OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 09/30/2024)

1. BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Zhou, Xin

eRA COMMONS USER NAME (credential, e.g., agency login): xzhou7

POSITION TITLE: Postdoc Fellow

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Fudan University, Shanghai, Shanghai	BS	07/2011	Biological Sciences
University Of Connecticut Health Center, Farmington, CT	PHD	04/2019	Genetics and Genomic Sciences

A. Personal Statement

My academic journey has provided me with a comprehensive foundation in a diverse range of biological disciplines, spanning from molecular biology and virology to biochemistry, immunology, and bioinformatics. This journey began at Fudan University under the mentorship of Dr. Juan Lin, where I investigated the medicinal properties of herbal natural products and mushrooms. I was involved in the identification and classification of species producing specific natural products, such as curcin and JcLEA, a novel protein found in *J. curcas*. My explorations also led me into the realm of medicinal mushrooms, where I studied the bioactive components of *Ganoderma* and *Chinese Cordyceps* species. Following this, my interests were drawn towards viral immunology during my pre-doctoral research with Dr. Daniel Popkin at Case Western Reserve University. I developed proficiency in animal model handling and cell culture techniques and acquired a deep understanding of host immune responses to pathogenic microbes. My contributions extended to novel drug discovery against viral infections, where I helped innovate a pioneering drug delivery system using nanoparticles for targeted delivery of antiviral agents. In subsequent research, I ventured into exploring host-microbiome interactions under the guidance of Dr. George Weinstock, a world-renowned leader in the microbiome field. This opportunity enabled me to investigate the intricate relationships between the microbiome and various markers of immune and metabolic health. Through this work, I uncovered a potential interaction that connects individual immune profiles with the composition of the gut microbiome, which holds substantial implications for understanding the development and progression of Type 2 Diabetes. My scientific journey continued at Stanford University, under the mentorship of the renowned geneticist, Dr. Michael Snyder. This has been a transformative experience, allowing me to extend my knowledge of multi-omics and its applications in understanding and developing interventions for diseases. Collaborating closely with Dr. Snyder, we have co-published seven research articles and one review that underscores my ability to contribute substantially to innovative research and push the boundaries of knowledge in genomics. Our investigations incorporated advanced multi-omics and single-cell analysis techniques, providing a nuanced understanding of the complex interplay between the microbiome and the host. With a focus on various disease contexts such as aging, Pulmonary Arterial Hypertension (PAH), and lymphatic disorders, our contributions have furthered understanding of the role of the microbiome and inflammations in health and disease. The proposed research and training plan aims to further refine my skills in advanced bioinformatics, multi omics and immunology research, as well as enhance crucial professional development areas such as grant writing, public speaking, lab management, and student mentoring. This comprehensive approach aligns with my objective of becoming an independent investigator, dedicated to

elucidating the role of the microbiome in human diseases. My rich academic trajectory, marked by multiple accolades, honors, and valuable collaborations like that with Dr. Snyder, has shaped me into a researcher well-equipped to make significant contributions to the understanding and management of metabolic diseases related to the human microbiome.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2019 -	Postdoc Fellow, Stanford University, Stanford, CA
2013 - 2019	Graduate Research Assistant, The Jackson Laboratory of Genomic Medicine, The Jackson Laboratory of Genomic Medicine, Farmington, CT
2011 - 2013	Research Assistant, Case Western Reserve University, Cleveland, OH

Honors

2022	Trainee Poster Award, American Association of Immunologists
2021	Resource Centers for Minority Aging Research Scientist, National Institute on Aging
2016	Travel Award for Talk, Cold Spring Harbor Asia: Microbiology and the Environment
2009	Study Section Chair, FDU Undergraduates Research Opportunities Program
2009	People's Scholarship, Fudan University
2008	Xi Yuan Scholar, Fudan University

