J Bacteriol. 2017 Jan 30;199(4). pii: e00595-16. doi: 10.1128/JB.00595-16. Print 2017 Feb 15.

Genetic Characterization of the Galactitol Utilization Pathway of Salmonella enterica Serovar Typhimurium.

Nolle N[1], Felsl A[1], Heermann R[2], Fuchs TM[3,4].

Author information

Abstract

Galactitol degradation by salmonellae remains underinvestigated, although this metabolic capability contributes to growth in animals (R. R. Chaudhuri et al., PLoS Genet 9:e1003456, 2013, https://doi.org/10.1371/journal.pgen.1003456). The genes responsible for this metabolic capability are part of a 9.6-kb gene cluster that spans from gatY to gatR (STM3253 to STM3262) and encodes a phosphotransferase system, four enzymes, and a transporter of the major facilitator superfamily. Genome comparison revealed the presence of this genetic determinant in nearly all Salmonella strains. The generation time of Salmonella enterica serovar Typhimurium strain ST4/74 was higher in minimal medium with galactitol than with glucose. Knockout of STM3254 and gatC resulted in a growth-deficient phenotype of S Typhimurium, with galactitol as the sole carbon source. Partial deletion of gatR strongly reduced the lag phase of growth with galactitol, whereas strains overproducing GatR exhibited a near-zero growth phenotype. Luciferase reporter assays demonstrated strong induction of the gatY and gatZ promoters, which control all genes of this cluster except gatR, in the presence of galactitol but not glucose. Purified GatR bound to these two main gat gene cluster promoters as well as to its own promoter, demonstrating that this autoregulated repressor controls galactitol degradation. Surface plasmon resonance spectroscopy revealed distinct binding properties of GatR toward the three promoters, resulting in a model of differential gat gene expression. The cyclic AMP receptor protein (CRP) bound these promoters with similarly high affinities, and a mutant lacking crp showed severe growth attenuation, demonstrating that galactitol utilization is subject to catabolite repression. Here, we provide the first genetic characterization of galactitol degradation in Salmonella, revealing novel insights into the regulation of this dissimilatory pathway.

IMPORTANCE:

The knowledge of how pathogens adapt their metabolism to the compartments encountered in hosts is pivotal to our understanding of bacterial infections. Recent research revealed that enteropathogens have adapted specific metabolic pathways that contribute to their virulence properties, for example, by helping to overcome limitations in nutrient availability in the gut due to colonization resistance. The capability of Salmonella enterica serovar Typhimurium to degrade galactitol has already been demonstrated to play a role in vivo, but it has not been investigated so far on the genetic level. To our knowledge, this is the first molecular description of the galactitol degradation pathway of a pathogen.

KEYWORDS:

Salmonella Typhimurium; galactitol utilization; gene regulation; metabolism; regulation

PMID: 27956522 PMCID: PMC5287402 DOI: 10.1128/JB.00595-16