

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: Zhao, Yanan

eRA COMMONS USER NAME (credential, e.g., agency login): yananz1

POSITION TITLE: Associate Professor

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
Tongji Medical University, Wuhan	MD	07/1999	Preventive Medicine
Tongji Medical College, HUST, Wuhan	MS	07/2002	Epidemiology
Fudan University, Shanghai	PhD	07/2005	Molecular Epidemiology
Public Health Research Institute, UMDNJ, Newark, NJ	Postdoctoral Fellow	2009	Molecular Microbiology

A. Personal Statement

My research endeavors are centered on the development of preclinical antimicrobial drugs and the molecular diagnosis of various infectious diseases and drug resistance mechanisms. I have a strong track record of leading drug development projects, utilizing various small animal models such as mice and rats. I have also had the opportunity to collaborate with notable pharmaceutical companies, including Cidara, Astellas, Amplyx, Scynexis, and Matinas, to evaluate novel antifungal compounds. Currently, I am spearheading two NIH-funded projects aimed at developing antibody-drug conjugates to combat drug-resistant Gram-negative bacterial infections. Through these projects, I have acquired extensive knowledge and experience in various aspects of drug development, including compound synthesis, in vitro screening, in vivo PK/PD and efficacy evaluation, GLP tox screen, and pre-IND studies in non-human primates. I have recently been invited to play a key role in the Metropolitan AntiViral Drug Accelerator (MAVDA) program, a highly-funded initiative with over \$65.1M in funding from the NIAID, and led by two of the most renowned scientists in the field, Dr. David Perlin (CSO, HMH-CDI) and Dr. Charles Rice (2020 Nobel laureate). As the Scientific liaison, I help oversee and facilitate progress across all projects and cores, ensuring that all efforts are aligned to advance the program's goals.

In addition to my work in preclinical drug development, I am a renowned expert in molecular diagnostics. I have developed rapid diagnostic tests for important drug-resistant bacterial and fungal infections, such as KPC-producing *Klebsiella pneumoniae*, azole-resistant *Aspergillus fumigatus*, echinocandin-resistant *C. glabrata* and *C. auris*. At the onset of the COVID-19 pandemic, I invented an FDA-EUA approved diagnostic test, which played a significant role in rapidly implementing testing in the clinical laboratory at HUMC and serving over 10,000 patients. Furthermore, I created a high-throughput SARS-CoV-2 variant screening platform that was integrated into the NJDOH COVID surveillance program, greatly facilitating local epidemiological monitoring.

My contributions to the field are well-documented, with 62 original articles and reviews published, 6 patent applications, and serving on the editorial board of Microbial Drug Resistance. Furthermore, I am an active member of the CLSI antifungal subcommittee and have served as a study section reviewer for NIH special emphasis panel "Repurposing Target-Based Pharmaceutical Libraries for Discovery of Therapeutics against Eukaryotic Pathogens (R21/R33)". I am also a program committee member of ASM Microbe 2023 under the AAR track.

1. Yu S, Paderu P, Lee A, Eirekat S, Healey K, Chen L, Perlin DS, **Zhao Y**. Histone Acetylation Regulator Gcn5 Mediates Drug Resistance and Virulence of *Candida glabrata*. *Microbiol Spectr*. 2022 Jun 29;10(3):e0096322. doi: 10.1128/spectrum.00963-22. PubMed PMID: 35658596; PubMed Central PMCID: PMC9241792.
2. Lovey A, Krel M, Borchardt A, Brady T, Cole JN, Do QQ, Fortier J, Hough G, Jiang W, Noncovich A, Tari L, Zhao Q, Balkovec JM, **Zhao Y**, Perlin DS. Development of novel immunoprophylactic agents against multidrug resistant Gram-negative bacterial infections. *Antimicrob Agents Chemother*. 2021 Oct

18;65(11):e0098521. doi: 10.1128/AAC.00985-21. Epub 2021 Aug 9. PubMed PMID: 34370589; PubMed Central PMCID: PMC8522721.