C. Contribution to Science

1. In the initial stages of my academic career, I devoted my research efforts to exploring the medical applications of herbal natural products. This involved the identification and classification of species that produced specific natural products, such as curcin and JcLEA, a novel protein found in the plant *Jatropha curcas*. These proteins garnered interest due to their potential anti-tumor properties. Subsequently, my research interests evolved to encompass the study of mushrooms with medicinal properties. In collaboration with a team of researchers, I embarked on the isolation and characterization of bioactive components from medicinal mushrooms, specifically Ganoderma and *Chinese Cordyceps* species. This collective body of work equipped me with fundamental skills and knowledge in molecular experimentation. Additionally, it afforded me extensive experience in the development of novel therapeutic approaches and drug discovery, establishing a solid foundation for my ongoing research endeavors.

    a. Xia F*, **Zhou X***, Liu Y, Li Y, Bai X, Zhou X. Composition and predictive functional analysis of bacterial communities inhabiting Chinese Cordyceps insight into conserved core microbiome. BMC Microbiol. 2019 May 23;19(1):105. PubMed Central PMCID: PMC6533680.

    b. Lin J, Jin Y, **Zhou X,** Wang J. Molecular cloning and functional analysis of the gene encoding geranylgeranyl diphosphate synthase from Jatropha curcas. African Journal of Biotechnology. 2010 July; 9(23):3342-3351.

    c. Cai X, Pi Y, **Zhou X**, Wu S, Lin J. Hepatoma Cell Growth Inhibition by Inducing Apoptosis with Polysaccharide Isolated from Turkey Tail Medicinal Mushroom, Trametes versicolor (L.: Fr.) Lloyd (Aphyllophoromycetideae). International Journal of Medicinal Mushrooms. 2010; 12(3):257-263. DOI: 10.1615/IntJMedMushr.v12.i3.40

    d. Wu S, Guo X, **Zhou X,** Li X, Chen Y, Lin J. AFLP analysis of genetic diversity in main cultivated strains of Ganoderma spp. African Journal of Biotechnology. 2009 August 04; 8(15):3448-3454.

2. In addition to my primary research focus, my pursuits within the realm of viral immunology have granted me a profound understanding of the mechanisms governing host immune responses to pathogenic viruses. Throughout this process, I have honed my skills in working with animal models and cell cultures, providing me with an intimate familiarity of experimental procedures and methodologies in virology and cell biology. This work has also afforded me invaluable exposure to basic cellular immunology, enriching my knowledge of the intricate interactions between pathogens and host cells. In tandem with these endeavors, I have embarked on a path towards novel drug discovery for viral infections, with a particular focus on the creation of a pioneering drug delivery system. This system is designed to target antiviral agents with preferential toxicity, thereby optimizing the efficacy of treatment while minimizing undesirable side effects. Collectively, these experiences have broadened my scientific acumen in virology and immunology, while also contributing to the scientific community's understanding of viral pathogenesis and the development of innovative treatment strategies.

    a. Bartley JM*, **Zhou X***, Kuchel GA, Weinstock GM, Haynes L. Impact of Age, Caloric Restriction, and Influenza Infection on Mouse Gut Microbiome: An Exploratory Study of the Role of Age-Related Microbiome Changes on Influenza Responses. Front Immunol. 2017; 8:1164. PubMed Central PMCID: PMC5611400.
    b. Wen AM, Le N, **Zhou X**, Steinmetz NF, Popkin DL. Tropism of CPMV to Professional Antigen Presenting Cells Enables a Platform to Eliminate Chronic Infections. ACS Biomater Sci Eng. 2015 Nov 9;1(11):1050-1054. PubMed Central PMCID: PMC4894745.
    c. Hatter AD, **Zhou X,** Honda K, Popkin DL. Langerhans Cell Hyperplasia From Molluscum Contagiosum. Am J Dermatopathol. 2015 Aug;37(8): e93-5. PubMed Central PMCID: PMC4334759.
    d. **Zhou X,** Ramachandran S, Mann M, Popkin DL. Role of lymphocytic choriomeningitis virus (LCMV) in understanding viral immunology: past, present and future. Viruses. 2012 Oct 29;4(11):2650-69. PubMed Central PMCID: PMC3509666.

