Genes that are Affected in High Hydrostatic Pressure Treatments in a 
Listeria Monocytogenes Scott A ctsR Deletion Mutant

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Abstract

Listeria monocytogenes is a food-borne pathogen of significant threat to public health. High Hydrostatic Pressure (HHP) treatment can be used to control L. monocytogenes in food. The CtsR (class three stress gene repressor) protein negatively regulates the expression of class III heat shock genes. In a previous study, a spontaneous ctsR L. monocytogenes deletion mutant 2-1 that was able to survive under HHP treatment was identified; however, there is only limited information about the mechanisms of survival and adaptation of this mutant in response to high pressure. Microarray technology was used to monitor the gene expression profiles of ctsR mutant 2-1 under pressure treatments (450 Mpa, 3min). Some of the gene expression changes determined by microarray assays were confirmed by real-time RT-PCR analyses. Compared to non-pressure-treated ctsR mutant 2-1, 14 genes were induced (> 2-fold increase) in the ctsR deletion mutant whereas 219 genes were inhibited (< -2-fold decrease) by pressure treatments. The induced genes included genes encoding proteins involved in synthesis of purines, pyrimidines, nucleosides, and nucleotides, transport and binding, transcription, cell membrane, DNA and energy metabolism, protein synthesis, and unknown functions. The inhibited genes included genes encoding proteins for transport and binding, cell envelope, transcription, amino acid biosynthesis, regulatory functions, cellular processes and central intermediary metabolism. The information concerning L. monocytogenes survival under HHP at the molecular level may contribute to improved HHP treatments for food processing.

Keywords: Listeria monocytogenes; Scott A; microarray and real-time PCR; High hydrostatic pressure (HHP); ctsR mutant

Introduction

L. monocytogenes is a Gram-positive bacterium that can cause listeriosis in animal and human populations. Listeriosis is a foodborne disease with a high mortality rate (approximately 20 to 30% of cases) and occurs mostly in susceptible individuals such as pregnant women, newborns, the elderly, and immune-compromised patients. Outbreaks of listeriosis have been associated with the consumption of contaminated food products including ready-to-eat (RTE) meats and dairy products [1-2]. Because L. monocytogenes is widely distributed in the environment and survive under very harsh conditions, it is very difficult to eliminate this pathogen from foods and/or food processing plants.

High Hydrostatic processing (HHP) is a process that can inactivate microorganisms without significant deterioration of food quality. Foods treated with HHP generally have better sensory and nutritional qualities than products processed in more traditional ways. HHP has been used as a non-thermal preservation technique for processing of meats and dairy products to control L. monocytogenes and extend product shelf-life. In the food industry, pressures within the range of 300 to 600 MPa are used to inactivate vegetative cells of microorganisms, including pathogens such as L. monocytogenes. However, the efficiency of HHP depends on the pressure, time, and composition of the food [3]. For example, the inactivation of L. monocytogenes by HHP (600 MPa, 3min) ranged from 1.82 to 3.85 Log units, depending on the type of dry-cured ham [4].

The pressure tolerance of L. monocytogenes is also growth-stage dependent. Stationary-phase cells are often more resistant to pressure than the exponential-phase cells [5]. High pressure resulted in changes in viability, morphology, and physiology in bacteria such as E. coli and L. monocytogenes [6-9]. However, the molecular survival mechanisms of L. monocytogenes under high pressure remain unknown.

Microarrays have been used to study differential gene expression of L. monocytogenes and E. coli during HPP and some important genes have been identified [10-13].

The ctsR gene encodes a transcriptional regulator that represses the class III heat shock genes. CtsR has been shown to be related to high pressure since several pressure-tolerant mutants contained mutations in this gene [14-20]. L. monocytogenes Scott A ctsR mutant 2-1 exhibiting a higher level of viability under HPP and was less virulent, non-motile, heat and acid resistant, and sensitive to nisin [15]. Compared to the wild-type L. monocytogenes, genes that were differentially expressed in ctsR mutant 2-1 under high pressure treatment were identified [12]. However, why the ctsR mutant 2-1 survives better under HHP treatments is unknown.

In the present paper, we compared gene expression of the ctsR mutant 2-1 under HHP treatment vs. normal conditions. Our purpose was to explore what other genes contribute to the barotolerance of the ctsR mutant 2-1. Since ctsR mutants are most frequently isolated under high pressure treatments [18, 20], they represent a critical challenge in the tailing effect of HHP. Understanding the survival mechanism of the...
**ctsR** mutant under HHP may assist in developing strategies to reduce the tailing effects of HHP treatments.

