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Exploring the Connection Between Acid Exposure and Virulence in Listeria monocytogenes

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EXPLORING THE CONNECTION BETWEEN ACID EXPOSURE AND VIRULENCE IN *LISTERIA MONOCYTOGENES*

by

Minghao Li

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ABSTRACT

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Utah State University, 2020

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The ability of *Listeria monocytogenes* to tolerate low pH-environment has raised concern in food industry as organic acids are widely used as food decontaminants. Prior research has suggested that the use of organic acids in the food industry may unintentionally enhance pathogenicity of *L. monocytogenes*. In this study, we examined the impact of habituation to lactic acid and acetic acid on expression of transcription factors and genes related to acid resistance, bile resistance and virulence in *L. monocytogenes* strains N1-227 and R2-499 by qRT-PCR, as well as their *in vivo* virulence using the *Galleria mellonella* infection model. Organic acid habituation significantly induced expression of the acid and bile stress response genes in both strains, while expression of virulence genes was strain dependent. Habituation in organic acid increased virulence of both strains as evidenced by decreased LT50 (time required for 50 % mortality) of *G. mellonella* larvae.

We then examined and compared the transcriptional profile of *L. monocytogenes* strains N1-227 and R2-499 in the presence or absence of organic acid habituation by

RNA-seq. As compared to *L. monocytogenes* grown in standard media, more differentially expressed genes (DEGs) were identified when cells were habituated with organic acid compared to cells habituated with inorganic acid. Induced expression of acid and bile stress response genes and virulence genes profiled using RT-qPCR technique was validated by RNA-seq results. RNA-seq data were strongly correlated with the gene expression values obtained for those genes shared in the parallel qRT-PCR analysis (R^2 = 0.74 for strain N1-227 and R^2 = 0.79 for strain R2-499). Other DEGs included genes involved in cell motility, membrane transport, carbohydrate and amino acid metabolism and quorum sensing. Interestingly, the DEGs involved in flagella-mediated cell motility pathways were exclusively down-regulated in both of the tested strains, and this is consistent with enhanced virulence as loss of flagella and their antigenic determinants are key to *L. monocytogenes* avoiding the host defense systems. The majority of the DEGs involved in amino sugar and nucleotide sugar metabolism were down-regulated under organic acid habituation for both strains, suggesting that changes in cell wall architecture is part of the *L. monocytogenes* response to organic acid exposure.

Results from this study suggest that exposure to acetic or lactic acid can induce increased virulence in at least some *L. monocytogenes* strains and provide a comprehensive view of the mechanisms used by *L. monocytogenes* to adapt to organic acid exposure, which may provide new leads for research and help to develop better strategies to prevent *L. monocytogenes* contamination in food.

(214 pages)

PUBLIC ABSTRACT

Exploring the Connection Between Acid Exposure and Virulence in *Listeria monocytogenes*

Minghao Li

Listeria monocytogenes is a gram-positive food-borne pathogen that is widely dispersed in the environment and can cause listeriosis with high fatality rates when consumed in contaminated food products. They are capable of growing over a wide range condition. *Listeria* is also able to tolerate adverse conditions which allows the bacterium to survive in unfavorable environments. The ubiquitous nature of *L. monocytogenes* makes it difficult to eliminate from food systems. One major problem in the food industry is the survival of *L. monocytogenes* under sublethal low pH-environment since organic acids are widely used as food decontaminants. Prior research has suggested that the use of organic acids in the food industry may unintentionally enhance pathogenicity of *L. monocytogenes.* This study examined the stress response of two strains of *L. monocytogenes*, N1-227 and R2-499, after lactic acid or acetic acid habituation.

The first phase of the study investigated the impact of habituation to lactic acid and acetic acid on expression of transcription factors and genes related to acid resistance, bile resistance and virulence in *L. monocytogenes* strains N1-227 and R2-499 by qRT-PCR. *Listeria* cells were treated with a sublethal organic acid concentration and RNA samples were collected for transcriptome analysis after 20 minutes. Statistical analysis was performed to identify genes that increased or decreased in expression during organic

acid habituation compared to cells without organic acid habituation. Results showed that organic acid habituation significantly induced expression of the acid and bile stress response genes in both strains, while expression of virulence genes was strain dependent.

The second phase of this study investigated the *in vivo* virulence of habituated *L. monocytogenes* using the *Galleria mellonella* infection model. Virulence was determined by injecting the cells into *G. mellonella* larvae. After injection, the survival of *G. mellonella* and the *L. monocytogenes* growth kinetics in insects were evaluated and the median lethal time (LT_{50}) was determined. Results showed that habituation in organic acid increased virulence of both strains as evidenced by decreased LT_{50} of *G. mellonella* larvae. The growth of *L. monocytogenes* growth kinetics in insects between treatments for either strain showed no significant difference, indicating that the enhanced virulence observed in organic acid habituated cells is not due to enhanced survival or growth in the larvae.

The third phase of this study investigated comprehensive transcriptional profile of *L. monocytogenes* strains N1-227 and R2-499 by RNA-seq in the presence or absence of organic acid. Results revealed detailed information about the mechanisms of *L. monocytogenes* responses to organic acid. As compared to *L. monocytogenes* grown in standard media, more differentially expressed genes (DEGs) were identified when cells were habituated with organic acid compared to cells habituated with inorganic acid. Induced expression of acid and bile stress response genes and virulence genes profiled using RT-qPCR technique in phase one was also validated by RNA-seq results. RNA-seq data were strongly correlated with the gene expression values obtained for those genes shared in the parallel qRT-PCR analysis ($R^2 = 0.74$ for strain N1-227 and $R^2 = 0.79$ for

strain R2-499). Other DEGs included genes involved in cell motility, membrane transport and carbohydrate, amino acid metabolism and quorum sensing.

Results from this project have increased the understanding of organic acid stress response in *L. monocytogenes* and may provide new leads for research and help to develop better strategies to prevent *L. monocytogenes* contamination in food.

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Minghao Li

CONTENTS

Page

LIST OF TABLES

LIST OF FIGURES

CHAPTER I

INTRODUCTION AND OBJECTIVES

Listeria monocytogenes is an intracellular pathogen that causes listeriosis in humans and some animals. The bacterium is Gram-positive, non-spore-forming, rod-shaped and facultatively anaerobic. It can be found in water, soil, the intestinal tract of animals and humans, and decaying vegetables (1, 2). *L. monocytogenes* is capable of growing over a wide range of temperature (0 – 45 °C) and pH (4.5 – 9.0) (3). *Listeria* is also able to survive in 10 % (w/v) NaCl and grow at water activity below 0.93 (4, 5). The ability of *L. monocytogenes* to tolerate adverse conditions (e.g. refrigeration temperatures, high salt concentrations and low pH) allows the bacterium to survive in unfavorable environments.

Listeriosis in humans normally develops after consuming contaminated food products including soft cheeses, raw milk, deli meats, deli salads, hot dogs and raw vegetables (6). Soft and semi-soft cheeses are considered particularly favorable for *L. monocytogenes* growth because these kinds of cheeses are characterized by a pH of 4.5 – 6.5 and a NaCl concentration of 2.3% – 3.5%. Some investigators have suggested that these conditions may induce or enhance virulence of *L. monocytogenes* (7-9).

The frequency of foodborne disease due to *Listeria monocytogenes* is low compared to other foodborne pathogens such as *Salmonella* spp. However, when it does occur, it is often associated with much higher hospitalization (up to 90 %) and fatality rates (20 % – 30 % of the infected individuals), even when treated with recommended antimicrobial agents (10-12). Listeriosis most severely affects pregnant women, newborn

babies, elderly and immunocompromised adults, and the disease is manifested as septicemia, gastroenteritis, meningitis and miscarriage (5, 13, 14).

Listeria monocytogenes lives in the soil as a saprophyte but transits into a pathogen when it encounters stressors during passage through the host gastrointestinal tract (14). These stressors include low pH, reduced oxygen, bile and the endogenous microbiota (15-19). In response, *L. monocytogenes* induces mechanisms that protect them from these hurdles and prepare it for cellular invasion.

Bile, a yellow-green fluid produced by liver and stored in the gallbladder, is a mixture of inorganic and organic compounds that promote lipid digestion in the small intestine (22). The principal antimicrobial effects of bile include membrane damage (22), membrane macromolecule dissociation (23, 24), inducible DNA damage (25) and increased oxidative stress (26). Given the fact that no less than one liter of bile is produced from the liver into the duodenum every day (27), the ability for *L. monocytogenes* to withstand bile and survive and colonize in the GI tact is of great importance. Two major bile stress response systems are found in *L. monocytogenes*: bile salt hydrolase (BSH), a system exclusive to pathogenic versus non-pathogenic listerial species, and the bile exclusion system (BilE) (28-30).

If *L. monocytogenes* survives acid and bile, it may colonize the gut and subsequently move to cellular infection cycle. The intracellular infection cycle of *listeria* is initiated by cell invasion with the help of two listerial surface proteins, internalin A and B. Upon entering epithelial cells, *Listeria* are entrapped into phagocytic vacuoles which they escape by lysing the membrane of the vacuole through the pore-forming toxin listeriolysin O and two phospholipases (1). Once free of the vacuole, the permease uhpT

(Hexose Phosphate Transporter) and the surface protein ActA help facilitate intracellular multiplications before a new cycle of invasion can occur (1, 31, 32).

In the food industry, the ability of *L. monocytogenes* to tolerate low pH-environment is of major concern as organic acids are widely used as food decontaminants (16, 20, 21). Three major acid stress response systems are found in *L. monocytogenes*: F_1F_0 ATPase system, the glutamate decarboxylase (GAD) system and an arginine deiminase (ADI) system.

The relationship between acid exposure and the transition of *L. monocytogenes* from saprophyte to pathogen has led some researchers to suggest that the use of organic acids in the food industry may unintentionally enhance virulence in *L. monocytogenes* (8, 33). Prior research by our group further indicated that exposure to organic acid under mildly acidic conditions (pH = 6.0) induced acid and bile resistance in some strains of *L. monocytogenes* and may promote bacterial virulence by enhancing survival through the GI tract (34).

To better understand the molecular basis and potential consequences of induced acid and bile resistance in acid habituated strains, expression of key transcription factors and targeted genes under their control related to acid resistance, bile resistance and virulence in *L. monocytogenes* needs to be studied. Research described in this dissertation explores the hypothesis that exposure to organic acids under weakly acidic conditions induces mechanisms that promote virulence in *L. monocytogenes*.

To test this hypothesis, I addressed the following objectives:

1. Explore the effect of acid habituation on the expression of key transcription factors and targeted genes under their control relating to acid resistance and bile resistance in *L. monocytogenes*.
2. Explore the effect of acid habituation on the expression of key transcription factors and targeted genes under their control relating to virulence in *L. monocytogenes*.
3. Explore the effect of acid habituation on the *in vivo* virulence of *L. monocytogenes*.

Two *L. monocytogenes* strains which show inducible resistance to both acid and bile in response to organic acids were used in this project (34). To accomplish objective 1 and 2, strains were habituated with organic acids (acetic acid or acetic acid) and their RNA was isolated to generate cDNA for real-time quantitative PCR (Q-PCR). The gene expression data were then statistically analyzed. To accomplish objective 3, a *Galleria mellonella* wax worm model was used by directly injecting adapted *L. monocytogenes* cells to the insect larvae. Survival of the insect larvae was recorded.

Outcomes from this research are expected to:

- Provide a greater understanding of factors that influence virulence of *L. monocytogenes* in foods.
- Facilitate industry efforts to control the impact of this pathogen on public health.
- Improve risk assessment of *L. monocytogenes* in food production.

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CHAPTER II

LITERATURE REVIEW

Listeria species

The genus *Listeria* is comprised of Gram-positive, non-spore-forming, rod-shaped (0.4 x 0.5 μm by 0.5 - 2.0 μm with rounded ends), facultative anaerobic bacteria which can be found ubiquitously in the environment (1, 2). They are capable of growing over a wide range of temperature (0 – 45 °C) and pH (4.5 – 9.0) (3). *Listeria* are also able to survive in 10 % (w/v) NaCl and grow at water activity values below 0.93 (4, 5). The ability of *L. monocytogenes* to tolerate adverse conditions (e.g. refrigeration temperatures, high salt concentrations and low pH) allows the bacterium to survive and grow in unfavorable environments.

Taxonomically, *Listeria* consists of eight species: *L. monocytogenes*, *L. ivannovii*, *L. innocua*, *L. seeligeri*, *L. welshimeri*, *L. rocourtiae*, *L. grayi* and *L. marthii* (6). Among them, only *L. monocytogenes* and *L. ivannovii* are pathogenic (7); *L. ivannovii* primarily infects animals while *L. monocytogenes* shows pathogenicity towards both humans and animals (8).

Listeria monocytogenes in soil and foods

It has been reported that *Listeria monocytogenes* live as saprophytes in the soil, where survival of the bacterium is influenced by the humidity of the soil, the temperature, and the motility of the bacterium (9). In addition, other soil microbiota could be an important factor due to competition for nutrients (10).

By virtue of its presence in soil, *L. monocytogenes* can be readily found in polluted water and in plant materials that are potential sources of contamination for food

products such as dairy products, poultry, meat, fruits, vegetables and seafoods (2, 11). *L. monocytogenes* contamination is most commonly associated with raw milk and soft cheeses as well as ready-to-eat (RTE) meat foods (12).

According to the European Food Safety Authority (EFSA) and the European Center for Disease Prevention and Control (ECDC), *L. monocytogenes* was most frequently found in RTE meat and fish products during 2004 to 2006 (13). In 2011, the highest proportions of contaminated foods were soft and semi-soft cheeses, hard cheeses and RTE fish products (13). Among all cheese products, soft and semi-soft cheeses are particularly favorable for *L. monocytogenes* growth because these kinds of cheeses are characterized by pH of 4.5 – 6.5 and a final NaCl concentration of 2.3% – 3.5%. Some investigators have suggested these conditions for may induce or enhance virulence of *L. monocytogenes* (14-16).

Listeria intracellular infection cycle

After consumption of contaminated food products by the host, *L. monocytogenes* pass through the stomach and enter the intestine where they invade the epithelium and spread from cell to cell. They may pass into blood and later invade the liver, spleen, and even translocate into the central nervous system after crossing protective barriers. Consequently, listeriosis may be manifest in a variety of ways including septicemia, gastroenteritis, meningitis and, in pregnant women, miscarriage or stillbirth (17, 18).

Figure 2-1 represents the intracellular infection cycle of *L. monocytogenes*: Cell invasion is induced by two listerial surface proteins, internalin A and B (InlA and InlB), that interact with specific receptors on host cell (E-cadherin and the hepatocyte growth factor receptor c-Met, respectively). After entering the cell, *L. monocytogenes* will be

entrapped into phagocytic vacuoles which they escape by lysing the membrane of the vacuole through the secretion of enzymes including the pore-forming toxin listeriolysin O (LLO) and two phospholipases, PlcA and PlcB (1). Once inside the cytosol, the permease hexose phosphate transporter (uhpT) helps them use hexose phosphates as substrate to multiply rapidly (19). They also start to polymerize actin, creating a network of the characteristic actin tails in the cytoplasm (1). This polymerization process, mediated by surface protein ActA, helps propel bacteria through the cytoplasm (20). When *Listeria* bacteria reach the plasma membrane, they pass into neighboring cells by inducing the formation of protrusions of the cell membrane that spread them to adjacent cells (21). Entry into adjacent cells results in the formation of two membrane vacuole from which *Listeria* escape, initiating a new infection cycle. The direct cell-to-cell transition keeps *Listeria* away from extracellular host defenses and is a key component of *Listeria* pathogenesis (20).

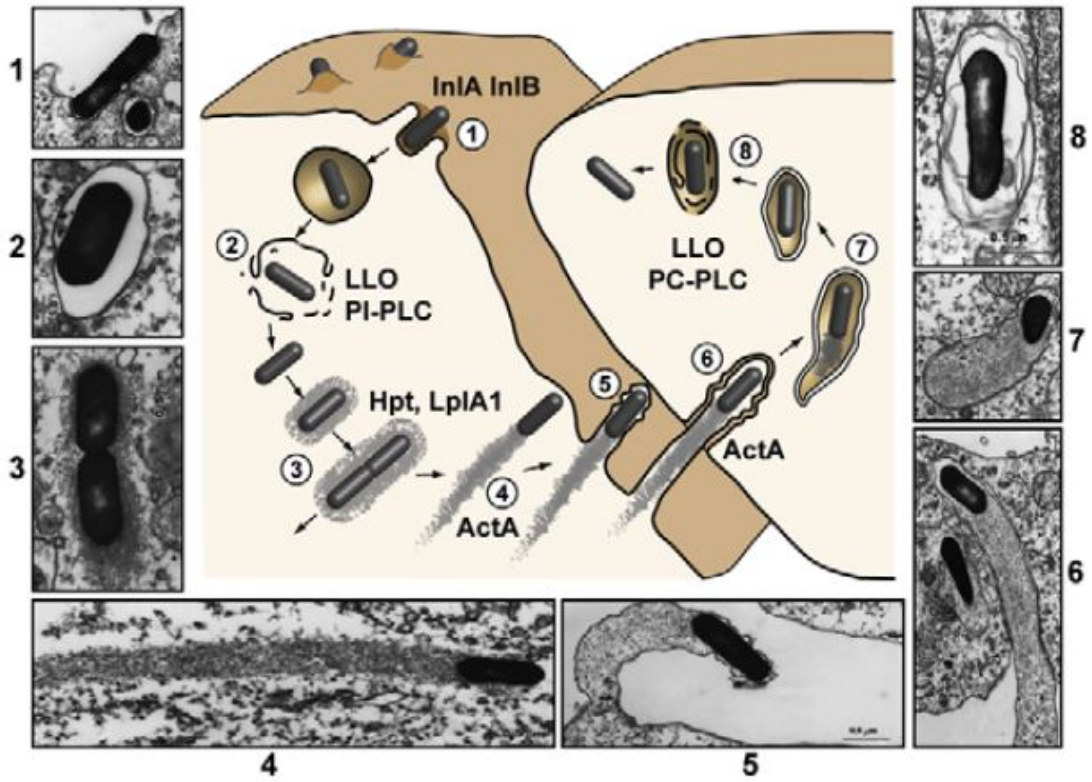


Figure 2-1 Electron-micrographs and schematic representation of the *Listeria monocytogenes* cell infectious circle. Source: (21)

The disease caused by *L. monocytogenes*, listeriosis, develops after consuming contaminated food products and most severely affects pregnant women, newborn babies, elderly and immunocompromised adults (5). Compared to other foodborne diseases, listeriosis has a low incidence but is often associated with a very high hospitalization and fatality rates, even when treated with recommended antimicrobial agents (6, 22, 23).

As indicated by the Centers for Disease Control and Prevention (CDC) in the United States (Table 2-1), The average annual prevalence of listeriosis in the United States was 0.3 cases per 100,000 population in 2018 (24). There were a total of 126 cases of listeriosis in 2018, of which 121 (96 %) resulted in hospitalizations and 26 deaths (21 % mortality) (24). As a result of its high hospitalization and mortality rate, *L. monocytogenes* has received substantial attention from scientists and the public.

Table 2-1 Number of cases of bacterial and parasitic infections, hospitalizations, and deaths, by pathogen, United States, 2018

Pathogen	Cases		Hospitalization		Deaths	
	No.	Incidence[a]	No.	(%)	No.	(%)
Bacteria						
Campylobacter	9,723	19.6	1,811	(18)	30	(0.3)
Salmonella	9,084	18.3	2,416	(27)	36	(0.4)
STEC	2,925	5.9	648	(22)	13	(0.4)
Shigella	2,414	4.9	632	(26)	1	(0.04)
Vibrio	537	1.1	151	(28)	9	(2)
Yersinia	465	0.9	95	(20)	4	(0.9)
Listeria	126	0.3	121	(96)	26	(21)
Parasites						
Cyclospora	332	0.7	19	(5)	1	(0.3)
Total	**25,606**	**—**	**5,893**	**(23)**	**120**	**(0.5)**

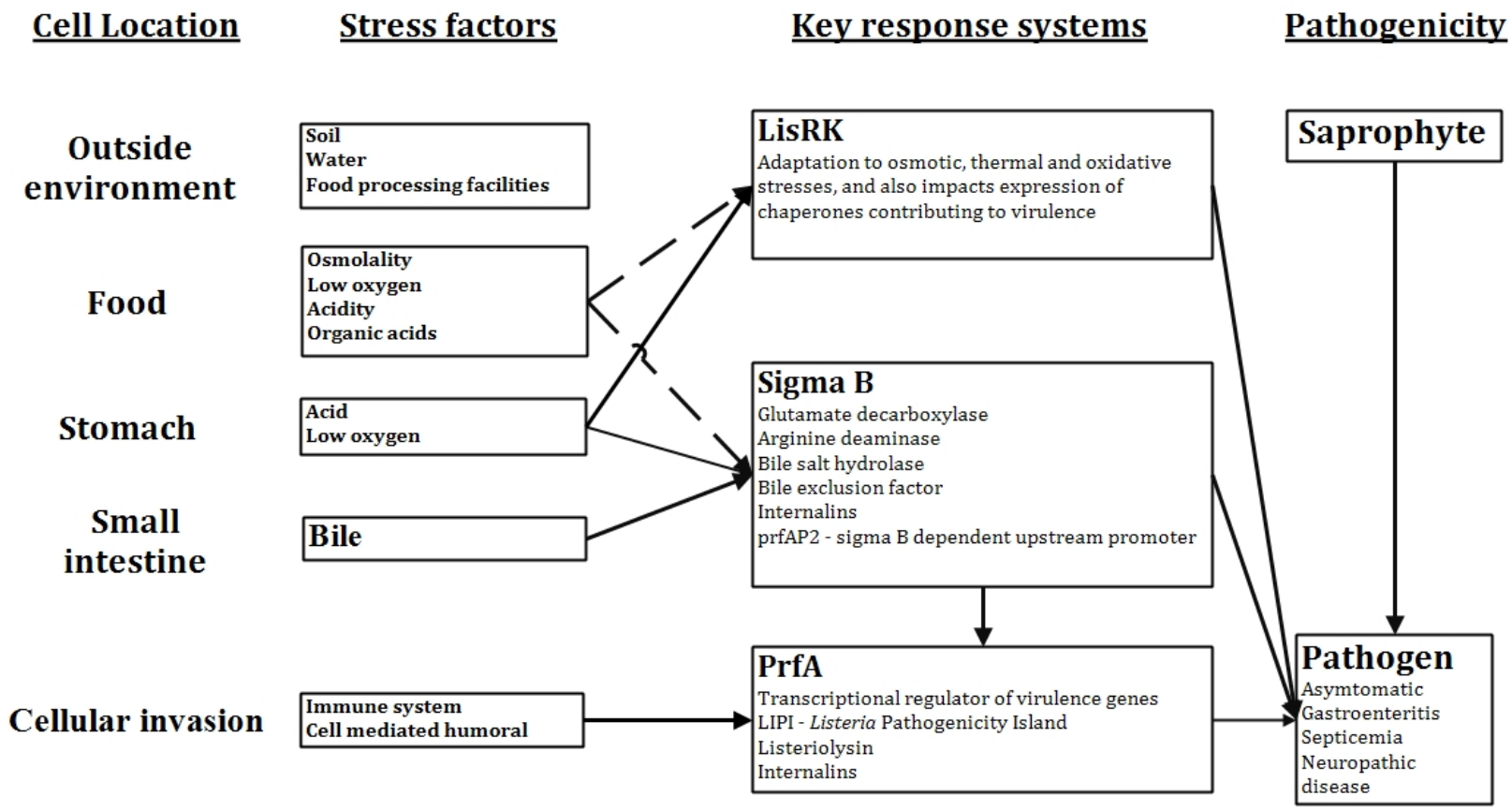
Abbreviations: STEC = Shiga toxin–producing Escherichia coli;
[a] Per 100,000 population;
Source: (24).

Transition from saprophyte to intracellular pathogen

L. monocytogenes lives in the soil as a saprophyte but transitions into a pathogen when it encounters stresses during its passage through the host gastrointestinal tract (Fig. 2-2) (18). This transition is based on the fact that stress response systems to resist acid and bile are intertwined via global regulators with the expression of virulence genes critical for infection. While substantial evidence exists for impact of GI stressors (solid lines in Fig. 2-2), others have suggested that stresses encountered in the food environment may also set listeria on the path to becoming a pathogen. Specifics of the latter have not been investigated in any detail (dashed lines in Fig. 2-2) and are the focus of this research. The main stressors encountered by *L.* monocytogenes as it passes through the gastrointestinal tract are reduced oxygen, acid and bile. *L. monocytogenes*

must adapt to those stresses in order to survive and three regulatory systems are involved in the transitions from saprophyte to pathogen: two-component system (LisRK, consist of a histidine kinase LisK and a response regulator LisR), the positive regulatory factor A (PrfA) and the general stress factor sigma B. The following introductory sections provide additional detail regarding the mechanisms and regulatory pathways involved with stress adaptations and virulence.

Figure 2-2 Transition of *Listeria monocytogenes* from saprophyte to pathogen



Solid lines: significant evidence in literature; Dashed lines: not yet established
LisRK: two component system consist of a histidine kinase LisK and a response regulator LisR
PrfA: positive regulatory factor A

LisRK

LisRK consists of a membrane-bound sensor histidine kinase (LisK) which monitors environmental conditions such as pH and O_2, and a cytoplasmic response regulator (LisR) which enables the cell to respond by regulating expression of specific target genes when the environmental condition changes (26, 27). It is a two-component signal transduction system in foodborne pathogen *L. monocytogenes* that is responsible for adaptation to osmotic, thermal and oxidative stresses, and also impacts expression of chaperones contributing to virulence (25, 26).

Previous studies have indicated that LisRK plays an essential role in stress sensing and virulence of *L. monocytogenes*. A mutant strain, LO28Δ*lisK (*with the deletion of gene *lisK)*, was approximately ten-fold less virulent than the parent wild-type strain (26). Furthermore, LisRK appears to be involved in the ability of *L. monocytogenes* to tolerate antimicrobial agents used in food and medicine such as nisin or the cephalosporin, respectively (25). The LisRK regulated locus, *htrA*, was identified as responsible for the growth at elevated osmolarity and the virulence of *L. monocytogenes* (28, 29). Additionally, disruption of *lisK* resulted in a significant reduction of survival rate of *L. monocytogenes* at elevated osmolarity (30).

PrfA

The positive regulatory factor A (listeriolysin PrfA protein), encoded by *prfA*, is the main regulator of *Listeria* virulence gene expression. It belongs to the cAMP receptor protein, also known as catabolite gene activator protein (Crp/Cap) – fumarate nitrate reductase regulator (Fnr) family of bacterial transcription factors (31). The expression of several key virulence genes is controlled and coordinated by PrfA in *L. monocytogenes*

(Table 2-2) and helps mediate the transition from bacterial saprophyte to human pathogen (32, 33).

Table 2-2 Pathogen/virulence genes regulated by positive regulatory factor A (PrfA).

Gene	Protein	Function
hly	Listeriolysin O (LLO)	Phagosome lysis
plcA	Phosphatidylinositol-specific phospholipase C (PI-PLC)	Phagosome lysis
plcB	Phosphatidylcholine phospholipase C (PC-PLC)	Phagosome lysis
mpl	Mpl	Metalloprotease that processes the PC-PLC precursor to its mature form
actA	Actin assembly-inducing ptotein (ActA)	Stimulates actin-based intracellular bacterial motility
uhpT	Hexose phosphate transporter (Hpt)	Intracellular bacterial growth
inlA	Internalin A (InlA)	Host cell invasion
inlB	Internalin B (InlB)	Host cell invasion
inlC	Internalin C (InlC)	Relaxes junctional tension through interaction with a regulator of the tight junction complex
prfA	Positive regulatory factor A (PrfA)	Required for the expression of *L. monocytogenes* virulence factors

Sources: (18, 20, 34)

Sigma B

Sigma B (σ^B), encoded by *sigB*, is a general stress responsive factor that exists in several Gram-positive bacteria including *L. monocytogenes*, *Staphylococcus aureus*, *Bacillus anthracis* and *Bacillus licheniformis* (35, 36). Studies have demonstrated that σ^B contributes to acid resistance, bile resistance, osmotic stress resistance and oxidative stress resistance (See Table 2-3 for a list of directly regulated genes) (36).

Table 2-3 Sigma B directly regulated genes of *L. monocytogenes*

Gene	Protein	Function
bsh	Bile salt hydrolase	Detoxify conjugated bile acid
bilEA/B	Bile exclusion protein	Exclude bile from cell
arcA	Arginine deiminase	Catalyze L-arginine to L-citrulline
arcB	Ornithine carbamoyltransferase	Catalyze reaction between ornithine and citrulline
arcC	carbamate kinase	Catalyze ADP and carbamoyl phosphate to form ATP
gadD1/D2/D3	Glutamate decarboxylase	Convert glutamate to GABA
gaDT1/T2/T3	Glutamate/γ-aminobutyrate antiporter (GABA)	Export GABA from cell
sigB	General stress-responsive sigma factor	Required for the expression of *L. monocytogenes* stress response factors

Source: (37, 38)

A *L. monocytogenes* Δ*sigB* mutant (with deletion of gene *sigB*) showed significantly reduced survival in acid conditions (pH 2.5) or oxidative conditions (cumene hydroperoxide) compared to the wild type (39, 40). The activity of σ^B also increased in high osmolarity medium (41). Sigma B also controls the transcription at the *prfAP2* promoter region, one of the three *prfA* transcription promoters, indicating that σ^B plays an important role in *L. monocytogenes* virulence (see Fig. 2-3 for the interaction network of SigB and PrfA regulated genes).

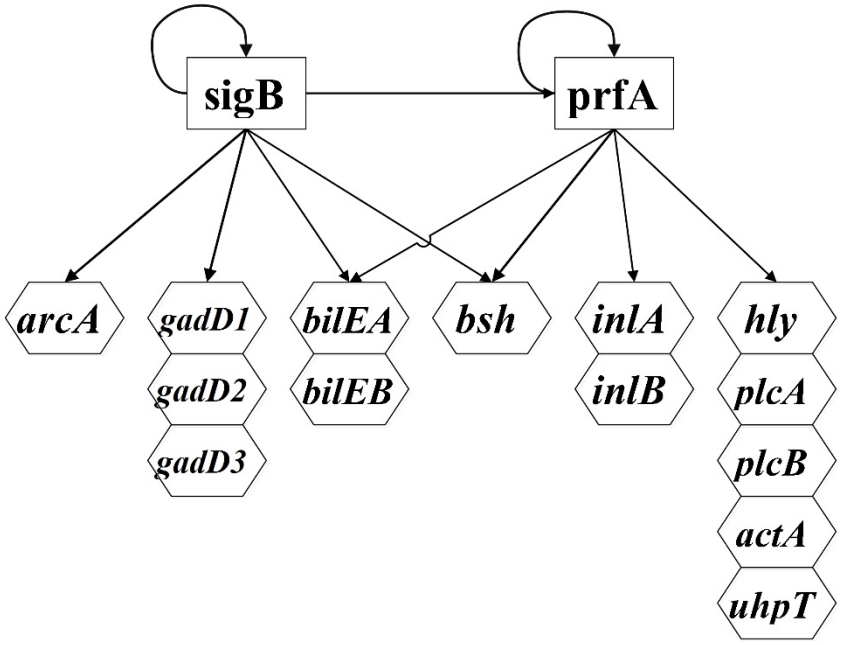


Figure 2-3 SigB and PrfA regulated genes in *L. monocytogenes* and their interaction network.

Acid stress responses of *L. monocytogenes*

During passage through the GI tract, *L. monocytogenes* encounters several stressors including low pH, reduced oxygen, bile and the endogenous microbiota (37, 38, 42-44). In response, *L. monocytogenes* induces several mechanisms that protect the cell from these hurdles and simultaneously lead toward pathogenicity. In the food industry, the ability of *L. monocytogenes* to tolerate low-pH environment is of major concern as organic acids are widely used as food decontaminants (38, 45, 46). Three major acid stress response systems are found in *L. monocytogenes*: F_1F_0 ATPase system, the glutamate decarboxylase (GAD) system and an arginine deiminase (ADI) system (Fig. 2-4).

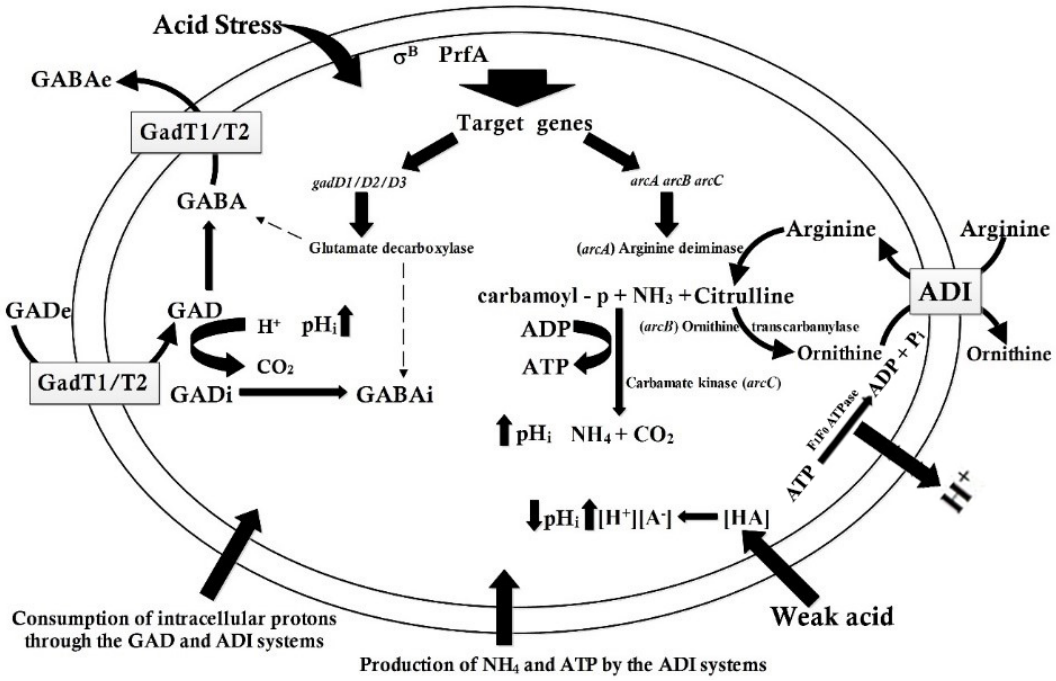


Figure 2-4 Major acid resistance systems in *L. monocytogenes. Source: (37, 38)*

F_1F_0 ATPase acid resistance system

The F_0F_1-ATPase is a multi-subunit enzyme consisting of a transmembrane channel (F_0) to translocate protons and a catalytic portion (F_1) that can synthesize or hydrolyze ATP (38, 47). Regeneration of ATP is catalyzed by the F_0F_1-APTase, which is driven by the flow of protons into the cell down an electrochemical gradient and forms ATP from ADP and inorganic phosphate (Pi). The catalysis is accomplished under aerobic condition as a result of protons entering the cell. The F_0F_1-ATPase complex can also work in the reverse direction by anaerobically hydrolyzing ATP into ADP and Pi and pumping protons to generate a proton motive force. The proton motive force accelerates the expelling of protons, resulting an increasing internal pH when the bacterial cells are stressed by acidic conditions (48, 49).

Glutamate decarboxylase (GAD) acid resistance system

The GAD system plays a significant role in pH homeostasis in *L. monocytogenes*. It has been reported that the *gadD2/T2* mutant (with the deletion of gene *gadD2* and *gadT2*) of *L. monocytogenes* showed impaired growth under acidic condition (50). Evidence also indicates that *gadT1/D1* (with the deletion of gene *gadD2* and *gadT2*) is important for growth in mildly acidic environments but provides no assistance under severe acidic conditions (51). The GAD system in *L. monocytogenes* is a complex mechanism that includes genes encoding two antiporters (GadT1 and GadT2) and three glutamate decarboxylase enzymes (GadD1, GadD2 and GadD3). These genes for their enzymes are organized in distinct combinations: *gadD1/T1*, *gadD2/T2* and a separate *gadD3* (38). When the cell is exposed to an acidic environment, the GAD system converts a molecule of glutamate to γ-aminobutyrate (GABA). The intracellular GABA is then exported from the cell via an antiporter that exchanges it for an extracellular glutamate. The net effects are the consumption of intracellular protons, alleviation of cytoplasmic acidity, and alkalization of the environment (50-52).

Arginine deiminase (ADI) acid resistance system

The arginine deiminase (ADI) system also contributes to the stabilization of the bacteria cytoplasmic pH. The ADI involves three enzymes, arginine deiminase, ornithine carbamoyltransferase and carbamate kinase, which are encoded by the genes *arcA*, *arcB* and *arc,* respectively. The ADI system catalyzes conversion of arginine to ornithine, with the resultant generation of ATP, CO_2 and ammonia. Ammonia combines with intracellular protons to yield ammonium (NH_4^+) to alleviate cytoplasmic acidity. Deletion

of *arcA* from *L. monocytogenes* adversely inhibited the growth as compared to the wild type under acidic conditions at pH 5.5 (53).

Bile stress responses of *L. monocytogenes*

Bile, a yellow-green fluid produced by the liver and stored in the gallbladder, is a mixture of inorganic and organic compounds (Table 2-4) that promote lipid digestion in the small intestine (54). The principal antimicrobial effects of bile include membrane damage (54), membrane macromolecule dissociation (55, 56), inducible DNA damage (57), and increased oxidative stress (58). Given the fact that no less than one liter of bile is produced from the liver into the duodenum every day (59), the ability of *L. monocytogenes* to withstand bile and survive and colonize in the GI tact is of great importance.

Table 2-4 Composition of human hepatic bile

Component	
Sodium (mmol/L)	145
Potassium (mmol/L)	4
Chloride (mmol/L)	90
Bile salts (mmol/L)	40
Cholesterol (mmol/L)	3
Phospholipids (mmol/L)	7
Dry weight (mg/mL)	20
Osmolality (mOsm/L)	280
pH	7.5 – 8.0

Source: (60)

One of the most important bile resistance mechanisms of *L. monocytogenes* is the ability to detoxify individual conjugated bile acids through bile salt hydrolase (BSH), a system exclusive to pathogenic as compared to non-pathogenic listerial species (Fig. 2-5)

(61, 62). It has been reported that the gene for bile salt hydrolase, *bsh*, is coordinately regulated by PrfA and σ^B in coordination and deletion of *bsh* results in impaired bile resistance (54, 61).

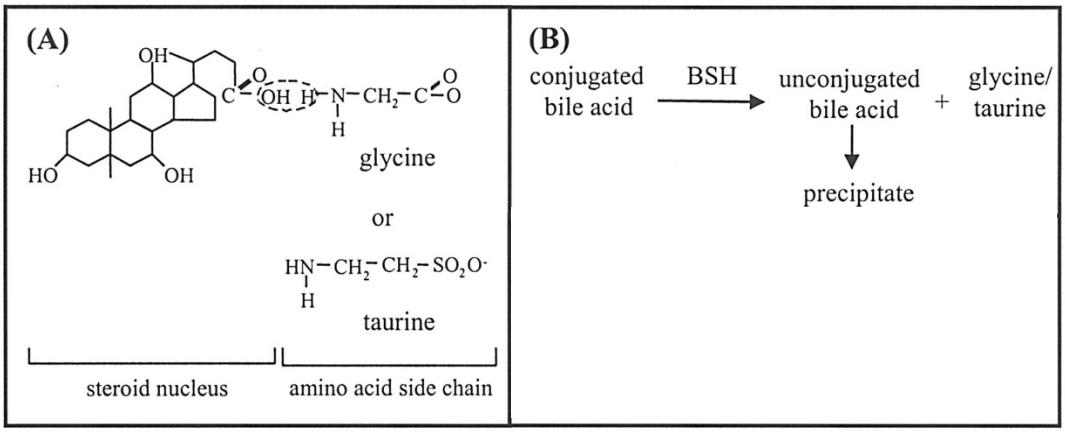


Figure 2-5 (A) Chemical structure of bile acids. (B) Reaction catalyzed by BSH. Source: (63)

The bile exclusion system (BilE) is another novel bile resistance system in *L. monocytogenes* (64). The genes encoding this system are present in a bicistronic operon and designated *bilEA* and *bilEB*, respectively. A mutant lacking *bilE* was shown to be 10^5 more sensitive to bile than the wild type (64). Additionally, significant reduction in *bilE* transcription was observed in a Δ*sigB* and Δ*prfA* mutant (with deletion of both *sigB* and *prfA* genes) but not in single mutant (deletion of either *sigB* or *prfA* gene), which suggested the *bilE* locus is regulated by σ^B and PrfA in combination. BilE acts to exclude the bile from the bacterial cell rather than detoxify the bile acid as does BSH. Confirmation was made through radio labelled bile accumulation studies which showed a Δ*bilE* mutant (with the deletion of *bilE* gene) maintained higher intracellular (approximately 1.5 times) concentration of bile salts than the wild type (64).

Prior research

In a previous study conducted by our group, the inducible resistance of two *L. monocytogenes* strains to acid and bile was tested, factors related to bacterial survival through the GI tract. Strains were grown either in media at pH 7.4 (baseline control) or at pH 6.0 containing 0 (pH control) or 4.75 mM organic acids (L-lactic acid, levulinic acid or acetic acid), harvested at mid-log phase and then challenged in medium at pH 3 or in medium with 0.2 % bile salts for 1 h.

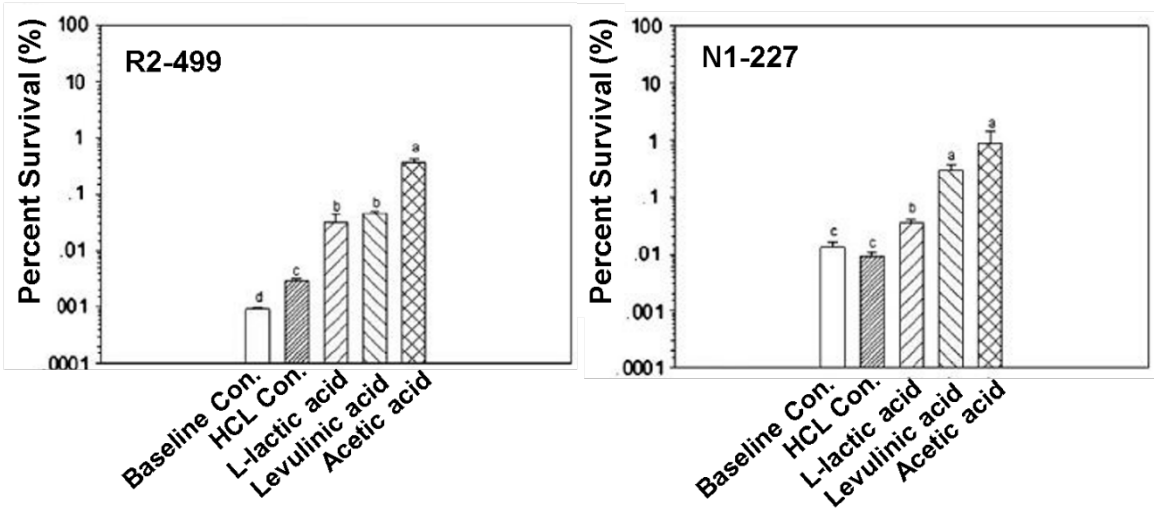


Figure 2-6 Survival of habituated log-phase *L. monocytogenes* strain R2-499 or N1-227 after 1 h challenge at pH 3.0. Treatments not sharing a letter are significantly different (P<0.05). *Source: (65)*

Growth of *L. monocytogenes* in medium at pH 6.0 with added organic acid induced an increase of more than 1 log survival against an acid challenge test compared to HCl control (Fig. 2-6). In addition, organic acid habituated cultures also showed increased survival in the 0.2 % bile salts challenge compared to HCl control. It is worth noting that inducible resistance to bile was particularly pronounced in *L. monocytogenes*

strain N1-227, which otherwise did not survive in the bile challenge test after habituation in the HCl control (Fig. 2-7) (65).

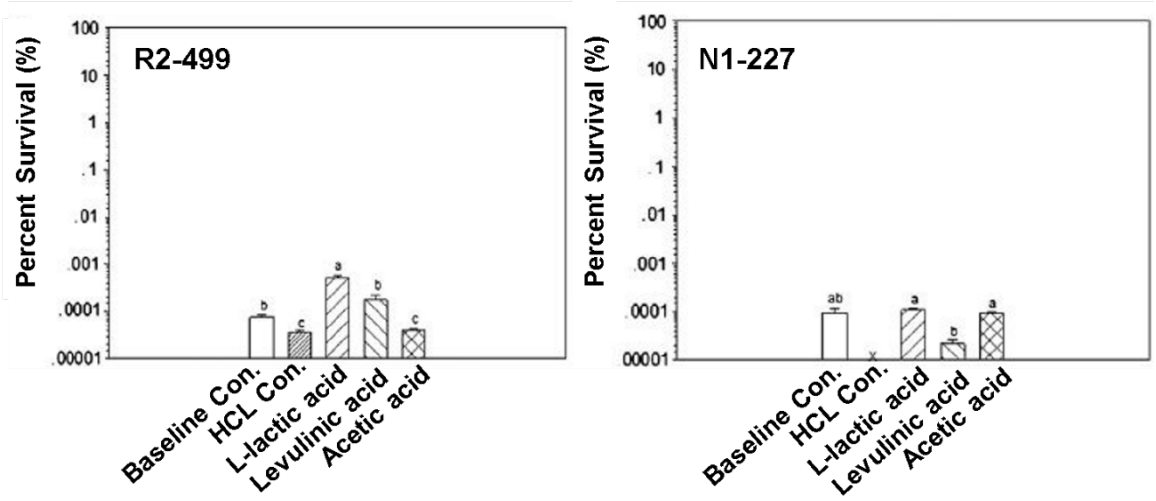


Figure 2-7 Survival of habituated log-phase *L. monocytogenes* strain R2-499 or N1-227 after 1 h challenge in TSB with 0.2% bile salts. Treatments not sharing a letter are significantly different (P<0.05). *Source: (65)*

Overall these results indicated that the exposure to organic acid under mildly acidic conditions (pH = 6.0) can induce acid and bile resistance in some strains of *L. monocytogenes* and may promote bacterial virulence by enhancing survival through the GI tract.