3. My recent investigations have delved into the intricate profiles of the microbiome and their complex interactions with the host immune system, providing a platform for me to accrue vital proficiency in bioinformatics and biostatistics. This research has necessitated the exploration of systemic interactions between gut microbiota and a myriad of immunological and metabolic markers. Through this rigorous inquiry, I have identified a potential novel interaction that interweaves personalized immune profiles with the composition of the gut microbiome, a finding with potential significance in the early onset and progression of Type 2 Diabetes. Concurrently, my immersion in bioinformatics has enabled me to contribute to the development of an innovative tool - DM-RPart. This tool excels in modeling high-dimensional host physiological data in parallel with high-dimensional sequencing data, underlining my acquired skills in bioinformatics and biostatistics. These lines of research have not only informed the wider understanding of the interplay between the microbiome and host immune response but have also been instrumental in honing my skills in bioinformatics and biostatistics. This collective work thus represents a significant personal and academic contribution to the field, offering valuable insights into the mechanisms governing microbiome and host interactions, as well as their implications for disease processes.

    a. Al-Muhanna FA, Dowdell AK, Al Eleq AH, Albaker WI, Brooks AW, Al-Sultan AI, Al-Rubaish AM, Alkharsah KR, Sulaiman RM, Al-Quorain AA, Cyrus C, Alali RA, Vatte C, Robinson FL, **Zhou X,** Snyder MP, Almuhanna AF, Keating BJ, Piening BD, Al-Ali AK. Gut microbiota analyses of Saudi populations for type 2 diabetes-related phenotypes reveals significant association. BMC Microbiol. 2022 Dec 13;22(1):301. PubMed Central PMCID: PMC9746012.

b. **Zhou X*,** Johnson JS*, Spakowicz D, Zhou W, Zhou Y, Sodergren E, Snyder M, Weinstock GM. Longitudinal Analysis of Serum Cytokine Levels and Gut Microbial Abundance Links IL-17/IL-22 With *Clostridia* and Insulin Sensitivity in Humans. Diabetes. 2020 Aug;69(8):1833-1842. PubMed Central PMCID: PMC7372073.

c. Yang D*, Johnson J*, **Zhou X***, Deych E, Shands B, Hanson B, Sodergren E, Weinstock G, Shannon WD. New statistical method identifies cytokines that distinguish stool microbiomes. Sci Rep. 2019 Dec 27;9(1):20082. PubMed Central PMCID: PMC6934614.

d. Zhou W, Sailani MR, Contrepois K, Zhou Y, Ahadi S, Leopold SR, Zhang MJ, Rao V, Avina M, Mishra T, Johnson J, Lee-McMullen B, Chen S, Metwally AA, Tran TDB, Nguyen H, **Zhou X**, Albright B, Hong BY, Petersen L, Bautista E, Hanson B, Chen L, Spakowicz D, Bahmani A, Salins D, Leopold B, Ashland M, Dagan-Rosenfeld O, Rego S, Limcaoco P, Colbert E, Allister C, Perelman D, Craig C, Wei E, Chaib H, Hornburg D, Dunn J, Liang L, Rose SMS, Kukurba K, Piening B, Rost H, Tse D, McLaughlin T, Sodergren E, Weinstock GM, Snyder M. Longitudinal multi-omics of host-microbe dynamics in prediabetes. Nature. 2019 May;569(7758):663-671. PubMed Central PMCID: PMC6666404.