**Materials and Methods**

**Bacterial strains and HHP treatments**

The *L. monocytogenes* Scott A *ctsR* mutant 2-1 and *L. monocytogenes* strain ScottA (wild-type) obtained from Dr. Joerger at University of Delaware were treated with high pressure (450 Mpa, 3 min) as described previously [12]. After pressure treatments, the suspension was centrifuged and the pellets were resuspended in RNA Later and followed by RNA isolation according to Liu et al., [12]. The *L. monocytogenes* Scott A *ctsR* mutant 2-1 using as control samples was held at room temperature at atmospheric pressure for 3 min before centrifugation.

**RNA isolation, microarray chip design, hybridization, and data analysis**

Total RNA was isolated and quantified as described previously [12]. A whole genome microarray was constructed as described previously [12]. All samples (both wild-type and the *ctsR* mutant 2-1) were hybridized twice with one experiment (chip 1) using Alexa Fluor 647 to label cDNA under pressure treatment and in the reciprocal experiment (chip2), Alexa Fluor 647 was used to label the cDNA under normal conditions and Alexa Fluor 555 to label the cDNA under pressure treatment. Microarray hybridization and washing was performed and the microarray slide was scanned, quantified as described previously [12]. A minimum threshold of a 2-fold change in gene expression with a p-value of <0.01 was used as the cut-off value.

**cDNA synthesis, primer design and real-time PCR analysis**

Synthesis of cDNA was carried out using Invitrogen’s SuperScript III First-Strand Synthesis SuperMix (Invitrogen, Carlsbad, CA) following the manufacturer’s instructions. Primers selected based on the gene sequences of *L. monocytogenes* F2365 strain (GenBank accession#AE017262) were designed using Primer3 (v.0.4.0) software. Primer sequences are listed in Table 1 and Table 2. The housekeeping gene (*spoG*) was used as the internal control gene for real-time PCR analysis (Primer sequences 5’TGACGTTGAATTCGCTGTAAT3’; 5’TACGCAAGAACCGATTGCA3’) since this gene had the least variation among other housekeeping genes including 16S rRNA and 5S rRNA.

**Microarray data accession number**

The microarray data have been deposited into the Gene Expression Omnibus (GEO) database under accession number GSE32172 (www.ncbi.nlm.nih.gov/geo).

**Results**

**Barotolerance of *L. monocytogenes* Scott A wild type and the *ctsR* mutant 2-1**

The response of wild type *L. monocytogenes* Scott A and its *ctsR* mutant 2-1 to high pressure treatment (450 Mpa, 3 minutes) was investigated. At the pressure of 450 Mpa, the wild type exhibited a reduction in viability by 8.6-log<sub>10</sub> units, while the *ctsR* mutant 2-1 exhibited 6.7-log<sub>10</sub> reduction in viability. Our data are consistent with the previously findings [15].

**Induced genes in *L. monocytogenes* Scott A *ctsR* mutant 2-1 strain under HHP treatment**

A total of 14 genes were expressed at higher levels in the *ctsR* mutant 2-1 under HPP treatment. The genes that were expressed at higher levels in the wildtype under pressure were also identified using microarray assays (Data not shown). There are 7 genes present in both wildtype and the *ctsR* mutant 2-1. The 7 unmatched genes that were only present in the *ctsR* mutant 2-1 are highlighted in boldface (Table 3). The unmatched genes are proposed to be pressure-resistant genes due to *ctsR* deletion. These genes are grouped into the following categories: genes encoding for proteins involved in transcription, regulatory functions, cell envelope, DNA and energy metabolism, and unknown functions.

LMO2365_1986 encoding for a transcriptional regulator in the Fur family was expressed at a moderate level in the *ctsR* mutant 2-1 under HPP treatment (Table 3). This gene has been shown to be involved in barotolerance in *L. monocytogenes* LO28 strains [22]. Disruption of the fur gene resulted in reduced virulence, increased resistance to hydrogen peroxide and sensitivity to low-iron conditions [23].

LMO2365_1515 encoding transcription elongation factor GreA was highly expressed in the *ctsR* mutant 2-1 under pressure. The elongation factor GreA binds to RNA polymerase and modulates transcriptional pausing. Deletion of this gene in *E. coli* resulted in reduced expression of many genes involved in transcription.