In a follow up study, the membrane fatty acid composition of organic acid habituated *L. monocytogenes* strains was investigated. The results indicated that the membrane profile of *L. monocytogenes* was altered by exposure to organic acids, but these changes did not explain the strain-specific increases in acid and bile resistance that had been previously observed (66).

Galleria mellonella wax worm model

The virulence of *Listeria* spp. is generally determined using an animal model (22). The well-established mouse model is considered useful for listeriosis due to their small

size, rapid reproduction and pathophysiology which is comparable to human beings (67, 68). However, it is not the most appropriate model for studying human pathogenicity of *L. monocytogenes* because the interaction between internalin A (InlA) and mouse E-cadherin, identified as InlA receptor in humans, is poor. This makes it difficult to promote *L. monocytogenes* entry into mouse epithelial cells (69, 70). Some of the alternative model systems that have been developed to explore the *L. monocytogenes* infectious process include *Drosophila melanogaster* (71, 72), *Caenorhabditis elegans* (73) and *Danio rerio* embryos (74).

Another model for researching *L. monocytogenes* virulence is the larvae of *Galleria mellonella* (75-77). Compared to the mouse model, the *G. mellonella* model estimates the virulence of *L. monocytogenes* by following its capacity for cellular invasion without the confounding effects of its acid and bile resistance. The immune system of *G. mellonella* is structurally and functionally similar to mammals and further offers the advantages of being inexpensive and easy to implement (78, 79). Studies can be carried out at various temperatures allowing for examination of human pathogens such as *L. monocytogenes* that are adapted at 37 °C (80, 81). The *G. mellonella* model allows for ready determination LT_{50} (Lethal Time; time to 50 % death) and monitoring the survival of bacteria in infected cells (82-84). This model has already been applied in conjunction with dairy foods (85).

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CHAPTER III

ACID EXPOSURE MAY ENHANCE VIRULENCE OF *LISTERIA MONOCYTOGENES*

ABSTRACT

Prior research has suggested that the use of organic acids in the food industry may unintentionally enhance pathogenicity of *Listeria monocytogenes*. This study aimed to evaluate the impact of habituation to lactic acid and acetic acid on expression of transcription factors (*sigB, prfA*) and genes related to acid resistance (*gadD2, gadD3* and *arcA*), bile resistance (*bsh, bilE*) stress response and virulence (*inlA, inlB, hly, plcA, plcB, uhpT* and *actA*) in *L. monocytogenes* strains N1-227 and R2-499, as well as their *in vivo* virulence using the *Galleria mellonella* wax worm infection model. Expression of these genes was determined by qRT-PCR, and virulence was determined by injecting the cells into *G. mellonella* larvae. After injection, the survival of *G. mellonella* and the *L. monocytogenes* growth kinetics in *G. mellonella* larvae were evaluated and the lethal time until 50 % population mortality (LT_{50}) was determined. Organic acid habituation significantly increased expression of the acid and bile stress response genes in both strains, while expression of virulence genes was strain dependent. The expression of transcription factor SigB was strain dependent and there was no significant change in the expression of transcription factor PrfA in both strains. Habituation to acid increased virulence of both strains as evidenced by decreased LT_{50} of larvae. In summary, habituation of *L. monocytogenes* to organic acids up-regulated expression of several stress and virulence genes and concurrently increased virulence as measured using the *G. mellonella* model.

INTRODUCTION

The genus *Listeria* is comprised of Gram-positive, non-spore-forming, rod-shaped, facultative anaerobic bacteria which can be found ubiquitously in the environment (1-3). Among *Listeria* species, only *L. monocytogenes* and *L. ivannovii* are pathogenic (4); *L. ivannovii* primarily infects animals while *L. monocytogenes* shows pathogenicity toward both humans and animals (5). During food production, *Listeria monocytogenes* can experience several stresses such as low pH and high salt environments. The ability of *Listeria* to adapt to these adverse conditions plays a crucial role in food contamination. In response to stress, *L. monocytogenes* may induce an acid tolerance response and other stress responses mechanisms that allow it to overcome these hurdles (6-8). *L. monocytogenes* is able to utilize a variety of regulators (over 100 different transcriptional regulators) to survive and grow in different environments (9, 10). Among those regulators, the alternative sigma B (σ^B) factor and the listeriolysin positive regulatory factor A (PrfA) are two essential transcriptional regulators for stress response and for host infection.

Alternative sigma B factor, encoded by *sigB*, is a general stress responsive initiation factor that has been identified in several Gram-positive bacteria including *L. monocytogenes* (11, 12). In *L. monocytogenes*, σ^B regulates a great number of genes that are associated with osmotic, oxidative, heat, acid and bile stress (7, 13-15). The acid stress response systems in *L. monocytogenes* include the glutamate decarboxylase (GAD) system and an arginine deiminase (ADI) system. The GAD system, which involves genes encoding three glutamate decarboxylase enzymes (*gadD1, gadD2 and gadD3*), plays a significant role in pH homeostasis in *L. monocytogenes* (7, 16). Expression of GAD

results in the decarboxylation of glutamate into γ-aminobutyrate with consumption of intracellular protons (16, 17). Additionally, the arginine deiminase (ADI) system also contributes to the stabilization of the bacterial cytoplasmic pH. The ADI pathway involves the enzymes arginine deiminase, ornithine carbamoyltransferase and carbamate kinase, which are encoded by *arcA*, *arcB* and *arcC* respectively (7). One of the most important bile resistance mechanisms that *L. monocytogenes* has developed is the ability to detoxify individual conjugated bile acid through bile salt hydrolase (BSH) (18, 19). The bile exclusion system (BilE) is another novel bile resistance system in *Listeria monocytogenes*, and acts to exclude bile from bacterial cells (20).

The listeriolysin positive regulatory factor A (PrfA), encoded by *prfA*, is a bacterial transcription factor that has been identified to control and coordinate the expression of several key virulence genes in *L. monocytogenes* (21-23). The intracellular infection cycle of *L. monocytogenes* involves cell invasion mediated by two surface proteins, internalin A and B (InlA and InlB). After entering the cell, *L. monocytogenes* are entrapped in a phagocytic vacuole from which they escape by lysing the membrane of the vacuole through the combined actions of the pore-forming toxin listeriolysin O (LLO, hly) and two phospholipases, PlcA and PlcB (1). Multiplication and invasion within host cells can then occur with the involvement of the permease UhpT (a hexose phosphate transporter) and the surface protein ActA. (1, 24, 25).

Research has suggested that the use of organic acids in the food industry may unintentionally enhance virulence of *L. monocytogenes* (26, 27). Prior research by our group showed that habituation of some strains of *L. monocytogenes* to organic acid under mildly acidic conditions (pH = 6.0) induces acid and bile resistance, which indicated

these treatments could promote bacterial virulence by enhancing survival as well as upregulating virulence genes through GI tract (28). That work also suggested the increased acid and bile resistance was likely due to the accumulation of intracellular organic acid anions rather than a decrease in pH (28, 29).

Virulence of *Listeria* spp. is frequently assessed using a murine model (30). However, this model has limitations for studying human pathogenicity of *L. monocytogenes* because the interaction between internalin A (InlA) and mouse E-cadherin (identified as InlA receptor in human) is poor, which makes *L. monocytogenes* entry into epithelial cells less efficient (31, 32). The larvae of *Galleria mellonella* have also been used as a model for *L. monocytogenes* virulence (2, 33-38). Compared to the mammalian model and other alternative models, the *G. mellonella* model offers several significant advantages, including structural and functional similarities with the mammalian immune system (39, 40). Additionally, the infection process can be performed over a range of temperatures (from 15°C to above 37°C), which enables use of the *G. mellonella* model to study the virulence of *L. monocytogenes* human pathogens at 37°C (41, 42).

To better understand the molecular basis and potential consequences of induced acid and bile resistance in organic acid habituated strains, we evaluated the expression of key transcription factors and some of their target genes related to acid or bile resistance or virulence in *L. monocytogenes* after habituation to 4.75 mM lactic acid or acetic acid at pH 6.0. Additionally, the *G. mellonella* infection model was used to analyze the *in vivo* virulence of control and acid habituated *L. monocytogenes* strains.

MATERIALS AND METHODS

Bacterial strains and growth conditions

Two *L. monocytogenes* strains which were previously shown to display inducible resistance to both acid and bile in response to organic acid habituation were used in this project (28) (Table 3-1). Original cultures were stored as frozen stocks at -80°C in tryptic soy broth (TSB, pH=7.4; Becton, Dickinson and Company, Sparks, MD) supplemented with 20 % v/v glycerol. Prior to use, cultures were first propagated on tryptic soy agar (TSA; Becton, Dickinson and Company, Sparks, MD) plate and incubated at 37°C for 24 h. A single colony from the TSA plate was transferred into TSB and incubated overnight at 37 ºC with shaking (220 rpm).

Table 3-1 *Listeria monocytogenes* strains used in this study

Strain	Ribotype	Lineage	Serotype	Source
FSL R2-499	DUP-1053A	II	1/2a	Human isolate associated with the US outbreak linked to sliced turkey, 2000
FSL N1-227	DUP-1044A	I	4b	Food isolate associated with the US outbreak, 1998–1999

Source: (28)

RNA isolation

Overnight cultures of each strain were harvested by centrifugation (2500 x g for 10 min; Sorvall RT1, Thermo Scientific, Germany) at 4°C, then diluted to an optical density at 600 nm (OD_{600}) of 0.03 in TSB. Cells were acid habituated as described by Zhang et al., (28). A 1 % inoculum (v/v) of diluted overnight cultures was transferred into 50 mL of standard TSB (pH 7.4) and incubated at 37 °C for 4 h with shaking (220 rpm). The mid-log phase cultures were collected by centrifugation (2500 x g for 10 min) at 4

°C and then suspended in 50 mL of either standard TSB (pH 7.4, baseline control) or TSB without dextrose (pH 6.0 adjusted with HCl, Becton, Dickinson and Company, Sparks, MD) containing 0 (pH control) or 4.75 mM of either L-lactic acid (Sigma Chemicals, St. Louis, MO) or acetic acid (A Johnson Matthey Company, Ward Hill, MA). The cultures were incubated at 37°C for 20, 40 or 60 minutes with shaking (240 rpm). After incubation, 100 mL of RNAprotect bacteria reagent (Qiagen, Inc., Valencia, CA) was added to each sample. Cells were incubated at room temperature for 10 min then collected by centrifugation (9,500 x g for 10 min). The supernatant was discarded and cell pellets were suspended in 900 µL of lysozyme solution (Sigma-Aldrich, 20 mg/mL in Tris-EDTA buffer) that contained 20 units of mutanolysin (Sigma-Aldrich). Samples were incubated for 30 min at 37°C on a shaker incubator at 240 rpm, then 20 µL of proteinase K (Omega Bio-Tek Inc., Norcross, GA) (20 mg/mL) was added and the samples were returned to the shaker/incubator for 30 min. Total RNA was isolated using an Aurum total RNA mini kit (Bio-Rad, Hercules, CA) following the vendor's recommended procedures. Residual DNA was removed using The Ambion® DNA-free™ DNase Treatment and Removal Reagents. RNA samples were then purified using the GeneJET RNA Cleanup and concentration Micro Kit PCR purification kit (Thermo Fisher Scientific, Lithuania). The amount and the quality of the RNA were measured using a NanoDrop Spectrophotometer (Thermo Scientific, USA) and TapeStation System (Agilent, Santa Clara, CA), respectively.

Synthesis of cDNA and qPCR

cDNA was synthesized from 10 µg of total RNA using random primers (Invitrogen, Carlsbad, CA) and SuperScript II reverse transcriptase (Invitrogen). The

qPCR was carried out in an Opticon II thermal cycler (MJ Research, Reno, NV) using HotStart-IT^{TM} SYBR Green qPCR Master Mix with UDG kit (Affymetrix, Inc). Each reaction was performed in triplicate and the relative gene expression of targeted genes was calculated by the Pfaffl Method (43). The primers used in this study are listed in Table S1 and *rpoB* was used as a housekeeping gene to normalize the gene expression data (44, 45). The amplification efficiency for each primer was tested by plotting the Ct (cycle threshold) value with different primer concentrations and fitting the data to a regression line (44, 46). The amplification efficiency for all the primers reached 90 % or above.

***Galleria mellonella* wax worm model**

The *in vivo* virulence of *L. monocytogenes* strains was determined using the *Galleria mellonella* wax worm model described by Ramarao *et al.*, (34). A 1 % inoculum (v/v) of freshly prepared *L.monocytogenes* cells was transferred into 50 mL of either standard TSB (pH 7.4, baseline control) or TSB without dextrose (pH 6.0 with HCl) containing 0 (pH control) or 4.75 mM of either L-lactic acid or acetic acid and incubated at 37 °C for 4 h with shaking (240 rpm). The mid-log phase cultures were collected by centrifugation (2500 x g for 10 min) at 4°C. The bacterial cells were then re-suspended with sterile PBS solution (pH 7.4) and diluted to an optical density at 600 nm (OD_{600}) of 0.25. Ten µL of 10^8 cfu/mL *L. monocytogenes*, either control or acid habituated, was injected into the haemocoel of the wax worms using an automated syringe pump (KDS 100, KD Scientific; 20 worms per treatment; see Figure 3-1 for injection order. Injection was done in two biological repetition). The larvae were placed in petri dish (5 per dish) and incubated at 37°C. Larvae survival was evaluated every 24 h for 5 days after

injection. The larvae were considered dead when they showed no movement in response to finger touch. Lethal times until 50 % population mortality (LT_{50}) for each treatment were then determined by Probit analysis (47, 48).

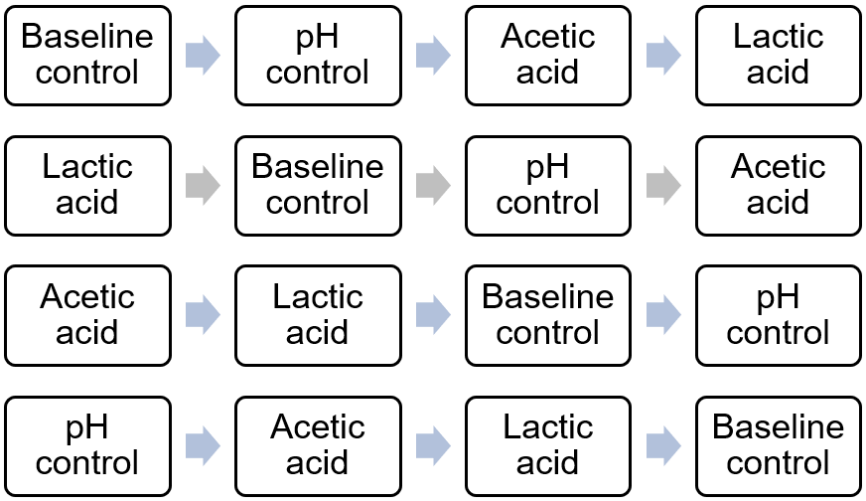


Figure 3-1 Injection order of one biological repetition

Examples of the whole injection process is shown on Figure 3-2:

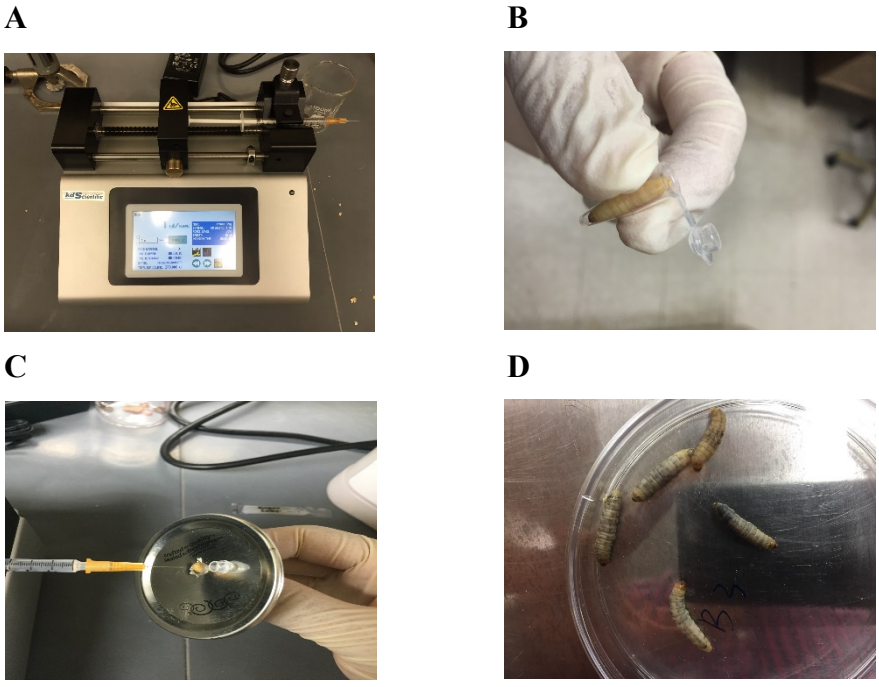


Figure 3-2 (A) Automated syringe pump injector. (B) Alive fresh *G. mellonella* larvae. (C) Bacteria are injected to *G. mellonella* larvae. (D) *G. mellonella* larvae after infection.

Viability of *Listeria monocytogenes* in *Galleria mellonella* wax worms

The viability of *L. monocytogenes* in *G. mellonella* larvae was determined at 5, 10, 15 and 20 h after injection. At each time point, 5 larvae were collected and homogenized in 9 mL of sterile peptone physiological solution (PPS) in a stomacher. Serial dilutions were made by pipetting 1 mL of diluted sample into 9 mL PPS, then 100µL of diluted samples were inoculated onto Palcam agar (*L. monocytogenes* selective media; Oxoid Limited, Hampshire, United Kingdom). Plates were incubated at 37°C for 48 h then *L. monocytogenes* colonies were enumerated. Microbiological count data were expressed as $\log_{10}$ of colony-forming units per larvae.

Statistical analysis

Quantitative data measuring the expression of the target genes were obtained by RT-qPCR according to the number of cycles required for optimal amplification generated fluorescence, in order to achieve a specific threshold detection value (i.e., the threshold cycle; CT value). The relative expression ratio (R) of each target genes' expression compared with that of a reference gene was calculated as previously described (43):

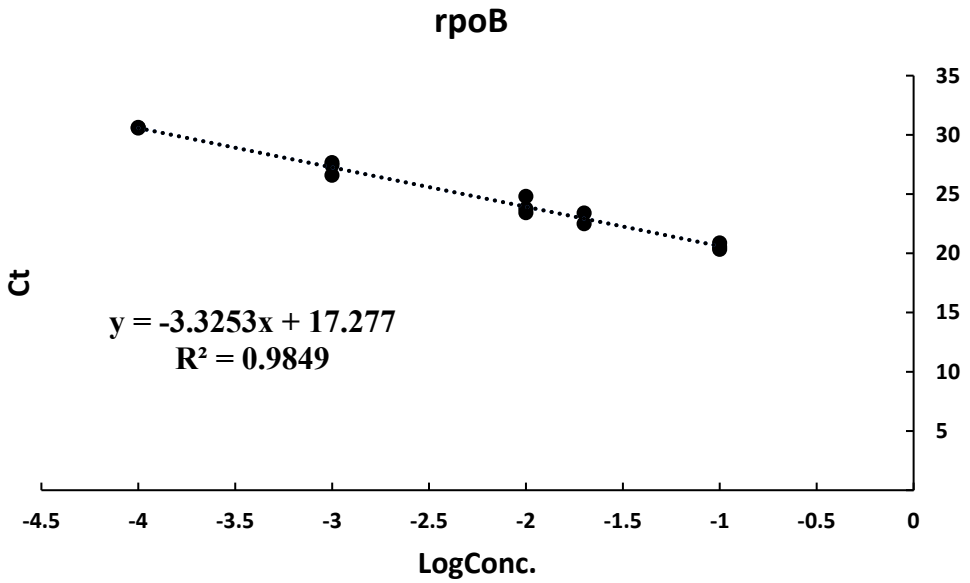
$$Relative\ expression\ ratio = \frac{(E_{target})^{\Delta C_T\ target(control-sample)}}{(E_{ref})^{\Delta C_T\ ref(control-sample)}}$$

Real-time PCR efficiencies (E) were calculated for each gene from the slope of the standard curve. Samples of DNA were diluted 1:10 and used to construct the standard curves, which were constructed by plotting CT versus $\log_{10}$ of DNA concentration. Dilutions were done three times independently and loaded singly. Using the slope of the standard curve, we calculated $E = 10^{(-1/slope)}$.

Relative expression ratio of targeted genes compared with reference genes was a continuous outcome variable for every categorical treatment variable (acidification treatments of *L. monocytogenes*). Testing for significant differences in gene expression outcomes between treatments was done using one-way analysis of variance (ANOVA) followed by Tukey's test to compare means of the gene expression outcome variables between treatments. Differences were considered significant at $P < 0.05$.

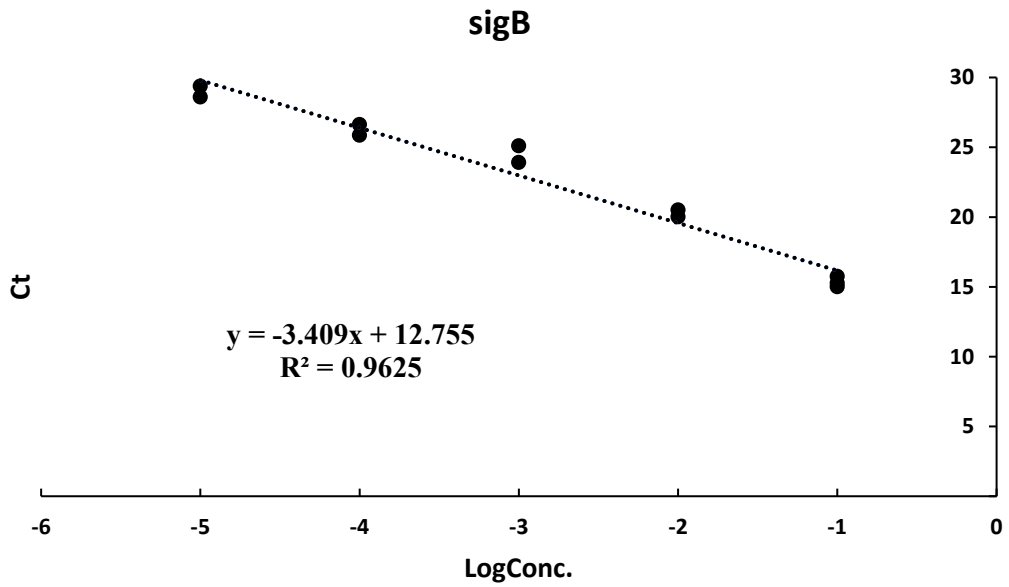
Example calculation:

Standard curve of *rpoB* (reference gene, housekeeping gene):



Slope: -3.3253, $E = 10^{(-1/slope)} = 1.99$.

Standard curve of *sigB* (target gene):



Slope: -3.409, $E = 10^{(-1/slope)} = 1.96$.

Ct value:

	rpoB	*sigB*
Baseline control	14.435	22.613
Lactic acid treatment	14.311	19.043

$$Relative\ expression\ ratio = \frac{(E_{target})^{\Delta C_T\ target(control-sample)}}{(E_{ref})^{\Delta C_T\ ref(control-sample)}} = \frac{1.96^{(22.613-19.043)}}{1.99^{(14.435-14.311)}} = 10.15$$

The survival rate of *G. mellonella* larvae was a continuous outcome variable for every categorical treatment variable (acidification treatments of *L. monocytogenes*). Testing for significant differences in larvae survival rate between treatments was done using one-way analysis of variance (ANOVA) followed by Tukey's test to compare

means of the survival rate outcome variables between treatments. Differences were considered significant at $P < 0.05$.

RESULTS AND DISCUSSION

The 40 minutes and 60 minutes habituation treatments resulted in less dramatic change of targeted gene expression compare to 20 min habituation for both strains (see Appendix Fig. A1-A4) which indicate that the adaptation process was likely done during the first 20 minutes of incubation. Therefore, the following results and discussion regarding qRT-PCR are based on 20 minutes organic acid habituation.

Influence of acid habituation on expression of acid and bile stress response genes

To elucidate the effect of organic acid habituation on the expression of the genes encoding important acid and bile stress response mechanisms, we used real-time quantitative PCR (q-PCR) to assess relative levels *gadD3*, *gadD2*, *arcA*, *bilE*, *bsh* and *sigB* in *Listeria monocytogenes*.

As shown in Figure 3-3, increased expression of *gadD3* and *gadD2* was observed for both strains in the pH control relative to the baseline control. However, acetic acid or lactic acid habituation resulted in significant ($P<0.05$, ANOVA) and dramatic upregulation of these genes in both strains. The glutamate decarboxylate (GAD) system serves as a key mechanism of *L. monocytogenes* surviving in acid environments. It has been reported that the *gadD2* mutant (with deletion of *gadD2* gene) of *L. monocytogenes* showed impaired growth under acidic condition (16). Furthermore, a revised model of how the GAD system functions was proposed by Karatzas et al. wherein GAD consists of two semi-independent intracellular and the extracellular systems (17). The intracellular GAD system involves the action of GadD3 utilizing intracellular glutamate whereas the

extracellular GAD system involves GadD2 decarboxylating the extracellular glutamate imported by antiporter GadT2 (17). Interestingly, the differential induction of *gadD3* versus *gadD2* in strains N1-227 and R2-499 suggests *gadD3* may play a more important role in acid protecting in N1-227, while *gadD2* serves as primary defense mechanism in R2-499. The q-PCR results for both strains also showed induction of *arcA* in the pH control relative to the baseline control, and that acetic acid or lactic acid habituation significantly ($P<0.05$) increased *arcA* expression in both strains (Fig. 3-3).

In contrast, transcription of genes related to bile tolerance showed strain to strain variability. Habituation to lactic acid or acetic acid significantly ($P<0.05$, ANOVA) increased *bsh* gene expression in comparison with the pH control for both strains. However, the pH control had no significant effect on in *bsh* gene expression relative to the baseline control in strain N1-227 (Fig. 3-3). Changes in the expression of *bilE* were strain dependent. For strain N1-227, *bilE* was significantly overexpressed ($P<0.05$) when cells were habituated to acetic or L-lactic acid, whereas no significant changes were observed in strain R2-499. Additionally, the expression level of *bilE* was lower than that of the *bsh* in both strains, which might be a consequence of cell growth phase. Sue et al. showed that *bilE* expression is growth-phase-dependent, with highest expression level observed in stationary phase cells (49). Finally, qRT-PCR data showed lactic acid or acetic acid treatment significantly ($P<0.05$) induced *sigB* expression in strain N1-227 cells compared to the baseline control. However, no significant change on *sigB* expression was observed between treatments in strain R2-499 (Fig. 3-3).

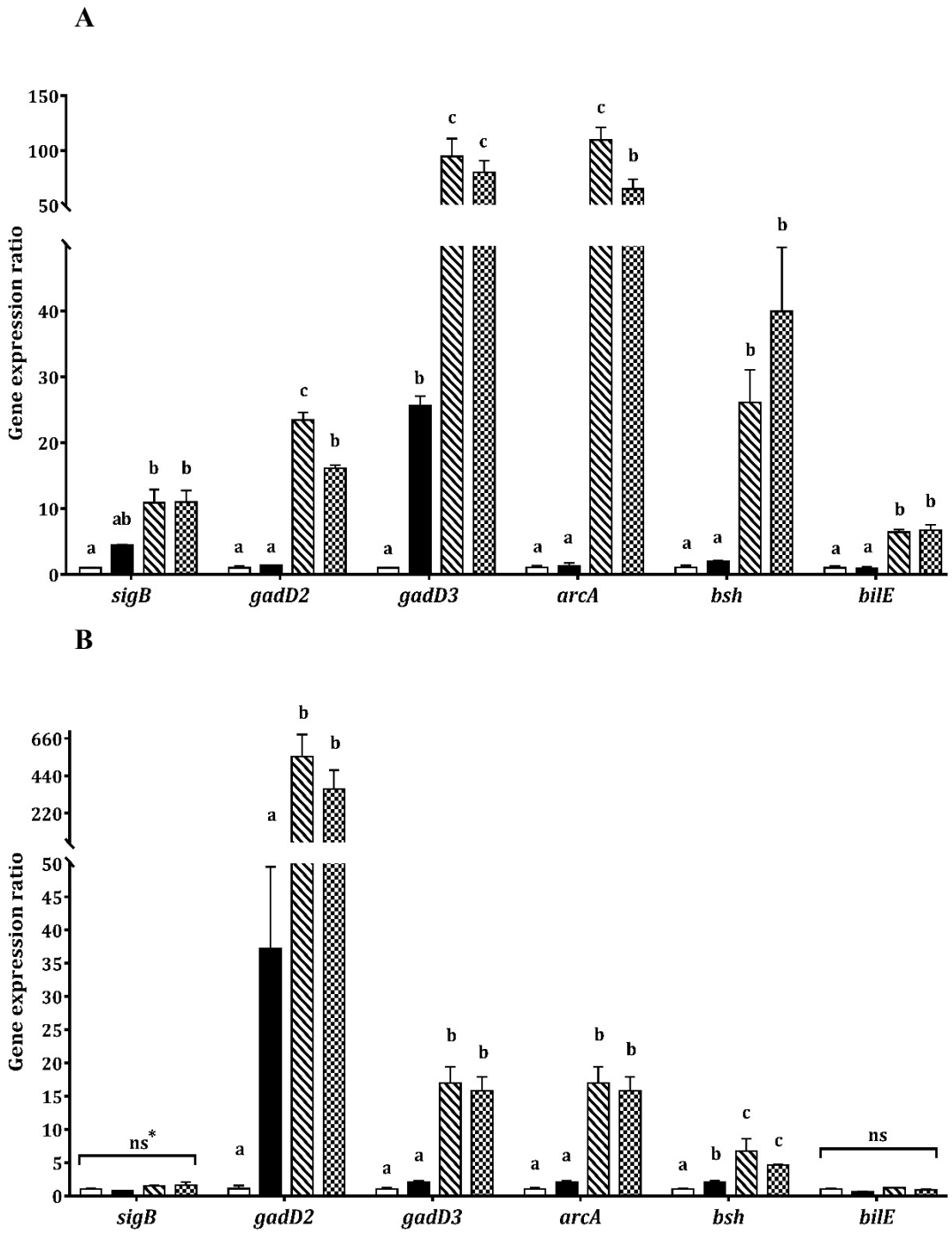


Figure 3-3 Relative gene expression of acid and bile stress response related genes in habituated *Listeria monocytogenes* strains N1-227 (panel A) and R2-499 (panel B) cells in comparison with non-habituated cells (baseline control, TSB pH 7.4, ▭). Habituated treatments include: TSB pH 6.0 (pH control, ■), TSB pH 6.0 w/ 4.75 mM of acetic acid (▨) and TSB pH 6.0 w/ 4.75 mM of L-lactic acid (▩). Error bars represent standard error of mean for two biological trials with three replicates for each trial. Different letters indicate that treatments are significantly different ($p<0.05$) as determined by one-way ANOVA with Tukey's post-hoc tests; *ns: non-significant.

Influence of acid habituation on expression of virulence genes

As was observed with stress genes, q-PCR results showed similarities and differences between strains with respect to virulence gene expression in response to organic acid habituation (Fig. 3-4). The transcription level of *prfA* or *uhpT* was not significantly different between treatments in either strain. However, expression of *inlA, inlB* and *hly* increased in both strains when the pH was decreased, and both strains showed significantly ($P<0.05$, ANOVA) increased expression of *inlA* and *inlB* in organic acid habituated cells compared to baseline control and pH control (Fig. 3-4). Furthermore, *hly* expression was significantly ($P<0.05$, ANOVA) increased in acetic acid or L-lactic acid habituated R2-499 cells relative to baseline control and pH control. However, for strain N1-227, significant ($P<0.05$, ANOVA) overexpression compared to baseline control was only observed in the pH control and acetic acid treatment.

The q-PCR results showed the expression profile for the other virulence genes (*plcA, plcB, actA*) was strain dependent (Fig. 3-4). No significant changes were observed in *plcA* expression for strain N1-227, while organic acid habituation significantly ($P<0.05$, ANOVA) increased expression of this gene in strain R2-499 compared to baseline control and pH control. All three acid treatments (pH control and organic acid habituated cells) significantly ($P<0.05$, ANOVA) induced *plcB* expression compared to baseline control in strain N1-227, whereas significant induction in strain R2-499 was only observed with acetic acid treatment. Conversely, no significant differences were recorded in actA expression for strain R2-499, and only acetic acid habituated N1-227 cells showed a significant ($P<0.05$, ANOVA) increase in the expression level of this gene (Fig. 3-4).

Infection of host cells by *L. monocytogenes* can be divided into three stages that require specific virulence factors: initial cell invasion (InlA and InlB), escape from vacuole (Hly, PlcA and PlcB) and cell to cell spread (ActA and UhpT) (1, 50-53). It has been reported that *L. monocytogenes* is able to sense different environments and host cell compartments and regulate virulence gene expression accordingly (10, 54). Specifically, *inlA* and *inlB* are induced prior to the cell invasion, *hly*, *plcB* and *plcA* are overexpressed within the phagosome and *uhpT* and *actA* are expressed in the cytosol (55). Our results are in agreement with these studies in that *inlA* and *inlB* were the only two virulence genes that showed same expression pattern for both strains when acid stress was introduced whereas expression for other virulence genes was strain-dependent.

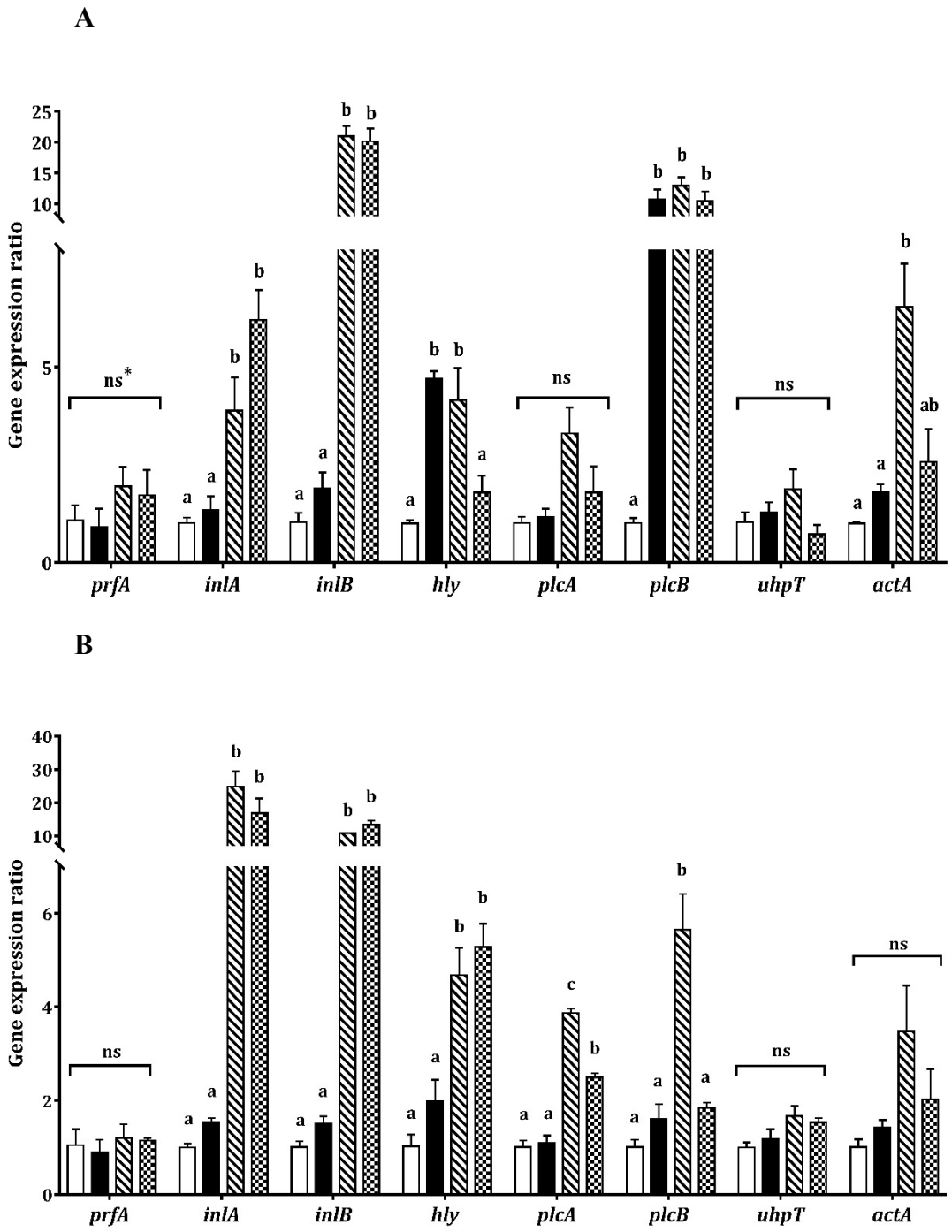
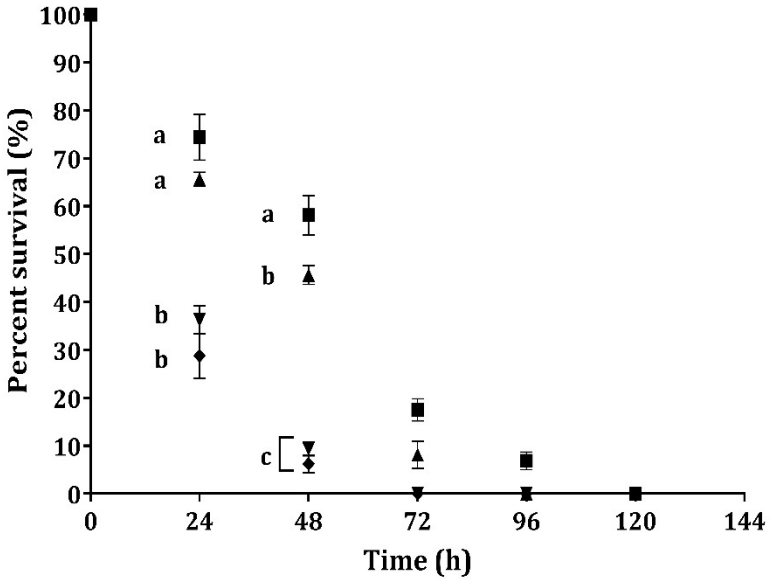


Figure 3-4 Relative gene expression of virulence related genes in habituated *Listeria monocytogenes* N1-227 (panel A) and R2-499 (panel B) cells in comparison with non-habituated cells (baseline control, TSB pH 7.4, ▭). Habituated treatments include: TSB pH 6.0 (pH control, ■), TSB pH 6.0 w/ 4.75 mM of acetic acid (▨) and TSB pH 6.0 w/ 4.75 mM of L-lactic acid (▩). Error bars represent standard error of mean for two biological trails with three replicates for each trail. Different letters indicate that treatments are significantly different ($p<0.05$) as determined by one-way ANOVA with Tukey's post-hoc tests. *ns: non-significant.

Effect of habituation to organic acid on *Galleria mellonella* survivability

Organic acid habituation affected the virulence of *L. monocytogenes* strains in the *G. mellonella* wax worm model observed 24 h after injection. A PBS-only control injection was also included and no larvae death was observed during the sampling time. Larvae injected with acid habituated N1-227 cells showed a significantly lower ($P<0.05$, ANOVA) survival rate (36 ± 3 % for acetic acid treatment and 29 ± 4 % for lactic acid treatment) after 24 h in comparison with the baseline control and pH control (74 ± 5 % and 66 ± 5 % respectively) (Fig. 3-5A). Significantly lower survivability ($P<0.05$, ANOVA) was also observed 48 h post-injection for the habituated cells compared to baseline control and pH control. The results for *L. monocytogenes* strain R2-499 were parallel to those for strain N1-227. However, larvae injected with acid habituated R2-499 cells showed lower survivability during the first two days after injection for all treatments (Fig. 3-5B). The lethal time to 50 % population mortality (LT_{50}) of each treatment for both strains are shown in Table 3-2. Larvae injected with non-habituated *L. monocytogenes* N1-227 cells had LT_{50} of 40.7 h. When cells were habituated with HCl, the LT_{50} decreased to 34.2 h, and an even more dramatic decrease of LT_{50} was observed when larvae were injected with organic acid habituated cells (19.8 h and 17.1 h for acetic acid and L-lactic acid treatment, respectively). A similar pattern was observed for strain R2-499, except that LT_{50} values were lower than N1-227 for all treatments. The LT_{50} result suggest that strain R2-499 may be more virulent and may escapes the vacuole more efficiently than N1-227 and therefore spreads and kills the host more rapidly.

A



B

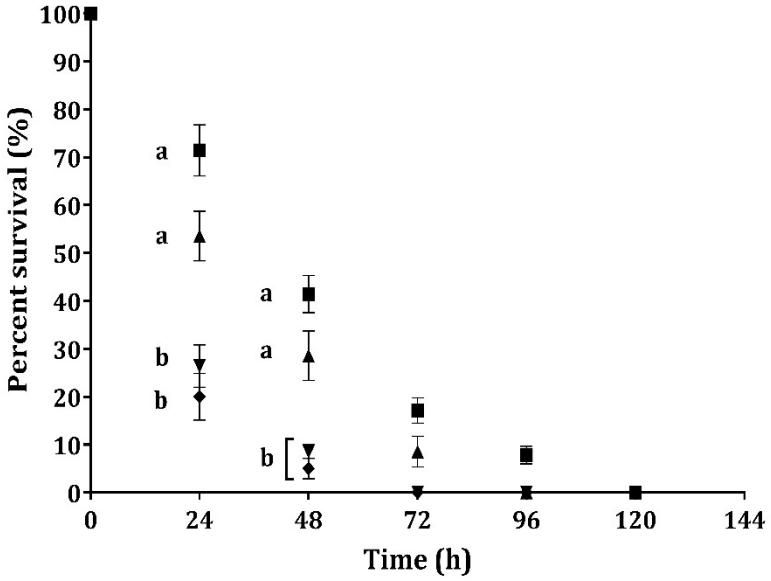


Figure 3-5 Survival of *Galleria mellonella* larvae after injection with habituated or non-habituated (baseline control, TSB pH 7.4, —■—) *Listeria monocytogenes* N1-227 (panel A) and R2-499 (panel B) cells. Media included in the habituated cells: TSB pH 6.0 (pH control, —▲—), TSB pH 6.0 w/ 4.75 mM of acetic acid (—▼—) and TSB pH 6.0 w/ 4.75 mM of L-lactic acid (—◆—). Error bars represent standard error of mean for two biological trails. Different letters indicate that treatments are significantly different ($p<0.05$) as determined by one-way ANOVA with Tukey's post-hoc tests.

Table 3-2 Probit analysis of lethal time to 50 % mortality (LT_{50}) with 95% confidence limit (95% CL) of *Listeria monocytogenes* on different treatments

Strain	Treatments	LT_{50} (Hours) (95 % CL)	Equation [a]
N1-227	Baseline	40.72 (32.58 – 50.90)	$y = 4.21x - 1.78$
	pH control	34.23 (26.28 – 44.59)	$y = 5.57x - 3.54$
	Acetic acid	19.76 (15.50 – 25.19)	$y = 4.69x - 0.68$
	L-lactic acid	17.14 (13.58 – 21.65)	$y = 4.05x + 0.01$
R2-499	Baseline	37.23 (31.22 – 44.39)	$y = 3.88x - 1.10$
	pH control	29.83 (22.79 – 39.04)	$y = 4.96x - 2.31$
	Acetic acid	17.14 (13.10 – 22.42)	$y = 4.00x + 0.06$
	L-lactic acid	14.01 (10.97 – 17.88)	$y = 3.62x + 0.85$

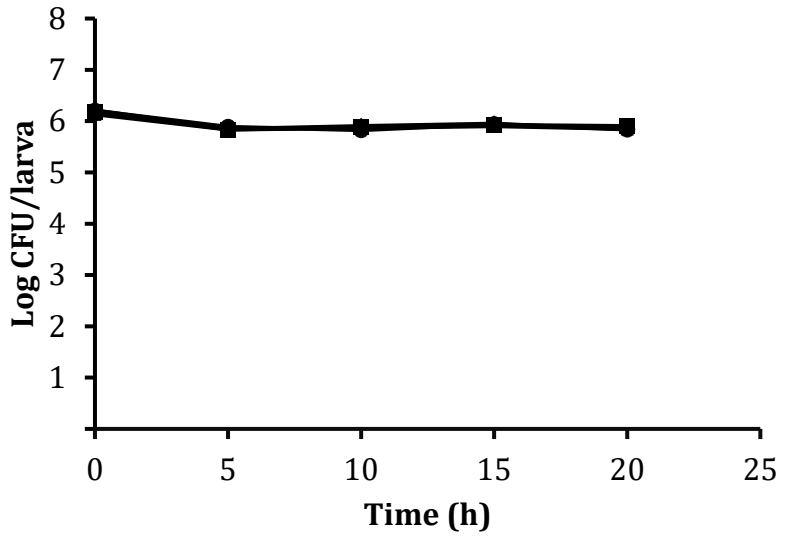
[a]: $Mortality\ (probit) = \ a * log(hour) + b$

Viability of *Listeria monocytogenes* in *Galleria mellonella*

To test whether the previous organic acid habituation affected the survival or growth of *L. monocytogenes* in *G. mellonella* larvae, post-injection bacterial cell numbers were determined over time. *L. monocytogenes* strains showed a slight decrease in number during the first 5 h then remained constant through the 20 h sampling period. Other researchers have also reported that *L. monocytogenes* cells decreased in number in the first 2 h post-injection (33, 38). No statistically significant differences were observed between treatments for either *L. monocytogenes* strain (Fig. 3-6), indicating that the

enhanced virulence observed in organic acid habituated cells is not due to enhanced survival or growth in the larvae.

