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Hydrogen stimulated glucarate catabolism in *Salmonella*

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Abstract

The pathogenic bacteria *Salmonella enterica* serovar Typhimurium are capable of surviving and growing in metabolically diverse environments both within and outside the host. The bacteria can grow and colonize within host tissues by utilizing host-produced H_2 by the activity of three H_2-oxidizing respiratory hydrogenases, all of which are required for virulence. Transcriptomic analyses of *S.* Typhimurium have revealed that high-level expression of genes associated with carbon uptake and metabolism occurs when the bacteria are exposed to H_2. Expression of the gene *gudT* that encodes a potential glucarate permease GudT, is significantly increased upon exposure of *S.* Typhimurium to H_2. Glucarate, an oxidized product of glucose, is a major serum organic acid in humans, and it is readily detected in tissues and body fluids. Still, its role as a carbon source for a pathogen has not been studied. In this study, we investigated the effects of deletion of *gudT* in the H_2-dependent growth and virulence of *S.* Typhimurium. We found that the *gudT*-deleted strain of *S.* Typhimurium is deficient in glucarate-dependent growth compared to its parent strain, and it exhibits attenuated virulence in mice. The mean time of death for mice inoculated with wild type was two days earlier than for the mice inoculated with the *gudT*-deleted strain. At four days post inoculation, liver and spleen homogenates from mice infected with *gudT*-deleted strain contained fewer viable *Salmonella* than mice infected with the parent strain. The parent strain grew well H_2-dependently in a minimal medium with amino acids and glucarate as the primary carbon-sources, whereas the *gudT*-deleted strain grew slower. Glucarate-mediated growth of a *hyc*-deleted mutant (that is deficient in H_2 production) was increased by H_2, presumably due to the positive transcriptional response of added H_2.