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Persisters

Dr. Ying Zhang is Professor at Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health. Dr. Zhang is a leader in drug resistance research and has made major contributions to our modern understanding of molecular basis of drug resistance in *M. tuberculosis*, including identification of the first TB drug resistance gene *katG* (catalase-peroxidase) in isoniazid (INH) resistance, *pncA* gene in pyrazinamide (PZA) resistance, and more recently identified two new PZA targets RpsA and PanD involved in PZA action and resistance. His work on the unique persister drug PZA, which is critical for shortening TB therapy, has provided important insights into key targets of persister bacteria and has impacted the development of new drugs that further shorten the TB therapy. He has also made a number of important contributions to the mechanisms and concept of bacterial persisters. He first pointed out the link and similarity of bacterial persisters and cancer stem cells in 2007, first proposed the heterogeneity of persisters and expanded the persister definition to include viable but nonculturable (VBNC) organisms as part of the persister continuum, as well as proposed common strategies for improved treatment of persistent infections by targeting both growing and non-growing persisters. More recently, Dr. Zhang applied the "PZA principle" to treatment of persistent Lyme disease,

and made paradigm-shifting contributions by identifying drugs that target *Borrelia* persistence for more effective treatment of persistent Lyme disease. Dr. Zhang has published over 200 original articles and review articles and book chapters, serves on various editorial boards and advisory boards, and has made important contributions to mechanisms of drug resistance and persistence that impact the control of drug resistant and persistent infections of several important bacterial pathogens including TB and Lyme disease.

Conference Lecture Summary

In this presentation, the causes as to why some patients continue to suffer from post-treatment Lyme disease syndrome (PTLDS) despite antibiotic treatment will be discussed. In particular, the relevance of *Borrelia* persistence in animal models and in vitro to the PTLDS condition in patients will be addressed. Different strategies for treating persistent infection will be presented in terms of drug combination treatment as compared to pulse dosing. In addition, an update on the search for practical and effective drug combinations that eradicate round bodies and biofilm-like structures in vitro will be presented. A path for translating these findings for more effective treatment of persistent Lyme disease will be discussed.