Xilin Zhao, Ph.D.

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Associate Professor, Department of Microbiology, Biochemistry, and Molecular Genetics
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Education

Dept. Biology, Nankai University, China, BS (Biochemistry 1988)
Institute of Molecular Biolology, Nankai University, China, MS (Molecular Biology 1990)
John Innes Centre/University of East Anglia, UK, Ph.D. (Mol. Biol. and Microbiol. 2003)

Positions and employment

1991-1992:	Assistant Researcher, Nankai University, China
1992-1993:	Research Assistant Professor, Nankai University, China
1994-2002:	Research Scientist, Public Health Research Institute (PHRI), New York
2003-present:	Research Associate Member/Principal Investigator, PHRI, New Jersey
2005-present:	Visiting Professor, PLA General (301) Hospital, Beijing, China
2006.06-2013:	Assistant/Associate Professor, Dept. Microbiology & Molecular Genetics, New Jersey Medical School, Univ. Med. and Dentistry of New Jersey
2012-present:	Professor, School of Public Health, Xiamen University, China
2013.07-present:	Associate Professor, Dept. Microbiology, Biochemistry, and Molecular Genetics, New Jersey Medical School, Rutgers Biomedical and Health Sciences, Rutgers, the State University of New Jersey

Honors and Awards

2003-present:	International Editor, Chinese Journal of Antibiotics
2004-present:	Member of American Society of Microbiology
2012-present:	Editorial Board, BioDiscovery.
2013-present:	Academic Editor, Microbial Cell
2016-present:	Editorial Board, Reactive Oxygen Species (ROS)

Bill & Melinda Gates Foundation Grand Challenge Exploration Award (2008)
Bill & Melinda Gates Foundation Grand Challenge Exploration Award (2009)
NIH Director's New Innovator Award (2010)
InnoCentive Extraordinary & Unorthodox Philanthropy Challenge Award (2011)

Research Interests

Overview. Dr. Zhao's work focuses on how to contain and overcome bacterial resistance to antimicrobial agents. His early work with Dr. Karl Drlica at PHRI developed the mutant selection window hypothesis into a framework for understanding relationships between antimicrobial concentration and selective enrichment of mutant subpopulations. Such work reveals a fundamental flaw in the way antibiotics have been dosed and calls for 1) antimicrobials to be dosed above the upper (mutant prevention concentration (MPC)) rather than the lower (minimum inhibitory concentration (MIC)) boundary of the selection window and 2) new compounds to be designed/developed to have a very narrow window in order to restrict enrichment of resistant mutant subpopulations. Zhao later shifted his effort to 1) better understanding of general mechanisms of antimicrobial killing, with a special emphasis on the bacterial stress response and programmed cell death, 2) developing new antimicrobials/antimicrobial potentiators and repurposing approved non-antimicrobial drugs for antimicrobial use, 3) reversing antimicrobial resistance with CRISPR-based technology, and 4) mitigating detrimental effects of antimicrobials on gut microbiota and on gut inflammation.

Bacterial stress response. Bacterial tolerance and persistence to antimicrobial treatment pose an alarming threat to human health. Stress-response networks underlie mechanisms of tolerance and persistence, thereby preventing bacteria from being killed by many antimicrobials. By understanding and subsequently perturbing stress responses, Dr. Zhao expects to stimulate the lethal action of both antimicrobial and host immune stresses. He has identified reactive oxygen species (ROS)-mediated post-stress bacterial programmed cell death (PCD) as a universal killing mechanism that is shared by many antimicrobial and non-antimicrobial stressors. His work has also identified four factors (MazF, EF4, Cpx, and superoxide) as having dual functions – at moderate levels of stress they protect cells, but at high levels of stress they assure death, largely through a cascade of ROS. Small-molecule inhibitors and enhancers of lethal stress-response factors are expected to both facilitate antimicrobial action and broaden our knowledge of bacterial stress-response networks.

Developing new antimicrobials and repurposing old drugs. With respect to developing new antimicrobials and repurposing old drugs for antimicrobial use, Dr. Zhao has focused on uncovering mechanisms of action of auranofin, gallium nitrate, and bicyclomycin. He has found a handful of compounds that not only synergistically enhance auranofin lethality against Gram-positive bacteria, but they may also help extend the spectrum of auranofin to cover Gram-negative pathogens. In addition, Zhao has identified a way to convert bicyclomycin from a largely static agent to a highly lethal one; with gallium, his laboratory has discovered two molecular targets involved in gallium-mediated bacterial killing. This type of work is expected to help contain multi-drug resistant pathogens.

CRISPR and microbiota. Dr. Zhao has also started an effort to reverse existing antimicrobial resistance by destroying genetic elements that confer antimicrobial resistance using CRISPR-based technology and phage-based delivery. Such work should make it possible to eliminate resistance genes without exerting selective pressure on pathogen populations. He has also been studying the destructive impact of antimicrobial use on gut microbiota and exploring ways to mitigate such detrimental effects on human health.