A



B

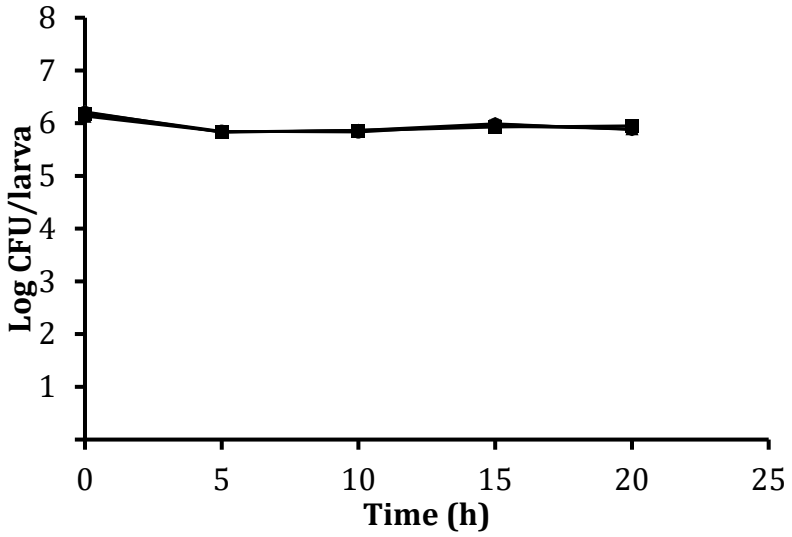


Figure 3-6 Growth of habituated and non-habituated *Listeria monocytogenes* N1-227 (A) and R2-499 (B) cells in *Galleria mellonella* after 5, 10, 15 and 20 h post injection. Media included: TSB pH 7.4 (baseline control, —●—), TSB pH 6.0 (pH control, —▲—), TSB pH 6.0 w/ 4.75 mM of acetic acid (—■—) and TSB pH 6.0 w/ 4.75 mM of L-lactic acid (—✕—). Error bars represent standard error of mean for two biological trails. Different letters indicate that treatments are significantly different ($p<0.05$) as determined by one-way ANOVA with Tukey's post-hoc tests.

CONCLUSION

Quantitative PCR demonstrated acid habituation induced similar and statistically significant increases in the expression of several genes associated with acid and bile stress resistance in two strains of *L. monocytogenes* that are known human pathogens.

Similar results were noted with expression of virulence genes, especially for the two internalin genes, while changes in other stress and virulence genes were strain dependent. In combination with lower LT_{50} time in the *G. mellonella* infection model that was observed for organic acid habituated *L. monocytogenes* cells, these findings strongly suggest that exposure to acetic or lactic acid can induce increased virulence in at least some *L. monocytogenes* strains. Because lactic and acetic acids are widely used in the food industry, the possibility that acid exposure triggers enhanced stress resistance and virulence in *L. monocytogenes* has important implications for food safety practices and should be explored further.

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CHAPTER IV

TRANSCRIPTOME RNA-SEQ ANALYSIS OF *LISTERIA MONOCYTOGENES* IN RESPONSE TO ORGANIC ACID HABITUATION

ABSTRACT

Listeria monocytogenes is a gram-positive, food-borne pathogen that can cause listeriosis with high mortality. Organic acids such as acetic acid or lactic acid are widely used in the food industry as antimicrobial agents to inhibit the growth of *L. monocytogenes*. However, studies suggest these acids may unintentionally enhance the pathogenicity of *L. monocytogenes*. Detailed understanding of the mechanisms by which *L. monocytogenes* responds to organic acid exposure is lacking. In this study, RNA-sequencing was conducted to compare the transcriptional profile of *L. monocytogenes* strains in the presence or absence of organic acid habituation. More differentially expressed genes (DEGs) were identified when *L. monocytogenes* cells were habituated with organic acid compared to *L. monocytogenes* cells without organic acid habituation. Induced expression of acid and bile stress response genes and virulence genes profiled in Chapter III using RT-qPCR technique was validated by RNA-seq results. Other DEGs included genes involved in two-component signal transduction systems, ATP-dependent (ABC-type) transporters, as well as enzymes associated with various phosphotransferase transport systems, carbohydrate metabolism, amino acid metabolism, quorum sensing, bacterial chemotaxis and flagellar assembly pathways. Interestingly, the DEGs involved in flagella-mediated cell motility pathways were exclusively down-regulated in both of the tested strains, and this is consistent with enhanced virulence as loss of flagella and their antigenic determinants are key to *L. monocytogenes* avoiding the host defense

systems. Results provide a more comprehensive view of the mechanisms used by *L. monocytogenes* to adapt to organic acid exposure, which may help to develop better strategies to prevent *L. monocytogenes* contamination in food.

INTRODUCTION

Listeria monocytogenes is a gram-positive foodborne pathogen that is widely dispersed in the environment and can cause listeriosis with high fatality rates when consumed in contaminated food products (1). The ubiquitous nature of *L. monocytogenes* makes it difficult to eliminate from food systems (2). Organic acids such as acetic acid and lactic acid are generally recognized as safe (GRAS) and approved as directly added antimicrobial agents in food products. However, research has suggested that exposure to organic acids may unintentionally enhance virulence of *L. monocytogenes* (3-5). Research outlined in Chapter III has further shown that habituation of *L. monocytogenes* to organic acids can lead to up regulated expression of several stress and virulence genes and concurrently increased virulence in a wax worm model. However, a detailed understanding of how *L. monocytogenes* adapts to organic acid exposure and how this adaptation bolsters virulence is still lacking.

The objective of this study was to gain a comprehensive view of the transcriptional response of *L. monocytogenes* to organic acid habituation using RNA-sequencing (RNA-seq). In order to achieve that objective, we compared the transcriptional profiles of *L. monocytogenes* in the presence and absence of 4.75 mM L-lactic or acetic acids at pH 6.0. The differentially expressed genes (DEGs) involved in *L. monocytogenes* response to organic acid were analyzed.

MATERIALS AND METHODS

Bacterial strains and growth conditions

Two *L. monocytogenes* strains, FSL N1-227 and FSL R2-499 which were previously shown to display inducible resistance to both acid and bile in response to organic acid habituation (5) were used in this project. Cells were maintained and grown as described by Zhang et al., (5).

RNA isolation and sequencing

Total RNA of *L. monocytogenes* was extracted as described in chapter III. Briefly, A 1 % inoculum (v/v) of diluted overnight cultures was transferred into standard TSB (pH 7.4) and incubated at 37 °C for 4 h. The mid-log phase cultures were collected and then suspended in either standard TSB (pH 7.4, baseline control) or TSB without dextrose (pH 6.0 adjusted with HCl) containing 0 (pH control) or 4.75 mM of either L-lactic acid or acetic acid and incubated at 37°C for 20 minutes. After incubation, Total RNA was isolated using an Aurum total RNA mini kit following the vendor's recommended procedures. Residual DNA was removed using The Ambion® DNA-free™ DNase Treatment and Removal Reagents. RNA samples were then purified using the GeneJET RNA Cleanup and concentration Micro Kit PCR purification kit. The quality of the RNA samples was measured using TapeStation System and samples with a RNA integrity number (RIN) between 9.7 and 10 were sent to the High-Throughput Genomics Shared Resource at the Huntsman Cancer Institute (University of Utah, Salt Lake City) for rRNA-depleted Illumina TruSeq Stranded Total RNA library prep with Ribo-Zero and NovaSeq 2 x 50 bp paired-end sequencing on the Illumina NovaSeq 6000 platform.

RNA-seq data analysis

The FastQC program was used to assess sequencing quality (6), and the Trimmomatic program was used to remove low-quality base pairs and Illumina adapter sequences (7). After the removal, 10 – 16 million reads remained for each sample. The Bowtie program (8) was then used to map the reads to the respective complete sequenced genome of *L. monocytogenes*. The aligned BAM files were used as input and raw counts for each gene were generated using the featureCounts tool (9). Raw counts were converted to fragments per kilobase per million (FPKM) values. Differential expressed genes (DEGs) analysis was performed using edgeR (10) in R (11). The DEGs were reported as Log2-fold changes and a threshold of p-value <0.05 and False Discovery Rate (FDR) < 0.05 were used to determine statistically significant DEGs. Functional enrichments of DEGs were conducted by Gene Ontology (GO) (12) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways (13).

RESULTS

Genome analysis summary

Reads for *L. monocytogenes* N1-227 and R2-499 were submitted to the comprehensive genome analysis service at PATRIC. Details of the analysis are provided below.

Genome assembly

L. monocytogenes N1-227 and R2-499 was assembled using SPAdes. For strain N1-227, there were 19 contigs, an estimated genome length of 3,078,586 bp, and an average G+C content of 37.79%. The N50 length, the shortest sequence length at 50% of

the genome, is 584,918 bp. The L50 count, the smallest number of contigs whose length sum produces N50, is 2. For strain R2-499, there were 21 contigs, an estimated genome length of 3,060,024 bp, and an average G+C content of 37.86%. The N50 length is 510,476 bp. The L50 count is 2 (Table 4-1).

Table 4-1 Assembly Details

	N1-227	**R2-499**
Contigs	19	21
GC Content	37.79 %	37.86
Plasmids	0	0
Contig L50	2	2
Genome Length	3,078,586 bp	3,060,024 bp
Contig N50	584,918	510,476

Genome annotation

The *L. monocytogenes* N1-227 and R2-499 genome was annotated using RAST tool kit (RASTtk). Strain N1-227 has 3,107 protein coding sequences (CDS), 59 transfer RNA (tRNA) genes, and 6 ribosomal RNA (rRNA) genes. Strain R2-499 has 3,100 protein coding sequences (CDS), 58 transfer RNA (tRNA) genes, and 8 ribosomal RNA (rRNA) genes. The annotation of N1-227 included 604 hypothetical proteins and 2,503 proteins with functional assignments. The annotation of R2-499 included 636 hypothetical proteins and 2,464 proteins with functional assignments. The annotated features are summarized in Table 4-2.

Table 4-2 Annotated genome features

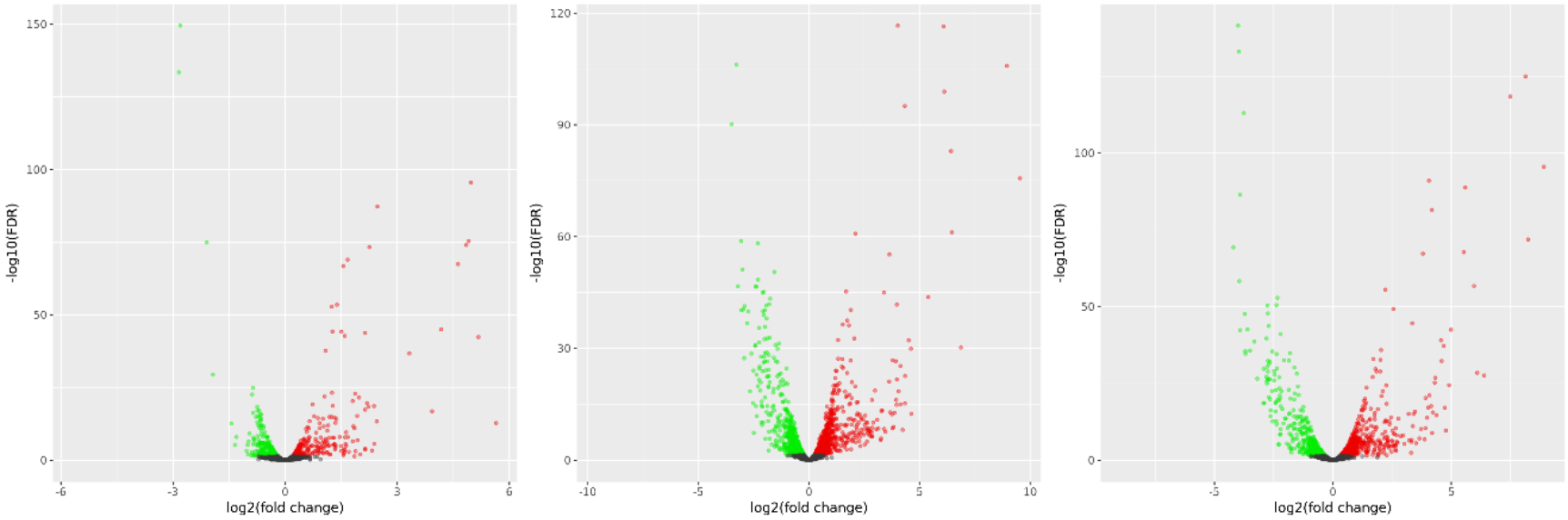
	N1-227	**R2-499**
CDS	3,107	3,100
tRNA	59	58
rRNA	6	8
Partial CDS	0	0
Miscellaneous RNA	0	0
Repeat Regions	58	0
Hypothetical proteins	604	636
Proteins with functional assignments	2503	2,464

Identification of DEGs induced by organic acid habituation

RNA-seq was performed to analyze the overall gene expression profile changes in *L. monocytogenes* strains after 20 minutes of organic acid habituation. When the baseline control was used as reference, there were 531 DEGs among the total 3234 genes analyzed in the pH control sample from *L. monocytogenes* strain N1-227. Within the 531 DEGs, 298 and 233 genes were up-regulated and down regulated, respectively (Fig. 4-1A). Acetic acid habituation increased the total number of DEGs in this strain to 1295 (693 up-regulated and 602 down-regulated), while L-lactic acid habituation resulted in 1109 DEGs (612 up-regulated and 497 down-regulated) (Fig. 4-1A).

There were a total of 3232 genes analyzed in *L. monocytogenes* strain R2-499, of which 238 were identified as DEGs (126 up-regulated and 112 down-regulated) in pH control samples (Fig. 4-1B). Acetic acid habituation of R2-499 increased the total number of DEGs to 994 (521 up-regulated and 473 down-regulated), and L-lactic acid habituation produced 839 DEGs (452 up-regulated and 387 down-regulated) (Fig. 4-1B).

A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log2(fold change)

B

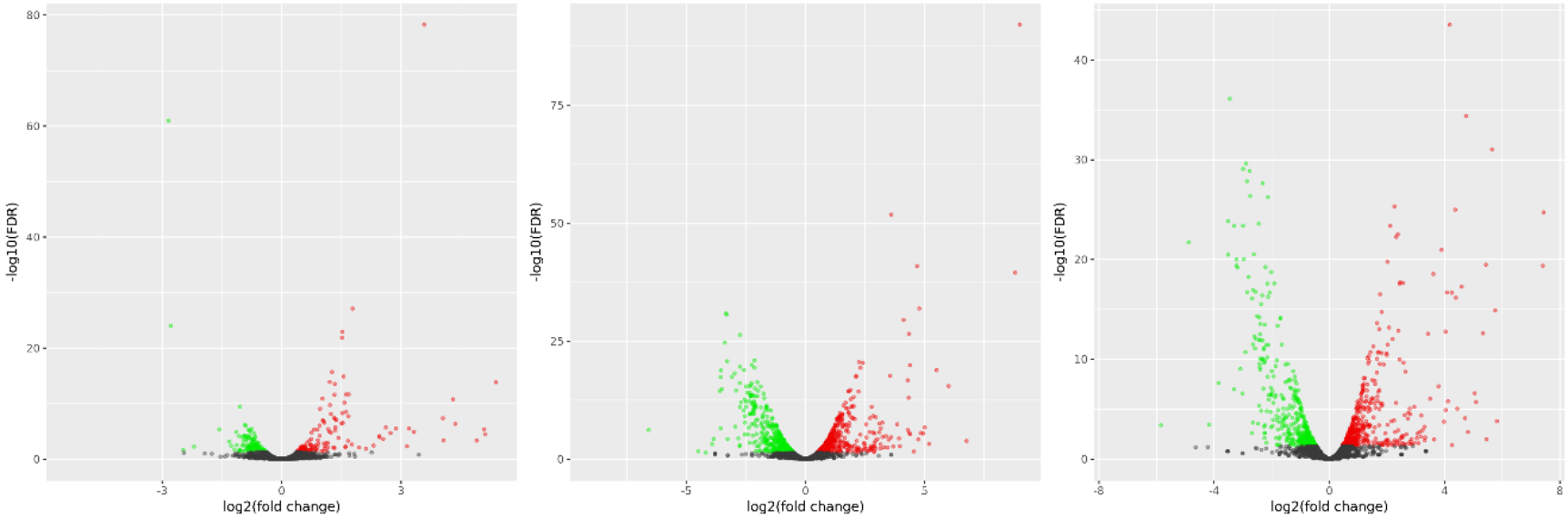
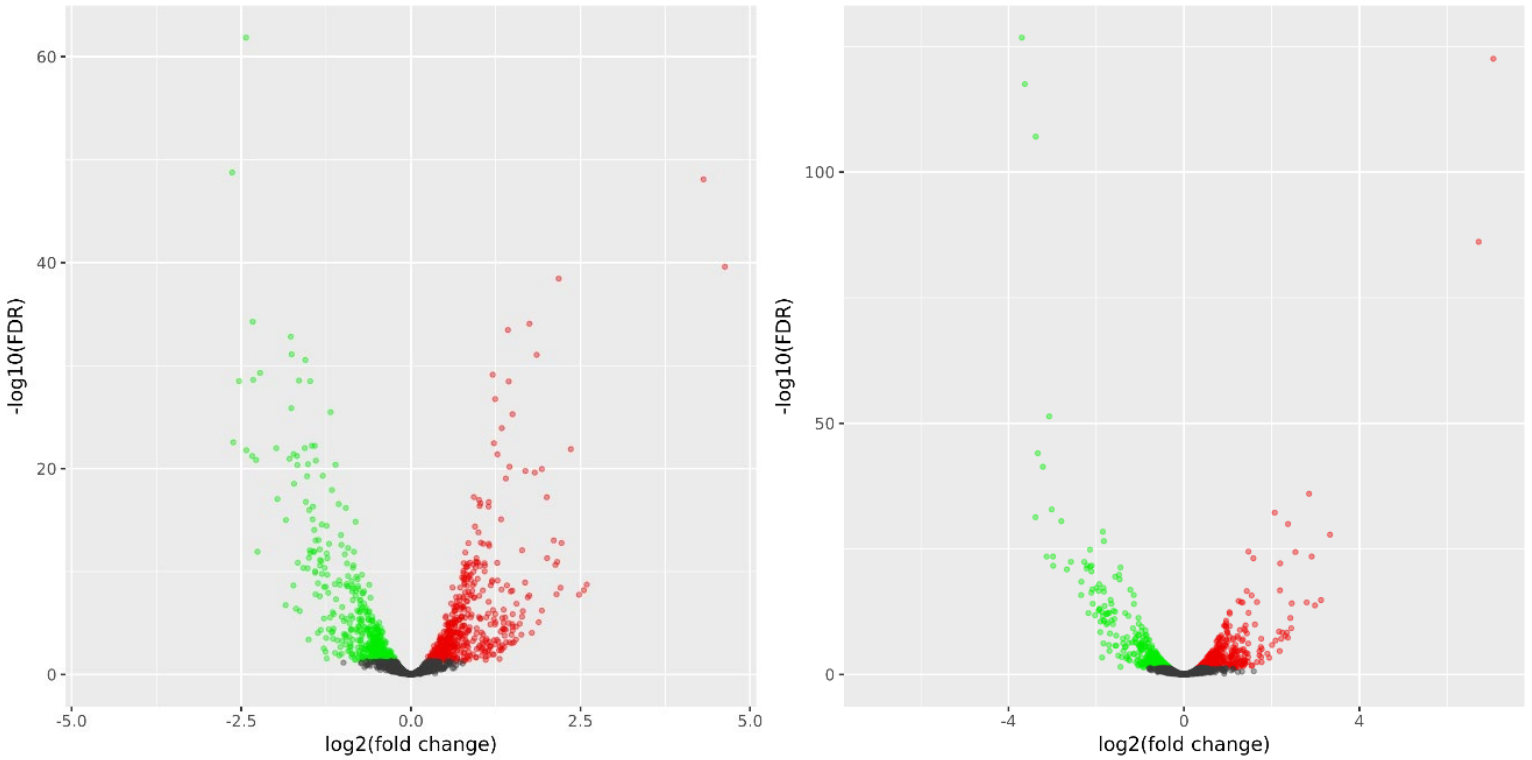


Figure 4-1 Volcano plot for transcription profile of pH control or organic acid habituated *Listeria monocytogenes* N1-227 (panel A) and R2-499 (panel B) cells compared to baseline control. From left to right: pH control, Acetic acid habituated and L- lactic acid habituated. Black dots represent the genes that are not significantly differentially expressed, while red and green dots are the genes that are significantly up- and down-regulated, respectively. Data was plotted with a threshold of FDR<0.05.

A


60
40
20
0
-log10(FDR)
-5.0
-2.5
0.0
2.5
5.0
log2(fold change)
100
50
0
-log10(FDR)
-4
0
4
log2(fold change)

B

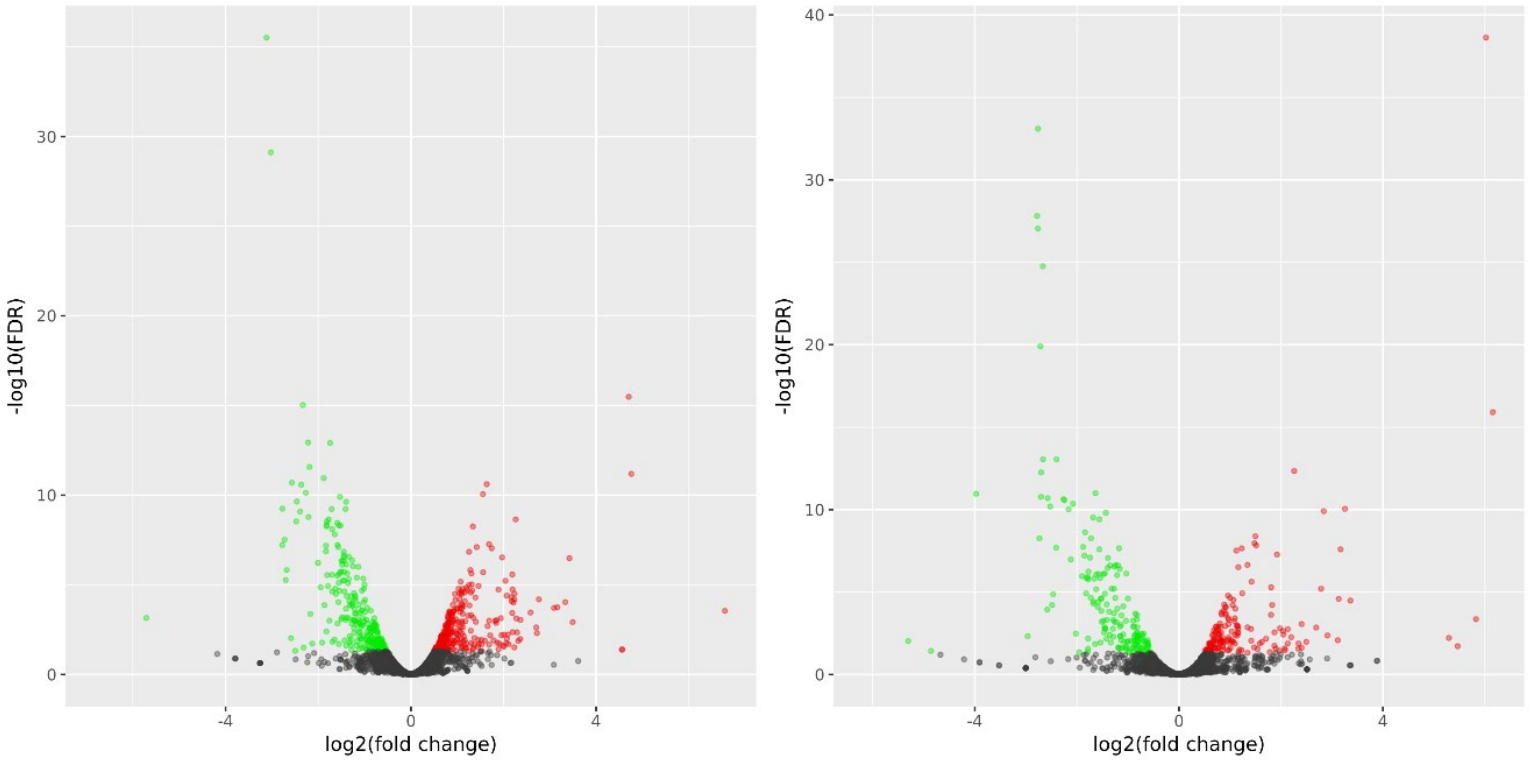


Figure 4-2 Volcano plot for transcription profile of organic acid habituated *Listeria monocytogenes* N1-227 (panel A) and R2-499 (panel B) cells compared to pH control. From left to right: Acetic acid habituated and L- lactic acid habituated. Black dots represent the genes that are not significantly differentially expressed, while red and green dots are the genes that are significantly up- and down-regulated, respectively. Data was plotted with a threshold of FDR<0.05.

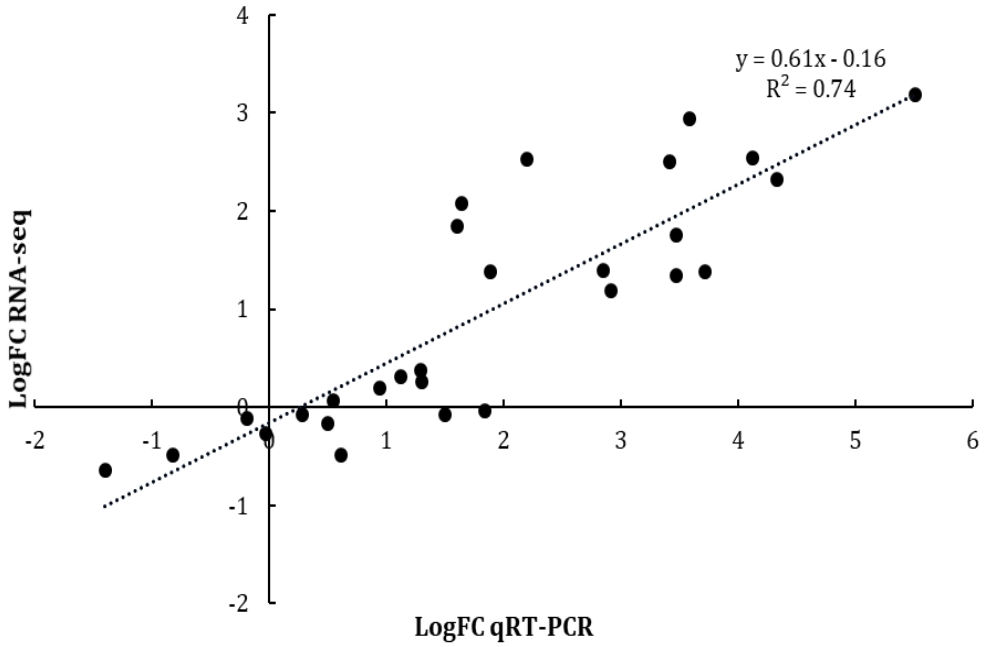
When the pH control treatment was used as a reference, 1025 DEGs (544 up-regulated and 481 down regulated) were identified in strain N1-227 after acetic acid habituation, and 765 DEGs (406 up-regulated and 359 down regulated) were detected after L-lactic acid habituation (Fig. 4-2A). A full list of up- and down-regulated DEGs in strain N1-227 is provided in Tables A2 and A3 in the appendices, respectively. Within the total pool of DEGs from acid habituated cells, 655 (353 up-regulated and 302 down-regulated) were discovered to be present in both acetic acid and L-lactic acid habituation samples (Table A2 and A3).

Acetic acid habituation of strain R2-499 resulted in 561 DEGs (304 up-regulated and 257 down regulated), and 335 DEGs (163 up-regulated and 172 down-regulated) were identified in L-lactic acid habituation samples (Fig. 4-2B). A full list of up- and down-regulated DEGs in strain R2-499 is provided in Tables A4 and A5, respectively. Once again there was overlap in the total pool of DEGs from acid habituated R2-499 cells, with 281 (134 up-regulated and 147 down-regulated) present in both strains in response to organic acid habituation (Table A4 and A5).

qRT-PCR validation

RNA-seq data was also used to validate the gene expression results of selected stress response genes and virulence genes from qRT-PCR results described in Chapter III. As expected, RNA-seq data were strongly corelated with the gene expression values obtained from qRT-PCR ($R^2 = 0.74$ for N1-227 and $R^2 = 0.79$ for R2-499) (Fig. 4-3).

A



B

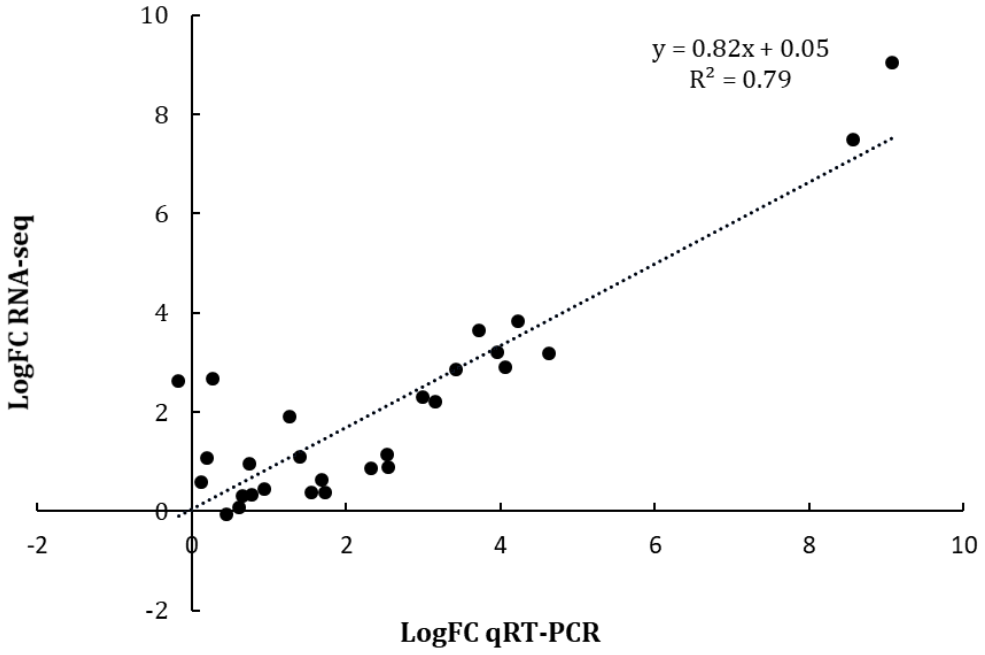


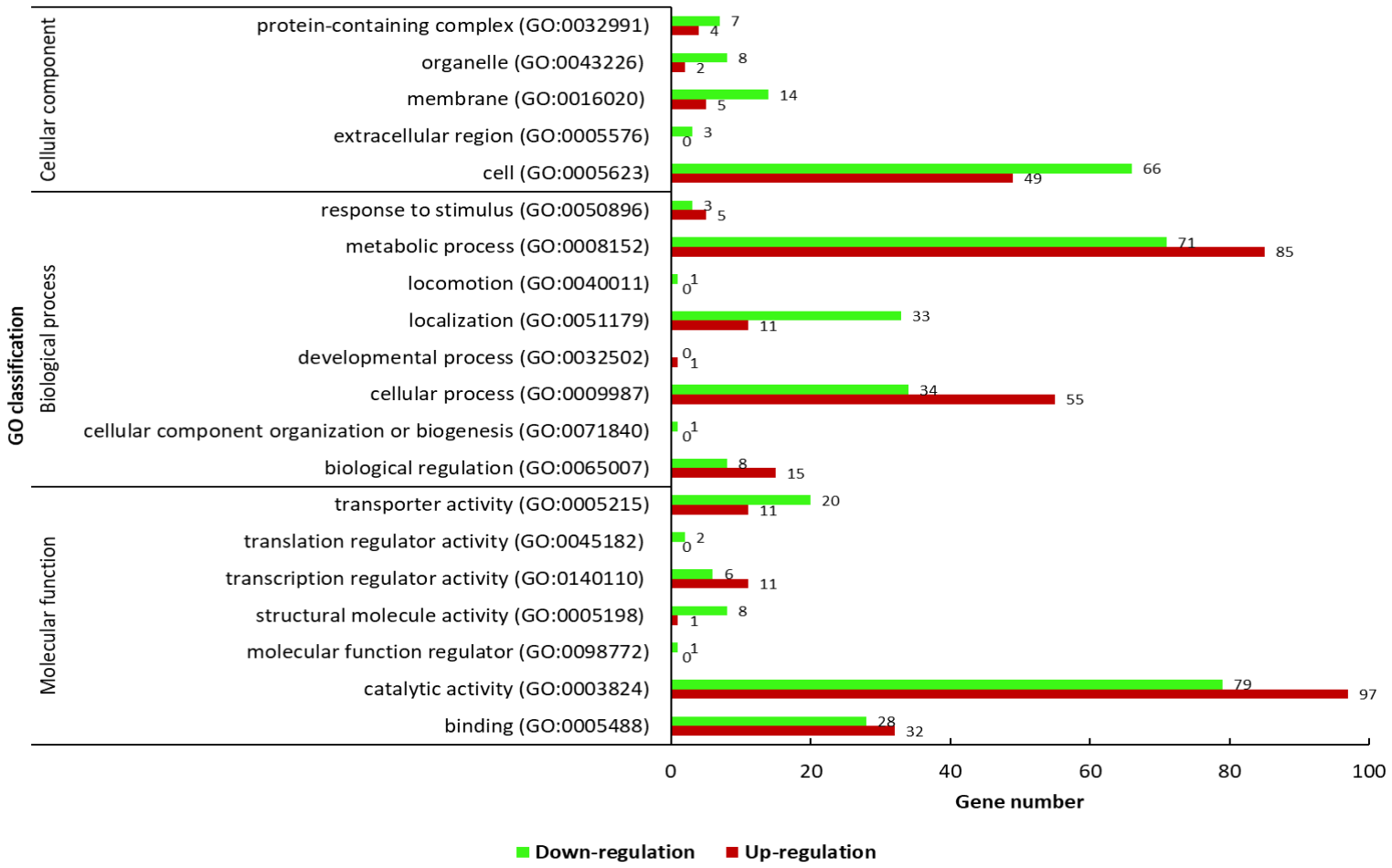
Figure 4-3 Correlation of fold change value from RNA-seq and qRT-PCR results for *Listeria monocytogenes* strain N1-227 (panel A) and R2-499 (panel B).

GO enrichment analysis of DEGs

Gene ontology (GO) analysis (12) was used to determine the functional characteristics of DEGs discovered in RNA-seq. For strain N1-227, 539 out of the 655 DEGs (82 %) identified in both acetic acid and L-lactic acid habituated samples were annotated to GO terms, in which 323 (172 up-regulated and 151 down-regulated) were annotated in biological process (GO: 0008150), 296 (152 up-regulated and 144 down-regulated) were annotated in molecular function (GO: 0003674) and 158 (60 up-regulated and 98 down-regulated) were annotated in cellular component (GO: 0005575) (Fig. 4-4A). The 539 GO-annotated DEGs were ultimately assigned to 20 categories, in which some of the categories including cell, metabolic process, localization, cellular process, biological regulation, transporter activity, catalytic activity and biding, were highly enriched (Fig. 4-4A).

For strain R2-499, 219 of the 281 DEGs (78 %) identified in both acetic acid and L-lactic acid habituated samples were annotated to the terms in the GO database. The DEGs were assigned to 16 categories, of which 120 DEGs (56 up-regulated and 64 down-regulated) were annotated in biological process (GO: 0008150), 110 DEGs (60 up-regulated and 50 down-regulated) were annotated in molecular function (GO: 0003674) and 80 DEGs (22 up-regulated and 58 down-regulated) were annotated in cellular component (GO: 0005575) with organic acids habituation (Fig. 4-3B). Among the 16 categories to which the 219 DEGs were assigned, the most enriched terms were cell, metabolic process, localization, cellular process and catalytic activity (Fig. 4-4B).

A


GO classification
Cellular component
Biological process
Molecular function
protein-containing complex (GO:0032991)
organelle (GO:0043226)
membrane (GO:0016020)
extracellular region (GO:0005576)
cell (GO:0005623)
response to stimulus (GO:0050896)
metabolic process (GO:0008152)
locomotion (GO:0040011)
localization (GO:0051179)
developmental process (GO:0032502)
cellular process (GO:0009987)
cellular component organization or biogenesis (GO:0071840)
biological regulation (GO:0065007)
transporter activity (GO:0005215)
translation regulator activity (GO:0045182)
transcription regulator activity (GO:0140110)
structural molecule activity (GO:0005198)
molecular function regulator (GO:0098772)
catalytic activity (GO:0003824)
binding (GO:0005488)
7
4
8
2
14
5
3
0
66
49
3
5
71
85
1
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33
11
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34
55
1
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8
15
20
11
2
0
6
11
8
1
1
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79
97
28
32
0
20
40
60
80
100
Gene number
Down-regulation
Up-regulation

B

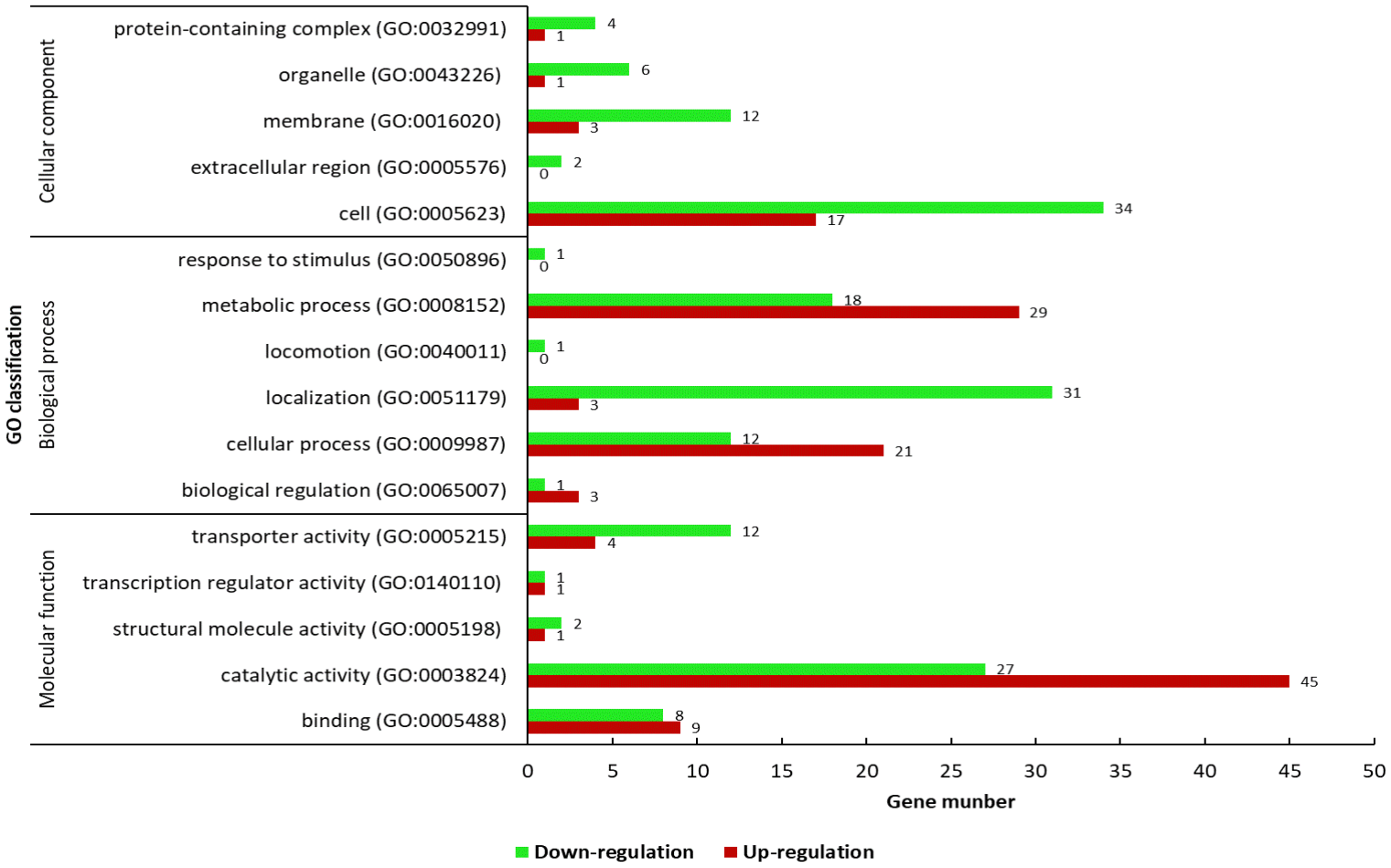

Figure 4-4 Gene Ontology (GO) classification of DEGs for *Listeria monocytogenes* strain N1-227 (panel A) and R2-499 (panel B)

KEGG pathway analysis of DEGs

KEGG pathway analysis (13) of DEGs (pH control as reference) was also conducted to explore the physiological response of *L. monocytogenes* to organic acid habituation. A total of 81 and 51 pathways were identified in strains N1-227 and R2-499, respectively (see Table A6 and Table A7 for full list). The enzymes and pathways that were most affected by habituation to organic acids included two-component signal transduction systems, ATP-dependent (ABC-type) transporters, as well as enzymes associated with various phosphotransferase transport systems, carbohydrate metabolism, amino acid metabolism, quorum sensing, bacterial chemotaxis and flagellar assembly pathways (Tables A6 and A7).

DISCUSSION

The combined GO and KEGG analysis of the DEG pool identified in both acetic acid and L-lactic acid habituated samples of *L. monocytogenes strain* N1-227 or R2-499 implicated two-component systems, ATP-dependent transporters, and enzymes associated with phosphotransferase uptake systems, carbohydrate metabolism, amino acid metabolism, quorum sensing, bacterial chemotaxis and flagellar assembly pathways as being particularly important to the physiology of this pathogen during exposure to organic acids.

Cell motility

Two-component systems (TCS) enable *Listeria monocytogenes* to sense and response to a wide variety of stresses including pH, temperature, osmolarity, nutrients, antibiotics and quorum signals (14, 15). A typical TCS consists of a histidine kinase

which monitors environmental stimulus, and a cognate response regulator which enables the bacterial cell to respond by regulating expression of specific target genes (14, 16). Chemotaxis protein CheA, a histidine kinase, and its cognate response regulator CheY transmit signals from chemoreceptors to the flagellar motors which result in changing the direction of flagellar rotation (17, 18). Bacterial chemotaxis allows cells to direct their movement toward a favorable environment or chemicals (positive chemotaxis) or avoid adverse environments or chemicals (negative chemotaxis) through flagellar rotation (19-21). Previous studies have shown that genes involved in flagellar assembly and motility are thermoregulated. *Listeria monocytogenes* strains are highly flagellated at 30ºC or below but there is a near complete absence of flagella-driven movement at 37ºC or above (18, 21-24). Loss of flagella may be related to successful infection since the bacterial flagellins (encoded by *fla*) are recognized by the innate immune system through Toll-like receptor 5-mediated signaling (25-27). Since transcription of *fla* is down-regulated at 37ºC, and this effect is associated with increased adhesion and invasion of Caco-2 cells, it has been proposed that down-regulation of flagellar assembly genes during in *vivo L. monocytogenes* infection may serve as an adaptive mechanism to avoid the recognition by the innate immune system of the host (17, 28-30).

In this study, genes involved in bacterial chemotaxis, including CheA and CheY, were significantly down regulated in both strains of *L. monocytogenes* after organic acid habituation compared to pH controls (Tables A3 and A5). All the genes involved in flagellar assembly, including *fla*, were also down regulated in both strains and the repression effect was significantly greater after organic acid habituation. It is worth noting that *fliG, fliM, fliY, motA* and *motB* are involved in both bacterial chemotaxis and

flagellar assembly pathways in both strains. It has been demonstrated that the chemotaxis stator protein MotA interacts with the rotor protein FliG electrostatically and plays a crucial role in bacterial flagellar motor rotation (31, 32). The finding that these genes were all down regulated during organic acid habituation, and that acid habituated cells became more virulent, is consistent with the hypothesis that reduced cell motility enhances virulence of *L. monocytogenes*.

