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Identification and Characterization of A Novel Regulator STM0029 which Contributes to *Salmonella* Intracellular Survival and Resistance to Antimicrobial Peptides

Heng-Chang Chen*, Peter Schwerk, Karsten Tedin
Institute of Microbiology and Epizootics, Freie University Berlin, Germany

Introduction:

Antimicrobial peptides (AMPs) are crucial components of the host innate immunity to eliminate pathogens. In this study, we report the identification of a novel regulator STM0029 involved in management of *Salmonella* intracellular survival.

Methods:

We first performed in vitro killing assay in various murine macrophage cell lines and peripheral blood mononuclear cells (PBMC) to determine intracellular survival ability between the wildtpy and ΔSTM0029 strain. Furthermore, different types of AMPs were tested the sensitivity of ΔSTM0029 strain comparing to the wildtype. Finally, the microarray analysis was performed to find out which genes were regulated.

Results:

An orphan putative transcriptional regulator STM0029 is 149 amino acid long. Comparing the wildtype and ΔSTM0029 mutant in murine macrophages as well as PBMC showed differences of the viable intracellular bacteria were observed between the wildtype and ΔSTM0029 after 24 hours post-infection. Further, expression data revealed that *Salmonella* STM0029 gene is affected by *pmrAB*, but not *phoPQ*. Since ΔSTM0029 mutant was more susceptible after infection in macrophage cell lines and PBMC, we therefore tested the bactericidal activity of α-defensin-1, LL-37, β-defensin-1/-2, lysozyme and polymyxin. ΔSTM0029 strain showed similar sensitivity patterns as Δ*pmrAB* strain whereas the wildtype was relatively resistant against AMPs. Finally, numerous of murein/peptidoglycan (PG) genes were found to be up-regulated under the ΔSTM0029 background, suggesting STM0029 is involved in the regulation of PG-related genes against intracellular receptors recognition.

Discussion:

We defined the function of STM0029, which is de-repressed by the *pmrAB* and further represses the expression of a set of PG-related genes to avoid being recognized by PAMP receptors as well as in resistance to antimicrobial peptides to establish the intracellular survival niche successfully. This finding gives us the new insight to identify the specific genes involved in pathogen survival issues as potential targets to control human infections.

Keywords: antimicrobial peptides, Salmonella peptidoglycan, pmrAB, intracellular survival