The Salmonella Typhi hlyE gene plays a role in invasion of cultured epithelial cells and its functional transfer to S. Typhimurium promotes deep organ infection in mice

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Abstract

Comparison of genome sequences of *Salmonella enterica* serovars Typhi and Typhimurium reveals that *S*. Typhi has a small 2.3 kb genomic island missing in *S*. Typhimurium, designated *Salmonella* pathogenicity island 18 (SPI-18), which includes two potential genes. One of these, *hlyE*, encodes a hemolysin related to the *Escherichia coli* K12 HlyE hemolysin. PCR assays show that SPI-18 is present in *S*. Typhi and in many other, but not all, serovars of *S*. *enterica* subsp. *enterica* belonging to the SARB collection. HlyE activity cannot be detected in *S.* Typhi by means of standard plate assays. Nevertheless, we were able to reveal this activity upon lysis of bacterial cells with phages, in the presence of ampicillin, and in a *ompA*genetic background, conditions that compromise the integrity of the bacterial envelope. Almost all serovars of the SARB collection shown to cause systemic infections in humans have SPI-18 and *hlyE* and express an active hemolysin revealed upon bacterial envelope destabilization. *S.* Typhi *hlyE*mutants are impaired in invasion of human epithelial cells *in vitro*, and its heterologous expression in *S.* Typhimurium improves the colonization of deep organs in mice, demonstrating that the HlyE hemolysin is a new virulence determinant.