Membrane transport

ATP-binding cassette (ABC-type) transporters are large integral membrane proteins that translocate substrate molecules such as sugars, ions, proteins, lipids and vitamins across cellular membranes through ATP binding and hydrolysis (33-35). They play an important role, directly or indirectly, in diverse cellular processes including metabolism, antibiotic resistance, homeostasis and nutrients uptake (33, 36). The arginine deiminase system (ADI), which catalyzes the synthesis of ornithine from arginine with production of ammonia and one ATP, is a primary component of the acid tolerance response (ATR) in *L. monocytogenes* (2, 37, 38). Ornithine is excreted out of the cell in an exchange for arginine entering the cell via the ADI pathway (38). A similar pathway termed the agmatine deiminase pathway (AgDI) has been described for agmatine, the decarboxylation product of arginine (39, 40). Carbamoyltransferase (Lmo0036; encoded by *lmo0036*) is one of the three enzymes in ADI system which catalyzes the synthesis of ornithine from arginine (38). Carbamoyltransferase is also involved in AgDI pathway, which converts agmatine to putrescine plus ammonia and an ATP (41). Similarly, putrescine leaves the cell in exchange for agmatine entering the cell in the AgDI pathway. In this study, the transcription level of over 35 and 20 ABC transporters,

including amino acid, carbohydrates and metal transporters, were significantly altered in the presence of organic acid for *L. monocytogenes* strain N1-227 and R2-499, respectively. Among them, putrescine ABC transporters were exclusively down regulated in both strains. In addition, arginine deiminase was significantly up regulated after organic acid habituation in both strains, and in contrast no significant change was found on the expression of arginine decarboxylase and agmatine deiminase was down regulated after organic acid habituation in both strains. These suggest that the AgDI pathway may have been repressed to facilitate the ADI pathway in our tested strains.

Listeria monocytogenes has the ability to utilize a variety of carbohydrates and the primary mechanism for sugar uptake in this species involves phophoenol pyruvate-dependent phosphotransferase systems (PTS) (42). The PTS consists of two non-sugar specific enzymes, EI and HPr, plus three or four sugar-specific components (enzymes EIIA, EIIB, EIIC and EIID) which are divided into seven protein families (PTS^{Man}, PTS^{Glc}, PTS^{Lac},PTS^{Gut}, PTS^{Fru}, PTS^{Asc} and PTS^{Gat}) (43, 44). Recent studies have shown that modulation of PrfA activity was cross-linked between the glucose-, mannose- and cellobiose-specific PTS permeases in *L. monocytogenes* wherein metabolism of these carbon sources represses PrfA-dependent gene expression (45-48). In this study, the expression of 13 genes (including 5 mannose- and 3 cellobiose-specific PTS permeases) were modified with organic acid habituation for both strains. The expression of mannose- and cellobiose-specific PTS permease genes in our study were exclusively down-regulated indicating that organic acid habituation may enhance the virulence of *L. monocytogenes* by repressing the metabolism of mannose or cellobiose.

Carbohydrate and amino acid metabolism

Carbohydrate and amino acid metabolism exert significant effects on *L. monocytogenes* stress response and virulence gene expression (45, 49, 50). In this study, the DEGs involved in carbohydrate metabolism pathways included glycolysis/glycogenesis, amino sugar and nucleotide sugar metabolism and fructose and mannose metabolism. Amino sugars and nucleotide sugar metabolism participate in polysaccharide biosynthesis which contributes to bacterial cell wall structure (51). The majority of the DEGs involved in amino sugar and nucleotide sugar metabolism were down-regulated under organic acid habituation for both strains, suggesting that changes in cell wall architecture are part of the *L. monocytogenes* response to organic acid exposure.

The DEGs associated with amino acid metabolism that were identified in acid habituated bacterial cells for both strains included genes for metabolism of D-alanine and glutathione metabolism (Table A6 and A7). D-alanine has been reported to associated with the cell wall structure of *L. monocytogenes* (56, 57). All genes involved in D-alanine metabolism were down regulated which provides further evidence that cell wall structure alteration was part of the *L. monocytogenes* response to organic acid habituation. Glutathione (GSH) has been proven to act as a binding cofactor to activate PrfA and evidence suggests that GSH binding to PrfA differentially affects PrfA-dependent gene expression (52, 53). In this study, all genes involved in GSH metabolism were up regulated.

Quorum sensing

When *L. monocytogenes* experience fluctuations in bacterial cell density due to external stimuli, they respond by using quorum sensing communications to regulate specific gene expression (58, 59). The response will activate or repress genes associated with a diverse array of activities such as virulence, antibiotic resistance, competence, motility, sporulation and biofilm formation (59). The two-component response regulator DegU in *L. monocytogenes* has been reported to contribute to motility (including quorum sensing and flagellar assembly), as well as virulence and biofilm formation (60-63). In this study, the expression level of 20 and 10 genes involved in quorum sensing were significantly altered for *L. monocytogenes* strain N1-227 and R2-499, respectively. Those genes included *gadD2* (acid stress response genes), ABC transporter genes, *lmo2854* (sporulation protein SpoJ), comK'(competence protein ComK) and two-component response regulator *degU*.

In summary, RNA-sequencing provided comprehensive insights on the response of *L. monocytogenes* to organic acid habituation. This information should provide new leads for research to improve control over *L. monocytogenes* in food and enhance the safety of food production. For instance, greater understanding of cell physiology in response to acid exposure may reveal new metabolic targets for antimicrobial interventions.

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CHAPTER V

SUMMARY AND CONCULSIONS

This study focused on the impact of habituation to lactic acid and acetic acid on transcriptional stress response of *Listeria monocytogenes*. The first phase of the study evaluated expression of transcription factors and genes related to acid resistance, bile resistance and virulence in *L. monocytogenes* strains N1-227 and R2-499. Two main acid stress response system, arginine deiminase (ADI) and glutamate decarboxylase, and their related gene expression were investigated in this study. Results showed that habituation of organic acid significantly increased the expression of *gadD2, gadD3* and *arcA* in both strains compared to *L. monocytogenes* without organic acid habituation. Results also showed significant increase in *bsh* (associated with bile salt hydrolase system) expression for both strains. However, changes in expression of *bilE*, which associated with bile exclusion system, were strain dependent. Finally, the expression profile for the virulence genes involved in *Listeria* infection cycle was strain dependent. Genes that helps with the cell invasion, *inlA* and *inlB,* were the only two virulence genes that showed same expression pattern for both strains when acid stress was introduced whereas expression for other virulence genes was strain-dependent.

The second phase of this study determined the *in vivo* virulence of organic acid habituated *L. monocytogenes* using the *Galleria mellonella* infection model. Organic acid habituation affected the virulence of *L. monocytogenes* strains in *G. mellonella* wax worm model observed 24 h and 48 h after injection. Significantly lower survivability was also observed 24 h and 48 h post-injection for the habituated cells compared to *L. monocytogenes* without organic acid habituation. Larvae injected with acid habituated

R2-499 cells showed lower survivability during the first two days after injection for all treatments compared to N1-227 cells. Decrease of LT_{50} was observed when larvae were injected with organic acid habituated cells. The growth of *L. monocytogenes* growth kinetics in insects between treatments for either strain showed no significantly difference, indicating that the enhanced virulence observed in organic acid habituated cells is not due to enhanced survival or growth in the larvae.

The third phase of this study explored a more comprehensive transcriptional profile of *L. monocytogenes* strains N1-227 and R2-499 using RNA-seq. Results showed that more differentially expressed genes (DEGs) were identified when *Listeria* cells were habituated with organic acid compared to *Listeria* cells without organic acid habituation. DEGs included genes involved in cell motility, membrane transport (including ATP-dependent (ABC-type) transporters and phosphotransferase transport systems), carbohydrate metabolism, amino acid metabolism and quorum sensing. Interestingly, the DEGs involved in bacterial chemotaxis and flagellar assembly pathways were exclusively down-regulated in both of the tested strains, indicating the motility of *L. monocytogenes* may be reduced by organic acid habituation and reduced cell motility enhances virulence of *L. monocytogenes*. Changes in cell wall architecture is also part of the *L. monocytogenes* response to organic acid exposure as the majority of the DEGs involved in amino sugar and nucleotide sugar metabolism and cell wall associated amino acid metabolism were down-regulated under organic acid habituation for both strains.

Results from this project have increased the understanding of organic acid stress response in *L. monocytogenes* and may provide new leads for research and help to develop better strategies to prevent *L. monocytogenes* contamination in food. According

to the FSIS *Listeria* Guideline, food product such as deli and hotdog which received an antimicrobial agent or process (AMAP; such as the addition of lactates or diacetates in the formulation) during the production does not required to have a testing program for food contact surfaces (FCS). However, results from this study suggests with the potential of some strains surviving after organic acid exposure, such regulations need to be re-evaluated and tightened. Future research will include gene expression of *L. monocytogenes* at different temperature or in response to different conditions (such as stomach acids, refrigerated storage). In addition, study of *L. monocytogenes* control on different food product other than meat product should be explored. Finally, to truly understand mechanisms discovered from the RNA-seq, functional studies involving genetic manipulation of *L. monocytogenes* is required. This will include developing reliable genetic manipulation methods and creating functional knockouts to understand the role of mechanisms described in this study such as cell motility, AgDI pathway as well as sugar and amino acid metabolism to the virulence of *L. monocytogenes*.

APPENDICES

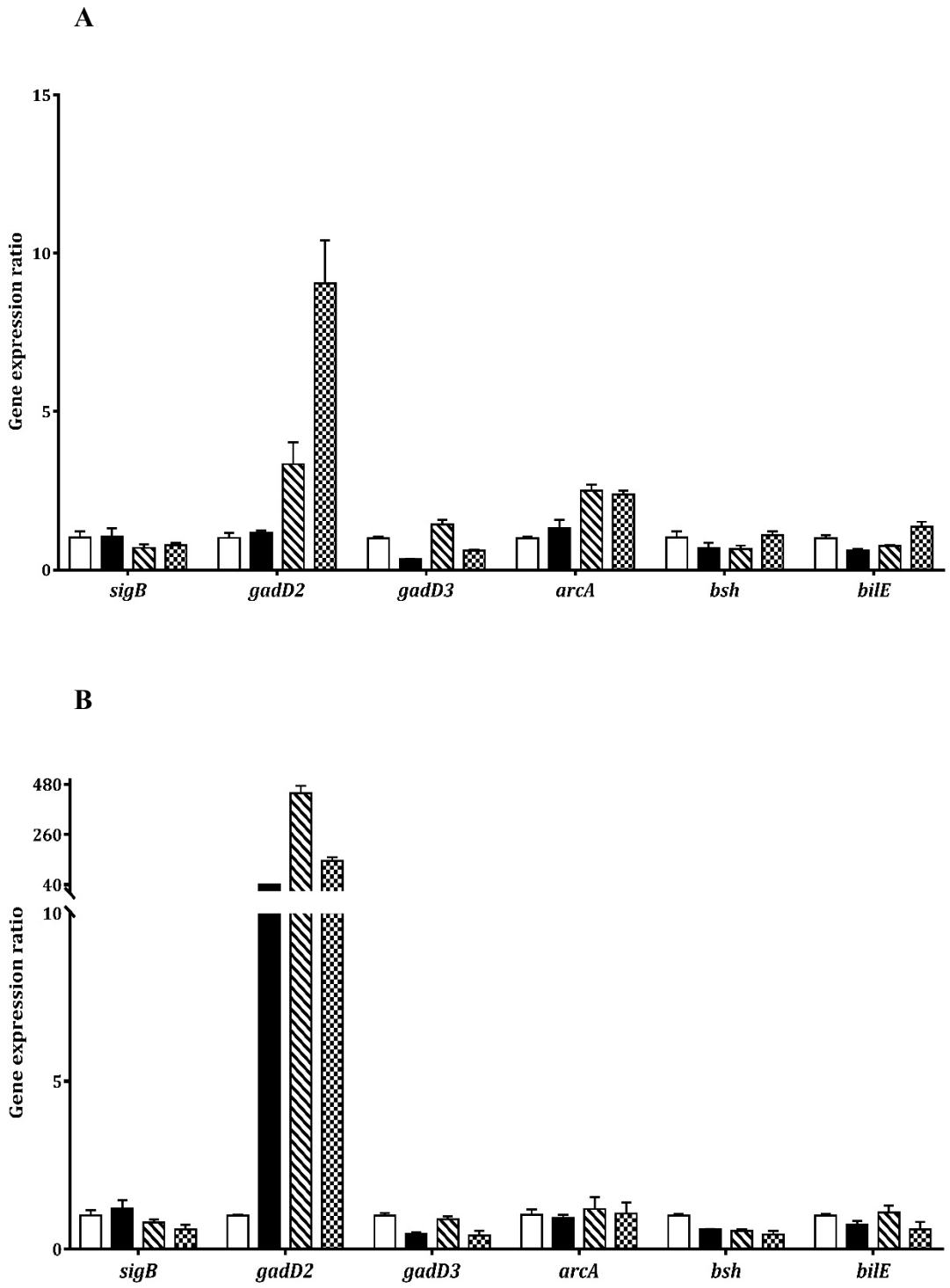

Figure A-1 Relative gene expression of acid and bile stress response related genes in 40 minutes habituated *Listeria monocytogenes* N1-227 (panel A) and R2-499 (panel B) cells in comparison with non-habituated cells (baseline control, TSB pH 7.4, ▭). Habituated treatments include: TSB pH 6.0 (pH control, ■), TSB pH 6.0 w/ 4.75 mM of acetic acid (▨) and TSB pH 6.0 w/ 4.75 mM of L-lactic acid (▩). Error bars represent standard error of mean for two biological trials with three replicates for each trial.

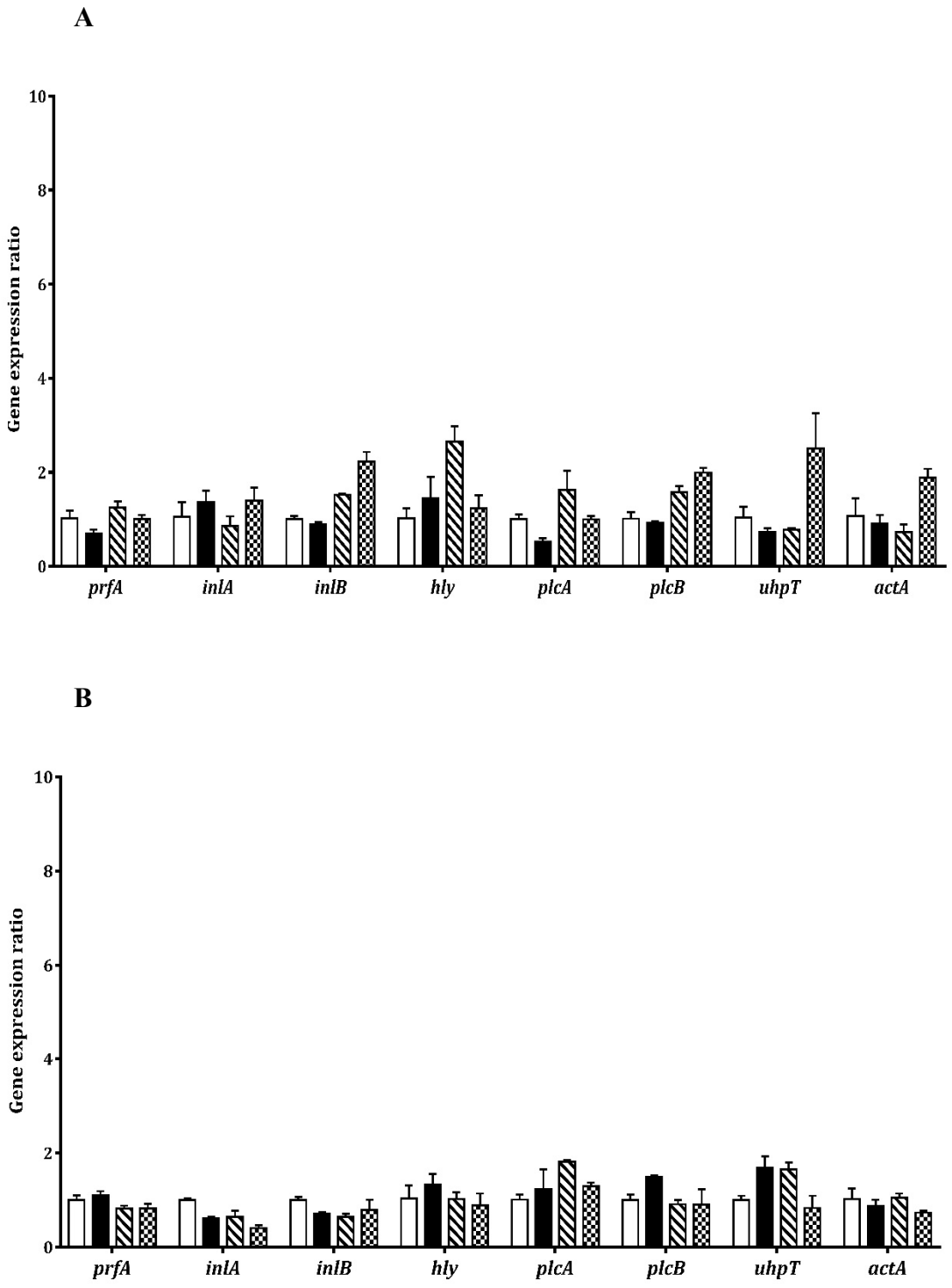

Figure A-2 Relative gene expression of virulence related genes in 40 minutes habituated *Listeria monocytogenes* N1-227 (panel A) and R2-499 (panel B) cells in comparison with non-habituated cells (baseline control, TSB pH 7.4, ▭). Habituated treatments include: TSB pH 6.0 (pH control, ■), TSB pH 6.0 w/ 4.75 mM of acetic acid (▨) and TSB pH 6.0 w/ 4.75 mM of L-lactic acid (▩). Error bars represent standard error of mean for two biological trails with three replicates for each trail.

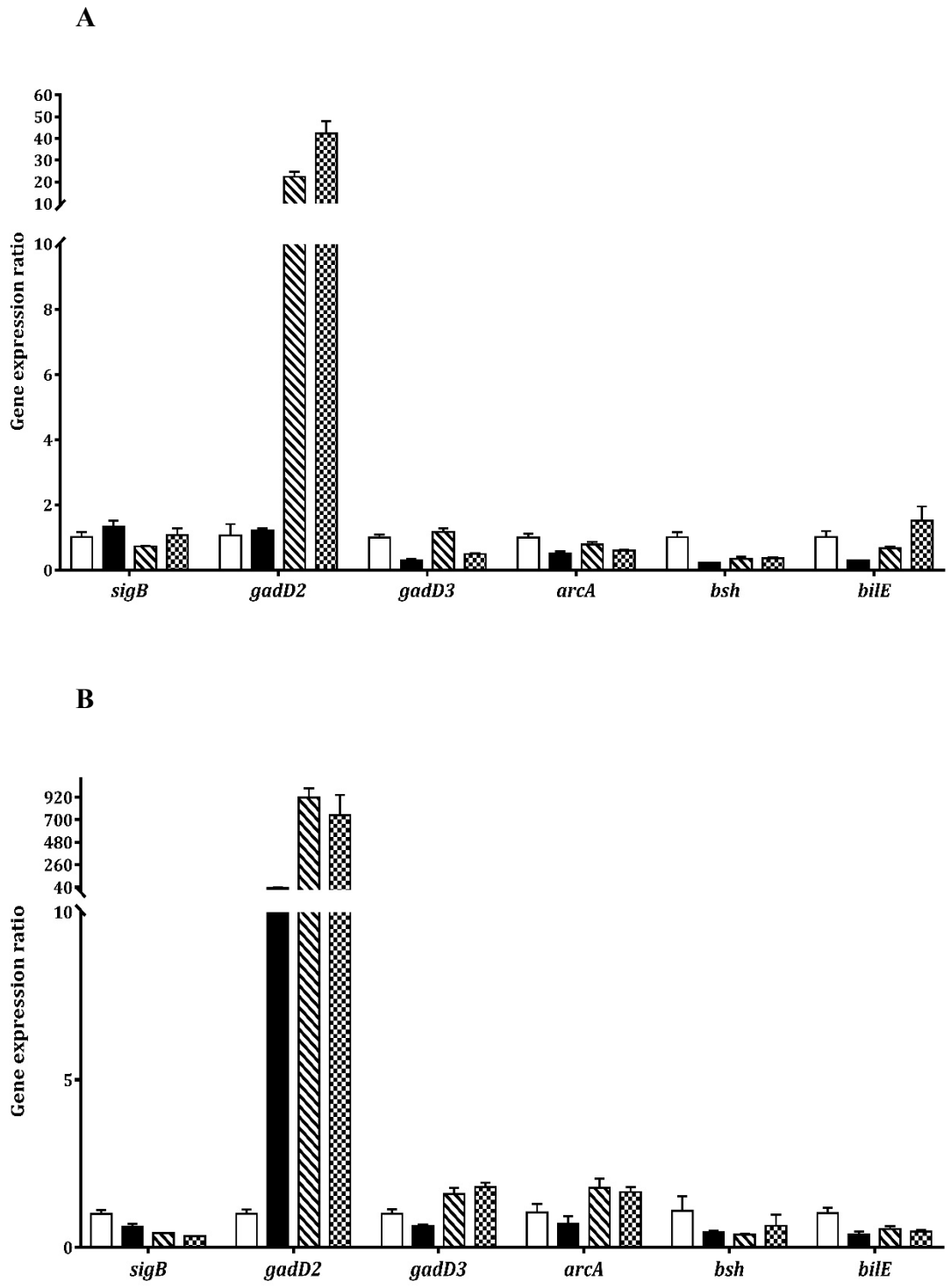

Figure A-3 Relative gene expression of acid and bile stress response related genes in 60 minutes habituated *Listeria monocytogenes* N1-227 (panel A) and R2-499 (panel B) cells in comparison with non-habituated cells (baseline control, TSB pH 7.4, ▭). Habituated treatments include: TSB pH 6.0 (pH control, ■), TSB pH 6.0 w/ 4.75 mM of acetic acid (▨) and TSB pH 6.0 w/ 4.75 mM of L-lactic acid (▩). Error bars represent standard error of mean for two biological trials with three replicates for each trial.

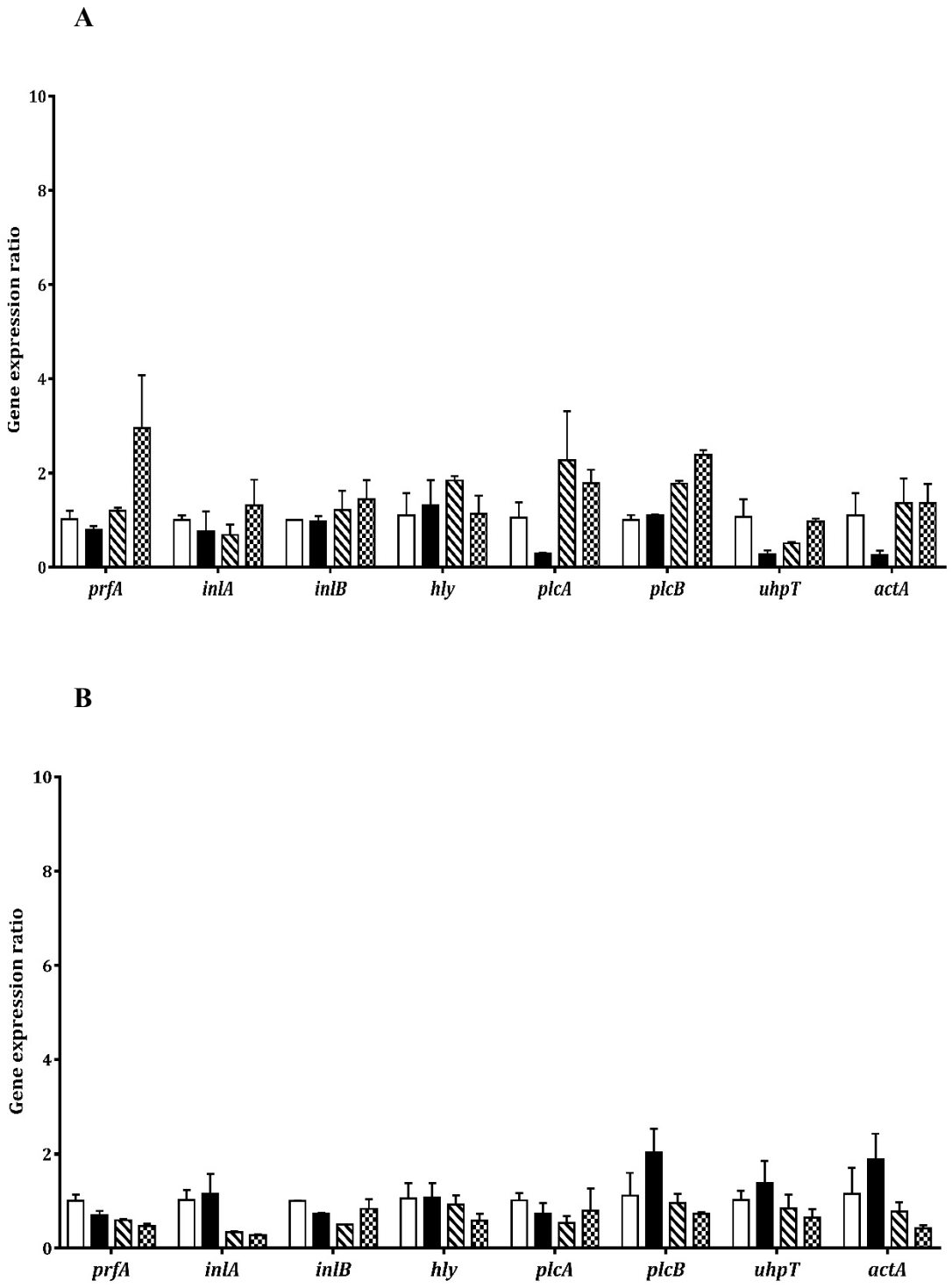

Figure A-4 Relative gene expression of virulence related genes in 60 minutes habituated *Listeria monocytogenes* N1-227 (panel A) and R2-499 (panel B) cells in comparison with non-habituated cells (baseline control, TSB pH 7.4, ▭). Habituated treatments include: TSB pH 6.0 (pH control, ■), TSB pH 6.0 w/ 4.75 mM of acetic acid (▨) and TSB pH 6.0 w/ 4.75 mM of L-lactic acid (▩). Error bars represent standard error of mean for two biological trails with three replicates for each trail.

Table A-1 Primer used in this project

Protein	Function	Gene		Sequence (5' –> 3')
General stress-responsive sigma factor B	Required for the expression of *L. monocytogenes* stress response factors	*sigB*	F	TGTTGGTGGTACGGATGATGG
			R	ACCCGTTTCTTTTTGACTGCG
Arginine deiminase	Catalyze L-arginine to L-citrulline	*arcA*	F	GCGTGATTGCGGAGGTTTTG
			R	CCCCATCATTCCACTGCTCT
Glutamate decarboxylase β	Convert glutamate to GABA	*gadD2*	F	ATCGATATGCGCGTTGTTCCA
			R	ATACCGAGGATGCCGACCACA
Glutamate decarboxylase γ	Convert glutamate to GABA	*gadD3*	F	TTCCGCATTGTTACGCCAG
			R	TCTTACTTGGGGACTTCGAC
Bile salt hydrolase	Detoxify conjugated bile acid	*bsh*	F	TTTGTTGTTCCACCGAGCCTA
			R	GGGCGGAATTGGCTTACCTG
Bile exclusion protein	Exclude bile from cell	*bilE*	F	CATCAACGGAGCCTGTCGAA
			R	TCCAGATGACGCGCTAAGAA
Positive regulatory factor A	Required for the expression of *L. monocytogenes* virulence factors	*prfA*	F	CGATGCCACTTGAATATCCT
			R	CTTGGCTCTATTTGCGGTCA
Internalin A	Host cell invasion	*inlA*	F	CTATACCTTTAGCCAACCTGT
			R	GGTTGTTTCTTTGCCGTCCAC
Internalin B	Host cell invasion	*inlB*	F	CTGGACTAAAGCGGAAAACCTT
			R	TCCAGACGCATTTCTCACTCTT

Listeriolysin O	Phagosome lysis	*hly*	F	ATGCAATTTCGAGCCTAACC
			R	ACGTTTTACAGGGAGAACATC
Phosphatidylinositol-specific phospholipase C	Phagosome lysis	*plcA*	F	ACCGTATTCCTGCTTCTAGTT
			R	ACACAACAAACCTAGCAGCG
Phosphatidylcholine phospholipase C	Phagosome lysis	*plcB*	F	TAGTCAACCTATGCACGCCAA
			R	TTTGCTACCATGTCTTCCGTT
Actin assembly-inducing ptotein	Stimulates actin-based intracellular bacterial motility	*actA*	F	TTATGCGTGCGATGATGGTG
			R	TTCTTCCCATTCATCTGTGT
Hexose phosphate transporter	Intracellular bacterial growth	*uhpT*	F	TTCAGCACCACAGAACTAGG
			R	GCATTTCTTCCATCCACGAC
RNA polymerase beta subunit	Housekeeping gene	*rpoB*	F	CTCTAGTAACGCAACAACCTC

Table A-2 Up-regulated DEGs of *Listeria monocytogenes* N1-227 during organic acid habituation compared to pH control; [a]: Acetic acid habituated; [b]: L-Lactic acid habituated; [c]: non-significant.

Gene name	Gene description	Log_2FC	
		A[a]	L[b]
lmo2362|gadT2	glutamate antiporter [Uniprot Acc. Q8Y4S1];	4.65	3.42
lmo2072|lmo2072	Redox-sensing transcriptional repressor Rex [Uniprot Acc. P60384];	0.95	0.51
lmo2212|hemE	Uroporphyrinogen decarboxylase [Uniprot Acc. Q8Y564];	0.87	1.04
lmo1830|lmo1830	short-chain dehydrogenase	2.37	2.62
lmo2371|lmo2371	ABC transporter permease [Uniprot Acc. Q8Y4R3];	0.54	0.45
lmo2366|lmo2366	DeoR family transcriptional regulator [Uniprot Acc. Q928R7];	0.69	0.78
lmo2369|lmo2369	general stress protein 13 (induced by heat shock, salt stress, oxidative stress, glucose limitation and oxygen limitation) [Uniprot Acc. Q8Y4R5];	0.43	0.65
lmo2166|lmo2166	hypothetical protein	0.67	0.78
lmo2670|lmo2670	hypothetical protein	1.08	1.10
lmo2158|lmo2158	hypothetical protein	2.20	2.46
lmo2338|pepC	Aminopeptidase C [Uniprot Acc. O69192];	0.99	1.12
lmo0871|lmo0871	hypothetical protein	0.81	1.05
lmo0870|lmo0870	hypothetical protein	1.34	1.48
lmo0558|lmo0558	hypothetical protein [Uniprot Acc. Q8Y9H0];	0.63	0.63
lmo0869|lmo0869	hypothetical protein [Uniprot Acc. Q8Y8M7];	1.23	1.40
lmo0602|lmo0602	transcripitonal regulator	2.22	2.24
lmo1065|lmo1065	hypothetical protein	0.56	0.65
lmo0866|lmo0866	ATP-dependent RNA helicase CshA [Uniprot Acc. Q8Y8N0];	0.36	0.41
lmo2211|hemH	Ferrochelatase [Uniprot Acc. Q8Y565];	0.80	1.01
lmo2210|lmo2210	hypothetical protein	1.66	2.28
lmo0581|lmo0581	hypothetical protein [Uniprot Acc. Q8Y9E8];	0.49	0.59
lmo2200|lmo2200	MarR family transcriptional regulator [Uniprot Acc. Q8Y575];	0.95	0.71
lmo2188|lmo2188	oligoendopeptidase [Uniprot Acc. Q8Y583];	0.57	0.55
lmo2177|lmo2177	hypothetical protein [Uniprot Acc. Q8Y592];	0.86	1.18
lmo2168|lmo2168	glyoxalase	0.70	0.76
lmo2167|lmo2167	hypothetical protein	0.43	0.59
lmo0588|lmo0588	DNA photolyase [Uniprot Acc. Q8Y9E2];	0.77	0.75
lmo2263|lmo2263	hypothetical protein [Uniprot Acc. Q8Y515];	0.58	0.67
lmo0553|lmo0553	hypothetical protein	0.35	0.56
lmo2818|lmo2818	MFS transporter [Uniprot Acc. Q8Y3L7];	1.60	2.15
lmo1059|lmo1059	hypothetical protein	0.42	0.55

lmo0288|lmo0288	two-component sensor histidine kinase [Uniprot Acc. Q8YA71];	0.29	0.32
lmo2113|lmo2113	Putative heme-dependent peroxidase lmo2113 [Uniprot Acc. Q8Y5F1];	0.58	1.12
lmo1425|opuCD	glycine/betaine ABC transporter permease, OpuCD protein [Uniprot Acc. Q7AP68];	1.51	1.53
lmo0591|lmo0591	hypothetical protein [Uniprot Acc. Q8Y9D9];	1.36	1.43
lmo2089|lmo2089	lipase [Uniprot Acc. Q8Y5H3];	0.77	0.69
lmo2085|lmo2085	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8Y5H7];	1.36	1.10
lmo2082|lmo2082	Putative fluoride ion transporter CrcB 2 [Uniprot Acc. Q8Y5I0];	0.56	0.71
lmo2817|lmo2817	peptidase [Uniprot Acc. Q8Y3L8];	1.40	1.82
lmo2213|lmo2213	hypothetical protein	1.12	1.23
lmo2067|bsh	bile acid hydrolase	1.38	2.32
lmo2064|mscL	Large-conductance mechanosensitive channel [Uniprot Acc. Q8Y5J6];	0.58	0.70
lmo2057|ctaB	Protoheme IX farnesyltransferase [Uniprot Acc. Q8Y5K3];	0.90	0.68
lmo2199|lmo2199	hypothetical protein [Uniprot Acc. Q8Y576];	0.95	0.82
lmo2570|lmo2570	hypothetical protein [Uniprot Acc. Q8Y485];	1.57	1.46
lmo2198|trpS	Tryptophan--tRNA ligase [Uniprot Acc. Q8Y577];	0.76	0.84
lmo2815|fabG	3-ketoacyl-ACP reductase	1.02	1.21
lmo1978|lmo1978	Glucose-6-phosphate 1-dehydrogenase [Uniprot Acc. Q8Y5S7];	0.45	0.47
lmo0612|lmo0612	MarR family transcriptional evidence [Uniprot Acc. Q8Y9C0];	1.19	1.49
lmo2055|lmo2055	hypothetical protein	0.41	0.69
lmo2692|lmo2692	hypothetical protein	0.66	0.66
lmo2724|lmo2724	hypothetical protein	1.26	1.28
lmo2785|kat	Catalase [Uniprot Acc. Q8Y3P9];	0.59	0.78
lmo0662|thiD	phosphomethylpyrimidine kinase [Uniprot Acc. Q8Y971];	0.42	0.50
lmo0663|lmo0663	hypothetical protein [Uniprot Acc. Q8Y970];	0.44	0.55
lmo1015|gbuB	glycine/betaine ABC transporter permease [Uniprot Acc. Q7AP75];	0.99	0.97
lmo0657|lmo0657	hypothetical protein	0.71	0.77
lmo0051|lmo0051	response regulator [Uniprot Acc. Q8YAR4];	0.63	0.63
lmo0019|lmo0019	hypothetical protein	2.25	2.45
lmo0658|lmo0658	hypothetical protein [Uniprot Acc. Q8Y975];	0.52	0.64
lmo0665|lmo0665	hypothetical protein	0.51	0.83
lmo0670|lmo0670	hypothetical protein	1.51	1.73
lmo0667|lmo0667	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y966];	0.66	0.64
lmo0589|lmo0589	hypothetical protein [Uniprot Acc. Q8Y9E1];	1.36	1.29

lmo0025|lmo0025	phosphoheptose isomerase [Uniprot Acc. Q8YAT8];	1.03	1.15
lmo0656|lmo0656	hypothetical protein [Uniprot Acc. Q8Y977];	0.46	0.54
lmo1269|lmo1269	Signal peptidase I [Uniprot Acc. Q8Y7K8];	0.79	0.63
lmo1282|lmo1282	hypothetical protein	0.54	0.76
lmo1281|lmo1281	hypothetical protein [Uniprot Acc. Q8Y7J6];	0.62	0.75
lmo1283|lmo1283	LacX protein [Uniprot Acc. Q8Y7J4];	0.47	0.67
lmo1270|lmo1270	Signal peptidase I [Uniprot Acc. Q8Y7K7];	0.57	0.54
lmo2363|gadD2	Glutamate decarboxylase beta [Uniprot Acc. Q9EYW9];	4.33	2.94
lmo1298|glnR	glutamine synthetase repressor [Uniprot Acc. Q92C55];	0.37	0.47
lmo2740|lmo2740	hypothetical protein	1.06	0.97
lmo0433|inlA	Internalin A [Uniprot Acc. P0DJM0];	1.84	2.53
lmo0452|lmo0452	hypothetical protein [Uniprot Acc. Q8Y9S1];	0.66	0.65
lmo0453|lmo0453	hypothetical protein [Uniprot Acc. Q8Y9S0];	0.76	0.89
lmo0450|lmo0450	hypothetical protein [Uniprot Acc. Q8Y9S3];	0.42	0.65
lmo0461|lmo0461	hypothetical protein	0.91	1.23
lmo0463|lmo0463	hypothetical protein [Uniprot Acc. Q8Y9R0];	0.63	1.43
lmo0462|lmo0462	hypothetical protein	1.15	1.53
lmo0464|lmo0464	transposase [Uniprot Acc. Q8Y9Q9];	1.18	1.83
lmo0611|acpD	FMN-dependent NADH-azoreductase 1 [Uniprot Acc. Q8Y9C1];	1.45	1.42
lmo0486|rpmF	50S ribosomal protein L32-1 [Uniprot Acc. Q8Y9N9];	0.61	0.49
lmo0518|lmo0518	hypothetical protein [Uniprot Acc. Q8Y9K9];	1.03	1.18
lmo0522|lmo0522	transcriptional regulator [Uniprot Acc. Q8Y9K5];	0.41	0.56
lmo0590|lmo0590	hypothetical protein [Uniprot Acc. Q8Y9E0];	1.49	1.32
lmo0851|lmo0851	hypothetical protein	0.51	0.66
lmo0539|lmo0539	Tagatose 1,6-diphosphate aldolase [Uniprot Acc. Q8Y9I9];	1.19	1.21
lmo2816|lmo2816	MFS transporter [Uniprot Acc. Q8Y3L9];	1.30	1.09
lmo1293|glpD	Glycerol-3-phosphate dehydrogenase [Uniprot Acc. Q8Y7I4];	0.79	0.71
lmo0836|lmo0836	phosphate-starvation-inducible protein PsiE [Uniprot Acc. Q8Y8Q9];	0.45	0.60
lmo0823|lmo0823	oxidoreductase [Uniprot Acc. Q8Y8S1];	0.82	0.81
lmo0822|lmo0822	transcriptional regulator [Uniprot Acc. Q8Y8S2];	0.69	0.82
lmo0815|lmo0815	transcriptional regulator [Uniprot Acc. Q8Y8S9];	0.63	0.58
lmo0800|lmo0800	hypothetical protein	1.35	1.49
lmo0796|lmo0796	hypothetical protein	1.13	1.16
lmo0779|lmo0779	hypothetical protein [Uniprot Acc. Q8Y8W3];	0.50	0.51

lmo0770|lmo0770	LacI family transcriptional regulator [Uniprot Acc. Q8Y8X2];	0.36	0.53
lmo0761|lmo0761	hypothetical protein [Uniprot Acc. Q8Y8Y1];	1.24	1.04
lmo0760|lmo0760	hypothetical protein [Uniprot Acc. Q8Y8Y2];	1.34	1.15
lmo1433|lmo1433	glutathione reductase [Uniprot Acc. Q8Y768];	1.90	1.83
lmo0759|lmo0759	hypothetical protein	1.29	1.15
lmo0758|lmo0758	hypothetical protein	1.36	1.44
lmo0597|lmo0597	Crp/Fnr family transcriptional regulator [Uniprot Acc. Q8Y9D3];	0.51	0.57
lmo1713|lmo1713	rod shape-determining protein MreB [Uniprot Acc. Q8Y6H3];	0.75	0.88
lmo1708|lmo1708	Aminoglycoside N(3)-acetyltransferase [Uniprot Acc. Q8Y6H6];	0.60	0.61
lmo1709|lmo1709	Methionine aminopeptidase [Uniprot Acc. Q8Y6H5];	0.31	0.41
lmo1704|lmo1704	hypothetical protein [Uniprot Acc. Q8Y6I0];	0.61	0.70
lmo1706|lmo1706	transporter [Uniprot Acc. Q8Y6H8];	0.42	0.60
lmo1698|lmo1698	ribosomal-protein-alanine N-acetyltransferase [Uniprot Acc. Q8Y6I6];	0.71	0.97
lmo1694|lmo1694	CDP-abequose synthase [Uniprot Acc. Q8Y6J0];	1.33	1.19
lmo1688|lmo1688	enoyl-ACP reductase	0.76	0.71
lmo1690|lmo1690	hypothetical protein [Uniprot Acc. Q8Y6J4];	0.85	1.05
lmo1689|lmo1689	Adenine DNA glycosylase [Uniprot Acc. Q8Y6J5];	0.93	0.86
lmo1687|lmo1687	hypothetical protein	0.53	0.68
lmo1684|lmo1684	glycerate dehydrogenase [Uniprot Acc. Q8Y6K0];	0.80	0.89
lmo1676|menF	menaquinone-specific isochorismate synthase [Uniprot Acc. Q8Y6K8];	0.85	0.82
lmo1673|menB	1,4-dihydroxy-2-naphthoyl-CoA synthase [Uniprot Acc. Q8Y6L1];	0.80	0.74
lmo1674|lmo1674	Putative 2-succinyl-6-hydroxy-2,4-cyclohexadiene-1-carboxylate synthase [Uniprot Acc. Q8Y6L0];	0.84	0.81
lmo1675|menD	2-succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylate synthase [Uniprot Acc. Q8Y6K9];	0.81	0.73
lmo1672|menE	2-succinylbenzoate--CoA ligase [Uniprot Acc. P58730];	1.01	0.79
lmo1635|lmo1635	hypothetical protein	0.43	0.58
lmo1628|trpB	Tryptophan synthase beta chain [Uniprot Acc. Q8Y6Q6];	0.97	0.82
lmo1627|trpA	Tryptophan synthase alpha chain [Uniprot Acc. Q8Y6Q7];	0.97	0.84
lmo1618|lmo1618	MarR family transcriptional regulator [Uniprot Acc. Q8Y6R5];	1.70	1.51

lmo1617|lmo1617	multidrug transporter [Uniprot Acc. Q8Y6R6];	1.71	1.45
lmo1611|lmo1611	aminopeptidase [Uniprot Acc. Q8Y6S2];	0.66	0.82
lmo1609|lmo1609	thioredoxin [Uniprot Acc. Q8Y6S4];	0.74	0.93
lmo1602|lmo1602	hypothetical protein [Uniprot Acc. Q8Y6T1];	0.80	0.85
lmo1601|lmo1601	general stress protein [Uniprot Acc. Q7AP59];	0.86	1.00
lmo1922|lmo1922	hypothetical protein	0.59	0.57
lmo1919|lmo1919	hypothetical protein [Uniprot Acc. Q8Y5Y4];	0.55	0.75
lmo1902|panB	3-methyl-2-oxobutanoate hydroxymethyltransferase [Uniprot Acc. Q8Y601];	1.00	0.98
lmo1900|panD	Aspartate 1-decarboxylase [Uniprot Acc. Q8Y603];	0.94	1.07
lmo1901|panC	Pantothenate synthetase [Uniprot Acc. Q8Y602];	1.11	1.07
lmo1921|lmo1921	hypothetical protein	0.38	0.48
lmo1889|lmo1889	hypothetical protein	0.82	0.78
lmo1877|lmo1877	Formate--tetrahydrofolate ligase [Uniprot Acc. Q8Y624];	0.41	0.52
lmo1878|lmo1878	HTH-type transcriptional regulator MntR [Uniprot Acc. Q8Y623];	0.60	0.69
lmo1854|lmo1854	hypothetical protein [Uniprot Acc. Q8Y646];	0.67	0.76
lmo1853|lmo1853	heavy metal-transporting ATPase [Uniprot Acc. Q8Y647];	0.45	0.52
lmo1852|lmo1852	mercury-binding protein [Uniprot Acc. Q8Y648];	0.63	0.70
lmo1847|lmo1847	Manganese-binding lipoprotein MntA [Uniprot Acc. Q8Y653];	0.59	0.73
lmo2572|lmo2572	dihydrofolate reductase subunit A [Uniprot Acc. Q8Y483];	1.51	1.32
lmo0604|lmo0604	hypothetical protein [Uniprot Acc. Q8Y9C8];	0.78	1.14
lmo1829|lmo1829	fibronectin-binding proteins [Uniprot Acc. Q8Y670];	0.42	0.62
lmo2169|lmo2169	hypothetical protein [Uniprot Acc. Q8Y5A0];	0.67	0.90
lmo2165|lmo2165	Crp/Fnr family transcriptional regulator	0.55	0.58
lmo1782|lmo1782	3'-exo-deoxyribonuclease [Uniprot Acc. Q8Y6A9];	0.95	1.20
lmo1779|lmo1779	hypothetical protein	0.70	0.90
lmo1776|lmo1776	hypothetical protein [Uniprot Acc. Q8Y6B5];	1.03	1.26
lmo1252|lmo1252	hypothetical protein [Uniprot Acc. Q8Y7M2];	0.84	0.88
lmo1250|lmo1250	antibiotic resistance protein [Uniprot Acc. Q8Y7M4];	1.13	7.15
lmo1608|lmo1608	hypothetical protein	0.86	0.89
lmo1243|lmo1243	hypothetical protein	0.48	0.62
lmo1241|lmo1241	hypothetical protein	2.16	2.25
lmo1233|trxA	Thioredoxin [Uniprot Acc. P0A4L3];	0.83	0.88
lmo1234|uvrC	excinuclease ABC subunit C [Uniprot Acc. Q8Y7P0];	0.45	0.43