**Table 1: Oligonucleotides used for real-time PCR to evaluate induced genes.**

<table>
<thead>
<tr>
<th>GENE</th>
<th>Forward primer sequence</th>
<th>Reverse primer sequence</th>
<th>Amplicon size (bp)</th>
</tr>
</thead>
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<td>LMO2365_0019</td>
<td>TCTAGCTTTGGCTGATCTCA</td>
<td>GATAATGCGGCAATAAA</td>
<td>111</td>
</tr>
<tr>
<td>LMO2365_0992</td>
<td>GCCCGCTAGGGTGTGATA</td>
<td>ATTTGATGAAGGCTTGCTTG</td>
<td>146</td>
</tr>
<tr>
<td>LMO2365_0993</td>
<td>AATATACATACTGCGGAAACCA</td>
<td>AGGTTTACGCTCTTGGAC</td>
<td>150</td>
</tr>
<tr>
<td>LMO2365_1036</td>
<td>CTTAGGTCCCCGTTGTTAT</td>
<td>CGCCAGAAATCTAAGTTCGA</td>
<td>135</td>
</tr>
<tr>
<td>LMO2365_1075</td>
<td>TCGGAGCAGATAACAGACAGC</td>
<td>CCGGAGACAGGATATTAGA</td>
<td>178</td>
</tr>
<tr>
<td>LMO2365_1076</td>
<td>CGGCCAAATAAGCACGAAAT</td>
<td>AGAGCGAGTTTGTGCTGAT</td>
<td>177</td>
</tr>
<tr>
<td>LMO2365_1438</td>
<td>CGCCGATAGATCAACAACTG</td>
<td>GATTTGTACGCTCGGGAAT</td>
<td>122</td>
</tr>
<tr>
<td>LMO2365_1515</td>
<td>CTGTCTTGCAGGATCATA</td>
<td>ATGACCTAGATAGGGAAAGC</td>
<td>145</td>
</tr>
<tr>
<td>LMO2365_1844</td>
<td>AATCACTAGCCGGTTCACA</td>
<td>TTAGGTGGCCGATTACAG</td>
<td>103</td>
</tr>
<tr>
<td>LMO2365_1920</td>
<td>TCAGCTAGCCAATGACAC</td>
<td>TACGTTCCAAAACGGATAT</td>
<td>134</td>
</tr>
<tr>
<td>LMO2365_1988</td>
<td>AAGAAACCTCTCTCGGACCT</td>
<td>GACGCCATTTAAGCACAAT</td>
<td>119</td>
</tr>
<tr>
<td>LMO2365_2230</td>
<td>TAGACCCGCTTCTATAATGTT</td>
<td>GCGATATGAAAGCGACTA</td>
<td>109</td>
</tr>
<tr>
<td>LMO2365_2305</td>
<td>AACCTGTGGTCAGCGGTC</td>
<td>AGACGGCAACGACAAAGAAG</td>
<td>119</td>
</tr>
<tr>
<td>LMO2365_2584</td>
<td>TCGGGAGCTTTCAATAACATT</td>
<td>ACGGTCTACCCGCTTGAGA</td>
<td>100</td>
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</table>

J Microbial Biochem Technol
ISSN:1948-5948 JMBT, an open access journal
of the 219 genes, 112 genes were repressed under pressure treatment were also identified by microarray analysis (supplemental table). The genes that were repressed in the wildtype strain under HPP treatment 

- GTP synthase, pyruvate dehydrogenase, and hypothetical proteins with unknown function. Only genes that encode for proteins involved in amino acid biosynthesis, cell envelope, transcription, transport and binding, regulatory functions, central intermediary metabolism and cellular processes were confirmed using real-time PCR assays. The 18 genes that were only repressed in the ctsR mutant 2-1 under pressure are highlighted in boldface (Table 4). These unmatched genes are likely to be pressure-resistant genes due to ctsR deletion.

The expression of the RNA polymerase σ-70 factor gene (LMO2365.0255) was inhibited in the ctsR mutant 2-1 (-10-fold in the microarray and -5-fold by real-time PCR), possibly suggesting compensation for HPP-induced inhibition of RNA synthesis. Bacterial σ-70 factor directs RNA polymerase (RNAP) to specific promoter sequences, and thus is important for transcriptional regulation [27]. Interestingly, RNA polymerase σ-70 factor was required for stabilization of a deep-sea piezophilic bacterium under high-pressure conditions [28]. Furthermore, several transcription-associated genes were also inhibited, including those encoding proteins involved in transcription regulation, and termination/antitermination activities (Table 4).

