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Regulation of Virulence Factors in *Escherichia coli* O157:H7 by Quorum Sensing

James B. Kaper

Professor of Microbiology & Immunology, University of Maryland School of Medicine, Baltimore, USA

Escherichia coli O157:H7 and other enterohemorrhagic *E. coli* (EHEC) are important causes of bloody diarrhea and hemolytic uremic syndrome. Two important virulence factors for EHEC are Shiga toxin (Stx) and the Locus of Enterocyte Effacement (LEE) pathogenicity island. The LEE plays a critical role in intestinal colonization and encodes a type III secretion system and the intimin adhesin. The majority of the LEE genes are organized in five operons (*LEE1-5*). The first gene of the LEE encodes a transcriptional regulator (Ler) essential for expression of the LEE genes (2).

Quorum sensing (QS) is a mechanism of gene regulation in which small molecules called autoinducers (AIs) activate gene expression in a density-dependent manner. We initially showed that the LEE genes and stx are regulated by QS in a process that requires AI-2, which is encoded by the *luxS* gene (3, 4). Gene array studies showed that approximately 10% of the shared *E. coli* K-12 and O157:H7 genes were regulated by the *luxS* gene, including genes involved in motility (4). Additional regulatory factors were discovered to be involved in QS in *E. coli* including QseA (1) and QseBC (6). The LEE genes were shown to be regulated by AIs produced by non-pathogenic *E. coli* and other commensal species suggesting a model in which expression of key EHEC virulence factors is activated in response to the high densities of commensal bacteria in the large intestine (3). Using purified and in vitro synthesized AI-2, we showed that this AI is not directly involved in regulation of the LEE but is essential for the production of a novel AI that we have designed AI-3 (5). Furthermore, we have shown that expression of the LEE genes can be induced by the mammalian hormones epinephrine and norepinephrine acting through the same regulatory factors involved in QS. These results suggest a novel “cross-talk” mechanism of signaling occurring between bacteria and their mammalian hosts.

References

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