lmo1216|lmo1216	N-acetylmuramoyl-L-alanine amidase [Uniprot Acc. Q8Y7Q6];	1.06	1.16
lmo1209|lmo1209	hypothetical protein	0.65	0.77
lmo1208|cbiP	Cobyric acid synthase [Uniprot Acc. Q8Y7R3];	0.79	0.75
lmo1212|lmo1212	hypothetical protein	0.93	1.00
lmo2352|lmo2352	LysR family transcriptional regulator [Uniprot Acc. Q8Y4T0];	1.94	1.42
lmo1140|lmo1140	hypothetical protein	1.24	1.37
lmo0603|lmo0603	hypothetical protein [Uniprot Acc. Q8Y9C9];	0.45	0.63
lmo2230|lmo2230	arsenate reductase	1.26	1.31
lmo0592|lmo0592	hypothetical protein [Uniprot Acc. Q8Y9D8];	0.52	0.63
lmo1095|lmo1095	PTS cellbiose transporter subunit IIB [Uniprot Acc. Q8Y823];	0.90	0.92
lmo1093|nadE	NH(3)-dependent NAD(+) synthetase [Uniprot Acc. Q8Y825];	0.43	0.45
lmo2204|lmo2204	hypothetical protein [Uniprot Acc. Q929G9];	0.56	0.86
lmo1058|lmo1058	hypothetical protein	0.65	0.71
lmo1056|lmo1056	hypothetical protein [Uniprot Acc. Q8Y861];	1.11	1.16
lmo1040|lmo1040	molybdenum ABC transporter permease [Uniprot Acc. Q8Y877];	0.77	0.70
lmo1392|lmo1392	peptidase [Uniprot Acc. Q8Y798];	0.59	0.52
lmo1038|lmo1038	Molybdenum cofactor guanylyltransferase [Uniprot Acc. Q8Y879];	0.61	0.60
lmo1890|lmo1890	hypothetical protein	0.76	0.79
lmo1016|gbuC	glycine/betaine ABC transporter substrate-binding protein [Uniprot Acc. Q8Y898];	1.05	1.12
lmo1014|gbuA	glycine/betaine ABC transporter ATP-binding protein [Uniprot Acc. Q7AP76];	1.02	1.07
lmo2844|lmo2844	hypothetical protein [Uniprot Acc. Q8Y3J1];	0.54	0.79
lmo0953|lmo0953	hypothetical protein [Uniprot Acc. Q8Y8F1];	1.66	1.79
lmo0609|lmo0609	phage shock protein E	0.88	1.00
lmo0995|lmo0995	hypothetical protein [Uniprot Acc. Q8Y8B3];	1.47	1.36
lmo0983|lmo0983	Glutathione peroxidase [Uniprot Acc. Q8Y8C5];	0.87	0.96
lmo0976|lmo0976	hypothetical protein [Uniprot Acc. Q8Y8D2];	0.74	0.52
lmo0975|lmo0975	Ribose-5-phosphate isomerase A [Uniprot Acc. Q8Y8D3];	0.93	0.85
lmo1426|opuCC	glycine/betaine ABC transporter substrate-binding protein [Uniprot Acc. Q7AP67];	1.50	1.39
lmo0964|lmo0964	hypothetical protein	0.45	0.60
lmo0075|lmo0075	carboxyphosphonoenolpyruvate phosphonomutase [Uniprot Acc. Q8YAP2];	0.87	1.32
lmo0958|lmo0958	GntR family transcirptional regulator [Uniprot Acc. Q8Y8E6];	0.61	0.81
lmo0957|lmo0957	Glucosamine-6-phosphate deaminase [Uniprot Acc. Q8Y8E7];	0.81	0.93

lmo1413|lmo1413	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8Y783];	0.73	1.06
lmo1432|lmo1432	hypothetical protein [Uniprot Acc. Q8Y769];	0.88	1.00
lmo0911|lmo0911	hypothetical protein	0.84	0.67
lmo1012|lmo1012	N-acetyldiaminopimelate deacetylase [Uniprot Acc. Q8Y8A0];	0.63	0.69
lmo0076|lmo0076	Lmo0076 protein [Uniprot Acc. Q8YAP1];	0.77	0.86
lmo0895|sigB	RNA polymerase sigma factor [Uniprot Acc. Q7AP79];	0.37	0.26
lmo0935|lmo0935	Putative tRNA (cytidine(34)-2'-O)-methyltransferase [Uniprot Acc. Q8Y8G9];	0.50	0.53
lmo0649|lmo0649	transcriptional regulator [Uniprot Acc. Q8Y984];	0.44	0.57
lmo0515|lmo0515	hypothetical protein	2.03	2.52
lmo0930|lmo0930	hypothetical protein	0.41	0.53
lmo0887|lmo0887	hypothetical protein [Uniprot Acc. Q8Y8L1];	0.34	0.53
lmo0931|lmo0931	Lipoate--protein ligase [Uniprot Acc. Q8Y8H3];	0.37	0.65
lmo2575|lmo2575	cation transporter [Uniprot Acc. Q8Y480];	1.52	1.74
lmo0100|lmo0100	hypothetical protein	0.57	0.92
lmo0101|lmo0101	transcriptional regulator [Uniprot Acc. Q8YAL7];	0.51	0.75
lmo0102|lmo0102	hypothetical protein	0.85	1.18
lmo0103|lmo0103	NADH oxidase [Uniprot Acc. Q8YAL5];	0.43	0.69
lmo0105|lmo0105	chitinase B [Uniprot Acc. Q8YAL3];	2.03	2.27
lmo2819|lmo2819	carboxypeptidase [Uniprot Acc. Q8Y3L6];	1.30	1.40
lmo0722|lmo0722	pyruvate oxidase [Uniprot Acc. Q8Y920];	1.46	1.42
lmo0133|lmo0133	hypothetical protein	2.61	3.25
lmo0134|lmo0134	hypothetical protein [Uniprot Acc. Q8YAJ1];	2.49	3.00
lmo1039|lmo1039	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y878];	0.62	0.85
lmo0135|lmo0135	peptide ABC transporter substrate-binding protein [Uniprot Acc. Q8YAJ0];	1.23	0.82
lmo0136|lmo0136	peptide ABC transporter permease [Uniprot Acc. Q92FC3];	1.29	0.86
lmo0137|lmo0137	peptide ABC transporter permease [Uniprot Acc. Q8YAI9];	1.24	0.82
lmo1423|lmo1423	hypothetical protein	0.54	0.65
lmo0956|lmo0956	N-acetylglucosamine-6P-phosphate deacetylase [Uniprot Acc. Q8Y8E8];	1.16	1.35
lmo1439|sod	Superoxide dismutase (Mn) [Uniprot Acc. P28764];	1.26	1.33
lmo2770|lmo2770	Glutathione biosynthesis bifunctional protein GshAB [Uniprot Acc. Q8Y3R3];	0.81	0.86
lmo0982|lmo0982	peptidase [Uniprot Acc. Q8Y8C6];	0.85	0.88
lmo1414|lmo1414	acetyl-CoA:acetyltransferase [Uniprot Acc. Q8Y782];	0.42	0.49

lmo0152|lmo0152	peptide ABC transporter substrate-binding protein [Uniprot Acc. Q8YAH4];	1.46	1.13
lmo1057|lmo1057	L-lactate dehydrogenase [Uniprot Acc. Q8Y860];	0.66	0.76
lmo0944|lmo0944	hypothetical protein	0.68	0.75
lmo1000|lmo1000	phytoene dehydrogenase [Uniprot Acc. Q8Y8A8];	0.77	0.72
lmo0943|fri	DNA protection during starvation protein [Uniprot Acc. Q8Y8G1];	0.66	1.04
lmo1030|lmo1030	LacI family transcriptional regulator [Uniprot Acc. Q8Y887];	0.34	0.57
lmo0579|lmo0579	hypothetical protein [Uniprot Acc. Q8Y9F0];	0.64	0.65
lmo2256|lmo2256	hypothetical protein	1.03	1.04
lmo0552|lmo0552	hypothetical protein [Uniprot Acc. Q8Y9H6];	1.09	1.19
lmo0169|lmo0169	Putative sugar uptake protein/glucose transporter [Uniprot Acc. Q8YAF7];	1.36	1.23
lmo0170|lmo0170	hypothetical protein	0.87	0.98
lmo0434|inlB	internalin B	1.76	2.50
lmo2829|lmo2829	nitroreductase [Uniprot Acc. Q8Y3K6];	0.70	0.82
lmo0906|lmo0906	glutathione reductase [Uniprot Acc. Q8Y8J5];	0.78	0.77
lmo1569|fxsA	FxsA, F exclusion of bacteriophage T7; overproduction of this protein in Escherichia coli inhibits the F plasmid-mediated exclusion of bacteriophage T7; interacts with the F plasmid-encoded PifA protein; inner membrane protein [Uniprot Acc. Q8Y6W2];	0.73	0.74
lmo0903|lmo0903	hypothetical protein	1.77	1.63
lmo0977|lmo0977	hypothetical protein	0.75	0.52
lmo1570|pykA	Pyruvate kinase [Uniprot Acc. Q8Y6W1];	0.27	0.55
lmo0905|lmo0905	hypothetical protein [Uniprot Acc. Q8Y8J6];	0.91	0.71
lmo0904|lmo0904	hypothetical protein	0.72	0.55
lmo1553|hemL	Glutamate-1-semialdehyde 2,1-aminomutase 1 [Uniprot Acc. Q8Y6X8];	0.58	0.58
lmo1557|hemA	Glutamyl-tRNA reductase [Uniprot Acc. Q8Y6X4];	0.68	0.70
lmo1554|hemB	Delta-aminolevulinic acid dehydratase [Uniprot Acc. Q8Y6X7];	0.60	0.57
lmo1556|hemC	Porphobilinogen deaminase [Uniprot Acc. Q8Y6X5];	0.64	0.68
lmo1555|hemD	uroporphyrinogen-III synthase [Uniprot Acc. Q8Y6X6];	0.66	0.61
lmo0907|lmo0907	phosphoglycerate mutase	0.64	0.76
lmo0913|lmo0913	Aldehyde dehydrogenase [Uniprot Acc. Q8Y8I9];	1.95	1.97
lmo1476|hemN	Oxygen-independent coproporphyrinogen-III oxidase-like protein [Uniprot Acc. Q8Y745];	0.37	0.55

lmo1580|lmo1580	Universal stress protein [Uniprot Acc. Q8Y6V1];	0.77	0.83
lmo1493|lmo1493	oligopeptidase [Uniprot Acc. Q8Y730];	0.49	0.59
lmo1500|lmo1500	hypothetical protein [Uniprot Acc. Q8Y724];	0.44	0.74
lmo0902|lmo0902	GntR family transcriptional regulator [Uniprot Acc. Q8Y8J9];	0.32	0.52
lmo1578|lmo1578	X-Pro dipeptidase [Uniprot Acc. Q8Y6V3];	0.83	0.89
lmo1576|lmo1576	hypothetical protein [Uniprot Acc. Q8Y6V5];	0.31	0.87
lmo2725|lmo2725	hypothetical protein [Uniprot Acc. Q8Y3V6];	0.70	0.75
lmo0185|lmo0185	hypothetical protein [Uniprot Acc. Q8YAE5];	0.47	0.50
lmo0203|mpl	Zinc metalloproteinase [Uniprot Acc. P23224];	0.55	0.73
lmo0209|lmo0209	hypothetical protein	0.64	1.52
lmo0211|ctc	50S ribosomal protein L25 [Uniprot Acc. Q8YAD3];	0.82	0.82
lmo2743|lmo2743	translaldolase [Uniprot Acc. Q8Y3T8];	0.87	0.67
lmo2739|lmo2739	NAD-dependent protein deacetylase [Uniprot Acc. Q8Y3U2];	0.79	0.96
lmo0223|cysK	Cysteine synthase [Uniprot Acc. Q8YAC3];	1.02	1.04
lmo0224|sul	Dihydropteroate synthase [Uniprot Acc. Q8YAC2];	0.81	0.92
lmo0225|folA	7,8-dihydroneopterin aldolase [Uniprot Acc. Q8YAC1];	0.60	0.72
lmo2726|lmo2726	MarR family transcriptional regulator [Uniprot Acc. Q8Y3V5];	0.78	0.88
lmo2720|lmo2720	acetate-CoA ligase [Uniprot Acc. Q8Y3W1];	0.81	0.64
lmo2719|lmo2719	tRNA-specific adenosine deaminase [Uniprot Acc. Q8Y3W2];	0.45	0.91
lmo0226|folK	7,8-dihydro-6-hydroxymethylpterin pyrophosphokinase [Uniprot Acc. Q8YAC0];	0.59	0.64
lmo2712|lmo2712	gluconate kinase [Uniprot Acc. Q8Y3W7];	0.91	0.75
lmo2697|lmo2697	PTS mannose transporter subunit IIA [Uniprot Acc. Q8Y3Y2];	2.15	2.38
lmo2696|lmo2696	dihydroxyacetone kinase [Uniprot Acc. Q8Y3Y3];	2.18	2.42
lmo2695|lmo2695	dihydroxyacetone kinase subunit DhaK [Uniprot Acc. Q8Y3Y4];	2.12	2.29
lmo0668|lmo0668	ABC transporter permease [Uniprot Acc. Q8Y965];	0.69	0.70
lmo0669|lmo0669	oxidoreductase [Uniprot Acc. Q8Y964];	1.74	1.84
lmo2673|lmo2673	hypothetical protein	1.53	1.47
lmo2672|lmo2672	AraC family transcriptional regulator [Uniprot Acc. Q8Y406];	1.06	1.28
lmo2671|lmo2671	hypothetical protein	1.24	1.32
lmo2603|lmo2603	hypothetical protein [Uniprot Acc. Q8Y452];	1.81	1.62
lmo2593|lmo2593	MerR family transcriptional regulator [Uniprot Acc. Q8Y462];	0.56	0.76
lmo2587|lmo2587	hypothetical protein	1.21	1.13

lmo2574|lmo2574	hypothetical protein [Uniprot Acc. Q8Y481];	0.85	0.96
lmo2573|lmo2573	zinc-binding dehydrogenase [Uniprot Acc. Q8Y482];	1.41	1.29
lmo2571|lmo2571	nicotinamidase [Uniprot Acc. Q8Y484];	1.52	1.41
lmo2557|lmo2557	lipid kinase [Uniprot Acc. Q8Y497];	0.66	0.70
lmo2527|lmo2527	hypothetical protein [Uniprot Acc. Q8Y4C3];	0.55	0.70
lmo2515|lmo2515	two-component response regulator DegU [Uniprot Acc. Q927X8];	0.28	0.46
lmo2507|ftsE	Cell division ATP-binding protein FtsE [Uniprot Acc. Q8Y4E0];	0.61	0.63
lmo2495|lmo2495	Phosphate import ATP-binding protein PstB 1 [Uniprot Acc. P63363];	1.23	1.20
lmo2478|trxB	Thioredoxin reductase [Uniprot Acc. O32823];	0.68	0.74
lmo2472|lmo2472	cell division protein WhiA [Uniprot Acc. Q8Y4H0];	0.58	0.57
lmo2471|lmo2471	NADPH dehydrogenase [Uniprot Acc. Q8Y4H1];	0.58	0.52
lmo0265|lmo0265	succinyl-diaminopimelate desuccinylase [Uniprot Acc. Q7AP85];	1.57	1.46
lmo2453|lmo2453	epoxide hydrolase [Uniprot Acc. Q8Y4I6];	0.70	0.68
lmo2439|lmo2439	hypothetical protein	0.67	1.18
lmo0613|lmo0613	oxidoreductase [Uniprot Acc. Q8Y9B9];	1.08	1.20
lmo2434|gadD3	glutamate decarboxylase gamma [Uniprot Acc. Q8Y4K4];	1.38	2.08
lmo2433|lmo2433	acetylesterase [Uniprot Acc. Q8Y4K5];	1.87	1.67
lmo2432|lmo2432	hypothetical protein	1.31	1.65
lmo2426|lmo2426	hypothetical protein	0.36	0.51
lmo0292|htrA	heat-shock protein htrA serine protease [Uniprot Acc. Q8YA67];	0.86	0.92
lmo0296|lmo0296	hypothetical protein [Uniprot Acc. Q8YA63];	0.73	0.82
lmo2406|lmo2406	hypothetical protein	0.54	0.62
lmo2405|lmo2405	hypothetical protein [Uniprot Acc. Q8Y4N1];	0.71	0.70
lmo2404|lmo2404	membrane transporter protein [Uniprot Acc. Q8Y4N2];	0.74	0.55
lmo2403|lmo2403	hypothetical protein [Uniprot Acc. Q8Y4N3];	0.56	0.66
lmo2401|lmo2401	hypothetical protein [Uniprot Acc. Q8Y4N4];	0.43	0.44
lmo2398|ltrC	Low temperature requirement C protein, also similar to B. subtilis YutG protein [Uniprot Acc. Q8Y4N7];	1.42	1.55
lmo2397|lmo2397	NifU protein [Uniprot Acc. Q8Y4N8];	0.62	0.72
lmo0321|lmo0321	hypothetical protein [Uniprot Acc. Q8YA43];	1.56	1.44
lmo2393|lmo2393	hypothetical protein	1.08	1.30
lmo2392|lmo2392	hypothetical protein	1.17	1.25
lmo2391|lmo2391	hypothetical protein	1.51	1.41
lmo2390|lmo2390	Ferredoxin--NADP reductase 2 [Uniprot Acc. Q8Y4P5];	0.79	0.71

lmo2389|lmo2389	NADH dehydrogenase [Uniprot Acc. Q8Y4P6];	1.16	1.02
lmo2387|lmo2387	hypothetical protein [Uniprot Acc. Q8Y4P8];	1.40	1.24
lmo2386|lmo2386	hypothetical protein [Uniprot Acc. Q8Y4P9];	0.63	0.66
lmo0356|lmo0356	oxidoreductase [Uniprot Acc. Q8YA10];	0.44	0.52
lmo0375|lmo0375	hypothetical protein	0.55	0.82
lmo0389|ltrA	Low temperature requirement protein A [Uniprot Acc. Q8Y9X8];	0.87	0.68
lmo0394|lmo0394	Cell wall-associated hydrolase	0.49	1.27
lmo0395|lmo0395	blasticidin S-acetyltransferase [Uniprot Acc. Q8Y9X3];	0.94	1.23
lmo1365|tktB	1-deoxy-D-xylulose-5-phosphate synthase [Uniprot Acc. Q8Y7C1];	0.45	0.53
lmo1304|lmo1304	UPF0291 protein hypothetical protein [Uniprot Acc. Q8Y7H5];	0.55	0.58
lmo1329|ribC	Riboflavin biosynthesis protein [Uniprot Acc. Q8Y7F2];	0.48	0.64
lmo1354|lmo1354	aminopeptidase P [Uniprot Acc. Q8Y7C9];	0.54	0.65
lmo2513|comFA	competence protein comFA [Uniprot Acc. Q8Y4D6];	0.83	0.83
lmo1504|alaS	Alanine--tRNA ligase [Uniprot Acc. Q8Y722];	0.37	0.46
lmo1583|tpx	Thiol peroxidase [Uniprot Acc. Q8Y6U8];	1.05	0.92
lmo1515|lmo1515	hypothetical protein [Uniprot Acc. Q8Y711];	0.45	0.68
lmo1518|lmo1518	hypothetical protein [Uniprot Acc. Q7AP60];	0.44	0.75
lmo1383|lmo1383	Isopentenyl-diphosphate delta-isomerase [Uniprot Acc. Q8Y7A5];	0.67	0.64
lmo1382|lmo1382	hypothetical protein	0.78	0.91
lmo1381|lmo1381	Acylphosphatase [Uniprot Acc. Q8Y7A7];	0.66	0.78
lmo0932|lmo0932	hypothetical protein [Uniprot Acc. Q8Y8H2];	0.72	0.90
lmo1376|lmo1376	6-phosphogluconate dehydrogenase, decarboxylating [Uniprot Acc. Q8Y7B0];	0.38	0.41
lmo0937|lmo0937	hypothetical protein [Uniprot Acc. Q8Y8G7];	1.52	1.70
lmo2114|lmo2114	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y5F0];	0.64	0.84
lmo2494|lmo2494	Phosphate-specific transport system accessory protein PhoU [Uniprot Acc. Q8Y4F0];	1.15	1.05
lmo2522|lmo2522	cell wall-binding protein [Uniprot Acc. Q8Y4C8];	1.43	1.82
lmo2506|ftsX	Cell division protein FtsX [Uniprot Acc. Q8Y4E1];	0.46	0.43
lmo2061|lmo2061	hypothetical protein [Uniprot Acc. Q8Y5J9];	0.46	0.54
lmo2375|lmo2375	hypothetical protein	0.80	0.82
lmo2028|lmo2028	hypothetical protein [Uniprot Acc. Q8Y5M9];	0.49	0.51
lmo2115|lmo2115	ABC transporter permease [Uniprot Acc. Q8Y5E9];	0.55	0.61
lmo2156|lmo2156	hypothetical protein	0.65	1.16
lmo2269|lmo2269	hypothetical protein	1.18	0.97

lmo2536a|lmo2536a	hypothetical protein	0.80	1.55
lmos08|lmos08	miscRNA	2.61	2.90
lmos03|lmos03	miscRNA	1.47	1.26
lmos36|lmos36	miscRNA	0.96	1.54
lmos81|lmos81	miscRNA	1.43	1.37
lmos91|lmos91	miscRNA	0.79	0.86
lmo2784|lmo2784	transcriptional antiterminator [Uniprot Acc. Q8Y3Q0];	0.44	NS[C]
lmo1053|PdhB	pyruvate dehydrogenase subunit E1 beta [Uniprot Acc. Q8Y864];	0.90	NS
lmo2642|lmo2642	hypothetical protein [Uniprot Acc. Q8Y432];	NS	0.73
lmo2372|lmo2372	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y4R2];	0.45	NS
lmo0551|lmo0551	hypothetical protein	0.64	NS
lmo2365|lmo2365	RofA family transcriptional regulator	NS	1.03
lmo2343|lmo2343	nitrilotriacetate monooxygenase [Uniprot Acc. Q8Y4T9];	1.39	NS
lmo2101|lmo2101	Pyridoxal 5'-phosphate synthase subunit PdxS [Uniprot Acc. Q8Y5G2];	0.80	NS
lmo2238|lmo2238	MFS transporter [Uniprot Acc. Q8Y538];	NS	0.78
lmo2231|lmo2231	hypothetical protein [Uniprot Acc. Q8Y545];	1.31	NS
lmo0578|lmo0578	Putative conserved membrane protein [Uniprot Acc. Q8Y9F1];	0.41	NS
lmo2187|lmo2187	hypothetical protein	NS	1.91
lmo2173|lmo2173	sigma-54-dependent transcriptional regulator [Uniprot Acc. Q8Y596];	NS	1.30
lmo2748|lmo2748	hypothetical protein [Uniprot Acc. Q8Y3T3];	1.03	NS
lmo2131|lmo2131	hypothetical protein	1.28	NS
lmo2120|lmo2120	Diadenylate cyclase [Uniprot Acc. Q8Y5E4];	0.39	NS
lmo2102|lmo2102	Pyridoxal 5'-phosphate synthase subunit PdxT [Uniprot Acc. Q8Y5G1];	0.78	NS
lmo2060|lmo2060	hypothetical protein [Uniprot Acc. Q8Y5K0];	0.47	NS
lmo0009|lmo0009	spermidine acetyltransferase [Uniprot Acc. Q8YAV4];	0.36	NS
lmo2658|lmo2658	acyltransferase [Uniprot Acc. Q8Y419];	0.45	NS
lmo0615|lmo0615	hypothetical protein	0.65	NS
lmo0010|lmo0010	mevalonate kinase [Uniprot Acc. Q8YAV3];	0.49	NS
lmo2190|mecA	Adapter protein MecA [Uniprot Acc. Q9RGW9];	0.44	NS
lmo0011|lmo0011	mevalonate diphosphate decarboxylase [Uniprot Acc. Q8YAV2];	0.39	NS
lmo0012|lmo0012	mevalonate kinase [Uniprot Acc. Q8YAV1];	0.30	NS
lmo0013|qoxA	Quinol oxidase subunit 2 [Uniprot Acc. Q8YAV0];	1.04	NS
lmo0897|lmo0897	transporter [Uniprot Acc. Q8Y8K4];	NS	0.75
lmo2721|lmo2721	6-phosphogluconolactonase [Uniprot Acc. Q8Y3W0];	0.78	NS

lmo0014|qoxB	AA3-600 quinol oxidase subunit I [Uniprot Acc. Q8YAU9];	1.10	NS
lmo0628|lmo0628	hypothetical protein	1.67	NS
lmo0015|qoxC	AA3-600 quinol oxidase subunit III [Uniprot Acc. Q8YAU8];	1.17	NS
lmo0646|lmo0646	hypothetical protein [Uniprot Acc. Q8Y987];	NS	0.73
lmo0016|qoxD	quinol oxidase aa3-600 subunit IV [Uniprot Acc. Q8YAU7];	1.22	NS
lmo0651|lmo0651	transcriptional regulator [Uniprot Acc. Q8Y982];	0.60	NS
lmo0650|lmo0650	hypothetical protein [Uniprot Acc. Q8Y983];	0.62	NS
lmo0654|lmo0654	hypothetical protein	1.13	NS
lmo0655|lmo0655	phosphoprotein phosphatase [Uniprot Acc. Q8Y978];	1.11	NS
lmo1268|clpX	ATP-dependent Clp protease ATP-binding subunit ClpX [Uniprot Acc. Q8Y7K9];	0.28	NS
lmo1271|lmo1271	Signal peptidase I [Uniprot Acc. Q8Y7K6];	0.40	NS
lmo0029|lmo0029	hypothetical protein [Uniprot Acc. Q8YAT4];	NS	0.81
lmo1291|lmo1291	acyltransferase [Uniprot Acc. Q8Y7I6];	0.31	NS
lmo1295|lmo1295	RNA-binding protein Hfq [Uniprot Acc. Q92C58];	NS	0.61
lmo0037|lmo0037	amino acid transporter [Uniprot Acc. Q8YAS6];	NS	0.89
lmo0439|lmo0439	hypothetical protein	1.16	NS
lmo0449|lmo0449	hypothetical protein [Uniprot Acc. Q8Y9S4];	NS	0.55
lmo0454|lmo0454	hypothetical protein [Uniprot Acc. Q8Y9R9];	0.48	NS
lmo0451|lmo0451	hypothetical protein	0.40	NS
lmo0460|lmo0460	membrane associated lipoprotein	0.95	NS
lmo0481|lmo0481	hypothetical protein [Uniprot Acc. Q8Y9P3];	NS	0.63
lmo2255|lmo2255	hypothetical protein [Uniprot Acc. Q8Y522];	NS	0.61
lmo0527|lmo0527	Transmembrane protein [Uniprot Acc. Q8Y9K0];	0.47	NS
lmo0537|lmo0537	allantoate amidohydrolase [Uniprot Acc. Q8Y9J1];	0.43	NS
lmo0641|lmo0641	heavy metal-transporting ATPase [Uniprot Acc. Q8Y992];	1.16	NS
lmo0830|fbp	Fructose-1,6-bisphosphatase class 3 [Uniprot Acc. Q8Y8R5];	0.48	NS
lmo0459|lmo0459	transcriptional regulator	0.66	NS
lmo0538|lmo0538	N-acyl-L-amino acid amidohydrolase [Uniprot Acc. Q8Y9J0];	0.45	NS
lmo0811|lmo0811	carbonic anhydrase [Uniprot Acc. Q8Y8T3];	0.96	NS
lmo1471|prmA	Ribosomal protein L11 methyltransferase [Uniprot Acc. P0DJO9];	0.49	NS
lmo0803|lmo0803	Na+/H+ antiporter [Uniprot Acc. Q8Y8U0];	0.45	NS
lmo0043|arcA	Arginine deiminase [Uniprot Acc. Q8YAS0];	1.34	NS
lmo0799|lmo0799	Blue-light photoreceptor [Uniprot Acc. P58724];	0.35	NS
lmo0795|lmo0795	hypothetical protein [Uniprot Acc. Q8Y8U7];	0.49	NS

lmo0794|lmo0794	hypothetical protein	1.09	NS
lmo0790|lmo0790	Cys-tRNA(Pro)/Cys-tRNA(Cys) deacylase, transcriptional regulator [Uniprot Acc. Q8Y8V2];	0.55	NS
lmo0788|lmo0788	hypothetical protein	NS	1.39
lmo0782|lmo0782	PTS mannose transporter subunit IIC [Uniprot Acc. Q8Y8W0];	0.78	NS
lmo0781|lmo0781	PTS mannose transporter subunit IID [Uniprot Acc. Q8Y8W1];	0.99	NS
lmo0775|lmo0775	hypothetical protein	NS	0.65
lmo0626|lmo0626	hypothetical protein [Uniprot Acc. Q8Y9A6];	0.56	NS
lmo0610|lmo0610	internalin [Uniprot Acc. Q8Y9C2];	1.07	NS
lmo0755|lmo0755	hypothetical protein [Uniprot Acc. Q8Y8Y7];	0.60	NS
lmo1731|lmo1731	sugar ABC transporter permease [Uniprot Acc. Q8Y6F6];	NS	1.46
lmo1650|lmo1650	hypothetical protein [Uniprot Acc. Q8Y6N4];	0.55	NS
lmo2112|lmo2112	hypothetical protein [Uniprot Acc. Q8Y5F2];	NS	0.66
lmo1705|lmo1705	deoxyguanosine kinase/deoxyadenosine kinase [Uniprot Acc. Q8Y6H9];	0.41	NS
lmo2657|lmo2657	Deoxyguanosinetriphosphate triphosphohydrolase [Uniprot Acc. Q8Y420];	0.34	NS
lmo1726|lmo1726	hypothetical protein [Uniprot Acc. Q8Y6G1];	0.35	NS
lmo1678|lmo1678	bifunctional homocysteine S-methyltransferase/5,10-methylenetetrahydrofolate reductase [Uniprot Acc. Q8Y6K6];	0.83	NS
lmo1670|lmo1670	Putative membrane protein insertion efficiency factor [Uniprot Acc. Q8Y6L4];	0.58	NS
lmo1644|lmo1644	helicase SNF2 [Uniprot Acc. Q8Y6P0];	0.42	NS
lmo1637|lmo1637	hypothetical protein [Uniprot Acc. Q8Y6P7];	0.62	NS
lmo1634|lmo1634	Aldehyde-alcohol dehydrogenase [Uniprot Acc. Q8Y6Q0];	NS	2.16
lmo1620|lmo1620	dipeptidase PepV [Uniprot Acc. Q8Y6R4];	0.31	NS
lmo1613|lmo1613	hypothetical protein [Uniprot Acc. Q8Y6S0];	NS	0.99
lmo2376|lmo2376	Peptidyl-prolyl cis-trans isomerase [Uniprot Acc. Q8Y4Q8];	NS	0.40
lmo1917|pflA	pyruvate formate-lyase [Uniprot Acc. Q8Y5Y6];	NS	0.46
lmo1910|lmo1910	oxidoreductase [Uniprot Acc. Q8Y5Z3];	0.82	NS
lmo1899|dinG	3'-5' exonuclease DinG [Uniprot Acc. Q8Y604];	0.59	NS
lmo1427|opuCB	glycine/betaine ABC transporter permease [Uniprot Acc. Q7AP66];	1.39	NS
lmo1849|lmo1849	Manganese transport system ATP-binding protein MntB [Uniprot Acc. Q8Y651];	NS	0.62
lmo2514|lmo2514	DegV domain-containing protein lmo2514 [Uniprot Acc. Q8Y4D5];	NS	0.44
lmo1812|lmo1812	L-serine dehydratase [Uniprot Acc. Q8Y685];	0.52	NS

lmo1811|lmo1811	ATP-dependent DNA helicase RecG [Uniprot Acc. Q8Y686];	0.38	NS
lmo1799|lmo1799	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8Y697];	0.70	NS
lmo1257|lmo1257	hypothetical protein	NS	1.45
lmo1251|lmo1251	Fnr/Crp family transcriptional regulator [Uniprot Acc. Q8Y7M3];	NS	3.09
lmo1883|lmo1883	chitinase [Uniprot Acc. Q8Y619];	0.68	NS
lmo1246|lmo1246	ATP-dependent RNA helicase DbpA [Uniprot Acc. Q8Y7M8];	0.32	NS
lmo1249|lmo1249	hypothetical protein	NS	6.80
lmo1225|lmo1225	MarR family transcriptional regulator [Uniprot Acc. Q8Y7P8];	0.42	NS
lmo1595|lmo1595	hypothetical protein [Uniprot Acc. Q8Y6T7];	0.53	NS
lmo1124|lmo1124	hypothetical protein	NS	1.49
lmo1122|lmo1122	hypothetical protein	NS	0.87
lmo1123|lmo1123	hypothetical protein	NS	1.31
lmo1121|lmo1121	hypothetical protein	NS	0.92
lmo1120|lmo1120	hypothetical protein	NS	1.18
lmo1992|lmo1992	Alpha-acetolactate decarboxylase [Uniprot Acc. Q8Y5R4];	1.17	NS
lmo1094|lmo1094	hypothetical protein	0.50	NS
lmo1092|lmo1092	Nicotinate phosphoribosyltransferase [Uniprot Acc. Q8Y826];	0.45	NS
lmo1011|lmo1011	2,3,4,5-tetrahydropyridine-2,6-dicarboxylate N-acetyltransferase [Uniprot Acc. Q8Y8A1];	0.38	NS
lmo0728|lmo0728	riboflavin kinase / FAD synthase [Uniprot Acc. Q8Y914];	0.56	NS
lmo1054|pdhC	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex [Uniprot Acc. Q8Y863];	0.94	NS
lmo1027|lmo1027	Ribonuclease J [Uniprot Acc. Q92CZ5];	0.38	NS
lmo1416|lmo1416	hypothetical protein [Uniprot Acc. Q8Y780];	NS	0.67
lmo0994|lmo0994	hypothetical protein [Uniprot Acc. Q8Y8B4];	1.18	NS
lmo1415|lmo1415	hydroxy-3-methylglutaryl-CoA synthase [Uniprot Acc. Q8Y781];	0.33	NS
lmo0909|lmo0909	GntR family transcriptional regulator [Uniprot Acc. Q8Y8J2];	0.56	NS
lmo1055|PdhD	Dihydrolipoyl dehydrogenase [Uniprot Acc. Q8Y862];	0.98	NS
lmo1028|lmo1028	hypothetical protein	0.39	NS
lmo0880|lmo0880	wall associated protein precursor [Uniprot Acc. Q8Y8L7];	1.17	NS
lmo2825|serC	Phosphoserine aminotransferase [Uniprot Acc. Q8Y3L0];	0.55	NS
lmo0580|lmo0580	hypothetical protein [Uniprot Acc. Q8Y9E9];	0.59	NS

lmo0934|lmo0934	Epoxyqueuosine reductase [Uniprot Acc. Q8Y8H0];	0.43	NS
lmo0112|lmo0112	Fnr/Crp family transcriptional regulator [Uniprot Acc. Q8YAK6];	NS	0.63
lmo2759|lmo2759	hypothetical protein	0.42	NS
lmo1467|lmo1467	phosphate starvation-induced protein PhoH [Uniprot Acc. Q7AP63];	0.36	NS
lmo0131|lmo0131	hypothetical protein	NS	0.76
lmo2536|atpI	ATP synthase subunit I [Uniprot Acc. Q8Y4B5];	NS	0.50
lmo1393|lmo1393	peptidase [Uniprot Acc. Q8Y797];	0.50	NS
lmo1052|pdhA	pyruvate dehydrogenase subunit E1 alpha [Uniprot Acc. Q8Y865];	0.89	NS
lmo1048|lmo1048	Molybdenum cofactor biosynthesis protein B [Uniprot Acc. Q8Y869];	0.51	NS
lmo1424|lmo1424	Divalent metal cation transporter MntH/manganese transporter [Uniprot Acc. Q8Y773];	0.69	NS
lmo2761|lmo2761	beta-glucosidase [Uniprot Acc. Q8Y3S1];	0.69	NS
lmo2755|lmo2755	CoA-transferase [Uniprot Acc. Q8Y3S6];	0.97	NS
lmo1563|coaE	Dephospho-CoA kinase [Uniprot Acc. Q8Y6W8];	0.51	NS
lmo1026|lmo1026	LytR protein [Uniprot Acc. Q8Y889];	0.36	NS
lmo1567|citZ	Citrate synthase [Uniprot Acc. Q8Y6W4];	0.44	NS
lmo1568|lmo1568	UPF0756 membrane protein [Uniprot Acc. Q8Y6W3];	0.52	NS
lmo1565|polA	DNA polymerase I [Uniprot Acc. Q8Y6W6];	0.55	NS
lmo1564|mutM	Formamidopyrimidine-DNA glycosylase [Uniprot Acc. Q8Y6W7];	0.59	NS
lmo1566|citC	Isocitrate dehydrogenase (NADP) [Uniprot Acc. Q8Y6W5];	0.47	NS
lmo1575|lmo1575	hypothetical protein [Uniprot Acc. Q8Y6V6];	NS	0.78
lmo0912|lmo0912	formate transporter [Uniprot Acc. Q92DA4];	NS	0.87
lmo1418|lmo1418	hypothetical protein [Uniprot Acc. Q8Y778];	0.38	NS
lmo1577|lmo1577	UPF0173 metal-dependent hydrolase [Uniprot Acc. Q8Y6V4];	NS	0.95
lmo0186|lmo0186	hypothetical protein [Uniprot Acc. Q8YAE4];	NS	0.70
lmo0189|lmo0189	Veg protein [Uniprot Acc. Q92F78];	0.41	NS
lmo0190|ipk	4-diphosphocytidyl-2-C-methyl-D-erythritol kinase [Uniprot Acc. Q8YAE1];	0.36	NS
lmo0191|lmo0191	Carbohydrate deacetylase [Uniprot Acc. Q8YAE0];	0.30	NS
lmo0200|prfA	Listeriolysin regulatory protein [Uniprot Acc. P22262];	0.31	NS
lmo0208|lmo0208	hypothetical protein	NS	0.72
lmo0210|ldh	L-lactate dehydrogenase 1 [Uniprot Acc. P33380];	NS	1.05

lmo0648|lmo0648	hypothetical protein [Uniprot Acc. Q8Y985];	0.65	NS
lmo2742|lmo2742	hypothetical protein	0.71	NS
lmo0221|lmo0221	Type III pantothenate kinase [Uniprot Acc. Q8YAC5];	0.32	NS
lmo2737|lmo2737	LacI family transcriptional regulator [Uniprot Acc. Q8Y3U4];	0.54	NS
lmo2727|lmo2727	hypothetical protein [Uniprot Acc. Q8Y3V4];	NS	0.55
lmo0664|lmo0664	acetyl transferase [Uniprot Acc. Q8Y969];	0.51	NS
lmo0666|lmo0666	hypothetical protein [Uniprot Acc. Q8Y967];	0.49	NS
lmo2681|kdpB	Potassium-transporting ATPase ATP-binding subunit [Uniprot Acc. Q8Y3Z7];	NS	1.96
lmo2669|lmo2669	hypothetical protein [Uniprot Acc. Q8Y409];	NS	1.06
lmo2602|lmo2602	hypothetical protein [Uniprot Acc. Q8Y453];	1.65	NS
lmo2592|lmo2592	aldo/keto reductase [Uniprot Acc. Q8Y463];	0.45	NS
lmo0238|cysE	Serine acetyltransferase [Uniprot Acc. Q8YAB2];	0.51	NS
lmo2564|lmo2564	4-oxalocrotonate isomerase [Uniprot Acc. Q8Y491];	NS	0.77
lmo2554|lmo2554	galactosyltransferase	0.36	NS
lmo0239|cysS	Cysteine--tRNA ligase [Uniprot Acc. Q8YAB1];	0.49	NS
lmo2553|lmo2553	Phosphatidylglycerol lysyltransferase [Uniprot Acc. Q8Y4A1];	0.33	NS
lmo0240|lmo0240	Mini-ribonuclease 3 [Uniprot Acc. Q8YAB0];	0.55	NS
lmo0241|lmo0241	hypothetical protein [Uniprot Acc. Q92F34];	0.50	NS
lmo0242|lmo0242	hypothetical protein	0.36	NS
lmo2512|comFC	competence protein ComFC [Uniprot Acc. Q8Y4D7];	0.69	NS
lmo2490|lmo2490	CsbA protein [Uniprot Acc. Q8Y4F4];	0.52	NS
lmo2489|uvrB	UvrABC system excinuclease ABC subunit B [Uniprot Acc. Q8Y4F5];	0.45	NS
lmo2488|uvrA	UvrABC system excinuclease ABC subunit A [Uniprot Acc. Q8Y4F6];	0.31	NS
lmo2474|lmo2474	Nucleotide-binding protein [Uniprot Acc. Q8Y4G9];	0.48	NS
lmo2473|lmo2473	Gluconeogenesis factor [Uniprot Acc. P58588];	0.45	NS
lmo0263|inlH	Internalin H [Uniprot Acc. Q7AP87];	1.12	NS
lmo2467|lmo2467	chitin-binding protein [Uniprot Acc. Q8Y4H4];	0.53	NS
lmo2463|lmo2463	multidrug transporter [Uniprot Acc. Q8Y4H8];	0.80	NS
lmo2460|lmo2460	transcriptional regulator [Uniprot Acc. Q8Y4I0];	0.65	NS
lmo2459|gap	Glyceraldehyde-3-phosphate dehydrogenase [Uniprot Acc. Q8Y4I1];	0.54	NS
lmo2458|pgk	Phosphoglycerate kinase [Uniprot Acc. Q8Y4I2];	0.53	NS
lmo2457|tpiA	Triosephosphate isomerase 1 [Uniprot Acc. Q8Y4I3];	0.47	NS

lmo2456|pgm	2,3-bisphosphoglycerate-independent phosphoglycerate mutase [Uniprot Acc. Q8Y4I4];	0.45	NS
lmo2455|eno	Enolase [Uniprot Acc. P64074];	0.40	NS
lmo2454|lmo2454	hypothetical protein	0.85	NS
lmo2444|lmo2444	glycosidase [Uniprot Acc. Q8Y4J4];	0.52	NS
lmo2442|lmo2442	hypothetical protein [Uniprot Acc. Q8Y4J6];	NS	1.22
lmo2441|lmo2441	transcriptional regulator	0.43	NS
lmo0281|lmo0281	hypothetical protein	0.35	NS
lmo0282|lmo0282	hypothetical protein [Uniprot Acc. Q8YA77];	0.48	NS
lmo2425|lmo2425	Glycine cleavage system H protein [Uniprot Acc. Q8Y4L2];	0.31	NS
lmo0291|lmo0291	hypothetical protein	0.47	NS
lmo2424|lmo2424	thioredoxin [Uniprot Acc. Q8Y4L3];	0.67	NS
lmo2420|lmo2420	hypothetical protein [Uniprot Acc. Q8Y4L7];	NS	0.56
lmo2402|lmo2402	hypothetical protein	0.51	NS
lmo2400|lmo2400	acetyltransferase [Uniprot Acc. Q8Y4N5];	0.74	NS
lmo2399|lmo2399	hypothetical protein [Uniprot Acc. Q8Y4N6];	0.66	NS
lmo0307|lmo0307	hypothetical protein	NS	1.03
lmo0355|lmo0355	fumarate reductase subunit A [Uniprot Acc. Q8YA11];	NS	0.82
lmo0377|lmo0377	hypothetical protein	0.44	NS
lmo0918|lmo0918	transcription antiterminator BglG [Uniprot Acc. Q8Y8I4];	0.55	NS
lmo1371|lmo1371	Dihydrolipoyl dehydrogenase [Uniprot Acc. Q8Y7B5];	0.36	NS
lmo1370|lmo1370	butyrate kinase [Uniprot Acc. Q8Y7B6];	0.41	NS
lmo1349|lmo1349	glycine dehydrogenase (decarboxylating) subunit 1 [Uniprot Acc. Q8Y7D4];	0.60	NS
lmo1350|lmo1350	glycine dehydrogenase (decarboxylating) subunit 2 [Uniprot Acc. Q8Y7D3];	0.68	NS
lmo1513|lmo1513	iron-sulfur cofactor synthesis protein [Uniprot Acc. Q8Y713];	0.35	NS
lmo0405|lmo0405	phosphate transporter [Uniprot Acc. Q8Y9W4];	1.10	NS
lmo0406|lmo0406	hypothetical protein	NS	0.62
lmo1520|hisS	Histidine--tRNA ligase [Uniprot Acc. Q8Y708];	0.31	NS
lmo0409|lmo0409	internalin	0.98	NS
lmo1525|lmo1525	recombination protein RecJ [Uniprot Acc. Q8Y705];	0.29	NS
lmo1532|ruvB	Holliday junction ATP-dependent DNA helicase RuvB [Uniprot Acc. Q8Y6Z8];	0.29	NS
lmo1538|glpK	Glycerol kinase [Uniprot Acc. Q8Y6Z2];	0.87	NS
lmo0412|lmo0412	hypothetical protein [Uniprot Acc. Q8Y9V8];	NS	1.25
lmo1539|lmo1539	glycerol transporter [Uniprot Acc. Q8Y6Z1];	1.04	NS
lmo0970|lmo0970	Enoyl-(acyl-carrier-protein) reductase (NADH) [Uniprot Acc. Q8Y8D5];	0.30	NS

lmo1466|lmo1466	glycerol transporter [Uniprot Acc. Q8Y746];	0.30	NS
lmo1387|lmo1387	pyrroline-5-carboxylate reductase [Uniprot Acc. Q8Y7A2];	0.73	NS
lmo1384|lmo1384	hypothetical protein	0.84	NS
lmo0951|lmo0951	hypothetical protein [Uniprot Acc. Q8Y8F3];	0.38	NS
lmo1375|lmo1375	aminotripeptidase [Uniprot Acc. Q8Y7B1];	0.89	NS
lmo1372|lmo1372	2-oxoisovalerate dehydrogenase subunit alpha [Uniprot Acc. Q8Y7B4];	0.38	NS
lmo1374|lmo1374	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex [Uniprot Acc. Q8Y7B2];	0.35	NS
lmo1363|lmo1363	geranyltranstransferase [Uniprot Acc. Q8Y7C2];	0.40	NS
lmo1362|lmo1362	Exodeoxyribonuclease 7 small subunit [Uniprot Acc. Q8Y7C3];	0.53	NS
lmo1428|opuCA	glycine/betaine ABC transporter ATP-binding protein [Uniprot Acc. Q7AP65];	1.26	NS
lmo2492|lmo2492	hypothetical protein [Uniprot Acc. Q8Y4F2];	NS	0.56
lmo2493|lmo2493	ArsR family transcriptional regulator [Uniprot Acc. Q8Y4F1];	NS	0.57
lmo2103|eutD	phosphotransacetylase [Uniprot Acc. Q8Y5G0];	0.33	NS
lmo2100|lmo2100	GntR family transcriptional regulator [Uniprot Acc. Q8Y5G3];	1.04	NS
lmo2062|lmo2062	copper transporter [Uniprot Acc. Q8Y5J8];	0.60	NS
lmo2377|lmo2377	multidrug transporter [Uniprot Acc. Q8Y4Q7];	0.37	NS
lmo2345|lmo2345	hypothetical protein [Uniprot Acc. Q8Y4T7];	0.82	NS
lmo2006|alsS	acetolactate synthase [Uniprot Acc. Q8Y5Q0];	1.36	NS
lmo1964|lmo1964	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y5U1];	NS	0.65
lmo1933|folE	GTP cyclohydrolase 1 [Uniprot Acc. Q8Y5X1];	0.33	NS
lmo1963|lmo1963	hypothetical protein [Uniprot Acc. Q8Y5U2];	0.49	NS
lmo2157|sepA	SepA protein [Uniprot Acc. Q8Y5B0];	1.16	NS
lmo2140|lmo2140	ABC transporter permease [Uniprot Acc. Q8Y5C5];	0.52	NS
lmot16|lmot16	tRNA	0.71	NS
lmo2760a|lmo2760a	hypothetical protein	0.64	NS
lmos50|lmos50	miscRNA	1.31	NS
lmos38|lmos38	miscRNA	0.88	NS

Table A-3 Down-regulated DEGs of *Listeria monocytogenes* N1-227 during organic acid habituation compared to pH control; [a]: Acetic acid habituated; [b]: L-Lactic acid habituated; [c]: non-significant.

