Oxidoreductases and RNA degradosome controlling virulence-associated traits of *Salmonella enterica* serovar Typhimurium

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ABSTRACT

The oxidative stress response is a fundamental and primitive mode of innate immune defense in nearly all forms of life. The host oxidative stress response becomes truly important and effective especially against intracellular pathogens such as Salmonella. Pathogens have evolved diverse mechanisms to withstand the oxidative responses. These include the use of oxidoreductases to neutralize oxidative products and repair oxidative damages, rapid alteration in their transcriptome and diversion of such oxidative products in cellular signaling, for their survival and successful infection.

In the first study in this thesis, we have introduced the putative SesABCD oxidoreductases of the thioredoxin superfamily for their role in oxidative stress tolerance and virulence of S. Typhimurium. We demonstrated that SesABCD proteins are dispensable for invasion in cultured epithelial cells under normal invasive conditions, although SesABCD acts as a suppressor of SPI-1 mediated invasion upon oxidative stress. Our results have further shown a functional association between SesABCD and thioredoxin 1 (TrxA) oxidoreductase of S. Typhimurium. In this, we demonstrated that absence of SesABCD restored the invasiveness of a trxA mutant in epithelial cells and its virulence in C. elegans. (Paper I).

Next, we present the analyses on the role of periplasmic Dsb oxidoreductase system in S. Typhimurium’s biofilm-development, specifically under redox stress. In this, we show that DsbA and DsbB act as suppressors of rdaA-morphotype development and affect biofilm-regulation using either Csg-dependent or-independent mechanism, respectively. Our results further reveal that oxidative stress abrogates rdaA-morphotype of S. Typhimurium, whereas reductive stress reduces rdaA-morphotype with concomitant plentiful release of extracellular slimy material containing, notably, the extracellular DNA (eDNA). Furthermore, we have demonstrated the oxidative recovery of swimming motility defects of a ddbA mutant. (Paper II).

Finally, we have demonstrated that exoribonuclease, PNPase and its genetic associate membrane lipoprotein Nlp1 constitute an operon and are functionally connected (Paper III and IV). PNPase was required for rdaA-morphotype development whereas, Nlp1 suppresses the biofilm formation. In addition, we established the association of PNPase with d-di-GMP metabolism in biofilm regulation. Moreover, we showed that both PNPase and Nlp1 are required, independently, for cold adaptation of S. Typhimurium.