3. Lee A, Wang N, Carter CL, Zimmerman M, Dartois V, Shaw KJ, Perlin DS, **Zhao Y**. Therapeutic Potential of Fosmanogepix (APX001) for Intra-abdominal Candidiasis: from Lesion Penetration to Efficacy in a Mouse Model. *Antimicrob Agents Chemother*. 2021 Mar 18;65(4). doi: 10.1128/AAC.02476-20. PubMed PMID: 33468476; PubMed Central PMCID: PMC8097442.
4. Lee A, Prideaux B, Zimmerman M, Carter C, Barat S, Angulo D, Dartois V, Perlin DS, **Zhao Y**. Penetration of Ibrexafungerp (Formerly SCY-078) at the Site of Infection in an Intra-abdominal Candidiasis Mouse Model. *Antimicrob Agents Chemother*. 2020 Feb 21;64(3). doi: 10.1128/AAC.02268-19. PubMed PMID: 31871074; PubMed Central PMCID: PMC7038262.

Highlighted Ongoing and Recently Completed Research Projects:

1U19AI171401, NIH-NIAID Perlin & Rice (PI) 05/16/22-04/30/25

Metropolitan AntiViral Drug Accelerator

Role: Key role (Scientific Liaison)

1R01AI141183, NIH-NIAID Perlin (PI) 02/21/19-01/31/24

Novel bi-specific immunotherapeutic against high-threat Gram-negative pathogens

Role: Co-Investigator

1R01AI138986, NIH-NIAID Perlin (PI) 05/01/18-04/30/24

Novel bi-specific immunoprophylactics against multi-drug resistant Gram-negative bacterial infections

Role: Co-Investigator

2R01AI109025, NIH-NIAID Perlin (PI) 08/01/14-06/30/23

Critical Factors Influencing Echinocandin Resistance in *Candida glabrata*

Role: Co-Investigator

Amplix Pharmaceuticals Zhao & Perlin (PI) 09/16/19-09/16/20

Penetration of APX001/APX001A at the Site of Infection in an Intra-abdominal Candidiasis Mouse Model

Role: PI

Scynexis, Inc. Zhao & Perlin (PI) 05/01/18-05/01/19

Penetration of SCY-078 at the Site of Infection in an Intra-abdominal Candidiasis Mouse Model

Role: PI

Astellas Pharma Inc. Perlin & Zhao (PI) 01/01/17-01/01/18

Tissue Distribution and Prophylactic Efficacy Evaluation of High Dose Isavuconazole in Experimental Invasive Pulmonary Aspergillosis

Role: Co-PI

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2019 - Associate Professor, Hackensack Meridian School of Medicine, Nutley, NJ

2015 - 2019 Assistant Professor, PHRI, NJMS, Rutgers University, Newark, NJ

2009 - 2015 Research Associate, PHRI, NJMS, Rutgers University, Newark, NJ

2006 - 2009 Postdoctoral Fellow, PHRI, UMDNJ, Newark, NJ

2005 - 2006 Lecturer of Epidemiology, School of Public Health, Fudan University, Shanghai

Other Experience and Professional Memberships

2022- Member, ASM Microbe Program Committee

2021- Editorial Board, Microbial Drug Resistance

2018 - Reviewer, Clinical and Laboratory Standards Institute (CLSI), Antifungal Subcommittee
2018 - Associate Editor, Frontiers In Cellular And Infection Microbiology, Fungal Pathogenesis

Honors

2007 Preventive Medicine Award of China, China Preventive Medicine Association
2007 Science and Technology Progress Award of the Institute of Higher Education of China, Ministry of Education of China
2005 Outstanding Graduate of Shanghai, Shanghai Municipal Education Commission
2005 The 19th Shanghai Excellent Invention Competition, Municipal Science and Technology Commission