Selected Articles (past 5 years, for a full list of publications see link below)
https://www.ncbi.nlm.nih.gov/sites/myncbi/xilin.zhao.1/bibliography/40899190/public/?sort=date&direction=ascending

1. Dorsey-Oresto A, Lu T, Mosel M, Wang X, Salz T, Drlica K, **Zhao X***. (2013) YihE kinase is a central regulator of programmed cell death in bacteria. Cell Reports 3 (2): 528-537.
2. Mosel M, Li L, Drlica K, **Zhao X***. (2013) Superoxide-mediated protection of *Escherichia coli* from antimicrobials. Antimicrobial Agents and Chemotherapy 57: 5755-9.
3. Yuan X, Liu Y, Bai C, Luo Y, Wang R, Wang R, Cai Y, **Zhao X*** (2014) Mycoplasma pneumoniae infection is associated with subacute cough. Eur Respir J. 43: 1178-81.
4. Mustaev A, Malik M, **Zhao** X, Kurepina N, Luan G, Oppegard LM, Hiasa H, Marks KR, Kerns RJ, Berger JM, Drlica K. (2014) Fluoroquinolone-Gyrase-DNA Complexes: Two Modes of Drug Binding. J Biol Chem 289:12300-12.
5. Malik M, Li L, **Zhao X***, Kerns RJ, Berger JM, and Drlica K*. (2014) Lethal synergy involving bicyclomycin: an approach for reviving old antibiotics. J. Antimicrob. Chemother. 69: 3227-35
6. **Zhao X***, Drlica K. (2014) Reactive oxygen species and the bacterial response to lethal stress. Curr. Opin. Microbiol. 21C: 1-6
7. **Zhao X***, Malik M, Hong Y, Li L, Drlica K. (2014) Quinolones. Reference Module in Biomedical Research. doi:10.1016/B978-0-12-801238-3.02418-1
8. Li L, Hong Y, Luan G, Mosel M, Malik M, Drlica K, **Zhao X*** (2014) Ribosomal elongation factor 4 promotes cell death associated with lethal stress. mBio 5 (6): e01708.
9. **Zhao X**, Hong Y, Drlica K. (2015) Moving forward with reactive oxygen species involvement in antimicrobial lethality. J. Antimicrob. Chemother. 70: 639-42.
10. Long Q, Du Q, Fu T, Drlica K, **Zhao X***, Xie J*. (2015) Involvement of Holliday junction resolvase in fluoroquinolone-mediated killing of *Mycobacterium smegmatis*. Antimicrobial Agents and Chemotherapy 59: 1782-5.
11. Malik M, Mustaev A, Schwanz HA, Luan G, Shah N, Oppegard LM, de Souza EC, Hiasa H, **Zhao X**, Kerns RJ, Drlica K. (2016). Suppression of gyrase-mediated resistance by C7 aryl fluoroquinolones. Nucleic Acids Res. 44: 3304-16.
12. Liu Y, Zhou J, Qu Y, Yang X, Shi G, Wang X, Hong Y, Drlica K, **Zhao X***. (2016). Resveratrol Antagonizes Antimicrobial Lethality and Stimulates Recovery of Bacterial Mutants. PLoS One. 11(4):e0153023.
13. Mi H, Wang D, Xue Y, Zhang Z, Niu J, Hong Y, Drlica K, **Zhao X***. (2016). Dimethyl Sulfoxide Protects Escherichia coli from Rapid Antimicrobial-Mediated Killing. Antimicrob Agents Chemother. 60(8):5054-8.
14. Zeng X, Li H, Zheng R, Kurepina N, Kreiswirth BN, **Zhao X**, Xu Y, Li Q. (2016). Spoligotyping of *Mycobacterium tuberculosis* Complex Isolates by Use of Ligation-Based Amplification and Melting Curve Analysis. J Clin Microbiol. 54(9):2384-7. PMCID: PMC5005503.
15. Carley Tasker, Selvakumar Subbian, Pan Gao, Jennifer Couret, Carly Levine, Saleena Ghanny, Patricia Soteropoulos, **Xilin Zhao**, Nathaniel Landau, Wuyuan Lu, and Theresa L. Chang (2016). IFN-ε protects primary macrophages against HIV infection. *JCI Insight*. 1(20): e88255
16. Theresa Li-Yun Chang, Carley Tasker, Selvakumar Subbian, Pan Gao, Jennifer Couret, Carly Levin, Saleena Ghanny, Patricia Soteropoulos, **Xilin Zhao**, Nathaniel Landau, Wuyuan Lu (2017). Interferon epsilon protects primary macrophages against HIV infection. The Journal of Immunology 198 (1 Supplement), 158.15-158.15
17. Y Hong, L Li, G Luan, K Drlica, **X Zhao*** (2017). Contribution of reactive oxygen species to thymineless death in *Escherichia coli*. Nature microbiology 2 (12), 1667

18. G Luan, Y Hong, K Drlica, **X Zhao*** (2017). Suppression of reactive-oxygen-species accumulation accounts for paradoxical bacterial survival at high quinolone concentration. Antimicrobial Agents and Chemotherapy, AAC. 01622-17 (In press).