Some genes related to the cell envelope were inhibited in the ctsR mutant 2-1 under HPP treatment. For example, LMO2365.0345 encoding for a leucine rich repeat domain/LPXTG-motif cell wall anchor domain protein was inhibited (-5-fold in microarray and 10-fold in real-time PCR).
also investigated. After comparison, the genes that were induced
The wildtype under normal and pressure-treated conditions were
conditions (no high pressure treatment) was used as a control.
These ABC transporters remain to be characterized.
uptake of beta-glucosides under pressure. Gene expression of several
mutant 2-1 are beta-glucoside-specific, indicating inhibition of the
Interestingly, three of the five PTS systems that were inhibited in the
Deletion of this gene in ctsR mutant 2-1 (not in the wildtype) are in boldface.
Table 3: Genes induced in L. monocytogenes strain ScottA ctsR mutant 2-1 under pressure treatment (450 Mpa, 3 minutes) as identified by microarray* and real-time PCR analysis. Gene induced only in the ctsR mutant 2-1 (not in the wildtype) are in boldface.

<table>
<thead>
<tr>
<th>Category/Gene</th>
<th>Function*</th>
<th>Fold change* Microarray</th>
<th>RT-PCR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genes encoding proteins involved in transport and binding</td>
<td>LMO2365_2305</td>
<td>PTS system; fructose-specific; IIABC component</td>
<td>6.5 2.1</td>
</tr>
<tr>
<td>LMO2365_1036</td>
<td>glycine betaine/L-proline ABC transporter; permease protein</td>
<td>34.3 7.7</td>
<td></td>
</tr>
<tr>
<td>Genes encoding proteins involved in cell envelope</td>
<td>LMO2365_0992</td>
<td>O-aminocarrier protein</td>
<td>5.0 3.2</td>
</tr>
<tr>
<td>LMO2365_0993</td>
<td>dtIB protein</td>
<td>4.6 7.0</td>
<td></td>
</tr>
<tr>
<td>LMO2365_1438</td>
<td>putative membrane protein</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>Genes encoding proteins involved in DNA metabolism</td>
<td>LMO2365_1920</td>
<td>recombination protein U</td>
<td>3.2 2.7</td>
</tr>
<tr>
<td>Genes encoding hypothetical or unknown function proteins</td>
<td>LMO2365_2230</td>
<td>hypothetical protein</td>
<td>2.3 2.4</td>
</tr>
<tr>
<td>Genes encoding proteins involved in transcription</td>
<td>LMO2365_1515</td>
<td>transcription elongation factor GreA</td>
<td>2.5 2.5</td>
</tr>
<tr>
<td>Genes encoding proteins involved in regulatory functions</td>
<td>LMO2365_1986</td>
<td>transcriptional regulator, Fur family</td>
<td>2.0 2.8</td>
</tr>
<tr>
<td>Genes encoding proteins of purines, pyrimidines, nucleosides, and nucleotides</td>
<td>LMO2365_2584</td>
<td>adenylate kinase</td>
<td>3.4 3.2</td>
</tr>
<tr>
<td>Genes encoding proteins involved in protein synthesis</td>
<td>LMO2365_1844</td>
<td>ribosomal protein L28</td>
<td>2.2 1.8</td>
</tr>
<tr>
<td>Genes encoding proteins involved in energy metabolism</td>
<td>LMO2365_1075</td>
<td>dihydrolipoamide acetyltransferase</td>
<td>2.6 1.9</td>
</tr>
<tr>
<td>LMO2365_1076</td>
<td>dihydrolipoamide dehydrogenase</td>
<td>2.6 4.1</td>
<td></td>
</tr>
<tr>
<td>LMO2365_0019</td>
<td>cytochrome aa3 quinol oxidase, subunit IV</td>
<td>1.2 119</td>
<td></td>
</tr>
</tbody>
</table>

*Only the genes that met the stringent criteria for being up-regulated in the ctsR mutant 2-1 of L. monocytogenes Scott A (i.e., fold change >2 fold; p<0.01) are listed here.

