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Abstract

"Molecular Chaperone ClpB: Protein Disaggregase Becomes a Novel Antimicrobial Target"

Irreversible aggregation of misfolded polypeptides is a common nuisance in biochemical laboratories and a major challenge in the cellular protein homeostasis. An ATP-dependent chaperone ClpB from the Hsp100 family resolubilizes and reactivates aggregated proteins in cooperation with DnaK/Hsp70. While no ClpB orthologs are found in metazoan proteomes, ClpB is essential for survival of many microorganisms under stress, including a number of pathogens. Thus, we started to explore a potential of this chaperone to become a target for the development of novel antimicrobials. I will describe our ongoing studies on the biological role and biochemical mechanism of the ClpB-mediated protein disaggregation in *Escherichia coli* and two vector-borne pathogens: *Plasmodium falciparum* and *Ehrlichia chaffeensis*. I will also outline our strategies for developing ClpB inhibitors, which might potentially target a previously unexplored vulnerability of pathogens linked to protein misfolding and aggregation.

Bio-Summary

Dr. Zolkiewski obtained his B.S./M.S. in Biophysics from the University of Warsaw, Poland and Ph.D. in Chemistry from the Polish Academy of Sciences. He worked as a Fogarty Fellow and Visiting Associate at the National Institutes of Health in Bethesda, Maryland between 1990 and 1997. He has been a faculty member at Kansas State University since 1997 and is currently a Professor and Head of the Department of Biochemistry and Molecular Biophysics.