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

**Robert J. Maier, Reena Lamicchane-Khadka and Mykeshia McNorton**
University of Georgia, USA

$H_2$-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 enteric* serovar Typhimurium 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 glucarate permease gudT 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 *Shigella flexneri* 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 J. 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. His work in the past 12 years has been focused on these attributes that aid survival of pathogenic bacteria within the host.

rmaier@uga.edu