Oral Defense Announcement
University of Missouri – St. Louis Graduate School

An oral examination in defense of the dissertation for the degree
Doctor of Philosophy in Biology with emphasis in Cell and Molecular biology

Srinivas Silpi Thota
M.Sc in Biotechnology, Jawaharlal Nehru University, Hyderabad, India

The Role of Multidrug Resistance Regulators MarA, SoxS, Rob and RamA in Regulating Virulence
Traits in Salmonella enterica

Date:  November 21st, 2019
Time:  2:00 p.m. to 5:00 p.m.
Place: 230 Benton Hall

Abstract
Enteric pathogens sense numerous signals specific to the anatomical location in the intestine and integrate them with the complex regulatory networks to temporally and spatially regulate their virulence genes. MarA, SoxS, Rob and RamA are homologous transcription factors that belong to AraC family of proteins in Salmonella enterica that primarily were thought to be involved in rendering antibiotic resistance to bacteria by up regulating efflux pumps and down regulating outer membrane porins. The fact that these transcription factors respond to the same intestinal compounds that regulate virulence genes in Salmonella motivated us to look for other roles of these transcription factors.

We performed RNA-Seq analysis on Salmonella strains overexpressing MarA, SoxS, Rob and RamA and found that the expression of flagellar, fimbrial and SPI1 genes are repressed. Our genetic tests showed flhDC, the master regulator of flagellar genes, and hilA, the master regulator of the SPI-1 encoded type 3 secretion system (T3SS), are repressed by MarA, SoxS, Rob and RamA. We discovered that MarA and Rob directly repress flhDC transcription, while SoxS represses flhDC via a post-transcriptional mechanism. Additionally, we delineate direct and indirect contributions of MarA, SoxS, Rob and RamA in repressing hilA and currently designing in vitro invasion assays to identify their role in inhibiting infection. Finally, we demonstrate the role of MarA, SoxS, Rob, and RamA in responding to known virulence attenuating compounds.

Flagella, fimbriae, and the SPI1 T3SS are three key components of Salmonella virulence. Tight regulation of these genes is necessary for successful infection by Salmonella. Our study identified that multidrug resistance transcription factors MarA, SoxS, Rob and RamA strongly repress these key virulence traits. Chemotherapeutic activation of these transcription factors may reduce the virulence of Salmonella before or during infection.

Defense of Dissertation Committee
Dr. Lon Chubiz, Ph.D.
Dr. Teresa Thiel, Ph.D.
Dr. Wendy Olivas, Ph.D.
Dr. Aimee Dunlap Ph.D.