4. I have extended my work on the interactions between the gut microbiome and host into a variety of different disease contexts. These include, but are not limited to, conditions such as aging, Pulmonary Arterial Hypertension (PAH), and several lymphatic disorders. This expansion has underscored the significant role that the gut microbiome plays in health and disease, contributing to metabolic homeostasis and potentially influencing the development of cardiovascular complications. Throughout these explorations, I have incorporated advanced multi-omics and single-cell analysis techniques. These methodologies have enabled a nuanced understanding of the complex interplay between the gut microbiome and the host, offering a holistic view of the disease mechanisms in question. The expertise I've developed in these areas has been instrumental in broadening the applications of the disease models I've been working with and has deepened our understanding of the gut microbiome's role in various health conditions. This comprehensive approach to investigating the gut microbiome's role in health and disease has equipped me with the essential skills to contribute meaningfully to this rapidly evolving field. The knowledge and experience I've gained positions me well to continue exploring and developing therapeutic interventions informed by these insights.

a. Lyu L*, Li X*, Feng R*, **Zhou X*,** Guha TK, Yu X, Chen GQ, Yao Y, Su B, Zou D, Snyder MP, Chen L. Simultaneous profiling of host expression and microbial abundance by spatial metatranscriptome sequencing. Genome Res. 2023 Mar;33(3):401-411. PubMed Central PMCID: PMC10078289.

b. **Zhou X*,** Wang B*, Demkowicz PC*, Johnson JS, Chen Y, Spakowicz DJ, Zhou Y, Dorsett Y, Chen L, Sodergren E, Kuchel GA, Weinstock GM. Exploratory studies of oral and fecal microbiome in healthy human aging. Front Aging. 2022;3:1002405. PubMed Central PMCID: PMC9631447.

c. Yu Z*, **Zhou X***, Liu Z, Pastrana-Gomez V, Liu Y, Guo M, Tian L, Nelson TJ, Wang N, Mital S, Chitayat D, Wu JC, Rabinovitch M, Wu SM, Snyder MP, Miao Y, Gu M. KMT2D-NOTCH Mediates Coronary Abnormalities in Hypoplastic Left Heart Syndrome. Circ Res. 2022 Jul 22;131(3):280-282. PubMed Central PMCID: PMC9308708.

d. Rockson SG*, **Zhou X*,** Zhao L*, Hosseini DK, Jiang X, Sweatt AJ, Kim D, Tian W, Snyder MP, Nicolls MR. Exploring disease interrelationships in patients with lymphatic disorders: A single center retrospective experience. Clin Transl Med. 2022 Apr;12(4):e760. PubMed Central PMCID: PMC9028099.

Complete List of Published Work in My Bibliography: https://www.ncbi.nlm.nih.gov/myncbi/xin.zhou.16/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Stanford/Rambam Pilot Grant Snyder/**Zhou**/Pitashny/Chen/Weiss (MPI) 06/01/2022-06/30/2024
Stanford Medicine (USA) – RAMBAM Health Care Campus (Israel)
Stanford University School of Medicine & Rambam Health Care Campus Collaboration Award
The project is designed to apply multi-omics characterization of dietary related dysbiosis and autoimmune signatures among Type 1 Diabetes(T1D) patients.
Role: Co-investigator

Stanford Pilot Grant Snyder/Nadeau/Armstrong/Lan/**Zhou** (MPI) 09/30/2022-09/30/2023
The Stanford Institute for Immunity, Transplantation and Infection (ITI) And the Stanford Autoimmune & Allergy Supergroup (SAAS) Interdisciplinary Research Awards
This grant sponsors the Longitudinal Analyses of Long COVID, ME/CFS and PTLDS Using Wearable Devices and Micro sampling.
Role: Co-investigator

Stanford (IMA-1051) Snyder/Davis/**Zhou**/Chen (MPI) 12/01/2021 -08/31/2023
Prototyping using Tonsils-in-a-Dish Award, Stanford Innovative Medicine Accelerator
The goal for this grant is to identify novel *Clostridia* strains that modulate immune response in human tonsil organoids.
Role: Co-Investigator

Completed Research Support

SAGE Fellowship (P30AG059307) **Zhou** (PI) 06/01/2021-06/30/2022
NIA/Stanford Resource Centers for Minority Aging Research (RCMAR) Fellowship
The project is to explore relationships between gastrointestinal dysbiosis and cardiovascular diseases such as pulmonary arterial hypertension with evidence of the dysbiosis related rapid vascular aging.
Role: PI