Transcriptomic response of *Listeria monocytogenes* during transition into the long-term-survival phase.

Wen, J., X. Deng, Z. Li, E. Dudley, R. Anantheswaran, S.Knabel, W. Zhang.

Abstract

We recently reported that *Listeria monocytogenes* can change cellular morphology from bacilli to cocci during the long-term-survival (LTS) phase, where they become extremely resistant to heat and high pressure. However, the underlying mechanisms that trigger transition to the LTS phase remain largely unknown. We compared the transcriptomic profiles of a fully sequenced *L. monocytogenes* serotype 4b strain F2365 at various growth phases in Trypticase Soy Broth with Yeast Extract using a whole-genome DNA microarray approach. A large number of genes were differentially regulated during transition to the LTS phase. Genes related to cell envelope structure, energy metabolism and material transport were significantly upregulated during transition to the LTS phase, in contrast to the downregulation of genes associated with amino acid and protein biosyntheses. We also observed significant degradation of ribosomal RNA in the LTS phase. The transcription profiles of resuscitated LTS cells after transfer into fresh broth resembled those of log phase cells ($r = 0.94$). Upregulation of compatible solute transporters in the LTS phase may lead to accumulation of cellular solutes and thus lower water activity, which might enhance resistance to heat and high pressure. This, along with downregulation of genes associated with protein synthesis in the LTS phase, indicates these cells may be dormant persister cells. Upon exposure to fresh nutrients, LTS cells quickly resumed metabolic activities, transitioned to the log phase and became sensitive to heat and high pressure.

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