Gene name	Gene description	Log_2FC	
		A[a]	L[b]
lmo1993|pdp	pyrimidine-nucleoside phosphorylase [Uniprot Acc. Q8Y5R3];	-1.65	-1.58
lmo2800|lmo2800	dehydrogenase [Uniprot Acc. Q8Y3N5];	-1.19	-0.96
lmo1949|lmo1949	Pseudouridine synthase [Uniprot Acc. Q8Y5V6];	-0.55	-0.44
lmo2354|lmo2354	hypothetical protein [Uniprot Acc. Q8Y4S8];	-0.42	-0.78
lmo2353|lmo2353	Na+/H+ antiporter [Uniprot Acc. Q8Y4S9];	-0.37	-0.37
lmo2752|lmo2752	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y3S9];	-0.55	-0.32
lmo2340|lmo2340	Pseudouridine-5'-phosphate glycosidase [Uniprot Acc. Q8Y4U2];	-0.45	-0.46
lmo2336|fruB	Tagatose-6-phosphate kinase [Uniprot Acc. Q8Y4U5];	-0.58	-1.06
lmo2335|fruA	PTS fructose transporter subunit IIABC [Uniprot Acc. Q8Y4U6];	-0.59	-1.14
lmo2382|lmo2382	monovalent cation/H+ antiporter subunit E [Uniprot Acc. Q8Y4Q2];	-0.45	-0.54
lmo2183|lmo2183	ferrichrome ABC transporter permease [Uniprot Acc. Q8Y586];	-0.82	-0.92
lmo2264|lmo2264	hypothetical protein [Uniprot Acc. Q8Y514];	-0.32	-0.40
lmo2591|lmo2591	Surface protein, N-acetylmuramoyl-L-alanine amidase [Uniprot Acc. Q8Y464];	-0.59	-0.43
lmo0867|lmo0867	hypothetical protein [Uniprot Acc. Q8Y8M9];	-0.85	-0.60
lmo2248|lmo2248	hypothetical protein	-0.83	-0.86
lmo0574|lmo0574	beta-glucosidase [Uniprot Acc. Q8Y9F4];	-0.62	-0.49
lmo2152|lmo2152	thioredoxin [Uniprot Acc. Q929L9];	-0.73	-0.95
lmo2229|lmo2229	penicillin-binding protein [Uniprot Acc. Q8Y547];	-0.47	-0.57
lmo1588|argD	Acetylornithine aminotransferase [Uniprot Acc. Q8Y6U4];	-1.58	-0.86
lmo2208|lmo2208	hypothetical protein [Uniprot Acc. Q8Y568];	-0.49	-0.40
lmo2194|lmo2194	peptide ABC transporter permease [Uniprot Acc. Q8Y580];	-0.43	-0.88
lmo2193|lmo2193	peptide ABC transporter ATP-binding protein [Uniprot Acc. Q7AP53];	-0.41	-0.77
lmo2192|lmo2192	peptide ABC transporter ATP-binding protein [Uniprot Acc. Q8Y581];	-0.37	-0.58
lmo2612|secY	preprotein translocase subunit SecY [Uniprot Acc. Q8Y448];	-0.44	-0.68
lmo0585|lmo0585	secreted protein	-0.82	-0.98

lmo2154|nrdF	Ribonucleoside-diphosphate reductase subunit beta [Uniprot Acc. Q8Y5B3];	-0.82	-0.95
lmo2251|lmo2251	amino acid ABC transporter ATP-binding protein [Uniprot Acc. Q8Y526];	-0.94	-0.65
lmo2606|rpoA	DNA-directed RNA polymerase subunit alpha [Uniprot Acc. P66699];	-0.23	-0.34
lmo2155|lmo2155	Ribonucleoside-diphosphate reductase [Uniprot Acc. Q8Y5B2];	-0.67	-0.88
lmo1943|lmo1943	hypothetical protein	-0.35	-0.40
lmo2186|lmo2186	Hemin/hemoglobin-binding protein 1 [Uniprot Acc. Q8Y585];	-1.22	-1.30
lmo2545|thrB	Homoserine kinase [Uniprot Acc. Q8Y4A6];	-0.74	-0.92
lmo2079|lmo2079	hypothetical protein	-1.22	-6.14
lmo2130|lmo2130	hypothetical protein [Uniprot Acc. Q8Y5D5];	-0.80	-3.13
lmo0007|gyrA	DNA gyrase subunit A [Uniprot Acc. Q8YAV6];	-0.24	-0.79
lmo0593|lmo0593	formate transporter [Uniprot Acc. Q8Y9D7];	-0.91	-0.41
lmo2185|lmo2185	Hemin/hemoglobin-binding protein 2 [Uniprot Acc. Q7AP54];	-1.48	-1.81
lmo1984|ilvB	Acetolactate synthase [Uniprot Acc. Q8Y5S1];	-1.31	-1.39
lmo1388|tcsA	CD4+ T-cell-stimulating antigen [Uniprot Acc. Q48754];	-1.74	-2.05
lmo0711|flgC	Flagellar basal-body rod protein FlgC [Uniprot Acc. Q92DU3];	-1.41	-1.79
lmo1389|lmo1389	sugar ABC transporter ATP-binding protein [Uniprot Acc. Q8Y7A1];	-0.51	-0.65
lmo0601|lmo0601	cell surface protein	-0.55	-0.77
lmo2249|lmo2249	low-affinity inorganic phosphate transporter [Uniprot Acc. Q8Y528];	-1.00	-1.05
lmo2003|lmo2003	GntR family transcriptional regulator [Uniprot Acc. Q8Y5Q3];	-0.93	-1.13
lmo1994|lmo1994	LacI family transcriptional regulator [Uniprot Acc. Q8Y5R2];	-0.48	-0.34
lmo1939|cmk	Cytidylate kinase [Uniprot Acc. Q8Y5W6];	-0.41	-0.37
lmo2341|lmo2341	sugar kinase [Uniprot Acc. Q8Y4U1];	-0.53	-0.50
lmo1390|lmo1390	ABC transporter permease [Uniprot Acc. Q8Y7A0];	-0.69	-0.80
lmo2254|lmo2254	hypothetical protein [Uniprot Acc. Q8Y523];	-1.28	-1.20
lmo2195|lmo2195	peptide ABC transporter permease [Uniprot Acc. Q8Y579];	-0.49	-0.95
lmo2196|lmo2196	peptide ABC transporter substrate-binding protein [Uniprot Acc. Q7AP52];	-1.16	-1.39
lmo2378|lmo2378	monovalent cation/H+ antiporter subunit A [Uniprot Acc. Q8Y4Q6];	-0.47	-0.61
lmo0547|lmo0547	DeoR family transcriptional regulator [Uniprot Acc. Q8Y9I1];	-0.45	-0.50

lmo0681|lmo0681	flagellar biosynthesis regulator FlhF [Uniprot Acc. Q8Y953];	-2.21	-2.70
lmo0676|fliP	flagellar biosynthesis protein FliP [Uniprot Acc. Q8Y958];	-1.52	-1.76
lmo0677|fliQ	flagellar biosynthesis protein FliQ [Uniprot Acc. Q8Y957];	-1.83	-1.87
lmo0678|fliR	flagellar biosynthesis protein FliR [Uniprot Acc. Q8Y956];	-1.33	-2.14
lmo1950|lmo1950	Segregation and condensation protein B [Uniprot Acc. Q8Y5V5];	-0.44	-0.49
lmo0859|lmo0859	sugar ABC transporter substrate-binding protein	-0.78	-0.80
lmo0684|lmo0684	hypothetical protein	-2.31	-2.85
lmo0687|lmo0687	hypothetical protein	-2.40	-3.04
lmo0682|flgG	flagellar basal body rod protein FlgG [Uniprot Acc. Q8Y952];	-1.96	-2.47
lmo0683|lmo0683	Chemotaxis protein methyltransferase [Uniprot Acc. Q9XDE8];	-2.29	-2.91
lmo0692|cheA	Chemotaxis protein CheA [Uniprot Acc. Q48768];	-1.10	-1.54
lmo0694|lmo0694	hypothetical protein	-1.31	-1.88
lmo0702|lmo0702	hypothetical protein [Uniprot Acc. Q8Y939];	-1.43	-1.88
lmo0693|lmo0693	flagellar motor switch protein FliY [Uniprot Acc. Q8Y947];	-1.28	-1.99
lmo0685|lmo0685	flagellar motor protein MotA [Uniprot Acc. Q7AP82];	-2.30	-3.15
lmo0695|lmo0695	hypothetical protein	-1.25	-1.64
lmo0696|flgD	flagellar basal body rod modification protein [Uniprot Acc. Q8Y944];	-1.18	-1.84
lmo0698|lmo0698	flagellar motor switch protein [Uniprot Acc. Q8Y943];	-1.40	-1.79
lmo0707|fliD	Flagellar hook-associated protein 2 [Uniprot Acc. Q8Y934];	-1.38	-2.04
lmo0704|lmo0704	hypothetical protein	-1.24	-1.28
lmo0697|flgE	Flagellar hook protein FlgE [Uniprot Acc. Q92DV7];	-1.23	-2.04
lmo0708|lmo0708	flagellar protein [Uniprot Acc. Q8Y933];	-1.41	-2.03
lmo0700|lmo0700	flagellar motor switch protein FliY [Uniprot Acc. Q8Y941];	-1.33	-2.15
lmo0701|lmo0701	hypothetical protein [Uniprot Acc. Q8Y940];	-1.55	-2.25
lmo0691|cheY	Chemotaxis protein CheY [Uniprot Acc. P0A4H5];	-1.00	-1.57
lmo0703|lmo0703	hypothetical protein	-1.42	-1.73
lmo0706|flgL	flagellar hook-associated protein FlgL [Uniprot Acc. Q8Y935];	-1.40	-1.70
lmo0705|flgK	Flagellar hook-associated protein 1 [Uniprot Acc. Q8Y936];	-1.29	-1.74

lmo0710|flgB	Flagellar basal body rod protein FlgB [Uniprot Acc. Q8Y931];	-1.51	-2.02
lmo0712|fliE	Flagellar hook-basal body complex protein FliE [Uniprot Acc. Q8Y930];	-1.45	-1.68
lmo0713|fliF	flagellar MS-ring protein FliF [Uniprot Acc. Q8Y929];	-1.51	-2.03
lmo0714|fliG	flagellar motor switch protein FliG [Uniprot Acc. Q8Y928];	-1.47	-1.67
lmo0715|fliH	flagellar assembly protein H	-1.40	-1.49
lmo0716|fliI	flagellum-specific ATP synthase [Uniprot Acc. Q8Y926];	-1.54	-1.92
lmo0027|lmo0027	PTS beta-glucoside transporter subunit IIABC [Uniprot Acc. Q8YAT6];	-1.18	-0.99
lmo0718|lmo0718	hypothetical protein	-1.66	-1.85
lmo0709|lmo0709	hypothetical protein	-1.39	-1.63
lmo2652|lmo2652	transcriptional antiterminator [Uniprot Acc. Q8Y423];	-0.38	-0.39
lmo1266|lmo1266	hypothetical protein	-0.48	-0.53
lmo0605|lmo0605	hypothetical protein [Uniprot Acc. Q8Y9C7];	-0.83	-0.86
lmo1267|tig	Trigger factor [Uniprot Acc. Q8Y7L0];	-0.39	-0.31
lmo0031|lmo0031	Transcriptional regulator LacI family [Uniprot Acc. Q8YAT2];	-0.50	-0.39
lmo1294|miaA	tRNA dimethylallyltransferase [Uniprot Acc. Q8Y7I3];	-0.77	-0.57
lmo0429|lmo0429	sugar hydrolase [Uniprot Acc. Q8Y9U1];	-0.60	-0.88
lmo1593|lmo1593	iron-sulfur cofactor synthesis protein NifS [Uniprot Acc. Q8Y6T9];	-0.49	-0.45
lmo0856|murF	UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D-alanine ligase [Uniprot Acc. Q8Y8P0];	-0.33	-0.33
lmo0488|lmo0488	LysR family transcriptional regulator [Uniprot Acc. Q8Y9N7];	-0.86	-0.50
lmo0514|lmo0514	internalin [Uniprot Acc. Q8Y9L3];	-1.12	-1.20
lmo0516|lmo0516	encapsulation protein CapA	-0.71	-0.57
lmo2142|lmo2142	hypothetical protein	-0.61	-0.51
lmo0534|lmo0534	hypothetical protein	-0.38	-0.38
lmo0536|lmo0536	6-phospho-beta-glucosidase [Uniprot Acc. Q92EC0];	-0.59	-0.47
lmo0848|lmo0848	amino acid ABC transporter ATP-binding protein [Uniprot Acc. Q8Y8P8];	-1.70	-1.74
lmo0847|lmo0847	glutamine ABC transporter [Uniprot Acc. Q8Y8P9];	-1.73	-1.74
lmo0837|lmo0837	hypothetical protein	-0.52	-0.75
lmo0826|lmo0826	transporter, Na+/phosphate symporter [Uniprot Acc. Q8Y8R8];	-0.84	-0.74
lmo0825|lmo0825	3-hydroxy-3-methylglutaryl coenzyme A reductase [Uniprot Acc. Q8Y8R9];	-0.51	-0.62

lmo0824|lmo0824	hypothetical protein	-0.39	-0.61
lmo0810|lmo0810	spermidine/putrescine ABC transporter substrate-binding protein [Uniprot Acc. Q8Y8T4];	-1.49	-1.54
lmo0809|lmo0809	spermidine/putrescine ABC transporter permease [Uniprot Acc. Q92DL4];	-1.30	-1.68
lmo0808|lmo0808	spermidine/putrescine ABC transporter permease [Uniprot Acc. Q8Y8T5];	-1.47	-1.70
lmo0807|lmo0807	Spermidine/putrescine import ATP-binding protein PotA [Uniprot Acc. Q8Y8T6];	-1.39	-1.58
lmo0806|lmo0806	transcriptional regulator [Uniprot Acc. Q8Y8T7];	-1.31	-1.51
lmo0798|lmo0798	lysine-specific permease [Uniprot Acc. Q8Y8U4];	-0.84	-1.08
lmo0793|lmo0793	hypothetical protein [Uniprot Acc. Q8Y8U9];	-0.56	-0.54
lmo0791|lmo0791	hypothetical protein	-1.02	-1.01
lmo0785|lmo0785	Sigma54-associated activator ManR [Uniprot Acc. Q7BC73]; Lmo0785 protein [Uniprot Acc. Q8Y8V7];	-1.04	-1.37
lmo0616|lmo0616	C-terminal domain similar to glycerophosphoryl diester phosphodiesterase [Uniprot Acc. Q8Y9B6];	-0.48	-0.47
lmo1936|gpsA	Glycerol-3-phosphate dehydrogenase (NAD(P)+) [Uniprot Acc. Q8Y5W9];	-0.49	-0.44
lmo1755|gatA	Glutamyl-tRNA(Gln) amidotransferase subunit A [Uniprot Acc. Q8Y6D2];	-0.29	-0.29
lmo1754|gatB	Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit B [Uniprot Acc. Q8Y6D3];	-0.30	-0.26
lmo1626|lmo1626	hypothetical protein [Uniprot Acc. Q8Y6Q8];	-0.42	-0.36
lmo2381|lmo2381	monovalent cation/H+ antiporter subunit D [Uniprot Acc. Q8Y4Q3];	-0.43	-0.69
lmo1700|lmo1700	hypothetical protein	-1.30	-0.94
lmo1699|lmo1699	chemotaxis protein [Uniprot Acc. Q8Y6I5];	-1.44	-1.09
lmo2153|lmo2153	flavodoxin [Uniprot Acc. Q8Y5B4];	-0.72	-0.78
lmo1671|lmo1671	ABC transporter [Uniprot Acc. Q8Y6L3];	-2.51	-2.24
lmo1662|lmo1662	hypothetical protein	-0.51	-0.57
lmo1652|lmo1652	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y6N2];	-0.87	-1.02
lmo1651|lmo1651	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y6N3];	-0.70	-0.90
lmo1649|lmo1649	hypothetical protein	-0.26	-0.37
lmo1625|lmo1625	transporter [Uniprot Acc. Q8Y6Q9];	-0.48	-0.37
lmo1603|lmo1603	aminopeptidase [Uniprot Acc. Q8Y6T0];	-0.30	-0.30
lmo1884|lmo1884	xanthine permease [Uniprot Acc. Q8Y618];	-0.43	-0.64
lmo1879|cspD	cold-shock protein [Uniprot Acc. Q92AD0];	-1.23	-1.59
lmo1856|deoD	Purine nucleoside phosphorylase DeoD-type [Uniprot Acc. Q8Y644];	-0.33	-0.38

lmo1851|lmo1851	carboxy-terminal processing proteinase [Uniprot Acc. Q8Y649];	-0.38	-0.50
lmo1850|lmo1850	MarR family transcriptional regulator [Uniprot Acc. Q8Y650];	-0.48	-0.40
lmo0573|lmo0573	hypothetical protein [Uniprot Acc. Q8Y9F5];	-0.59	-0.79
lmo1843|lmo1843	Pseudouridine synthase [Uniprot Acc. Q8Y657];	-0.43	-0.36
lmo1846|lmo1846	multidrug transporter, multidrug efflux protein [Uniprot Acc. Q8Y654];	-0.58	-0.55
lmo1844|lspA	Lipoprotein signal peptidase [Uniprot Acc. Q8Y656];	-0.42	-0.49
lmo2218|lmo2218	uracil permease [Uniprot Acc. Q8Y558];	-0.85	-0.67
lmo1833|pyrD	Dihydroorotate dehydrogenase B (NAD(+)), catalytic subunit [Uniprot Acc. Q8Y667];	-0.76	-1.24
lmo1835|carB	Carbamoyl-phosphate synthase large chain [Uniprot Acc. Q8Y665];	-0.51	-0.97
lmo1834|pyrDII	Dihydroorotate dehydrogenase B (NAD(+)), electron transfer subunit [Uniprot Acc. Q8Y666];	-0.94	-1.26
lmo1832|pyrF	Orotidine 5'-phosphate decarboxylase [Uniprot Acc. P58641];	-1.19	-1.48
lmo1831|pyrE	Orotate phosphoribosyltransferase [Uniprot Acc. Q8Y668];	-1.22	-1.28
lmo1871|lmo1871	phosphoglucomutase [Uniprot Acc. Q8Y629];	-0.57	-0.42
lmo1797|rpsP	30S ribosomal protein S16 [Uniprot Acc. Q8Y699];	-0.77	-0.60
lmo1796|lmo1796	hypothetical protein [Uniprot Acc. P67234];	-0.86	-0.64
lmo1775|purE	N5-carboxyaminoimidazole ribonucleotide mutase [Uniprot Acc. Q8Y6B6];	-0.43	-0.42
lmo1765|purH	Bifunctional purine biosynthesis protein PurH [Uniprot Acc. Q8Y6C5];	-0.40	-0.64
lmo1761|lmo1761	sodium-dependent transporter [Uniprot Acc. Q8Y6C7];	-0.72	-0.75
lmo1255|lmo1255	PTS trehalose transporter subunit IIBC [Uniprot Acc. Q8Y7L9];	-1.14	-1.48
lmo1254|lmo1254	alpha,alpha-phosphotrehalase [Uniprot Acc. Q8Y7M0];	-1.01	-1.25
lmo1239|lmo1239	dITP/XTP pyrophosphatase [Uniprot Acc. Q8Y7N5];	-0.44	-0.41
lmo1238|rph	Ribonuclease PH [Uniprot Acc. Q8Y7N6];	-0.36	-0.39
lmo1224|lmo1224	hypothetical protein [Uniprot Acc. Q8Y7P9];	-0.57	-0.51
lmo0055|purA	Adenylosuccinate synthetase [Uniprot Acc. Q8YAR1];	-0.67	-0.48
lmo1173|lmo1173	two-component sensor histidine kinase	-0.69	-0.50
lmo1172|lmo1172	two-component response regulator [Uniprot Acc. Q92CN5];	-0.46	-0.67
lmo1445|zurR	Transcriptional regulator ZurR [Uniprot Acc. P0A3E6];	-0.60	-0.56

lmo0731|lmo0731	hypothetical protein [Uniprot Acc. Q8Y911];	-0.62	-0.56
lmo0482|lmo0482	ribosomal RNA large subunit methyltransferase N [Uniprot Acc. Q8Y9P2];	-0.66	-0.36
lmo1096|guaA	GMP synthase (glutamine-hydrolyzing) [Uniprot Acc. Q8Y822];	-0.55	-0.69
lmo2760|lmo2760	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y3S2];	-0.75	-0.69
lmo0541|lmo0541	ABC transporter substrate-binding protein [Uniprot Acc. Q8Y9I7];	-1.13	-0.89
lmo0688|lmo0688	hypothetical protein	-2.41	-2.98
lmo2638|lmo2638	NADH dehydrogenase [Uniprot Acc. Q8Y435];	-0.48	-0.37
lmo0679|flhB	flagellar biosynthesis protein FlhB [Uniprot Acc. Q8Y955];	-1.63	-2.14
lmo0680|flhA	flagellar biosynthesis protein FlhA [Uniprot Acc. Q8Y954];	-1.76	-2.21
lmo2270|comK'	competence protein ComK [Uniprot Acc. Q8Y508];	-1.11	-1.45
lmo0727|lmo0727	Glutamine--fructose-6-phosphate aminotransferase (isomerizing) [Uniprot Acc. Q8Y915];	-0.25	-0.44
lmo1479|lepA	Elongation factor 4 [Uniprot Acc. Q8Y742];	-0.61	-0.56
lmo1019|lmo1019	hypothetical protein [Uniprot Acc. Q8Y895];	-0.45	-0.44
lmo2854|lmo2854	Membrane protein insertase YidC 2 [Uniprot Acc. Q8Y3I2];	-0.33	-0.38
lmo2853|lmo2853	hypothetical protein [Uniprot Acc. Q8Y3I3];	-0.30	-0.41
lmo1592|lmo1592	thiamine biosynthesis protein ThiI [Uniprot Acc. Q8Y6U0];	-0.52	-0.47
lmo0971|dltD	DltD protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid [Uniprot Acc. Q7AP78];	-0.70	-0.89
lmo0973|dltB	DltB protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid [Uniprot Acc. Q7AP77];	-0.76	-0.95
lmo0040|lmo0040	Agmatine deiminase [Uniprot Acc. Q8YAS3];	-0.56	-0.43
lmo0974|dltA	D-alanine--D-alanyl carrier protein ligase [Uniprot Acc. Q8Y8D4];	-0.71	-0.81
lmo0972|dltC	D-alanyl carrier protein [Uniprot Acc. Q9S389];	-0.79	-0.89
lmo0961|lmo0961	protease [Uniprot Acc. Q8Y8E3];	-1.39	-0.66
lmo0960|lmo0960	protease [Uniprot Acc. Q8Y8E4];	-1.19	-0.58
lmo0963|lmo0963	heat shock protein HtpX homolog [Uniprot Acc. Q8Y8E1];	-0.40	-0.26
lmo1391|lmo1391	sugar ABC transporter permease [Uniprot Acc. Q8Y799];	-0.65	-0.89
lmo2538|upp	Uracil phosphoribosyltransferase [Uniprot Acc. Q8Y4B3];	-0.46	-0.32
lmo2546|thrC	Threonine synthase [Uniprot Acc. Q8Y4A5];	-0.75	-0.88

lmo1073|lmo1073	metal ABC transporter substrate-binding protein	-0.31	-0.68
lmo2832|lmo2832	hypothetical protein [Uniprot Acc. Q8Y3K3];	-0.53	-0.68
lmo1937|engA	GTP-binding protein EngA, GTPase Der [Uniprot Acc. Q8Y5W8];	-0.46	-0.39
lmo0883|lmo0883	hypothetical protein [Uniprot Acc. Q8Y8L4];	-0.91	-0.93
lmo0882|lmo0882	hypothetical protein [Uniprot Acc. Q8Y8L5];	-0.92	-0.93
lmo1736|lmo1736	hypothetical protein [Uniprot Acc. Q8Y6F1];	-0.49	-0.42
lmo2544|lmo2544	Thymidine kinase [Uniprot Acc. Q8Y4A7];	-0.54	-0.40
lmo0096|lmo0096	EIIMant PTS permease IIAB subunit [Uniprot Acc. Q7BC72]; Lmo0096 protein [Uniprot Acc. Q8YAM2];	-1.49	-3.61
lmo0097|lmo0097	EIIMant PTS permease IIC subunit [Uniprot Acc. Q7BC71]; Lmo0097 protein [Uniprot Acc. Q8YAM1];	-1.63	-3.54
lmo2831|lmo2831	phosphoglucomutase [Uniprot Acc. Q8Y3K4];	-0.74	-0.89
lmo2233|lmo2233	LysR family transcriptional regulator [Uniprot Acc. Q8Y543];	-0.72	-0.63
lmo0098|lmo0098	EIIMant PTS permease IID subunit [Uniprot Acc. Q7BC70]; Lmo0098 protein [Uniprot Acc. Q8YAM0];	-1.53	-3.29
lmo0099|lmo0099	hypothetical protein	-0.83	-1.38
lmo2542|lmo2542	Release factor glutamine methyltransferase [Uniprot Acc. Q8Y4A9];	-0.58	-0.46
lmo2337|lmo2337	DeoR family transcriptional regulator [Uniprot Acc. Q8Y4U4];	-0.44	-0.84
lmo1447|zurA	Zinc uptake system ATP-binding protein ZurA [Uniprot Acc. Q9XDA6];	-0.46	-0.48
lmo2801|lmo2801	Putative N-acetylmannosamine-6-phosphate 2-epimerase [Uniprot Acc. Q8Y3N4];	-1.75	-1.45
lmo0130|lmo0130	Cell wall protein Lmo0130 [Uniprot Acc. Q8YAJ5];	-1.34	-1.83
lmo2799|lmo2799	PTS mannitol transporter subunit IIBC [Uniprot Acc. Q8Y3N6];	-1.31	-0.87
lmo2543|prfA	Peptide chain release factor 1 [Uniprot Acc. Q8Y4A8];	-0.43	-0.46
lmo0981|lmo0981	transporter [Uniprot Acc. Q8Y8C7];	-0.60	-0.73
lmo2779|ychF	Ribosome-binding ATPase YchF [Uniprot Acc. Q926X1];	-0.55	-0.39
lmo2773|lmo2773	transcriptional antiterminator [Uniprot Acc. Q8Y3R0];	-1.07	-0.99
lmo0997|clpE	ATP-dependent protease [Uniprot Acc. Q8Y8B1];	-1.10	-0.95
lmo2767|lmo2767	hypothetical protein [Uniprot Acc. Q8Y3R6];	-0.73	-0.67
lmo0560|lmo0560	Glutamate dehydrogenase [Uniprot Acc. Q8Y9G8];	-0.46	-0.67

lmo0153|lmo0153	zinc ABC transporter substrate-binding protein [Uniprot Acc. Q8YAH3];	-2.20	-1.71
lmo2525|mbl	rod shape-determining protein MreB [Uniprot Acc. Q8Y4C5];	-0.76	-0.55
lmo0160|lmo0160	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8YAG6];	-0.93	-1.24
lmo1594|lmo1594	Septation ring formation regulator EzrA [Uniprot Acc. Q8Y6T8];	-0.27	-0.36
lmo0162|lmo0162	DNA polymerase III subunit delta' [Uniprot Acc. Q8YAG4];	-0.44	-0.44
lmo0686|motB	flagellar motor rotation MotB [Uniprot Acc. Q7AP81];	-2.26	-2.90
lmo0163|lmo0163	hypothetical protein [Uniprot Acc. Q8YAG3];	-0.46	-0.48
lmo2676|lmo2676	DNA polymerase IV [Uniprot Acc. Q8Y402];	-0.39	-0.60
lmo0164|lmo0164	Initiation-control protein YabA [Uniprot Acc. Q8YAG2];	-0.48	-0.39
lmo0167|lmo0167	Ribosomal RNA small subunit methyltransferase I [Uniprot Acc. Q8YAF9];	-0.44	-0.38
lmo0177|metS	Methionine--tRNA ligase [Uniprot Acc. Q8YAF2];	-0.50	-0.47
lmo1584|lmo1584	hypothetical protein [Uniprot Acc. Q8Y6U7];	-0.73	-0.76
lmo0178|lmo0178	xylose repressor [Uniprot Acc. Q8YAF1];	-0.44	-0.40
lmo0180|lmo0180	sugar ABC transporter permease [Uniprot Acc. Q8YAF0];	-1.12	-1.06
lmo0181|lmo0181	sugar ABC transporter substrate-binding protein	-1.10	-1.03
lmo0182|lmo0182	alpha-glucosidase [Uniprot Acc. Q8YAE8];	-0.84	-1.27
lmo1446|zurM	Metal (Zinc) transport protein (ABC transporter,permease protein) [Uniprot Acc. Q8Y758];	-0.54	-0.52
lmo1572|accA	Acetyl-coenzyme A carboxylase carboxyl transferase subunit alpha [Uniprot Acc. Q8Y6V9];	-0.43	-0.31
lmo0183|lmo0183	alpha-glucosidase [Uniprot Acc. Q8YAE7];	-0.61	-0.79
lmo2747|serS	Serine--tRNA ligase [Uniprot Acc. Q8Y3T4];	-0.33	-0.27
lmo0192|lmo0192	PurR family transcriptional regulator [Uniprot Acc. Q8YAD9];	-0.29	-0.33
lmo0198|glmU	bifunctional N-acetylglucosamine-1-phosphate uridyltransferase/glucosamine-1-phosphate acetyltransferase GlmU [Uniprot Acc. Q8YAD4];	-0.46	-0.26
lmo0199|prs	Ribose-phosphate pyrophosphokinase 1 [Uniprot Acc. Q48793];	-0.70	-0.55
lmo2714|lmo2714	Cell wall protein/pepdidoglycan bound protein [Uniprot Acc. Q8Y3W5];	-0.83	-0.90
lmo2713|lmo2713	internalin	-0.27	-0.41
lmo2708|lmo2708	Permease IIC component [Uniprot Acc. Q8Y3X1];	-1.04	-1.50

lmo2690|lmo2690	TetR family transcriptional regulator [Uniprot Acc. Q8Y3Y9];	-1.04	-0.75
lmo2689|lmo2689	magnesium-translocating P-type ATPase [Uniprot Acc. Q8Y3Z0];	-1.68	-0.90
lmo2685|lmo2685	PTS cellbiose transporter subunit IIA [Uniprot Acc. Q927F6];	-0.90	-1.33
lmo0675|lmo0675	hypothetical protein [Uniprot Acc. Q8Y959];	-1.29	-1.71
lmo2683|lmo2683	PTS cellbiose transporter subunit IIB [Uniprot Acc. Q8Y3Z5];	-1.93	-2.56
lmo2665|lmo2665	PTS galacticol transporter subunit IIC [Uniprot Acc. Q8Y412];	-0.58	-0.70
lmo0689|lmo0689	chemotaxis protein CheV [Uniprot Acc. Q8Y948];	-2.61	-3.23
lmo2653|tuf	Elongation factor Tu [Uniprot Acc. Q8Y422];	-0.27	-0.29
lmo0690|flaA	Flagellin [Uniprot Acc. Q02551];	-0.51	-0.53
lmo0699|fliM	flagellar motor switch protein FliM [Uniprot Acc. Q8Y942];	-1.24	-1.78
lmo2616|rplR	50S ribosomal protein L18 [Uniprot Acc. Q8Y445];	-0.32	-0.65
lmo2615|rpsE	30S ribosomal protein S5 [Uniprot Acc. Q8Y446];	-0.43	-0.74
lmo2614|rpmD	50S ribosomal protein L30 [Uniprot Acc. Q927M5];	-0.30	-0.60
lmo2613|rplO	50S ribosomal protein L15 [Uniprot Acc. Q8Y447];	-0.32	-0.66
lmo0717|lmo0717	transglycosylase	-1.71	-2.06
lmo2569|lmo2569	peptide ABC transporter substrate-binding protein [Uniprot Acc. Q8Y486];	-0.74	-1.77
lmo2558|ami	Autolysin, amidase [Uniprot Acc. Q8Y496];	-0.44	-0.46
lmo2547|hom	Homoserine dehydrogenase [Uniprot Acc. Q8Y4A4];	-0.63	-0.71
lmo2524|fabZ	3-hydroxyacyl-(acyl-carrier-protein) dehydratase FabZ [Uniprot Acc. Q8Y4C6];	-0.70	-0.66
lmo2517|lmo2517	hypothetical protein [Uniprot Acc. Q8Y4D3];	-0.59	-0.59
lmo0248|rplK	50S ribosomal protein L11 [Uniprot Acc. P66054];	-0.35	-0.29
lmo0249|rplA	50S ribosomal protein L1 [Uniprot Acc. Q8YAA4];	-0.42	-0.42
lmo0250|rplJ	50S ribosomal protein L10 [Uniprot Acc. P66042];	-0.54	-0.35
lmo0251|rplL	50S ribosomal protein L7/L12 [Uniprot Acc. Q8YAA3];	-0.46	-0.35
lmo2479|lmo2479	hypothetical protein	-0.45	-0.37
lmo2469|lmo2469	amino acid transporter [Uniprot Acc. Q8Y4H3];	-0.95	-0.63
lmo2466|lmo2466	hypothetical protein [Uniprot Acc. Q8Y4H5];	-0.75	-0.72
lmo0275|lmo0275	hypothetical protein	-0.50	-0.46

lmo0278|lmo0278	sugar ABC transporter ATP-binding protein [Uniprot Acc. Q8YA81];	-2.59	-3.28
lmo0279|lmo0279	Class III anaerobic ribonucleoside-triphosphate reductase catalytic subunit [Uniprot Acc. F0V6T8]; Lmo0279 protein [Uniprot Acc. Q8YA80];	-1.46	-0.36
lmo0280|lmo0280	Anaerobic ribonucleoside-triphosphate reductase-activating protein [Uniprot Acc. F0V6T9];	-1.75	-0.59
lmo0289|lmo0289	Two-component signal transduction system YycFG, regulatory protein YycH [Uniprot Acc. Q8YA70];	-0.41	-0.53
lmo0290|lmo0290	Two-component signal transduction system YycFG, regulatory protein YycI [Uniprot Acc. Q8YA69];	-0.44	-0.46
lmo2416|lmo2416	hypothetical protein	-1.21	-1.18
lmo0297|lmo0297	transcriptional antiterminator BglG [Uniprot Acc. Q8YA62];	-0.55	-0.68
lmo2384|lmo2384	monovalent cation/H+ antiporter subunit G [Uniprot Acc. Q8Y4Q1];	-0.53	-0.47
lmo0369|lmo0369	Probable transcriptional regulatory protein lmo0369 [Uniprot Acc. Q8Y9Z8];	-0.48	-0.34
lmo0370|lmo0370	hypothetical protein [Uniprot Acc. Q8Y9Z7];	-0.49	-0.42
lmo0372|lmo0372	beta-glucosidase [Uniprot Acc. Q8Y9Z5];	-1.39	-1.30
lmo0373|lmo0373	Permease IIC component [Uniprot Acc. Q8Y9Z4];	-1.80	-1.57
lmo0391|lmo0391	hypothetical protein	-0.49	-0.57
lmo0392|lmo0392	hypothetical protein [Uniprot Acc. Q92EP8];	-0.65	-0.79
lmo0393|lmo0393	hypothetical protein [Uniprot Acc. Q8Y9X5];	-0.71	-0.59
lmo1585|lmo1585	peptidase [Uniprot Acc. Q8Y6U6];	-0.70	-0.57
lmo1529|lmo1529	hypothetical protein [Uniprot Acc. Q8Y701];	-0.31	-0.26
lmo0418|lmo0418	hypothetical protein	-0.64	-0.45
lmo2502|lmo2502	hypothetical protein [Uniprot Acc. Q8Y4E4];	-0.35	-0.40
lmo2004|lmo2004	GntR family transcriptional regulator [Uniprot Acc. Q8Y5Q2];	-1.00	-1.07
lmo1998|lmo1998	Fructosamine deglycase [Uniprot Acc. Q8Y5Q8];	-1.13	-0.83
lmo1955|lmo1955	Tyrosine recombinase XerD [Uniprot Acc. Q8Y5V0];	-0.64	-0.65
lmo1953|pnp	Purine nucleoside phosphorylase [Uniprot Acc. Q8Y5V2];	-0.78	-0.88
lmo1954|drm	Phosphopentomutase [Uniprot Acc. Q8Y5V1];	-0.72	-0.78
lmo1942|recS	ATP-dependent DNA helicase/RecS protein [Uniprot Acc. Q8Y5W3];	-0.47	-0.53
lmo1940|lmo1940	asparaginase [Uniprot Acc. Q8Y5W5];	-0.30	-0.32
lmo1952|lysA	Diaminopimelate decarboxylase [Uniprot Acc. Q8Y5V3];	-0.52	-0.44

lmo1956|fur	Fur family transcriptional regulator [Uniprot Acc. Q8Y5U9];	-1.09	-0.70
lmo0428|lmo0428	PTS fructose transporter subunit IIC [Uniprot Acc. Q8Y9U2];	NS[C]	-0.87
lmo2379|lmo2379	monovalent cation/H+ antiporter subunit B [Uniprot Acc. Q8Y4Q5];	-0.40	-0.61
lmo2642|lmo2642	hypothetical protein [Uniprot Acc. Q8Y432];	-0.29	NS
lmo2374|lmo2374	Aspartokinase [Uniprot Acc. Q8Y4R0];	NS	-0.42
lmo2677|lmo2677	esterase	-0.42	NS
lmo2104|lmo2104	hypothetical protein [Uniprot Acc. Q929R6];	-0.57	NS
lmo2361|lmo2361	hypothetical protein [Uniprot Acc. Q928S1];	NS	-0.78
lmo2360|lmo2360	Transmembrane protein [Uniprot Acc. Q8Y4S2];	NS	-0.57
lmo0496|lmo0496	UPF0291 hypothetical protein [Uniprot Acc. P60073];	-0.85	NS
lmo2611|adk	Adenylate kinase [Uniprot Acc. Q8Y449];	NS	-0.65
lmo2608|rpsM	30S ribosomal protein S13 [Uniprot Acc. P66383];	NS	-0.34
lmo2252|lmo2252	Aminotransferase [Uniprot Acc. Q8Y525];	-0.72	NS
lmo2250|arpJ	amino acid ABC transporter permease [Uniprot Acc. Q8Y527];	-0.86	NS
lmo2238|lmo2238	MFS transporter [Uniprot Acc. Q8Y538];	-0.68	NS
lmo2209|lmo2209	hypothetical protein [Uniprot Acc. Q8Y567];	-0.34	NS
lmo2197|lmo2197	hypothetical protein [Uniprot Acc. Q8Y578];	-0.59	NS
lmo2184|lmo2184	ferrichrome ABC transporter substrate-binding protein [Uniprot Acc. Q7AP55];	NS	-1.15
lmo2182|lmo2182	ferrichrome ABC transporter ATP-binding protein [Uniprot Acc. Q8Y587];	-0.62	NS
lmo2181|lmo2181	Sortase B [Uniprot Acc. Q8Y588];	-0.59	NS
lmo2751|lmo2751	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y3T0];	-0.50	NS
lmo2151|lmo2151	hypothetical protein [Uniprot Acc. Q8Y5B5];	-0.74	NS
lmo1591|argC	N-acetyl-gamma-glutamyl-phosphate reductase [Uniprot Acc. Q8Y6U1];	-0.96	NS
lmo2150|lmo2150	hypothetical protein [Uniprot Acc. Q929M1];	-0.57	NS
lmo2149|lmo2149	hypothetical protein	-0.99	NS
lmo2063|lmo2063	hypothetical protein [Uniprot Acc. Q8Y5J7];	-0.89	NS
lmo2039|pbpB	penicillin-binding protein 2B [Uniprot Acc. Q8Y5L8];	-0.25	NS
lmo1959|lmo1959	ferrichrome-binding protein [Uniprot Acc. Q8Y5U6];	-0.96	NS
lmo1958|fhuB	ferrichrome ABC transporter permease [Uniprot Acc. Q8Y5U7];	-0.42	NS
lmo2253|lmo2253	phosphoglucomutase [Uniprot Acc. Q8Y524];	-0.37	NS
lmo0013|qoxA	Quinol oxidase subunit 2 [Uniprot Acc. Q8YAV0];	NS	-0.61
lmo0619|lmo0619	hypothetical protein	NS	-0.64

lmo0627|lmo0627	Peptidoglycan bound protein (LPXTG motif) similar to adhesin [Uniprot Acc. Q8Y9A5];	NS	-0.75
lmo2041|mraW	Ribosomal RNA small subunit methyltransferase H [Uniprot Acc. Q8Y5L7];	-0.27	NS
lmo0645|lmo0645	amino acid transporter [Uniprot Acc. Q8Y988];	-0.57	NS
lmo0018|lmo0018	Beta-glucosidase [Uniprot Acc. Q8YAU5];	-0.50	NS
lmo0030|lmo0030	hypothetical protein [Uniprot Acc. Q8YAT3];	-0.48	NS
lmo1280|codY	GTP-sensing transcriptional pleiotropic repressor CodY [Uniprot Acc. Q8Y7J7];	-0.26	NS
lmo2629|rplB	50S ribosomal protein L2 [Uniprot Acc. P60426];	NS	-0.34
lmo0440|lmo0440	hypothetical protein	-0.64	NS
lmo0857|lmo0857	carboxylesterase [Uniprot Acc. Q8Y8N9];	NS	-0.34
lmo0455|lmo0455	hypothetical protein	-0.46	NS
lmo0457|lmo0457	hypothetical protein	NS	-0.76
lmo0855|ddl	D-alanine--D-alanine ligase [Uniprot Acc. Q8Y8P1];	-0.28	NS
lmo0509|prs	Putative ribose-phosphate pyrophosphokinase 2 [Uniprot Acc. Q8Y9L8];	-0.28	NS
lmo0510|lmo0510	hypothetical protein	-0.40	NS
lmo1658|rpsB	30S ribosomal protein S2 [Uniprot Acc. Q8Y6M6];	-0.36	NS
lmo0042|lmo0042	DedA protein [Uniprot Acc. Q8YAS1];	-0.34	NS
lmo0600|lmo0600	hypothetical protein [Uniprot Acc. Q8Y9D2];	NS	-0.85
lmo0835|lmo0835	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8Y8R0];	-0.88	NS
lmo0832|lmo0832	transposase [Uniprot Acc. Q8Y8R3];	-0.68	NS
lmo2688|lmo2688	cell division protein FtsW [Uniprot Acc. Q8Y3Z1];	-0.88	NS
lmo0829|nifJ	Pyruvate-flavodoxin oxidoreductase [Uniprot Acc. Q8Y8R6];	-0.38	NS
lmo0814|lmo0814	oxidoreductase [Uniprot Acc. Q8Y8T0];	-0.93	NS
lmo0813|lmo0813	fructokinase [Uniprot Acc. Q8Y8T1];	-0.50	NS
lmo2206|clpB	Clp protease subunit B, Chaperone protein ClpB [Uniprot Acc. Q8Y570];	-0.46	NS
lmo0797|lmo0797	hypothetical protein [Uniprot Acc. Q8Y8U5];	-0.61	NS
lmo0788|lmo0788	hypothetical protein	-0.49	NS
lmo0786|lmo0786	FMN-dependent NADH-azoreductase 2 [Uniprot Acc. Q8Y8V6];	-0.54	NS
lmo0778|lmo0778	hypothetical protein [Uniprot Acc. Q8Y8W4];	-0.67	NS
lmo2826|lmo2826	MFS transporter [Uniprot Acc. Q8Y3K9];	-0.41	NS
lmo0765|lmo0765	hypothetical protein [Uniprot Acc. Q8Y8X7];	-0.74	NS
lmo0614|lmo0614	hypothetical protein	-0.38	NS
lmo0046|rpsR	30S ribosomal protein S18 [Uniprot Acc. P66461];	-0.31	NS