C. Contribution to Science

1. **Preclinical drug discovery and development.** The problem of drug resistance, particularly multidrug-resistance, poses a significant threat to healthcare globally and in the U.S. Despite this, there has been a dearth of new drugs coming to market in recent decades. There is a pressing need for new therapeutics to treat drug-resistant bacterial and fungal infections. I have been at the forefront of addressing this need, leading multiple preclinical studies of novel antimicrobial and antifungal compounds, utilizing small animal models. To gain a deeper understanding of drug penetration at infected tissue sites, I have developed a novel platform using MALDI imaging mass spectrometry and laser capture microdissection directed LC-MS/MS drug quantification, which is applicable to multiple small molecule drugs. This cutting-edge approach has the potential to unlock new treatments for drug-resistant infections and improve patient outcomes.
 - a. Lovey A, Krel M, Borchardt A, Brady T, Cole JN, Do QQ, Fortier J, Hough G, Jiang W, Noncovich A, Tari L, Zhao Q, Balkovec JM, **Zhao Y**, Perlin DS. Development of novel immunoprophylactic agents against multidrug resistant Gram-negative bacterial infections. *Antimicrob Agents Chemother.* 2021 Oct 18;65(11):e0098521. doi: 10.1128/AAC.00985-21. PubMed PMID: 34370589; PubMed Central PMCID: PMC8522721.
 - b. Lee A, Wang N, Carter CL, Zimmerman M, Dartois V, Shaw KJ, Perlin DS, **Zhao Y**. Therapeutic Potential of Fosmanogepix (APX001) for Intra-abdominal Candidiasis: from Lesion Penetration to Efficacy in a Mouse Model. *Antimicrob Agents Chemother.* 2021 Mar 18;65(4). doi: 10.1128/AAC.02476-20. PubMed PMID: 33468476; PubMed Central PMCID: PMC8097442.
 - c. Lee A, Prideaux B, Zimmerman M, Carter C, Barat S, Angulo D, Dartois V, Perlin DS, **Zhao Y**. Penetration of Ibrexafungerp (Formerly SCY-078) at the Site of Infection in an Intra-abdominal Candidiasis Mouse Model. *Antimicrob Agents Chemother.* 2020 Feb 21;64(3) PubMed Central PMCID: PMC7038262.
 - d. Lee A, Prideaux B, Lee MH, Zimmerman M, Dolgov E, Perlin DS, **Zhao Y**. Tissue Distribution and Penetration of Isavuconazole at the Site of Infection in Experimental Invasive Aspergillosis in Mice with Underlying Chronic Granulomatous Disease. *Antimicrob Agents Chemother.* 2019 Jun;63(6) PubMed Central PMCID: PMC6535567.
2. **Molecular mechanisms of antifungal resistance.** Antifungal drug resistance continues to be a disturbing problem in medical mycology. I have studied the molecular mechanisms of drug resistance in *Aspergillus* and *Candida* species and developed comprehensive molecular diagnostic assays to detect resistance in these fungi. I led a project funded by NIH to investigate azole resistance in *A. fumigatus* and created rapid diagnostic tools for *C. glabrata* and *C. auris*. Additionally, I successfully developed a GI colonization mouse model and incorporated rapid diagnostic tools to study genetic factors contributing to echinocandin resistance emergence.
 - a. Yu S, Paderu P, Lee A, Eirekat S, Healey K, Chen L, Perlin DS, **Zhao Y**. Histone Acetylation Regulator Gcn5 Mediates Drug Resistance and Virulence of *Candida glabrata*. *Microbiol Spectr.* 2022 Jun 6;:e0096322. doi: 10.1128/spectrum.00963-22. [Epub ahead of print] PubMed PMID: 35658596.
 - b. Hou X, Healey KR, Shor E, Kordalewska M, Ortigosa CJ, Paderu P, Xiao M, Wang H, Zhao Y, Lin LY, Zhang YH, Li YZ, Xu YC, Perlin DS, **Zhao Y**. Novel *FKS1* and *FKS2* modifications in a high-level

echinocandin resistant clinical isolate of *Candida glabrata*. *Emerg Microbes Infect.* 2019;8(1):1619-1625. PubMed Central PMCID: PMC6853239.

