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## A mass spectrometry perspective on dormancy and antibiotic tolerance in bacteria

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Dormancy is a protective state where diverse bacteria including *M. tuberculosis*, *S. aureus*, *T. pallidum* (syphilis), and *B. burgdorferi* (Lyme Disease) curtail metabolic activity to survive severe external stresses including antibiotics. Dormancy appears to consist of a continuum of interrelated states including viable but nonculturable (VBNC) and persistence states implicated in antibiotic tolerance, reemergence from latent infections, and even quorum sensing and biofilm formation. To *eliminate dormancy as a mechanism for antibiotic tolerance, we must bridge a critical gap in current knowledge; our limited understanding of the protein mechanisms regulating persistence and VBNC dormancy states.* To elucidate some of these mechanisms, we have queried the VBNC state of Micrococcus luteus NCTC 2665 (MI-2665) by quantitative proteomics combining gel electrophoresis, HPLC and tandem mass spectrometry. MI-2665 is well suited for these studies being a non-pathogenic actinobacterium containing a small 2.5 Mb, high GC-content genome and exhibiting a well-defined VBNC state induced by nutrient deprivation. The MI-2665 VBNC state demonstrated a loss of protein diversity accompanied by upregulation of 18 proteins that are conserved across Actinobacteria, of which 14 have not been previously identified. In this talk, I will discuss these proteins and their implication of an anaplerotic strategy in VBNC transition exploiting the glyoxylate shunt, redox and amino acid metabolism, and ribosomal regulation. These results indicate a VBNC protein-level signature and suggest the viability of MI-2665 as model for dissecting the protein mechanisms underlying this stress response. I will also discuss the broader implications of our results for understanding protein regulation of dormancy and for therapeutic targeting of dormant bacterial infections.

## Biography

Steven J. Bark obtained his Ph.D. from The Scripps Research Institute (TSRI) with Professor Stephen B.H. Kent. He has served as the Director of the Center for Protein Sciences at TSRI before joining University of California San Diego as an Associate Project Scientist, Adjunct Assistant Professor, and Member of the Clinical and Translational Sciences Institute. Dr. Bark is currently an Assistant Professor in the Department of Biology and Biochemistry at University of Houston. His research program applies mass spectrometry, analytical chemistry, and systems biology to understand how dormancy stress responses regulate bacterial pathogenesis and evasion of antibiotics.

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