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Hydrogen-stimulated carbon catabolism in enteric pathogens *Salmonella* and *Shigella*

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Abstract

H_2-oxidizing nickel-containing hydrogenases allow enteric and other pathogens to use H_2 within host tissues, and aids pathogen survival within macrophages. Among the genes up-expressed by exposure of *Salmonella enterica*serovartyphimurium to H_2—a byproduct of intestinal commensal metabolism, are carbon uptake and catabolism-related genes. 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. High-level expression of a potential glucaratepermeasegudT occurs when *Salmonella* is exposed to H_2 gas. A *gudT* mutant strain of *Salmonella* is deficient in glucarate dependent growth, and it exhibits attenuated virulence (i.e. morbidity and mortality) in mice. The mean time of death for wild type-infected mice was two days earlier than for *gudT*-inoculated animals. At four days post inoculation, liver and spleen homogenates from *gudT*-inoculated mice contained fewer viable *Salmonella* than parental strain-inoculated animals. The parent strain grew well H_2-dependently in a minimal medium with amino acids and glucarate as the primary C-sources, whereas the *gudT* strain achieved ~60% of the parent strain's yield. Glucarate-mediated growth of a *hyc* mutant (cannot produce H_2) was stimulated by H_2, presumably due to the positive transcriptional response of added H_2. Hydrogenase deficient *Shigellaflexneri* exhibited poor acid tolerance but an energy deficiency response; compared to the H_2-utilizing parent it had increased production of glycolytic, nucleosidase, peptidase, and ATP synthase enzymes. Hydrogenases can be inhibited by nickel chelation approaches.

Biography

Robert Maier is the Georgia Research Alliance Professor of Microbial Physiology and has published more than 170 manuscripts on bacterial physiology and biochemistry, many involving roles of metalloenzymes and hydrogen metabolism enzymes. Work in the past 12 years has been focused on these attributes that aid survival of pathogenic bacteria within the host.