Mycobacterium tuberculosis toxin; antitoxin genes: Modulators of growth and fibromyalgia

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One aspect of Mtb's (*Mycobacterium tuberculosis*) pathogenic success is undoubtedly its ability to adapt to adverse environments encountered during infection of human macrophages. By mechanisms not fully understood, Mtb is able to transition from active growth to dormancy and can persist for extensive periods of time, with the potential of causing reactivation disease. Remarkably, Mtb encodes 90+ TA modules belonging to TA families relBE, vapBC, parDE, higBA and mazEF, suggesting involvement of toxin: antitoxin genes in Mtb pathogenesis. This talk will focus on the role of TA modules as regulators of cell growth and potential effectors of mycobacterial persistence, with an emphasis on the relBE family. We have established that the mycobacterial RelEMtb toxin negatively impacts growth and the structural integrity of the mycobacterial envelope in the absence of its cognate RelBMtb antitoxin, generating cells with aberrant forms that are prone to extensive aggregation. At a time coincident with growth defects, RelEMtb mediates mRNA degradation *in vivo* resulting in significant changes to the proteome. We establish that relMtb modules are stress responsive, as all three operons are transcriptionally activated following mycobacterial exposure to specific adverse environments. Overall, analysis reveals that the relMtb toxin: antitoxin family is stress-responsive and, through the degradation of mRNA, the RelEMtb toxin influences the growth, proteome and morphology of mycobacterial cells.

Speaker Biography

Shaleen B Korch has received her PhD in Microbiology and Immunology from the University of North Dakota (USA) in 2005. After completing her PhD, she did a Post-doctoral fellowship at the Bio design Institute at Arizona State University (USA) which is focused on characterizing the first toxin: antitoxin modules in *Mycobacterium tuberculosis*. Currently, she is an Associate Professor of Pharmacology at Midwestern University, with research interests in *M. tuberculosis* pathogenicity and the role of toxin: antitoxin modules in *M. tuberculosis* persistence. In addition, she evaluates novel, synthetic man-made proteins as potential antimicrobial chemotherapeutics and biological tools.

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