A number of genes encoding transport and binding proteins were
inhibited in the ctsR mutant 2-1 under HHP treatment (Table 4).
Interestingly, three of the five PTS systems that were inhibited in the
ctsR mutant 2-1 are beta-glucoside-specific, indicating inhibition of the
uptake of beta-glucosides under pressure. Gene expression of several
ABC transporters was also inhibited under pressure. The substrates for
these ABC transporters remain to be characterized.

Three genes encoding for amino acid biosynthesis were inhibited in
the ctsR mutant 2-1 under pressure. Thus, reduction in amino acid
synthesis may be related to the survival of the ctsR mutant 2-1 under
pressure.

Discussion
In this study, microarrays were used to identify genes that are
differentially expressed in a pressure tolerant ctsR mutant strain
2-1 under HPP treatment. The ctsR mutant 2-1 held under normal
conditions (no high pressure treatment) was used as a control.
The wildtype under normal and pressure-treated conditions were
also investigated. After comparison, the genes that were induced
or repressed only in the ctsR mutant 2-1 (highlighted in boldface in
Supplement (Table, Table 3 and Table 4) were proposed to be pressure-
resistant related genes due to ctsR deletion. All of the induced genes
identified by microarray analysis in ctsR mutant 2-1 were confirmed by
quantitative reverse transcriptase real-time PCR (qRT-PCR). Some of
the repressed genes identified by microarray analysis were confirmed by
qRT-PCR. The gene expression changes in the ctsR mutant 2-1 to
may contribute to the barotolerance and adaptation/survival of the ctsR
mutant 2-1 under pressure.

We chose our HPP treatment to mimic HPP exposure procedures
and exposure times typically used for food processing. The conditions
we used (450 Mpa, 3 min) resulted in a 6.7 log reduction of the ctsR
mutant 2-1 whereas a 8.6 log reduction was observed in wild-type
L. monocytogenes Scott A. The gene expression levels of the house-
keeping gene (spoG) in the ctsR mutant 2-1 remained the same under
HPP vs. normal conditions, suggesting that RNA synthesis was not
inhibited under these conditions. However, it has been shown that
with increased pressure levels HHP combined with extended exposure
times in L. monocytogenes [10], resulted in inhibition of RNA synthesis
[30].

A problem observed during high pressure treatment is that a small
portion of a bacterial population can be relatively resistant after a certain
applied pressure. This phenomenon is called the tailing effect [31], and it is a major challenge for the food industry. There are indications that high pressure results in genetic changes in the pressure-resistant subpopulation. A majority of pressure-resistant mutants contained mutations in the ctsR gene [16,18-20], indicating the involvement of this gene in the tailing effect. Understanding how the ctsR mutant 2-1 survives under HHP may help develop better strategies to eliminate the tailing effect of HHP in food processing. For example, LMO2365_0345 encoding for a leucine rich repeat domain/LPXTG-motif cell wall anchor domain protein was repressed in the ctsR mutant 2-1. Since deletion of this gene resulted in greater sensitivity to nisin [29], the reduced expression of LMO2365_0345 in ctsR mutant 2-1 provides an explanation for the sensitivity of this mutant to nisin under high pressure. This suggests that combination of a nisin and HPP treatment may inhibit the growth of L. monocytogenes. This notion has been supported by a study showing that a combination of high pressure treatment with nisin inhibited the growth of L. monocytogenes [4], in dry-cured ham, therefore, preventing the tailing effect.

Although the enhanced barotolerance of the ctsR mutant 2-1 made

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**Table 4**: Genes repressed in L. monocytogenes strain ScottA ctsR mutant 2-1 under pressure treatment as identified by microarray and real-time PCR analysis. Gene repressed only in the ctsR mutant 2-1 (not in the wildtype) are in boldface.