lmo1756|gatC	Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit C [Uniprot Acc. P58817];	NS	-0.32
lmo1750|lmo1750	hypothetical protein	-0.34	NS
lmo1742|adeC	Adenine deaminase [Uniprot Acc. Q8Y6E5];	NS	-0.30
lmo1737|lmo1737	glycerol dehydrogenase [Uniprot Acc. Q8Y6F0];	-0.41	NS
lmo1722|lmo1722	ATP-dependent RNA helicase [Uniprot Acc. Q8Y6G5];	-0.34	NS
lmo1716|lmo1716	transcriptional regulator [Uniprot Acc. Q8Y6H0];	-0.58	NS
lmo1710|lmo1710	flavodoxin [Uniprot Acc. Q92AU7];	-0.46	NS
lmo1661|lmo1661	hypothetical protein [Uniprot Acc. Q8Y6M3];	-0.42	NS
lmo1657|tsf	Elongation factor Ts [Uniprot Acc. Q8Y6M7];	-0.28	NS
lmo1639|lmo1639	DNA-3-methyladenine glycosidase [Uniprot Acc. Q8Y6P5];	-0.47	NS
lmo0050|lmo0050	histidine kinase [Uniprot Acc. Q8YAR5];	-0.36	NS
lmo1638|lmo1638	hypothetical protein	-0.53	NS
lmo1634|lmo1634	Aldehyde-alcohol dehydrogenase [Uniprot Acc. Q8Y6Q0];	-0.91	NS
lmo1619|daaA	D-alanine aminotransferase [Uniprot Acc. P0DJL9];	-0.38	NS
lmo1596|rpsD	30S ribosomal protein S4 [Uniprot Acc. Q8Y6T6];	-0.29	NS
lmo1604|lmo1604	2-cys peroxiredoxin [Uniprot Acc. Q8Y6S9];	-0.44	NS
lmo1917|pflA	multidrug transporter [Uniprot Acc. Q8Y5Y6];	-0.58	NS
lmo1915|lmo1915	malate dehydrogenase [Uniprot Acc. Q8Y5Y8];	-0.42	NS
lmo1913|lmo1913	hypothetical protein [Uniprot Acc. Q8Y5Z0];	NS	-0.40
lmo1916|lmo1916	peptidase, Beta-lactamase	-0.33	NS
lmo1892|pbpA	penicillin-binding protein 2A [Uniprot Acc. Q8Y610];	NS	-0.26
lmo1885|lmo1885	Xanthine phosphoribosyltransferase [Uniprot Acc. Q8Y617];	NS	-0.36
lmo1870|lmo1870	alkaline phosphatase [Uniprot Acc. Q8Y630];	-0.41	NS
lmo1867|lmo1867	Pyruvate, phosphate dikinase [Uniprot Acc. Q8Y633];	NS	-0.78
lmo1866|lmo1866	Putative pyruvate, phosphate dikinase regulatory protein 2 [Uniprot Acc. Q8Y634];	NS	-0.49
lmo1855|lmo1855	D-alanyl-D-alanine carboxypeptidase [Uniprot Acc. Q8Y645];	-0.26	NS
lmo1842|lmo1842	hypothetical protein	-0.68	NS
lmo1839|pyrP	uracil permease [Uniprot Acc. Q8Y661];	NS	-0.67
lmo1837|pyrC	Dihydroorotase [Uniprot Acc. Q8Y663];	NS	-0.66
lmo1836|pyrAa	Carbamoyl-phosphate synthase small chain [Uniprot Acc. Q8Y664];	NS	-0.90
lmo1803|lmo1803	Signal recognition particle receptor FtsY [Uniprot Acc. Q8Y693];	NS	-0.33

lmo1787|rplS	50S ribosomal protein L19 [Uniprot Acc. O53083];	-0.40	NS
lmo1764|purD	Phosphoribosylamine--glycine ligase [Uniprot Acc. Q8Y6C6];	-0.41	NS
lmo2355|lmo2355	multidrug resistance protein [Uniprot Acc. Q8Y4S7];	NS	-0.48
lmo1262|lmo1262	transcriptional regulator [Uniprot Acc. Q8Y7L5];	-0.41	NS
lmo1240|lmo1240	Phosphoesterase [Uniprot Acc. Q8Y7N4];	-0.37	NS
lmo1806|acpP	Acyl carrier protein [Uniprot Acc. P63439];	-0.41	NS
lmo1236|lmo1236	hypothetical protein	-0.41	NS
lmo1223|lmo1223	ABC transporter ATP-binding proteins [Uniprot Acc. Q8Y7Q0];	-0.36	NS
lmo0054|dnaC	Replicative DNA helicase [Uniprot Acc. Q92FQ6];	-0.25	NS
lmo0056|lmo0056	heat shock protein	-0.60	NS
lmo1168|AckA2	Acetate kinase 2 [Uniprot Acc. Q8Y7V1];	-0.43	NS
lmo1003|lmo1003	Phosphoenolpyruvate-protein phosphotransferase [Uniprot Acc. O31149];	-0.22	NS
lmo1406|pflB	Pyruvate formate-lyase [Uniprot Acc. Q8Y786];	-0.79	NS
lmo1132|lmo1132	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y7Y7];	-0.78	NS
lmo1117|lmo1117	hypothetical protein	-0.64	NS
lmo2768|lmo2768	hypothetical membrane protein [Uniprot Acc. Q8Y3R5];	-0.46	NS
lmo2556|fbaA	fructose-1,6-bisphosphate aldolase [Uniprot Acc. Q8Y498];	-0.45	NS
lmo0575|lmo0575	GntR family transcriptional regulator [Uniprot Acc. Q8Y9F3];	-0.39	NS
lmo1749|lmo1749	Shikimate kinase [Uniprot Acc. Q8Y6D8];	-0.43	NS
lmo1024|lmo1024	hypothetical protein [Uniprot Acc. Q8Y891];	-0.41	NS
lmo2851|lmo2851	AraC family transcriptional regulator [Uniprot Acc. Q8Y3I5];	-1.01	NS
lmo0962|lemA	Listeria epitope LemA [Uniprot Acc. Q8Y8E2];	-0.27	NS
lmo1407|pflC	Pyruvate formate-lyase-activating enzyme [Uniprot Acc. P0A442];	-0.60	NS
lmo2519|lmo2519	teichoic acid linkage unit synthesis protein [Uniprot Acc. Q8Y4D1];	-0.27	NS
lmo1050|lmo1050	hypothetical protein [Uniprot Acc. Q8Y867];	-0.45	NS
lmo1131|lmo1131	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y7Y8];	-0.69	NS
lmo0078|lmo0078	phosphoglycerate dehydrogenase [Uniprot Acc. Q8YAN9];	-0.30	NS
lmo1116|lmo1116	regulatory protein [Uniprot Acc. Q8Y803];	-0.70	NS
lmo2654|fus	Elongation factor G [Uniprot Acc. Q8Y421];	NS	-0.32
lmo2159|lmo2159	oxidoreductase [Uniprot Acc. Q8Y5A9];	NS	-0.92
lmo2823|lmo2823	sporulation protein SpoOJ	NS	-0.57

lmo2820|lmo2820	Amino-terminal domain similar to transcription regulators [Uniprot Acc. Q8Y3L5];	-0.43	NS
lmo1748|lmo1748	hypothetical protein [Uniprot Acc. Q8Y6D9];	-0.40	-0.37
lmo0118|lmaA	antigen A	NS	-0.69
lmo1025|lmo1025	hypothetical protein [Uniprot Acc. Q8Y890];	-0.52	NS
lmo1431|lmo1431	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y770];	-0.36	NS
lmo0952|lmo0952	hypothetical protein [Uniprot Acc. Q8Y8F2];	-0.40	NS
lmo2778|lmo2778	hypothetical protein [Uniprot Acc. Q8Y3Q5];	-0.55	NS
lmo2539|glyA	Serine hydroxymethyltransferase [Uniprot Acc. Q8Y4B2];	NS	-0.28
lmo0156|lmo0156	hypothetical protein	-0.84	NS
lmo2758|guaB	Inosine-5'-monophosphate dehydrogenase [Uniprot Acc. Q926Y9];	NS	-0.35
lmo2754|lmo2754	D-alanyl-D-alanine carboxypeptidase [Uniprot Acc. Q8Y3S7];	NS	-0.27
lmo1487|lmo1487	hypothetical protein	-0.44	NS
lmo1480|rpsT	30S ribosomal protein S20 [Uniprot Acc. P66503];	-0.28	NS
lmo0176|lmo0176	Putative sugar uptake protein lmo0176 [Uniprot Acc. Q8YAF3];	-0.66	NS
lmo1483|comEB	competence protein ComEB [Uniprot Acc. Q8Y739];	-0.44	NS
lmo1488|nadD	nicotinic acid mononucleotide adenylyltransferase [Uniprot Acc. Q8Y735];	-0.36	NS
lmo1490|lmo1490	Shikimate dehydrogenase (NADP(+)) [Uniprot Acc. Q8Y733];	-0.27	NS
lmo0179|lmo0179	sugar ABC transporter permease [Uniprot Acc. Q92F88];	NS	-0.63
lmo1559|thrS	Threonine--tRNA ligase [Uniprot Acc. Q8Y6X2];	-0.26	NS
lmo0912|lmo0912	formate transporter [Uniprot Acc. Q92DA4];	-0.62	NS
lmo1497|udk	Uridine kinase [Uniprot Acc. Q8Y727];	-0.31	NS
lmo1486|lmo1486	Ribosomal silencing factor RsfS [Uniprot Acc. Q92BM7];	-0.35	NS
lmo1573|accD	Acetyl-coenzyme A carboxylase carboxyl transferase subunit beta [Uniprot Acc. Q8Y6V8];	-0.36	NS
lmo1485|lmo1485	hypothetical protein	-0.49	NS
lmo0184|lmo0184	oligo-1,6-glucosidase [Uniprot Acc. Q8YAE6];	-0.59	NS
lmo0188|ksgA	Ribosomal RNA small subunit methyltransferase A [Uniprot Acc. Q8YAE2];	-0.32	NS
lmo0202|hly	Listeriolysin O [Uniprot Acc. P13128];	NS	-0.65
lmo0218|lmo0218	Polyribonucleotide nucleotidyltransferase domain present [Uniprot Acc. Q8YAC8];	-0.29	NS
lmo0228|lysS	Lysine--tRNA ligase [Uniprot Acc. Q8YAB8];	-0.28	NS
lmo2710|lmo2710	hypothetical protein [Uniprot Acc. Q8Y3W9];	NS	-0.37

lmo2684|lmo2684	Permease IIC component [Uniprot Acc. Q8Y3Z4];	-0.92	NS
lmo2667|lmo2667	PTS galacticol transporter subunit IIA [Uniprot Acc. Q8Y411];	NS	-0.72
lmo2666|lmo2666	PTS galacticol transporter subunit IIB [Uniprot Acc. Q927H3];	-0.76	NS
lmo2637|lmo2637	hypothetical protein [Uniprot Acc. Q8Y436];	-0.94	NS
lmo2636|lmo2636	FAD:protein FMN transferase [Uniprot Acc. Q8Y437];	-0.76	NS
lmo2635|lmo2635	1,4-dihydroxy-2-naphthoate octaprenyltransferase [Uniprot Acc. Q8Y438];	-0.42	NS
lmo2626|rpsC	30S ribosomal protein S3 [Uniprot Acc. P66548];	NS	-0.46
lmo2621|rplX	50S ribosomal protein L24 [Uniprot Acc. Q8Y443];	NS	-0.39
lmo2620|rplE	50S ribosomal protein L5 [Uniprot Acc. Q927L9];	NS	-0.58
lmo2619|rpsN	30S ribosomal protein S14 type Z [Uniprot Acc. P66401];	NS	-0.45
lmo2618|rpsH	30S ribosomal protein S8 [Uniprot Acc. P66623];	NS	-0.65
lmo2617|rplF	50S ribosomal protein L6 [Uniprot Acc. Q8Y444];	NS	-0.67
lmo2596|rpsI	30S ribosomal protein S9 [Uniprot Acc. Q8Y459];	-0.21	NS
lmo2577|lmo2577	hypothetical protein [Uniprot Acc. Q8Y478];	-0.36	NS
lmo2560|lmo2560	DNA-directed RNA polymerase subunit delta [Uniprot Acc. Q8Y494];	-0.23	NS
lmo2559|pyrG	CTP synthase [Uniprot Acc. Q8Y495];	-0.26	NS
lmo2548|rpmE2	50S ribosomal protein L31 type B [Uniprot Acc. P0A485];	-0.42	NS
lmo0245|secE	Protein translocase subunit SecE [Uniprot Acc. Q8YAA7];	-0.34	NS
lmo2516|lmo2516	hypothetical protein	-0.51	NS
lmo0256|lmo0256	hypothetical protein [Uniprot Acc. Q8YA98];	-0.43	NS
lmo0259|rpoC	DNA-directed RNA polymerase subunit beta' [Uniprot Acc. Q8YA96];	NS	-0.38
lmo0261|lmo0261	phospho-beta-glucosidase [Uniprot Acc. Q8YA94];	-0.33	NS
lmo2462|lmo2462	dipeptidase [Uniprot Acc. Q8Y4H9];	-0.38	NS
lmo2447|lmo2447	transcriptional regulator [Uniprot Acc. Q8Y4J1];	-0.86	NS
lmo0269|lmo0269	transporter [Uniprot Acc. Q8YA90];	NS	-0.50
lmo0271|lmo0271	phospho-beta-glucosidase [Uniprot Acc. Q8YA88];	-0.26	NS
lmo0272|lmo0272	hypothetical protein [Uniprot Acc. Q8YA87];	-0.37	NS
lmo0273|lmo0273	hypothetical protein [Uniprot Acc. Q8YA86];	-0.48	NS
lmo2435|lmo2435	hypothetical protein [Uniprot Acc. Q8Y4K3];	-0.71	NS

lmo0283|lmo0283	ABC transporter permease [Uniprot Acc. Q8YA76];	NS	-0.60
lmo0284|lmo0284	Methionine import ATP-binding protein MetN 1 [Uniprot Acc. Q8YA75];	NS	-0.48
lmo0285|lmo0285	lipoprotein	NS	-0.46
lmo2537|lmo2537	UDP-N-acetylglucosamine 2-epimerase [Uniprot Acc. Q8Y4B4];	-0.32	NS
lmo0306|lmo0306	hypothetical protein	-0.47	NS
lmo0327|lmo0327	cell surface protein [Uniprot Acc. Q8YA37];	-0.51	NS
lmo0331|lmo0331	internalin [Uniprot Acc. Q8YA34];	-0.66	NS
lmo0352|lmo0352	DeoR family transcriptional regulator [Uniprot Acc. Q8YA14];	-0.51	NS
lmo0354|lmo0354	fatty-acid--CoA ligase [Uniprot Acc. Q8YA12];	-0.63	NS
lmo0355|lmo0355	fumarate reductase subunit A [Uniprot Acc. Q8YA11];	-0.45	NS
lmo0371|lmo0371	GntR family transcriptional regulator [Uniprot Acc. Q8Y9Z6];	-0.51	NS
lmo0382|lmo0382	transcriptional regulator [Uniprot Acc. Q8Y9Y5];	-0.70	NS
lmo1138|lmo1138	ATP-dependent Clp protease proteolytic subunit [Uniprot Acc. Q8Y7Y1];	-0.49	NS
lmo1228|rnhC	Ribonuclease HIII [Uniprot Acc. Q8Y7P5];	-0.38	NS
lmo1306|lmo1306	hypothetical protein [Uniprot Acc. P67288];	-0.57	NS
lmo1314|frr	Ribosome-recycling factor [Uniprot Acc. Q8Y7G7];	-0.31	NS
lmo1319|proS	Proline--tRNA ligase [Uniprot Acc. Q8Y7G2];	-0.42	-0.52
lmo1320|polC	DNA polymerase III PolC-type [Uniprot Acc. Q8Y7G1];	NS	-0.27
lmo1330|rpsO	30S ribosomal protein S15 [Uniprot Acc. Q92C24];	-0.29	NS
lmo1332|lmo1332	Small ribosomal subunit biogenesis GTPase RsgA 1 [Uniprot Acc. Q8Y7F0];	-0.31	NS
lmo1333|lmo1333	hypothetical protein	-0.43	NS
lmo1355|efp	Elongation factor P [Uniprot Acc. P64032];	-0.28	NS
lmo0403|lmo0403	hypothetical protein [Uniprot Acc. Q8Y9W6];	-0.56	NS
lmo0404|lmo0404	hypothetical protein [Uniprot Acc. Q8Y9W5];	-0.43	NS
lmo1516|lmo1516	Ammonium transporter [Uniprot Acc. Q8Y710];	-0.57	NS
lmo1517|lmo1517	nitrogen regulatory PII protein [Uniprot Acc. Q7AP61];	-0.98	NS
lmo0412|lmo0412	hypothetical protein [Uniprot Acc. Q8Y9V8];	-0.68	NS
lmo0414|lmo0414	hypothetical protein [Uniprot Acc. Q8Y9V6];	-0.42	NS
lmo0424|lmo0424	Putative sugar uptake protein lmo0424 [Uniprot Acc. Q8Y9U6];	NS	-0.93
lmo0425|lmo0425	transcriptional antiterminator BglG [Uniprot Acc. Q8Y9U5];	NS	-0.85
lmo1757|lmo1757	hypothetical protein	NS	-0.30

lmo2105|lmo2105	Ferrous iron transport protein B [Uniprot Acc. Q8Y5F9];	-0.92	NS
lmo2086|lmo2086	hypothetical protein [Uniprot Acc. Q8Y5H6];	-0.51	NS
lmo2065|lmo2065	hypothetical protein [Uniprot Acc. Q8Y5J5];	-0.51	NS
lmo2050|lmo2050	excinuclease ABC subunit A [Uniprot Acc. Q8Y5K9];	-0.51	NS
lmo2040|ftsL	Cell division protein FtsL [Uniprot Acc. Q929X7];	-0.32	NS
lmo2380|lmo2380	monovalent cation/H+ antiporter subunit C [Uniprot Acc. Q8Y4Q4];	NS	-0.60
lmo1951|scpA	Segregation and condensation protein A [Uniprot Acc. Q8Y5V4];	-0.37	NS
lmo1938|rpsA	30S ribosomal protein S1 [Uniprot Acc. Q8Y5W7];	-0.46	NS
lmo1941|lmo1941	hypothetical protein [Uniprot Acc. Q8Y5W4];	-0.52	NS
lmo1957|fhuG	ferrichrome ABC transporter permease [Uniprot Acc. Q8Y5U8];	-0.54	NS
lmot43|lmot43	tRNA	NS	-0.57
lmot58|lmot58	tRNA	-0.85	NS
lmot19|lmot19	tRNA	-0.66	NS
lmo2104a|lmo2104a	hypothetical protein	-1.00	NS
lmo2689a|lmo2689a	hypothetical protein	-0.93	NS
lmos28|lmos28	miscRNA	-0.35	NS
lmos12|lmos12	miscRNA	-0.39	NS
lmos13|lmos13	miscRNA	-0.50	NS

Table A-4 Up-regulated DEGs of *Listeria monocytogenes* R2-499 during organic acid habituation compared to pH control; [a]: Acetic acid habituated; [b]: L-Lactic acid habituated; [c]: non-significant.

Gene name	Gene description	Log_2FC	
		A[a]	L[b]
lmo2362|gadT2	amino acid (glutamate) antiporter/inner membrane transporter [Uniprot Acc. Q8Y4S1];	4.76	3.37
lmo2072|lmo2072	Redox-sensing transcriptional repressor Rex [Uniprot Acc. P60384];	1.10	0.69
lmo2212|hemE	Uroporphyrinogen decarboxylase [Uniprot Acc. Q8Y564];	0.67	0.85
lmo1830|lmo1830	short-chain dehydrogenase	3.43	3.18
lmo2369|lmo2369	general stress protein 13 [Uniprot Acc. Q8Y4R5];	0.80	0.58
lmo2166|lmo2166	hypothetical protein	0.67	0.63
lmo2670|lmo2670	hypothetical protein	1.00	1.04
lmo2158|lmo2158	hypothetical protein	2.12	2.09
lmo0558|lmo0558	hypothetical protein [Uniprot Acc. Q8Y9H0];	0.83	0.69
lmo0602|lmo0602	transcripitonal regulator	3.34	2.93
lmo1065|lmo1065	hypothetical protein	0.77	0.68
lmo2211|hemH	Ferrochelatase [Uniprot Acc. Q8Y565];	0.69	0.90
lmo2210|lmo2210	hypothetical protein	1.82	1.88
lmo2202|lmo2202	3-oxoacyl-(acyl-carrier-protein) synthase 3 [Uniprot Acc. Q8Y573];	0.91	0.82
lmo2177|lmo2177	hypothetical protein [Uniprot Acc. Q8Y592];	0.92	1.06
lmo2168|lmo2168	glyoxalase	0.90	0.63
lmo2167|lmo2167	hypothetical protein	0.64	0.61
lmo2263|lmo2263	hypothetical protein [Uniprot Acc. Q8Y515];	0.72	0.61
lmo1059|lmo1059	hypothetical protein	0.65	0.55
lmo2113|lmo2113	Putative heme-dependent peroxidase lmo2113 [Uniprot Acc. Q8Y5F1];	0.81	1.14
lmo2089|lmo2089	lipase [Uniprot Acc. Q8Y5H3];	0.67	0.63
lmo2815|fabG	3-ketoacyl-ACP reductase	0.86	0.78
lmo0612|lmo0612	MarR family transcriptional evidence [Uniprot Acc. Q8Y9C0];	1.39	0.96
lmo2692|lmo2692	hypothetical protein	0.88	0.55
lmo0019|lmo0019	hypothetical protein	3.10	2.70
lmo0670|lmo0670	hypothetical protein	2.25	2.21
lmo0656|lmo0656	hypothetical protein [Uniprot Acc. Q8Y977];	0.82	0.64
lmo2363|gadD2	Glutamate decarboxylase beta [Uniprot Acc. Q9EYW9];	4.70	3.15
lmo1300|lmo1300	Arsenical pump membrane protein [Uniprot Acc. Q8Y7H9];	1.06	0.85
lmo0433|inlA	Internalin A [Uniprot Acc. P0DJM0];	2.17	2.80
lmo0448|gadT1	amino acid (glutamate) antiporter [Uniprot Acc. Q8Y9S5];	0.93	0.50

lmo0611|acpD	FMN-dependent NADH-azoreductase 1 [Uniprot Acc. Q8Y9C1];	1.64	1.17
lmo0851|lmo0851	hypothetical protein	0.80	0.69
lmo0539|lmo0539	Tagatose 1,6-diphosphate aldolase [Uniprot Acc. Q8Y9I9];	2.30	2.09
lmo1293|glpD	Glycerol-3-phosphate dehydrogenase [Uniprot Acc. Q8Y7I4];	1.26	0.78
lmo0823|lmo0823	oxidoreductase [Uniprot Acc. Q8Y8S1];	1.09	0.79
lmo0802|lmo0802	hypothetical protein [Uniprot Acc. Q8Y8U1];	1.07	1.15
lmo0800|lmo0800	hypothetical protein	1.55	1.25
lmo0796|lmo0796	hypothetical protein	1.37	1.24
lmo0761|lmo0761	hypothetical protein [Uniprot Acc. Q8Y8Y1];	1.24	1.17
lmo0760|lmo0760	hypothetical protein [Uniprot Acc. Q8Y8Y2];	1.27	1.10
lmo0759|lmo0759	hypothetical protein	1.29	1.15
lmo0758|lmo0758	hypothetical protein	1.32	1.17
lmo1713|lmo1713	rod shape-determining protein MreB [Uniprot Acc. Q8Y6H3];	1.20	1.11
lmo1690|lmo1690	hypothetical protein [Uniprot Acc. Q8Y6J4];	0.97	0.98
lmo1687|lmo1687	hypothetical protein	0.84	0.67
lmo1684|lmo1684	glycerate dehydrogenase [Uniprot Acc. Q8Y6K0];	0.77	0.66
lmo1676|menF	menaquinone-specific isochorismate synthase [Uniprot Acc. Q8Y6K8];	0.87	0.69
lmo1673|menB	1,4-dihydroxy-2-naphthoyl-CoA synthase [Uniprot Acc. Q8Y6L1];	0.78	0.62
lmo1675|menD	2-succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylate synthase [Uniprot Acc. Q8Y6K9];	0.74	0.58
lmo1672|menE	2-succinylbenzoate--CoA ligase [Uniprot Acc. P58730];	0.80	0.63
lmo1618|lmo1618	MarR family transcriptional regulator [Uniprot Acc. Q8Y6R5];	1.12	1.15
lmo1617|lmo1617	multidrug transporter [Uniprot Acc. Q8Y6R6];	1.17	0.98
lmo1611|lmo1611	aminopeptidase [Uniprot Acc. Q8Y6S2];	0.76	0.62
lmo1919|lmo1919	hypothetical protein [Uniprot Acc. Q8Y5Y4];	1.12	1.08
lmo1902|panB	3-methyl-2-oxobutanoate hydroxymethyltransferase [Uniprot Acc. Q8Y601];	1.75	1.53
lmo1900|panD	Aspartate 1-decarboxylase [Uniprot Acc. Q8Y603];	1.56	1.44
lmo1901|panC	Pantothenate synthetase [Uniprot Acc. Q8Y602];	1.69	1.51
lmo2165|lmo2165	Crp/Fnr family transcriptional regulator	0.77	0.64
lmo1782|lmo1782	3'-exo-deoxyribonuclease [Uniprot Acc. Q8Y6A9];	1.01	0.79
lmo1776|lmo1776	hypothetical protein [Uniprot Acc. Q8Y6B5];	1.06	0.89
lmo1241|lmo1241	hypothetical protein	1.48	1.41
lmo1233|trxA	Thioredoxin [Uniprot Acc. P0A4L3];	1.09	0.83
lmo1209|lmo1209	hypothetical protein	1.11	0.75
lmo2230|lmo2230	arsenate reductase	1.84	1.91

lmo1992|lmo1992	Alpha-acetolactate decarboxylase [Uniprot Acc. Q8Y5R4];	1.34	0.92
lmo2204|lmo2204	hypothetical protein [Uniprot Acc. Q929G9];	0.80	0.72
lmo1392|lmo1392	peptidase [Uniprot Acc. Q8Y798];	0.92	0.81
lmo1017|lmo1017	PTS glucose transporter subunit IIA [Uniprot Acc. Q8Y897];	0.56	0.61
lmo0953|lmo0953	hypothetical protein [Uniprot Acc. Q8Y8F1];	2.18	1.88
lmo0609|lmo0609	phage shock protein E	1.31	0.98
lmo0983|lmo0983	Glutathione peroxidase [Uniprot Acc. Q8Y8C5];	0.95	0.82
lmo0930|lmo0930	hypothetical protein	0.71	0.62
lmo2575|lmo2575	cation transporter [Uniprot Acc. Q8Y480];	1.21	1.36
lmo0105|lmo0105	chitinase B [Uniprot Acc. Q8YAL3];	0.99	1.19
lmo0722|lmo0722	pyruvate oxidase [Uniprot Acc. Q8Y920];	2.71	2.36
lmo0133|lmo0133	hypothetical protein	2.78	2.41
lmo0134|lmo0134	hypothetical protein [Uniprot Acc. Q8YAJ1];	3.18	3.27
lmo1393|lmo1393	peptidase [Uniprot Acc. Q8Y797];	0.79	0.72
lmo0956|lmo0956	N-acetylglucosamine-6P-phosphate deacetylase [Uniprot Acc. Q8Y8E8];	1.11	1.00
lmo1439|sod	Superoxide dismutase (Mn) [Uniprot Acc. P28764];	1.25	1.08
lmo2770|lmo2770	Glutathione biosynthesis bifunctional protein GshAB [Uniprot Acc. Q8Y3R3];	0.76	0.66
lmo0982|lmo0982	peptidase [Uniprot Acc. Q8Y8C6];	1.03	0.89
lmo0944|lmo0944	hypothetical protein	1.11	0.87
lmo1000|lmo1000	phytoene dehydrogenase [Uniprot Acc. Q8Y8A8];	1.13	0.87
lmo0943|fri	DNA protection during starvation protein [Uniprot Acc. Q8Y8G1];	1.30	1.43
lmo2256|lmo2256	hypothetical protein	0.91	0.74
lmo0434|inlB	Internalin B	2.07	2.85
lmo1569|fxsA	F exclusion of bacteriophage T7; interacts with the F plasmid-encoded PifA protein; inner membrane protein [Uniprot Acc. Q8Y6W2];	1.08	0.81
lmo1570|pykA	Pyruvate kinase [Uniprot Acc. Q8Y6W1];	0.51	0.52
lmo1553|hemL	Glutamate-1-semialdehyde 2,1-aminomutase 1 [Uniprot Acc. Q8Y6X8];	0.68	0.73
lmo1557|hemA	Glutamyl-tRNA reductase [Uniprot Acc. Q8Y6X4];	0.84	0.85
lmo1554|hemB	Delta-aminolevulinic acid dehydratase [Uniprot Acc. Q8Y6X7];	0.65	0.75
lmo1556|hemC	Porphobilinogen deaminase [Uniprot Acc. Q8Y6X5];	0.65	0.78
lmo0913|lmo0913	Aldehyde dehydrogenase [Uniprot Acc. Q8Y8I9];	3.50	3.13
lmo1580|lmo1580	Universal stress protein [Uniprot Acc. Q8Y6V1];	1.40	1.16
lmo1493|lmo1493	oligopeptidase [Uniprot Acc. Q8Y730];	0.65	0.55
lmo1578|lmo1578	X-Pro dipeptidase [Uniprot Acc. Q8Y6V3];	1.05	0.93
lmo0189|lmo0189	Veg protein [Uniprot Acc. Q92F78];	0.72	0.69

lmo0209|lmo0209	hypothetical protein	0.77	1.11
lmo0211|ctc	50S ribosomal protein L25 [Uniprot Acc. Q8YAD3];	1.02	0.83
lmo2720|lmo2720	acetate-CoA ligase [Uniprot Acc. Q8Y3W1];	2.19	1.82
lmo2697|lmo2697	PTS mannose transporter subunit IIA [Uniprot Acc. Q8Y3Y2];	2.28	1.99
lmo2696|lmo2696	dihydroxyacetone kinase [Uniprot Acc. Q8Y3Y3];	2.22	2.05
lmo2695|lmo2695	dihydroxyacetone kinase subunit DhaK [Uniprot Acc. Q8Y3Y4];	2.20	1.99
lmo0669|lmo0669	oxidoreductase [Uniprot Acc. Q8Y964];	2.19	2.15
lmo2672|lmo2672	AraC family transcriptional regulator [Uniprot Acc. Q8Y406];	1.35	1.17
lmo2602|lmo2602	hypothetical protein [Uniprot Acc. Q8Y453];	2.37	2.42
lmo2574|lmo2574	hypothetical protein [Uniprot Acc. Q8Y481];	0.90	0.84
lmo2454|lmo2454	hypothetical protein	1.03	0.88
lmo2453|lmo2453	epoxide hydrolase [Uniprot Acc. Q8Y4I6];	0.93	0.72
lmo0613|lmo0613	oxidoreductase [Uniprot Acc. Q8Y9B9];	1.46	1.09
lmo2434|gadD3	glutamate decarboxylase gamma [Uniprot Acc. Q8Y4K4];	1.85	2.15
lmo0292|lmo0292	heat-shock protein htrA serine protease [Uniprot Acc. Q8YA67];	1.30	1.35
lmo2398|ltrC	Low temperature requirement C protein, also similar to B. subtilis YutG protein [Uniprot Acc. Q8Y4N7];	2.26	1.93
lmo2391|lmo2391	hypothetical protein	2.04	1.82
lmo2390|lmo2390	Ferredoxin--NADP reductase 2 [Uniprot Acc. Q8Y4P5];	0.84	0.57
lmo2389|lmo2389	NADH dehydrogenase [Uniprot Acc. Q8Y4P6];	1.10	0.82
lmo0356|lmo0356	oxidoreductase [Uniprot Acc. Q8YA10];	1.05	0.77
lmo1583|tpx	Thiol peroxidase [Uniprot Acc. Q8Y6U8];	1.17	0.92
lmo1518|lmo1518	hypothetical protein [Uniprot Acc. Q7AP60];	1.11	1.11
lmo1383|lmo1383	Isopentenyl-diphosphate delta-isomerase [Uniprot Acc. Q8Y7A5];	0.78	0.58
lmo0932|lmo0932	hypothetical protein [Uniprot Acc. Q8Y8H2];	1.28	1.04
lmo1376|lmo1376	6-phosphogluconate dehydrogenase, decarboxylating [Uniprot Acc. Q8Y7B0];	0.63	0.54
lmo0937|lmo0937	hypothetical protein [Uniprot Acc. Q8Y8G7];	2.59	2.51
lmo2522|lmo2522	cell wall-binding protein [Uniprot Acc. Q8Y4C8];	1.86	1.55
lmo2191|spxA	Regulatory protein Spx [Uniprot Acc. Q9RGX0];	0.89	0.87
lmo2579a|lmo2579a	hypothetical protein	1.77	4.03
lmos08|lmos08	miscRNA	1.94	1.64
lmos09|lmos09	miscRNA	2.01	1.79
lmos10|lmos10	miscRNA	2.24	2.06
lmos07|lmos07	miscRNA	1.89	1.59
lmos36|lmos36	miscRNA	1.97	1.84
lmos81|lmos81	miscRNA	1.69	1.49

lmo2373|lmo2373	PTS beta-glucoside transporter subunit IIB [Uniprot Acc. Q8Y4R1];	0.58	NS[C]
lmo1053|PdhB	pyruvate dehydrogenase subunit E1 beta [Uniprot Acc. Q8Y864];	0.64	NS
lmo2642|lmo2642	hypothetical protein [Uniprot Acc. Q8Y432];	NS	0.84
lmo2366|lmo2366	DeoR family transcriptional regulator [Uniprot Acc. Q928R7];	0.68	NS
lmo2356|lmo2356	hypothetical protein	NS	1.19
lmo2101|lmo2101	Pyridoxal 5'-phosphate synthase subunit PdxS [Uniprot Acc. Q8Y5G2];	1.08	NS
lmo2338|pepC	Aminopeptidase C [Uniprot Acc. O69192];	0.74	NS
lmo2259|lmo2259	PTS beta-glucoside transporter subunit IIA [Uniprot Acc. Q8Y519];	0.68	NS
lmo2231|lmo2231	hypothetical protein [Uniprot Acc. Q8Y545];	2.00	NS
lmo2200|lmo2200	MarR family transcriptional regulator [Uniprot Acc. Q8Y575];	1.10	NS
lmo2188|lmo2188	oligoendopeptidase [Uniprot Acc. Q8Y583];	0.71	NS
lmo2176|lmo2176	TetR family transcriptional regulator [Uniprot Acc. Q8Y593];	0.69	NS
lmo2173|lmo2173	sigma-54-dependent transcriptional regulator [Uniprot Acc. Q8Y596];	NS	0.98
lmo2748|lmo2748	hypothetical protein [Uniprot Acc. Q8Y3T3];	1.72	NS
lmo0553|lmo0553	hypothetical protein	0.55	NS
lmo1425|opuCD	glycine/betaine ABC transporter permease [Uniprot Acc. Q7AP68];	2.24	NS
lmo2102|lmo2102	Pyridoxal 5'-phosphate synthase subunit PdxT [Uniprot Acc. Q8Y5G1];	0.91	NS
lmo0591|lmo0591	hypothetical protein [Uniprot Acc. Q8Y9D9];	1.46	NS
lmo2085|lmo2085	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8Y5H7];	1.96	NS
lmo2213|lmo2213	hypothetical protein	2.73	NS
lmo2339|lmo2339	hypothetical protein	0.78	NS
lmo2064|mscL	Large-conductance mechanosensitive channel [Uniprot Acc. Q8Y5J6];	0.68	NS
lmo2057|ctaB	Protoheme IX farnesyltransferase [Uniprot Acc. Q8Y5K3];	0.86	NS
lmo2199|lmo2199	hypothetical protein [Uniprot Acc. Q8Y576];	1.13	NS
lmo2570|lmo2570	hypothetical protein [Uniprot Acc. Q8Y485];	1.79	NS
lmo2198|trpS	Tryptophan--tRNA ligase [Uniprot Acc. Q8Y577];	0.66	NS
lmo1978|lmo1978	Glucose-6-phosphate 1-dehydrogenase [Uniprot Acc. Q8Y5S7];	0.56	NS
lmo2830|lmo2830	Thioredoxin [Uniprot Acc. Q8Y3K5];	0.67	NS
lmo0615|lmo0615	hypothetical protein	0.89	NS
lmo2724|lmo2724	hypothetical protein	1.20	NS
lmo2785|kat	Catalase [Uniprot Acc. Q8Y3P9];	1.11	NS
lmo0629|lmo0629	hypothetical protein [Uniprot Acc. Q8Y9A3];	0.64	NS

lmo0651|lmo0651	transcriptional regulator [Uniprot Acc. Q8Y982];	0.63	NS
lmo0654|lmo0654	hypothetical protein	0.98	NS
lmo0018|lmo0018	Beta-glucosidase [Uniprot Acc. Q8YAU5];	0.78	NS
lmo0655|lmo0655	phosphoprotein phosphatase [Uniprot Acc. Q8Y978];	1.04	NS
lmo0661|lmo0661	hypothetical protein [Uniprot Acc. Q8Y972];	1.27	NS
lmo0663|lmo0663	hypothetical protein [Uniprot Acc. Q8Y970];	0.56	NS
lmo0657|lmo0657	hypothetical protein	0.65	NS
lmo0658|lmo0658	hypothetical protein [Uniprot Acc. Q8Y975];	0.61	NS
lmo0660|lmo0660	transposase [Uniprot Acc. Q8Y973];	1.06	NS
lmo0589|lmo0589	hypothetical protein [Uniprot Acc. Q8Y9E1];	1.37	NS
lmo0719|lmo0719	hypothetical protein	0.62	NS
lmo1282|lmo1282	hypothetical protein	0.61	NS
lmo1281|lmo1281	hypothetical protein [Uniprot Acc. Q8Y7J6];	0.73	NS
lmo1283|lmo1283	LacX protein [Uniprot Acc. Q8Y7J4];	0.61	NS
lmo1292|lmo1292	glycerophosphodiester phosphodiesterase [Uniprot Acc. Q8Y7I5];	0.58	NS
lmo0464|lmo0464	transposase [Uniprot Acc. Q8Y9Q9];	1.36	NS
lmo2132|lmo2132	hypothetical protein [Uniprot Acc. Q8Y5D3];	0.92	NS
lmo0486|rpmF	50S ribosomal protein L32-1 [Uniprot Acc. Q8Y9N9];	0.80	NS
lmo0590|lmo0590	hypothetical protein [Uniprot Acc. Q8Y9E0];	1.31	NS
lmo0822|lmo0822	transcriptional regulator [Uniprot Acc. Q8Y8S2];	0.91	NS
lmo0811|lmo0811	carbonic anhydrase [Uniprot Acc. Q8Y8T3];	0.96	NS
lmo0799|lmo0799	Blue-light photoreceptor [Uniprot Acc. P58724];	0.75	NS
lmo0794|lmo0794	hypothetical protein	1.09	NS
lmo0790|lmo0790	Cys-tRNA(Pro)/Cys-tRNA(Cys) deacylase [Uniprot Acc. Q8Y8V2];	0.64	NS
lmo0788|lmo0788	hypothetical protein	NS	0.97
lmo0779|lmo0779	UPF0266 membrane protein [Uniprot Acc. Q8Y8W3];	0.71	NS
lmo0770|lmo0770	LacI family transcriptional regulator [Uniprot Acc. Q8Y8X2];	0.57	NS
lmo1433|lmo1433	glutathione reductase [Uniprot Acc. Q8Y768];	1.60	NS
lmo0597|lmo0597	Crp/Fnr family transcriptional regulator [Uniprot Acc. Q8Y9D3];	0.68	NS
lmo0740|lmo0740	transcriptional regulator	0.65	NS
lmo1704|lmo1704	hypothetical protein [Uniprot Acc. Q8Y6I0];	0.66	NS
lmo1726|lmo1726	hypothetical protein [Uniprot Acc. Q8Y6G1];	0.54	NS
lmo1694|lmo1694	CDP-abequose synthase [Uniprot Acc. Q8Y6J0];	2.32	NS
lmo1689|lmo1689	Adenine DNA glycosylase [Uniprot Acc. Q8Y6J5];	0.60	NS
lmo1674|lmo1674	Putative 2-succinyl-6-hydroxy-2,4-cyclohexadiene-1-carboxylate synthase [Uniprot Acc. Q8Y6L0];	0.60	NS
lmo1634|lmo1634	Aldehyde-alcohol dehydrogenase [Uniprot Acc. Q8Y6Q0];	NS	0.88

lmo1609|lmo1609	thioredoxin [Uniprot Acc. Q8Y6S4];	0.74	NS
lmo1607|pheT	Phenylalanine--tRNA ligase beta subunit [Uniprot Acc. Q8Y6S6];	0.51	NS
lmo1917|pflA	pyruvate formate-lyase [Uniprot Acc. Q8Y5Y6];	NS	0.78
lmo2349|lmo2349	amino acid ABC transporter substrate-binding protein	1.18	NS
lmo1889|lmo1889	hypothetical protein	0.76	NS
lmo1878|lmo1878	manganese transport transcriptional regulator [Uniprot Acc. Q8Y623];	0.62	NS
lmo2572|lmo2572	dihydrofolate reductase subunit A [Uniprot Acc. Q8Y483];	1.53	NS
lmo0604|lmo0604	hypothetical protein [Uniprot Acc. Q8Y9C8];	NS	0.77
lmo1841|lmo1841	hypothetical protein	0.98	NS
lmo1829|lmo1829	fibronectin-binding proteins [Uniprot Acc. Q8Y670];	0.57	NS
lmo2169|lmo2169	hypothetical protein [Uniprot Acc. Q8Y5A0];	0.71	NS
lmo1799|lmo1799	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8Y697];	0.86	NS
lmo1798|lmo1798	hypothetical protein [Uniprot Acc. Q8Y698];	0.88	NS
lmo1258|lmo1258	hypothetical protein [Uniprot Acc. Q8Y7L7];	0.84	NS
lmo1257|lmo1257	hypothetical protein	NS	1.05
lmo1251|lmo1251	Fnr/Crp family transcriptional regulator [Uniprot Acc. Q8Y7M3];	NS	2.27
lmo1250|lmo1250	antibiotic resistance protein [Uniprot Acc. Q8Y7M4];	NS	6.04
lmo1249|lmo1249	hypothetical protein	NS	6.27
lmo1608|lmo1608	hypothetical protein	0.73	NS
lmo1595|lmo1595	hypothetical protein [Uniprot Acc. Q8Y6T7];	1.00	NS
lmo1208|cbiP	Cobyric acid synthase [Uniprot Acc. Q8Y7R3];	1.00	NS
lmo2352|lmo2352	LysR family transcriptional regulator [Uniprot Acc. Q8Y4T0];	1.66	NS
lmo1406|pflB	Pyruvate formate-lyase [Uniprot Acc. Q8Y786];	NS	0.93
lmo1140|lmo1140	hypothetical protein	NS	1.71
lmo0603|lmo0603	hypothetical protein [Uniprot Acc. Q8Y9C9];	0.85	NS
lmo1056|lmo1056	hypothetical protein [Uniprot Acc. Q8Y861];	0.72	NS
lmo0728|lmo0728	riboflavin kinase / FAD synthase [Uniprot Acc. Q8Y914];	0.62	NS
lmo1054|pdhC	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex [Uniprot Acc. Q8Y863];	0.63	NS
lmo2174|lmo2174	hypothetical protein [Uniprot Acc. Q8Y595];	NS	1.02
lmo1890|lmo1890	hypothetical protein	0.87	NS
lmo1009|lmo1009	hypothetical protein	0.57	NS
lmo0995|lmo0995	hypothetical protein [Uniprot Acc. Q8Y8B3];	2.20	NS
lmo0994|lmo0994	hypothetical protein [Uniprot Acc. Q8Y8B4];	2.01	NS