- c. **Zhao Y**, Stensvold CR, Perlin DS, Arendrup MC. Azole resistance in *Aspergillus fumigatus* from bronchoalveolar lavage fluid samples of patients with chronic diseases. *J Antimicrob Chemother.* 2013 Jul;68(7):1497-504. PubMed Central ID: PMC3935014.
 - d. Healey KR, **Zhao Y**, Perez WB, Lockhart SR, Sobel JD, Farmakiotis D, Kontoyiannis DP, Sanglard D, Taj-Aldeen SJ, Alexander BD, Jimenez-Ortigosa C, Shor E, Perlin DS. Prevalent mutator genotype identified in fungal pathogen *Candida glabrata* promotes multi-drug resistance. *Nat Commun.* 2016 Mar 29;7:11128. PubMed Central PMCID: PMC5603725.
3. **Molecular diagnostics.** Rapid and accurate diagnosis is central to early and appropriate therapeutic management, directly impacting clinical outcome. I have extensive experience in developing and implementing cutting-edge technologies for the identification of various infectious diseases, including viral, bacterial, and fungal infections. For the past 17 years, I have been dedicated to advancing the field through the development of next-generation nucleic acid PCR- and RNA-based molecular beacon platforms for the rapid identification of high-threat pathogens and associated drug resistance. My work has been instrumental in improving patient outcomes, as demonstrated by the FDA EUA approval of my diagnostic test for COVID-19 during the pandemic, and its successful implementation in a clinical lab setting. Additionally, I have created a variant test that is currently being utilized as a rapid screening tool for tracking SARS-CoV-2 variants within HMH hospital network.
- a. **Zhao Y**, Lee A, Composto K, Cunningham MH, Mediavilla JR, Fennessey S, Corvelo A, Chow KF, Zody M, Chen L, Kreiswirth BN, Perlin DS. A novel diagnostic test to screen SARS-CoV-2 variants containing E484K and N501Y mutations. *Emerg Microbes Infect.* 2021 Dec;10(1):994-997. PubMed Central PMCID: PMC8168736.
 - b. **Zhao Y**, Cunningham MH, Mediavilla JR, Park S, Fitzgerald S, Ahn HS, Li X, Zhan C, Hong T, Munk G, Chow KF, Perlin DS. Diagnosis, clinical characteristics, and outcomes of COVID-19 patients from a large healthcare system in northern New Jersey. *Sci Rep.* 2021 Feb 23;11(1):4389. PubMed Central PMCID: PMC7902820.
 - c. Hou X, Lee A, Jiménez-Ortigosa C, Kordalewska M, Perlin DS, **Zhao Y**. Rapid Detection of *ERG11*-Associated Azole Resistance and *FKS*-Associated Echinocandin Resistance in *Candida auris*. *Antimicrob Agents Chemother.* 2019 Jan;63(1) PubMed Central PMCID: PMC6325222.
 - d. **Zhao Y**, Petraitiene R, Walsh TJ, Perlin DS. A real-time PCR assay for rapid detection and quantification of *Exserohilum rostratum*, a causative pathogen of fungal meningitis associated with injection of contaminated methylprednisolone. *J Clin Microbiol.* 2013 Mar;51(3):1034-6. PubMed Central PMCID: PMC3592047.

Complete List of My Published Work:

<https://www.ncbi.nlm.nih.gov/myncbi/10gldjVPIT35Q/bibliography/public/>

PATENT APPLICATIONS

1. 2022 **Zhao Y**, Perlin DS; “MPX-F3L assay for real-time detection of monkeypox” (Provisional Patent Application No. 63413075)
2. 2022 **Zhao Y**, Perlin DS; “MPX-HA Assay For Real-Time Detection of monkeypox” (Provisional Patent Application No. 63413089)
3. 2021 **Zhao Y**, L Chen, Perlin DS; “CDI Rapid Test For Covid-19 Variants of Concern” (Provisional Patent Application No. 63/231,424)
4. 2020 **Zhao Y**, Park S, Perlin DS; “CDI Enhanced COVID-19 Test” (Provisional Patent Application No. 62/985,602)
5. 2018 Perlin DS, **Zhao Y** and Weidman G; “Aptamers, biosensors and detection methods for common azole-class antifungal drugs” (PCT/US18/44834)
6. 2004 Jiang QW, **Zhao Y**, Jiang RJ, Chen YZ, Shen JJ; “New Echovirus 30 and its use”; National Patent Application No: 200410053431; Publication No: CN1651573; State Intellectual Property Office of P.R.China