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Abstract

"Targets and Mechanisms of Bacterial Glycosyltransferases "

Many Gram-negative bacteria interact with mammalian cells by using a specialized type III secretion system to inject proteins directly into infected host cells. A subset of these injected protein 'effectors' are enzymes that covalently modify mammalian proteins. Effectors play essential roles in bacterial virulence, yet the mechanisms by which they subvert host cell functions to promote pathogen survival are incompletely characterized and are thus important and significant topics for ongoing research. Understanding these host-pathogen dynamics in molecular detail may enhance the development of pharmacological approaches to prevent and treat infections. Particularly intriguing and important is the function of a conserved family of effectors named NleB in *E. coli* and SseK in *Salmonella*. These proteins are glycosyltransferases that modify protein substrates on arginine residues. Relatively little is known about the structure and function of these newly discovered bacterial *N*-GlcNAc-transferases, although we do know that NleB is extremely important to pathogen virulence. I will discuss our ongoing research designed to elucidate the structure and function of the NleB/SseK enzymes. This research includes determining 1) the mechanism by which NleB/SseK glycosylate host substrates; 2) why the NleB/SseK orthologs have different substrate specificities despite their high degree of sequence identity; 3) the extent to which effector glycosyltransferase activity affects diarrheal pathogen virulence.

Bio-Summary

Dr. Hardwidge is a Professor at Kansas State University, a Senior International Scientist of the Chinese Academy of Sciences, a Distinguished Professor of Yangzhou University, a Distinguished Professor of Jiangsu Academy of Agricultural Sciences, Station Representative for the NC-1202 Agricultural Experiment Station, and owner of Impact Factor Consulting, LLC.

Dr. Hardwidge directs a research program that identifies mechanisms by which diarrheal pathogens establish colonization niches in infected hosts by inhibiting immunological pathways. Dr. Hardwidge discovered several molecular mechanisms by which bacterial proteins (effectors) subvert the host innate immune system to promote bacterial colonization and transmission. He is now leveraging these data by engineering these proteins as cell-penetrating fusion proteins to study other human diseases such as colon cancer, psoriasis, and arthritis. The National Institutes of Health has funded Dr. Hardwidge's research continuously since 2006. He was named the recipient of the Zoetis Research Award in 2015.

Dr. Hardwidge has published 75 peer-reviewed publications and has delivered 152 invited presentations. He serves on the editorial boards of 3 journals, serves as an ad hoc reviewer for 24 other journals, and has served on 35 federal, university, commodity group, and international grant review panels.