied abroad to return to China and contribute to the country. Therefore, he has received the Contribution Award from the China Federation of Returned Overseas Chinese twice in 2014 and 2018.

Overall, Professor Yin's research accomplishments, along with his ability to secure funding,

publish influential papers, receive prestigious accolades, demonstrate leadership, and foster mentorship, position him as a highly esteemed researcher in the field of immunology. His work holds immense promise for the future of healthcare, with the potential to transform our understanding and treatment of diseases. Through his dedication and expertise, he continues to push the boundaries of scientific discovery and make a lasting impact on the field of immunology.

Complete Bibliography

First author/corresponding author^[1-89]

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