<table>
<thead>
<tr>
<th>Category/Gene</th>
<th>Function</th>
<th>Fold change</th>
<th>Microarray</th>
<th>RT-PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino acid biosynthesis</td>
<td>LMO2365_0624 O-acetylhomoserine (thiol)-lyase</td>
<td>-2.3</td>
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<td></td>
<td>LMO2365_1705 5-methyltetrahydropteroylglutamate--homocysteine S-methyltransferase</td>
<td>-4.3</td>
<td>-3.3</td>
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<td></td>
<td>LMO2365_2285 aspartate aminotransferase</td>
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<td>Cell envelope</td>
<td>LMO2365_0342 putative lipoprotein</td>
<td>-4.0</td>
<td>-1.4</td>
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<td></td>
<td>LMO2365_0345 leucine rich repeat domain/ LPXTG-motif cell wall anchor domain protein</td>
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<td>LMO2365_0694 cell wall surface anchor family protein</td>
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<td>-2.9</td>
<td>-28.6</td>
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<td></td>
<td>LMO2365_2610 putative lipoprotein</td>
<td>-3.0</td>
<td>-5.0</td>
<td></td>
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<td></td>
<td>LMO2365_2742 D-alanyl-D-alanine carboxypeptidase</td>
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<td>Transport and binding proteins</td>
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<td></td>
<td>LMO2365_0305 D-methionine ABC transporter, D-methionine-binding protein</td>
<td>-3.6</td>
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<td>LMO2365_0390 PTS system, beta-glucoside-specific, IIB component</td>
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<td>-7.7</td>
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<td>LMO2365_1445 glycine betaine/L-proline ABC transporter, glycine betaine/L-proline-binding protein</td>
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<td>-5.0</td>
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<td>Regulatory functions</td>
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<td>LMO2365_2805 transcriptional regulator, TetR family</td>
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<tr>
<td>Central intermediary metabolism</td>
<td>LMO2365_2238 putative glucosamine-6-phosphate isomerase</td>
<td>-2.3</td>
<td>-2.0</td>
<td></td>
</tr>
<tr>
<td>Cellular processes</td>
<td>LMO2365_0742 putative flagellar hook-associated protein FlgL</td>
<td>-2.1</td>
<td>-2.5</td>
<td></td>
</tr>
</tbody>
</table>

*a*Only the genes that met the stringent criteria for being up-regulated in the ctsR mutant 2-1 of L. monocytogenes Scott A (i.e., fold change >2 fold; p<0.01) are listed here.

*b*Gene functions are based on annotations provided by TIGR (http://cmr.jcvi.org/tigr-scripts/CMR/CmrHomePage.cgi).

*c*Fold change indicates the transcript ratios of the ctsR mutant 2-1 between pressure treatment (450 Mpa, 3 minutes) and normal conditions as determined by microarray and real-time PCR.

*d*Numbers are average values from two independent experiments.

*e*Numbers are average values from two independent experiments.

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it difficult to eliminate the HHP tailing effect, the enhanced stress tolerance feature of the ctsR mutant can be beneficial to lactic acid bacteria. Various ctsR deletion mutants have been used successfully in food and beverage fermentation. For example, the ctsR deletion mutant of Lactobacillus plantarum was shown to survive better under ethanol stress [32], suggesting that this mutant can be potentially used for making wine. In another study, a ctsR deletion mutant of Lactobacillus sakei improved raw sausage fermentation since it grew better under stress [33,34].

Several lines of evidence suggest that the ctsR mutant 2-1 and deep-sea bacteria are similar in terms of pressure tolerance. First, the stress related genes were expressed under normal conditions, i.e. no pressure treatment. In the ctsR mutant 2-1, the clpC operon was highly expressed; whereas in a deep-sea bacterium, stress related genes were also highly expressed [35]. Although the expressed stress genes were different in the ctsR mutant 2-1 and a deep-sea bacterium, they may represent the same mechanism to compromise the environment. Second, some genes that were induced in the ctsR mutant 2-1 under pressure were also found to be necessary in deep-sea bacteria under pressure, e.g. genes encoding for respiratory chain [35] and recombinant proteins [25]. This indicates that they may share some adaptation/survival strategies under high pressure.

In the present study, whole-genome microarrays were used to identify multiple genes that were induced or inhibited by HHP treatment in ctsR mutant 2-1. The induced genes and a portion of the repressed genes were confirmed by real-time PCR. Identification of these genes begins to reveal the molecular mechanisms responsible for the adaptation and survival of ctsR mutant 2-1 under HHP treatment. Our results will provide a useful list of genes as novel candidates for probing the molecular mechanism and physiology of the stress response. On the basis of proven or putative function, we provide an interpretation and speculation on these detected changes in gene transcription. Further studies including the creation of gene knockouts need to be performed to confirm/identify the actual function of these genes.

Acknowledgments

We thank Amy Ream for performing real-time PCR assays. We are grateful to Anna Porto-Fett, John Luchansky, Brad Shoyer, and Jeffery Call for their work on HHP treatments. We appreciate Dr. Pina Friatamico and Dr. James Smith (USDA, Agricultural Research Service, Eastern Regional Research Center, Wyndmoor, PA) for critical reading of the manuscript.

References


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