lmo1415|lmo1415	hydroxy-3-methylglutaryl-CoA synthase [Uniprot Acc. Q8Y781];	0.64	NS
lmo0975|lmo0975	Ribose-5-phosphate isomerase A [Uniprot Acc. Q8Y8D3];	0.80	NS
lmo0964|lmo0964	hypothetical protein	0.55	NS
lmo0957|lmo0957	Glucosamine-6-phosphate deaminase [Uniprot Acc. Q8Y8E7];	0.67	NS
lmo1407|pflC	Pyruvate formate-lyase-activating enzyme [Uniprot Acc. P0A442];	NS	1.01
lmo1413|lmo1413	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8Y783];	1.00	1.49
lmo0911|lmo0911	hypothetical protein	0.94	NS
lmo1012|lmo1012	N-acetyldiaminopimelate deacetylase [Uniprot Acc. Q8Y8A0];	0.66	NS
lmo1055|PdhD	Dihydrolipoyl dehydrogenase [Uniprot Acc. Q8Y862];	0.67	NS
lmo0515|lmo0515	hypothetical protein	2.10	NS
lmo0931|lmo0931	Lipoate--protein ligase [Uniprot Acc. Q8Y8H3];	0.52	NS
lmo0095|lmo0095	hypothetical protein	0.83	NS
lmo0100|lmo0100	hypothetical protein	0.53	NS
lmo0101|lmo0101	transcriptional regulator [Uniprot Acc. Q8YAL7];	0.65	NS
lmo0129|lmo0129	N-acetylmuramoyl-L-alanine amidase [Uniprot Acc. Q8YAJ6];	NS	1.35
lmo2511|lmo2511	Ribosome hibernation promoting factor [Uniprot Acc. Q927Y2];	NS	0.61
lmo1423|lmo1423	hypothetical protein	0.81	NS
lmo1052|pdhA	pyruvate dehydrogenase subunit E1 alpha [Uniprot Acc. Q8Y865];	0.64	NS
lmo1414|lmo1414	acetyl-CoA:acetyltransferase [Uniprot Acc. Q8Y782];	0.56	NS
lmo1057|lmo1057	L-lactate dehydrogenase [Uniprot Acc. Q8Y860];	0.65	NS
lmo2755|lmo2755	CoA-transferase [Uniprot Acc. Q8Y3S6];	0.70	NS
lmo0170|lmo0170	hypothetical protein	1.08	NS
lmo2829|lmo2829	nitroreductase [Uniprot Acc. Q8Y3K6];	0.66	NS
lmo0906|lmo0906	glutathione reductase [Uniprot Acc. Q8Y8J5];	0.74	NS
lmo1555|hemD	Lmo1555 protein [Uniprot Acc. Q8Y6X6];	NS	0.71
lmo0907|lmo0907	phosphoglycerate mutase	0.79	NS
lmo0912|lmo0912	formate transporter [Uniprot Acc. Q92DA4];	NS	0.74
lmo0185|lmo0185	hypothetical protein [Uniprot Acc. Q8YAE5];	0.63	NS
lmo0210|ldh	L-lactate dehydrogenase 1 [Uniprot Acc. P33380];	NS	0.93
lmo2743|lmo2743	translaldolase [Uniprot Acc. Q8Y3T8];	1.10	NS
lmo2742|lmo2742	hypothetical protein	0.91	NS
lmo0223|cysK	Cysteine synthase [Uniprot Acc. Q8YAC3];	0.80	NS
lmo2719|lmo2719	tRNA-specific adenosine deaminase [Uniprot Acc. Q8Y3W2];	NS	0.98
lmo2712|lmo2712	gluconate kinase [Uniprot Acc. Q8Y3W7];	0.64	NS

lmo0664|lmo0664	acetyl transferase [Uniprot Acc. Q8Y969];	0.78	NS
lmo0668|lmo0668	Transport permease protein [Uniprot Acc. Q8Y965];	0.57	NS
lmo2674|lmo2674	ribose-5-phosphate isomerase B [Uniprot Acc. Q8Y404];	0.65	NS
lmo2673|lmo2673	hypothetical protein	1.91	NS
lmo2669|lmo2669	hypothetical protein [Uniprot Acc. Q8Y409];	NS	1.02
lmo2604|lmo2604	hypothetical protein	0.65	NS
lmo2603|lmo2603	hypothetical protein [Uniprot Acc. Q8Y452];	1.69	NS
lmo2587|lmo2587	hypothetical protein	1.17	NS
lmo2573|lmo2573	zinc-binding dehydrogenase [Uniprot Acc. Q8Y482];	1.52	NS
lmo2571|lmo2571	nicotinamidase [Uniprot Acc. Q8Y484];	1.46	NS
lmo2557|lmo2557	lipid kinase [Uniprot Acc. Q8Y497];	0.80	NS
lmo2527|lmo2527	hypothetical protein [Uniprot Acc. Q8Y4C3];	0.70	NS
lmo2507|ftsE	Cell division ATP-binding protein FtsE [Uniprot Acc. Q8Y4E0];	NS	0.57
lmo2495|lmo2495	Phosphate import ATP-binding protein PstB 1 [Uniprot Acc. P63363];	1.35	NS
lmo2490|lmo2490	CsbA protein [Uniprot Acc. Q8Y4F4];	0.72	NS
lmo2478|trxB	Thioredoxin reductase [Uniprot Acc. O32823];	0.80	NS
lmo2474|lmo2474	Nucleotide-binding protein lmo2474 [Uniprot Acc. Q8Y4G9];	0.52	NS
lmo2473|lmo2473	Gluconeogenesis factor [Uniprot Acc. P58588];	0.52	NS
lmo2471|lmo2471	NADPH dehydrogenase [Uniprot Acc. Q8Y4H1];	0.61	NS
lmo0265|lmo0265	succinyl-diaminopimelate desuccinylase [Uniprot Acc. Q7AP85];	2.08	NS
lmo2467|lmo2467	chitin-binding protein [Uniprot Acc. Q8Y4H4];	0.74	NS
lmo2460|lmo2460	transcriptional regulator [Uniprot Acc. Q8Y4I0];	0.65	NS
lmo2459|gap	Glyceraldehyde-3-phosphate dehydrogenase [Uniprot Acc. Q8Y4I1];	0.83	NS
lmo2439|lmo2439	hypothetical protein	NS	0.95
lmo0281|lmo0281	hypothetical protein	0.61	NS
lmo2426|lmo2426	hypothetical protein	0.55	NS
lmo2425|lmo2425	Glycine cleavage system H protein [Uniprot Acc. Q8Y4L2];	0.54	NS
lmo2424|lmo2424	thioredoxin [Uniprot Acc. Q8Y4L3];	0.98	NS
lmo2406|lmo2406	hypothetical protein	0.77	NS
lmo2403|lmo2403	hypothetical protein [Uniprot Acc. Q8Y4N3];	0.64	NS
lmo2397|lmo2397	NifU; Fe-S cluster biogenesis protein [Uniprot Acc. Q8Y4N8];	0.69	NS
lmo0321|lmo0321	hypothetical protein [Uniprot Acc. Q8YA43];	1.90	NS
lmo2393|lmo2393	hypothetical protein	0.79	NS
lmo2392|lmo2392	hypothetical protein	0.90	NS
lmo2387|lmo2387	hypothetical protein [Uniprot Acc. Q8Y4P8];	2.07	NS
lmo2386|lmo2386	hypothetical protein [Uniprot Acc. Q8Y4P9];	0.88	NS

lmo0341|lmo0341	hypothetical protein	0.88	NS
lmo0377|lmo0377	hypothetical protein	0.82	NS
lmo0389|ltrA	Low temperature requirement protein A [Uniprot Acc. Q8Y9X8];	0.89	NS
lmo1329|ribC	Riboflavin biosynthesis protein [Uniprot Acc. Q8Y7F2];	0.69	NS
lmo1354|lmo1354	aminopeptidase P [Uniprot Acc. Q8Y7C9];	0.53	NS
lmo1514|lmo1514	recombination factor protein RarA [Uniprot Acc. Q8Y712];	0.59	NS
lmo1538|glpK	Glycerol kinase [Uniprot Acc. Q8Y6Z2];	1.15	NS
lmo1539|lmo1539	glycerol transporter [Uniprot Acc. Q8Y6Z1];	1.18	NS
lmo1387|lmo1387	pyrroline-5-carboxylate reductase [Uniprot Acc. Q8Y7A2];	0.88	NS
lmo1384|lmo1384	hypothetical protein	0.72	NS
lmo1382|lmo1382	hypothetical protein	0.87	NS
lmo2114|lmo2114	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y5F0];	NS	0.60
lmo2494|lmo2494	Phosphate-specific transport system accessory protein PhoU [Uniprot Acc. Q8Y4F0];	1.21	NS
lmo2103|eutD	phosphotransacetylase [Uniprot Acc. Q8Y5G0];	0.76	NS
lmo2375|lmo2375	hypothetical protein	0.68	NS
lmo2005|lmo2005	oxidoreductase [Uniprot Acc. Q8Y5Q1];	1.32	NS
lmo2011|lmo2011	Histidine kinase [Uniprot Acc. Q8Y5P5];	0.77	NS
lmo2006|alsS	acetolactate synthase [Uniprot Acc. Q8Y5Q0];	1.42	NS
lmo2028|lmo2028	hypothetical protein [Uniprot Acc. Q8Y5M9];	0.63	NS
lmo2157|sepA	SepA protein [Uniprot Acc. Q8Y5B0];	2.37	NS
lmo2189|lmo2189	competence protein CoiA	0.78	NS
lmo2269|lmo2269	hypothetical protein	1.17	NS
lmo2536a|lmo2536a	hypothetical protein	NS	1.24
lmos45|lmos45	miscRNA	NS	1.69
lmos49|lmos49	miscRNA	1.56	NS
lmos66|lmos66	miscRNA	NS	2.48

Table A-5 Down-regulated DEGs of *Listeria monocytogenes* R2-499 during organic acid habituation compared to pH control; [a]: Acetic acid habituated; [b]: L-Lactic acid habituated; [c]: non-significant.

Gene name	Gene description	Log_2FC	
		A[a]	L[b]
lmo1993|pdp	pyrimidine-nucleoside phosphorylase [Uniprot Acc. Q8Y5R3];	-1.33	-1.36
lmo2800|lmo2800	dehydrogenase [Uniprot Acc. Q8Y3N5];	-1.13	-1.52
lmo2183|lmo2183	ferrichrome ABC transporter permease [Uniprot Acc. Q8Y586];	-1.52	-1.24
lmo2264|lmo2264	hypothetical protein [Uniprot Acc. Q8Y514];	-0.60	-0.53
lmo2248|lmo2248	hypothetical protein	-1.01	-0.89
lmo2152|lmo2152	thioredoxin [Uniprot Acc. Q929L9];	-0.85	-0.79
lmo2194|lmo2194	peptide ABC transporter permease [Uniprot Acc. Q8Y580];	-0.85	-0.79
lmo2193|lmo2193	peptide ABC transporter ATP-binding protein [Uniprot Acc. Q7AP53];	-0.67	-0.60
lmo2184|lmo2184	ferrichrome ABC transporter substrate-binding protein [Uniprot Acc. Q7AP55];	-1.56	-1.31
lmo2182|lmo2182	ferrichrome ABC transporter ATP-binding protein [Uniprot Acc. Q8Y587];	-1.43	-1.26
lmo2181|lmo2181	Sortase B [Uniprot Acc. Q8Y588];	-1.43	-1.12
lmo2180|lmo2180	hypothetical protein [Uniprot Acc. Q8Y589];	-1.20	-1.02
lmo2162|lmo2162	hypothetical protein	-1.45	-2.04
lmo2154|nrdF	Ribonucleoside-diphosphate reductase subunit beta [Uniprot Acc. Q8Y5B3];	-0.94	-0.79
lmo1597|lmo1597	hypothetical protein	-1.81	-1.67
lmo2155|lmo2155	Ribonucleoside-diphosphate reductase [Uniprot Acc. Q8Y5B2];	-0.96	-0.80
lmo2186|lmo2186	Hemin/hemoglobin-binding protein 1 [Uniprot Acc. Q8Y585];	-1.74	-1.42
lmo2079|lmo2079	hypothetical protein	-1.27	-1.08
lmo2130|lmo2130	hypothetical protein [Uniprot Acc. Q8Y5D5];	-0.80	-0.70
lmo2185|lmo2185	Hemin/hemoglobin-binding protein 2 [Uniprot Acc. Q7AP54];	-1.88	-1.62
lmo1388|tcsA	CD4+ T-cell-stimulating antigen [Uniprot Acc. Q48754];	-1.69	-1.72
lmo0711|flgC	Flagellar basal-body rod protein FlgC [Uniprot Acc. Q92DU3];	-1.55	-1.76
lmo1389|lmo1389	sugar ABC transporter ATP-binding protein [Uniprot Acc. Q8Y7A1];	-1.01	-0.81
lmo2249|lmo2249	low-affinity inorganic phosphate transporter [Uniprot Acc. Q8Y528];	-1.10	-1.03
lmo2000|lmo2000	PTS mannose transporter subunit IID [Uniprot Acc. Q8Y5Q6];	-1.84	-2.58

lmo1959|lmo1959	ferrichrome-binding protein [Uniprot Acc. Q8Y5U6];	-1.34	-0.85
lmo1390|lmo1390	ABC transporter permease [Uniprot Acc. Q8Y7A0];	-1.00	-0.81
lmo2254|lmo2254	hypothetical protein [Uniprot Acc. Q8Y523];	-1.17	-1.08
lmo2195|lmo2195	peptide ABC transporter permease [Uniprot Acc. Q8Y579];	-0.85	-0.82
lmo2196|lmo2196	peptide ABC transporter substrate-binding protein [Uniprot Acc. Q7AP52];	-1.39	-1.38
lmo0681|lmo0681	flagellar biosynthesis regulator FlhF [Uniprot Acc. Q8Y953];	-2.27	-2.26
lmo0676|fliP	flagellar biosynthesis protein FliP [Uniprot Acc. Q8Y958];	-1.84	-1.83
lmo0677|fliQ	flagellar biosynthesis protein FliQ [Uniprot Acc. Q8Y957];	-2.02	-2.10
lmo0678|fliR	flagellar biosynthesis protein FliR [Uniprot Acc. Q8Y956];	-1.78	-1.86
lmo0684|lmo0684	hypothetical protein	-2.72	-3.92
lmo0687|lmo0687	hypothetical protein	-2.79	-2.75
lmo0682|flgG	flagellar basal body rod protein FlgG [Uniprot Acc. Q8Y952];	-2.40	-2.68
lmo0683|lmo0683	Chemotaxis protein methyltransferase [Uniprot Acc. Q9XDE8];	-2.47	-2.56
lmo0692|cheA	Chemotaxis protein CheA [Uniprot Acc. Q48768];	-1.27	-1.39
lmo0694|lmo0694	hypothetical protein	-1.21	-1.16
lmo0702|lmo0702	hypothetical protein [Uniprot Acc. Q8Y939];	-1.56	-1.69
lmo0693|lmo0693	flagellar motor switch protein FliY [Uniprot Acc. Q8Y947];	-1.27	-1.50
lmo0685|lmo0685	flagellar motor protein MotA [Uniprot Acc. Q7AP82];	-2.58	-2.69
lmo0695|lmo0695	hypothetical protein	-1.50	-1.29
lmo0696|flgD	flagellar basal body rod modification protein [Uniprot Acc. Q8Y944];	-1.36	-1.29
lmo0698|lmo0698	flagellar motor switch protein [Uniprot Acc. Q8Y943];	-1.80	-1.41
lmo0707|fliD	Flagellar hook-associated protein 2 [Uniprot Acc. Q8Y934];	-1.48	-1.54
lmo0704|lmo0704	hypothetical protein	-1.18	-1.59
lmo0697|flgE	Flagellar hook protein FlgE [Uniprot Acc. Q92DV7];	-1.37	-1.53
lmo0708|lmo0708	flagellar protein [Uniprot Acc. Q8Y933];	-1.63	-1.47
lmo0700|lmo0700	flagellar motor switch protein FliY [Uniprot Acc. Q8Y941];	-1.57	-1.67
lmo0701|lmo0701	hypothetical protein [Uniprot Acc. Q8Y940];	-1.70	-1.62

lmo0691|cheY	Chemotaxis protein CheY [Uniprot Acc. P0A4H5];	-1.03	-1.26
lmo0703|lmo0703	hypothetical protein	-1.11	-1.59
lmo0706|flgL	flagellar hook-associated protein FlgL [Uniprot Acc. Q8Y935];	-1.44	-1.57
lmo0705|flgK	Flagellar hook-associated protein 1 [Uniprot Acc. Q8Y936];	-1.45	-1.44
lmo0710|flgB	Flagellar basal body rod protein FlgB [Uniprot Acc. Q8Y931];	-1.59	-1.41
lmo0712|fliE	Flagellar hook-basal body complex protein FliE [Uniprot Acc. Q8Y930];	-1.32	-1.85
lmo0713|fliF	flagellar MS-ring protein FliF [Uniprot Acc. Q8Y929];	-1.71	-1.62
lmo0714|fliG	flagellar motor switch protein FliG [Uniprot Acc. Q8Y928];	-1.56	-1.81
lmo0715|fliH	flagellar assembly protein H	-1.34	-1.50
lmo0716|fliI	flagellum-specific ATP synthase [Uniprot Acc. Q8Y926];	-1.71	-1.76
lmo0027|lmo0027	PTS beta-glucoside transporter subunit IIABC [Uniprot Acc. Q8YAT6];	-1.09	-1.49
lmo0718|lmo0718	hypothetical protein	-1.51	-1.44
lmo0709|lmo0709	hypothetical protein	-1.62	-1.33
lmo1294|miaA	tRNA dimethylallyltransferase [Uniprot Acc. Q8Y7I3];	-0.79	-0.68
lmo0514|lmo0514	internalin [Uniprot Acc. Q8Y9L3];	-1.36	-1.14
lmo0848|lmo0848	amino acid ABC transporter ATP-binding protein [Uniprot Acc. Q8Y8P8];	-3.02	-2.71
lmo0847|lmo0847	glutamine ABC transporter [Uniprot Acc. Q8Y8P9];	-3.12	-2.75
lmo0837|lmo0837	hypothetical protein	-0.99	-0.80
lmo0826|lmo0826	transporter [Uniprot Acc. Q8Y8R8];	-0.81	-0.70
lmo0810|lmo0810	spermidine/putrescine ABC transporter substrate-binding protein [Uniprot Acc. Q8Y8T4];	-1.27	-1.00
lmo0809|lmo0809	spermidine/putrescine ABC transporter permease [Uniprot Acc. Q92DL4];	-1.18	-0.97
lmo0808|lmo0808	spermidine/putrescine ABC transporter permease [Uniprot Acc. Q8Y8T5];	-1.21	-0.91
lmo0807|lmo0807	Spermidine/putrescine import ATP-binding protein PotA [Uniprot Acc. Q8Y8T6];	-1.05	-0.77
lmo0791|lmo0791	hypothetical protein	-0.81	-0.93
lmo2381|lmo2381	monovalent cation/H+ antiporter subunit D [Uniprot Acc. Q8Y4Q3];	-0.83	-0.63
lmo1700|lmo1700	hypothetical protein	-1.24	-1.03
lmo1699|lmo1699	chemotaxis protein [Uniprot Acc. Q8Y6I5];	-1.23	-1.07
lmo2153|lmo2153	flavodoxin [Uniprot Acc. Q8Y5B4];	-0.89	-0.85

lmo1671|lmo1671	ABC transporter [Uniprot Acc. Q8Y6L3];	-2.33	-2.39
lmo1652|lmo1652	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y6N2];	-1.45	-1.22
lmo1651|lmo1651	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y6N3];	-1.44	-1.26
lmo1641|citB	Aconitate hydratase [Uniprot Acc. Q8Y6P3];	-0.83	-0.89
lmo1625|lmo1625	transporter [Uniprot Acc. Q8Y6Q9];	-0.73	-0.65
lmo1068|lmo1068	hypothetical protein	-0.58	-0.61
lmo1879|cspD	cold-shock protein [Uniprot Acc. Q92AD0];	-0.91	-1.10
lmo2218|lmo2218	hypothetical protein [Uniprot Acc. Q8Y558];	-1.06	-0.81
lmo1255|lmo1255	PTS trehalose transporter subunit IIBC [Uniprot Acc. Q8Y7L9];	-0.79	-1.34
lmo1254|lmo1254	alpha,alpha-phosphotrehalase [Uniprot Acc. Q8Y7M0];	-0.71	-1.26
lmo1188|lmo1188	hypothetical protein	-0.80	-0.79
lmo1079|lmo1079	hypothetical protein [Uniprot Acc. Q8Y839];	-1.01	-0.80
lmo1076|lmo1076	autolysin [Uniprot Acc. Q8Y842];	-0.75	-0.59
lmo0541|lmo0541	ABC transporter substrate-binding protein [Uniprot Acc. Q8Y9I7];	-1.13	-0.61
lmo0688|lmo0688	hypothetical protein	-2.73	-2.65
lmo0679|flhB	flagellar biosynthesis protein FlhB [Uniprot Acc. Q8Y955];	-1.82	-2.06
lmo0680|flhA	flagellar biosynthesis protein FlhA [Uniprot Acc. Q8Y954];	-2.19	-2.23
lmo2852|lmo2852	hypothetical protein	-0.69	-0.88
lmo0971|dltD	DltD protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid [Uniprot Acc. Q7AP78];	-1.48	-1.15
lmo0973|dltB	DltB protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid [Uniprot Acc. Q7AP77];	-1.53	-1.16
lmo0974|dltA	D-alanine--D-alanyl carrier protein ligase [Uniprot Acc. Q8Y8D4];	-1.40	-1.02
lmo0972|dltC	D-alanyl carrier protein [Uniprot Acc. Q9S389];	-1.59	-1.23
lmo1391|lmo1391	sugar ABC transporter permease [Uniprot Acc. Q8Y799];	-1.03	-0.84
lmo0883|lmo0883	hypothetical protein [Uniprot Acc. Q8Y8L4];	-0.84	-0.88
lmo0882|lmo0882	hypothetical protein [Uniprot Acc. Q8Y8L5];	-0.88	-0.86
lmo0096|lmo0096	EIIMant PTS permease IIAB subunit [Uniprot Acc. Q7BC72]; Lmo0096 protein [Uniprot Acc. Q8YAM2];	-1.13	-2.75
lmo0097|lmo0097	EIIMant PTS permease IIC subunit [Uniprot Acc. Q7BC71]; Lmo0097 protein [Uniprot Acc. Q8YAM1];	-1.20	-2.77

lmo0098|lmo0098	EIIMant PTS permease IID subunit [Uniprot Acc. Q7BC70]; Lmo0098 protein [Uniprot Acc. Q8YAM0];	-1.20	-2.66
lmo2801|lmo2801	Putative N-acetylmannosamine-6-phosphate 2-epimerase [Uniprot Acc. Q8Y3N4];	-1.14	-1.41
lmo0040|lmo0040	Agmatine deiminase [Uniprot Acc. Q8YAS3];	-0.41	-0.59
lmo0130|lmo0130	Cell wall protein Lmo0130 [Uniprot Acc. Q8YAJ5];	-1.29	-1.47
lmo2799|lmo2799	PTS mannitol transporter subunit IIBC [Uniprot Acc. Q8Y3N6];	-1.52	-1.15
lmo2788|bvrA	Transcription antiterminator [Uniprot Acc. Q8Y3P6];	-0.94	-0.99
lmo2773|lmo2773	transcriptional antiterminator [Uniprot Acc. Q8Y3R0];	-0.99	-1.20
lmo2772|lmo2772	PTS beta-glucoside transporter subunit IIABC [Uniprot Acc. Q8Y3R1];	-0.94	-1.07
lmo0153|lmo0153	zinc ABC transporter substrate-binding protein [Uniprot Acc. Q8YAH3];	-2.37	-1.91
lmo0154|lmo0154	zinc ABC transporter ATP-binding protein [Uniprot Acc. Q8YAH2];	-2.72	-1.74
lmo0686|motB	flagellar motor rotation MotB [Uniprot Acc. Q7AP81];	-2.78	-2.51
lmo0179|lmo0179	sugar ABC transporter permease [Uniprot Acc. Q92F88];	-1.18	-1.41
lmo0180|lmo0180	sugar ABC transporter permease [Uniprot Acc. Q8YAF0];	-1.81	-1.47
lmo0181|lmo0181	sugar ABC transporter substrate-binding protein	-1.33	-1.14
lmo0182|lmo0182	alpha-glucosidase [Uniprot Acc. Q8YAE8];	-1.03	-1.01
lmo2690|lmo2690	TetR family transcriptional regulator [Uniprot Acc. Q8Y3Y9];	-1.12	-0.88
lmo2689|lmo2689	magnesium-translocating P-type ATPase [Uniprot Acc. Q8Y3Z0];	-1.81	-0.83
lmo2685|lmo2685	PTS cellbiose transporter subunit IIA [Uniprot Acc. Q927F6];	-1.10	-1.43
lmo2684|lmo2684	Permease IIC component [Uniprot Acc. Q8Y3Z4];	-1.21	-0.86
lmo0675|lmo0675	hypothetical protein [Uniprot Acc. Q8Y959];	-1.47	-1.84
lmo2683|lmo2683	PTS cellbiose transporter subunit IIB [Uniprot Acc. Q8Y3Z5];	-1.64	-2.15
lmo0689|lmo0689	chemotaxis protein CheV [Uniprot Acc. Q8Y948];	-2.48	-2.39
lmo0699|fliM	flagellar motor switch protein FliM [Uniprot Acc. Q8Y942];	-1.59	-1.79
lmo2636|lmo2636	FAD:protein FMN transferase [Uniprot Acc. Q8Y437];	-0.79	-0.59

lmo2635|lmo2635	1,4-dihydroxy-2-naphthoate octaprenyltransferase [Uniprot Acc. Q8Y438];	-0.56	-0.60
lmo0717|lmo0717	transglycosylase	-1.51	-1.65
lmo2569|lmo2569	peptide ABC transporter substrate-binding protein [Uniprot Acc. Q8Y486];	-1.23	-1.55
lmo0257|lmo0257	hypothetical protein [Uniprot Acc. Q8YA97];	-0.76	-0.83
lmo2469|lmo2469	amino acid transporter [Uniprot Acc. Q8Y4H3];	-1.11	-0.72
lmo0278|lmo0278	sugar ABC transporter ATP-binding protein [Uniprot Acc. Q8YA81];	-1.65	-2.47
lmo2416|lmo2416	hypothetical protein	-1.41	-1.18
lmo0361|lmo0361	Sec-independent protein translocase protein TatC [Uniprot Acc. Q8YA05];	-1.06	-0.80
lmo0365|lmo0365	hypothetical protein [Uniprot Acc. Q8YA02];	-2.22	-1.71
lmo0366|lmo0366	hypothetical protein	-2.21	-1.74
lmo0367|lmo0367	Deferrochelatase/peroxidase [Uniprot Acc. Q8YA00];	-1.83	-1.55
lmo2001|lmo2001	PTS mannose transporter subunit IIC [Uniprot Acc. Q8Y5Q5];	-1.78	-2.41
lmo1955|lmo1955	Tyrosine recombinase XerD [Uniprot Acc. Q8Y5V0];	-0.59	-0.60
lmo1956|fur	Fur family transcriptional regulator [Uniprot Acc. Q8Y5U9];	-0.71	-0.68
lmo0597a|lmo0597a	hypothetical protein	-1.39	-1.11
lmo1596a|lmo1596a	hypothetical protein	-1.40	-1.41
lmos23|lmos23	miscRNA	-1.44	-1.65
lmo2630|rplW	50S ribosomal protein L23 [Uniprot Acc. Q8Y441];	-0.58	NS[C]
lmo2379|lmo2379	monovalent cation/H+ antiporter subunit B [Uniprot Acc. Q8Y4Q5];	-0.89	NS
lmo1949|lmo1949	Pseudouridine synthase [Uniprot Acc. Q8Y5V6];	-0.68	NS
lmo2104|lmo2104	hypothetical protein [Uniprot Acc. Q929R6];	-0.71	NS
lmo2354|lmo2354	hypothetical protein [Uniprot Acc. Q8Y4S8];	-0.63	NS
lmo1590|argJ	Arginine biosynthesis bifunctional protein ArgJ [Uniprot Acc. Q8Y6U2];	-1.31	NS
lmo2336|fruB	Tagatose-6-phosphate kinase [Uniprot Acc. Q8Y4U5];	NS	-0.76
lmo2335|fruA	PTS fructose transporter subunit IIABC [Uniprot Acc. Q8Y4U6];	NS	-0.78
lmo2250|arpJ	amino acid ABC transporter permease [Uniprot Acc. Q8Y527];	-1.21	NS
lmo0867|lmo0867	hypothetical protein [Uniprot Acc. Q8Y8M9];	-0.66	NS
lmo1588|argD	Acetylornithine aminotransferase [Uniprot Acc. Q8Y6U4];	-1.08	NS
lmo2192|lmo2192	peptide ABC transporter ATP-binding protein [Uniprot Acc. Q8Y581];	-0.54	NS

lmo2161|lmo2161	hypothetical protein	NS	-3.07
lmo0427|lmo0427	PTS fructose transporter subunit IIB [Uniprot Acc. Q8Y9U3];	-1.59	NS
lmo2151|lmo2151	hypothetical protein [Uniprot Acc. Q8Y5B5];	-1.39	NS
lmo2251|lmo2251	amino acid ABC transporter ATP-binding protein [Uniprot Acc. Q8Y526];	-1.13	NS
lmo2149|lmo2149	hypothetical protein	-0.59	NS
lmo1999|lmo1999	hypothetical protein [Uniprot Acc. Q8Y5Q7];	-2.18	NS
lmo0593|lmo0593	formate transporter [Uniprot Acc. Q8Y9D7];	-0.87	NS
lmo1958|fhuB	ferrichrome ABC transporter permease [Uniprot Acc. Q8Y5U7];	-0.72	NS
lmo2378|lmo2378	monovalent cation/H+ antiporter subunit A [Uniprot Acc. Q8Y4Q6];	-0.80	NS
lmo0659|lmo0659	transcriptional regulator [Uniprot Acc. Q8Y974];	-0.91	NS
lmo1950|lmo1950	Segregation and condensation protein B [Uniprot Acc. Q8Y5V5];	-0.71	NS
lmo1266|lmo1266	hypothetical protein	-0.63	NS
lmo0605|lmo0605	hypothetical protein [Uniprot Acc. Q8Y9C7];	-0.91	NS
lmo0503|lmo0503	PTS fructose transporter subunit IIA [Uniprot Acc. Q8Y9M3];	NS	-1.97
lmo0517|lmo0517	phosphoglycerate mutase	-1.90	NS
lmo0041|lmo0041	hypothetical protein [Uniprot Acc. Q8YAS2];	-0.71	NS
lmo2330|lmo2330	hypothetical protein [Uniprot Acc. Q8Y4V0];	-1.29	NS
lmo0838|uhpT	sugar:phosphate antiporter [Uniprot Acc. Q8Y8Q8];	NS	-1.13
lmo0834|lmo0834	hypothetical protein	-1.26	NS
lmo2688|lmo2688	cell division protein FtsW [Uniprot Acc. Q8Y3Z1];	-1.48	NS
lmo0814|lmo0814	oxidoreductase [Uniprot Acc. Q8Y8T0];	-0.85	NS
lmo0806|lmo0806	transcriptional regulator [Uniprot Acc. Q8Y8T7];	-0.92	NS
lmo0798|lmo0798	lysine-specific permease [Uniprot Acc. Q8Y8U4];	-0.88	NS
lmo0546|lmo0546	NAD(P)-dependent oxidoreductase	-0.97	NS
lmo2646|lmo2646	hypothetical protein [Uniprot Acc. Q8Y429];	-2.53	NS
lmo0737|lmo0737	hypothetical protein	-1.08	NS
lmo0736|lmo0736	ribose-5-phosphate isomerase B [Uniprot Acc. Q8Y906];	-1.07	NS
lmo1756|gatC	Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit C [Uniprot Acc. P58817];	-0.53	NS
lmo0785|lmo0785	Sigma54-associated activator ManR/transcriptional regulator [Uniprot Acc. Q7BC73]; Lmo0785 protein [Uniprot Acc. Q8Y8V7];	NS	-1.28

lmo0546|lmo0546	NAD(P)-dependent oxidoreductase	NS	-1.30
lmo0768|lmo0768	sugar ABC transporter substrate-binding protein	NS	-0.97
lmo0743|lmo0743	hypothetical protein [Uniprot Acc. Q8Y8Z9];	NS	-2.27
lmo0735|lmo0735	ribulose-5-phosphate 3-epimerase [Uniprot Acc. Q8Y907];	-1.31	NS
lmo1717|lmo1717	hypothetical protein [Uniprot Acc. Q8Y6G9];	-0.63	NS
lmo1885|lmo1885	Xanthine phosphoribosyltransferase [Uniprot Acc. Q8Y617];	-0.58	NS
lmo1884|lmo1884	xanthine permease [Uniprot Acc. Q8Y618];	-0.71	NS
lmo1869|lmo1869	hypothetical protein [Uniprot Acc. Q8Y631];	-0.86	NS
lmo1851|lmo1851	carboxy-terminal processing proteinase [Uniprot Acc. Q8Y649];	-0.54	NS
lmo0573|lmo0573	hypothetical protein [Uniprot Acc. Q8Y9F5];	-0.64	NS
lmo1838|pyrB	Aspartate carbamoyltransferase [Uniprot Acc. Q8Y662];	-0.79	NS
lmo1833|pyrD	Dihydroorotate dehydrogenase B (NAD(+)), catalytic subunit [Uniprot Acc. Q8Y667];	-1.08	NS
lmo1835|carB	Carbamoyl-phosphate synthase large chain [Uniprot Acc. Q8Y665];	-0.94	NS
lmo1834|pyrDII	Dihydroorotate dehydrogenase B (NAD(+)), electron transfer subunit [Uniprot Acc. Q8Y666];	-1.06	NS
lmo1832|pyrF	Orotidine 5'-phosphate decarboxylase [Uniprot Acc. P58641];	-1.23	NS
lmo1831|pyrE	Orotate phosphoribosyltransferase [Uniprot Acc. Q8Y668];	-1.26	NS
lmo1761|lmo1761	sodium-dependent transporter [Uniprot Acc. Q8Y6C7];	-0.63	NS
lmo2355|lmo2355	multidrug resistance protein [Uniprot Acc. Q8Y4S7];	-0.60	NS
lmo2716|cydC	ABC transporter [Uniprot Acc. Q8Y3W3];	-0.61	NS
lmo1224|lmo1224	hypothetical protein [Uniprot Acc. Q8Y7P9];	-0.82	NS
lmo1173|lmo1173	two-component sensor histidine kinase	-0.83	NS
lmo1172|lmo1172	two-component response regulator [Uniprot Acc. Q92CN5];	-0.97	NS
lmo1170|lmo1170	PduX; Protein involved in propanediol utilization, and related proteins [Uniprot Acc. Q8Y7U9];	-0.71	NS
lmo1149|lmo1149	alpha-ribazole-5'-phosphatase [Uniprot Acc. Q8Y7X0];	NS	NS
lmo1406|pflB	Pyruvate formate-lyase [Uniprot Acc. Q8Y786];	-0.78	NS
lmo1445|zurR	Transcriptional regulator ZurR [Uniprot Acc. P0A3E6];	NS	-0.69
lmo0482|lmo0482	ribosomal RNA large subunit methyltransferase N [Uniprot Acc. Q8Y9P2];	-0.72	NS

lmo2760|lmo2760	ABC transporter ATP-binding protein [Uniprot Acc. Q8Y3S2];	-0.95	NS
lmo0876|lmo0876	Permease IIC component [Uniprot Acc. Q8Y8M1];	-2.72	NS
lmo1019|lmo1019	Lmo1019 protein [Uniprot Acc. Q8Y895];	-0.66	NS
lmo0961|lmo0961	protease [Uniprot Acc. Q8Y8E3];	-1.45	NS
lmo0960|lmo0960	protease [Uniprot Acc. Q8Y8E4];	-1.25	NS
lmo1407|pflC	Pyruvate formate-lyase-activating enzyme [Uniprot Acc. P0A442];	-0.62	NS
lmo1073|lmo1073	metal ABC transporter substrate-binding protein	-0.62	NS
lmo2840|lmo2840	Sucrose phosphorylase [Uniprot Acc. Q8Y3J5];	NS	-1.68
lmo1937|engA	GTP-binding protein EngA [Uniprot Acc. Q8Y5W8];	-0.53	NS
lmo2838|lmo2838	sugar ABC transporter permease [Uniprot Acc. Q8Y3J7];	-2.20	NS
lmo2837|lmo2837	sugar ABC transporter permease [Uniprot Acc. Q8Y3J8];	-1.71	NS
lmo0085|lmo0085	hypothetical protein	NS	NS
lmo2233|lmo2233	LysR family transcriptional regulator [Uniprot Acc. Q8Y543];	-0.69	NS
lmo0099|lmo0099	hypothetical protein	NS	-1.20
lmo2332|int	Putative integrase (Bacteriophage A118) [Uniprot Acc. Q8Y4U8];	-0.93	NS
lmo2536|atpI	ATP synthase subunit I [Uniprot Acc. Q8Y4B5];	-0.56	NS
lmo2787|bvrB	Beta-glucoside-specific phosphotransferase enzyme II ABC component [Uniprot Acc. Q8Y3P7];	-1.58	NS
lmo2532|atpH	ATP synthase subunit delta [Uniprot Acc. Q8Y4B9];	-0.60	NS
lmo2767|lmo2767	hypothetical protein [Uniprot Acc. Q8Y3R6];	-0.69	NS
lmo0160|lmo0160	Putative peptidoglycan bound protein (LPXTG motif) [Uniprot Acc. Q8YAG6];	NS	-0.73
lmo0176|lmo0176	Putative sugar uptake protein lmo0176 [Uniprot Acc. Q8YAF3];	NS	-0.62
lmo1446|zurM	Metal (Zinc) transport protein (ABC transporter,permease protein) [Uniprot Acc. Q8Y758];	NS	-0.71
lmo0201|plcA	1-phosphatidylinositol phosphodiesterase [Uniprot Acc. P34024];	NS	-1.12
lmo0202|hly	Listeriolysin O [Uniprot Acc. P13128];	NS	-0.69
lmo0204|actA	Actin assembly-inducing protein [Uniprot Acc. P33379];	NS	-0.87
lmo0205|plcB	Phospholipase C [Uniprot Acc. P33378];	NS	-0.79
lmo2718|cydA	cytochrome D ubiquinol oxidase subunit I [Uniprot Acc. Q927C3];	-0.65	NS

lmo2714|lmo2714	Cell wall protein/pepdidoglycan bound protein [Uniprot Acc. Q8Y3W5];	-0.70	NS
lmo2687|lmo2687	cell division protein FtsW [Uniprot Acc. Q8Y3Z2];	-1.39	NS
lmor04|lmor04	16S ribosomal RNA	NS	NS
lmo2649|ulaA	PTS system ascorbate transporter subunit IIC [Uniprot Acc. Q8Y426];	NS	-1.23
lmo2637|lmo2637	hypothetical protein [Uniprot Acc. Q8Y436];	-0.73	NS
lmo2558|ami	Autolysin, amidase [Uniprot Acc. Q8Y496];	-0.71	NS
lmo2535|atpB	ATP synthase subunit a [Uniprot Acc. Q8Y4B6];	-0.63	NS
lmo2534|atpE	ATP synthase subunit c [Uniprot Acc. Q8Y4B7];	-0.59	NS
lmo2533|atpF	ATP synthase subunit b [Uniprot Acc. Q8Y4B8];	-0.54	NS
lmo0279|lmo0279	Class III anaerobic ribonucleoside-triphosphate reductase catalytic subunit [Uniprot Acc. F0V6T8]; Lmo0279 protein [Uniprot Acc. Q8YA80];	-1.95	NS
lmo0280|lmo0280	Anaerobic ribonucleoside-triphosphate reductase-activating protein [Uniprot Acc. F0V6T9];	-1.87	NS
lmo0303|lmo0303	putaive secreted, lysin rich protein	-0.70	NS
lmo2384|lmo2384	monovalent cation/H+ antiporter subunit G [Uniprot Acc. Q8Y4Q1];	-0.73	NS
lmo0349|lmo0349	hypothetical protein [Uniprot Acc. Q8YA17];	-2.63	NS
lmo0362|lmo0362	Sec-independent protein translocase protein TatA [Uniprot Acc. Q8YA04];	-0.87	NS
lmo0385|lmo0385	5-dehydro-2-deoxygluconokinase [Uniprot Acc. Q8Y9Y2];	-1.19	NS
lmo0421|lmo0421	rod shape-determining protein RodA [Uniprot Acc. Q8Y9U9];	NS	-0.77
lmo0391|lmo0391	hypothetical protein	-0.63	NS
lmo0403|lmo0403	hypothetical protein [Uniprot Acc. Q8Y9W6];	-0.60	NS
lmo1585|lmo1585	peptidase [Uniprot Acc. Q8Y6U6];	-0.88	NS
lmo0412|lmo0412	hypothetical protein [Uniprot Acc. Q8Y9V8];	-1.04	NS
lmo0421|lmo0421	rod shape-determining protein RodA [Uniprot Acc. Q8Y9U9];	-0.72	NS
lmo0423|lmo0423	RNA polymerase factor sigma C [Uniprot Acc. Q8Y9U7];	-0.85	NS
lmo0426|lmo0426	PTS fructose transporter subunit IIA [Uniprot Acc. Q8Y9U4];	-0.99	NS
lmo2839|lmo2839	sugar ABC transporter substrate-binding protein	-1.60	NS
lmo1757|lmo1757	hypothetical protein	-0.60	NS
lmo2105|lmo2105	Ferrous iron transport protein B [Uniprot Acc. Q8Y5F9];	-0.96	NS
lmo2050|lmo2050	excinuclease ABC subunit A [Uniprot Acc. Q8Y5K9];	-0.78	NS

lmo2040|ftsL	Cell division protein FtsL [Uniprot Acc. Q929X7];	-0.54	NS
lmo2380|lmo2380	monovalent cation/H+ antiporter subunit C [Uniprot Acc. Q8Y4Q4];	-0.77	NS
lmo1998|lmo1998	Fructosamine deglycase [Uniprot Acc. Q8Y5Q8];	-1.32	NS
lmo1951|scpA	Segregation and condensation protein A [Uniprot Acc. Q8Y5V4];	-0.74	NS
lmo1953|pnp	Purine nucleoside phosphorylase [Uniprot Acc. Q8Y5V2];	NS	-0.57
lmo1954|drm	Phosphopentomutase [Uniprot Acc. Q8Y5V1];	NS	-0.61
lmo1942|recS	ATP-dependent DNA helicase [Uniprot Acc. Q8Y5W3];	-0.77	NS
lmo1957|fhuG	ferrichrome ABC transporter permease [Uniprot Acc. Q8Y5U8];	-0.78	NS
lmot58|lmot58	tRNA	-0.81	NS
lmo2104a|lmo2104a	hypothetical protein	-0.85	NS
lmo2689a|lmo2689a	hypothetical protein	-0.75	NS
lmos12|lmos12	miscRNA	-0.60	NS

Table A-6 KEGG pathway analysis for DEGs of *Listeria monocytogenes* N1-227 during organic acid habituation compared to pH control.

No.	Pathway	DEGs count	Gene symbol/Description
	Metabolic		
	Carbohydrate metabolism		
1	Glycolysis / Gluconeogenesis (lmo00010)	4	lmo1570 pykA; pyruvate kinase
			lmo2720 acetate-CoA ligase
			lmo0536 6-phospho-beta-glucosidase
			lmo0574 beta-glucosidase
2	Pentose phosphate pathway (lmo00030)	8	lmo1978 glucose-6-phosphate 1-dehydrogenase
			lmo0558 hypothetical protein
			lmo1376 6-phosphogluconate dehydrogenase
			lmo2743 translaldolase
			lmo0975 ribose-5-phosphate isomerase A
			lmo1954 drm; phosphopentomutase
			lmo0199 prs; ribose-phosphate pyrophosphokinase
			lmo2712 gluconate kinase
3	Fructose and mannose metabolism (lmo00051)	6	lmo2336 fruB; fructose-1-phosphate kinase
			lmo2335 fruA; PTS fructose transporter subunit IIABC
			lmo0096 PTS mannose transporter subunit IIAB

			lmo0097 PTS mannose transporter subunit IIC
			lmo0098 PTS mannose transporter subunit IID
			lmo2799 PTS mannitol transporter subunit IIBC
4	Galactose metabolism (lmo00052)	3	lmo2665 PTS galacticol transporter subunit IIC
			lmo0539 tagatose 1
			lmo0183 alpha-glucosidase
5	Starch and sucrose metabolism (lmo00500)	12	lmo0183 alpha-glucosidase
			lmo0372 beta-glucosidase
			lmo2685 PTS cellbiose transporter subunit IIA
			lmo1095 PTS cellbiose transporter subunit IIB
			lmo2683 PTS cellbiose transporter subunit IIB
			lmo2708 PTS cellbiose transporter subunit IIC
			lmo0373 PTS beta-glucoside transporter subunit IIC
			lmo0536 6-phospho-beta-glucosidase
			lmo0574 beta-glucosidase
			lmo2831 phosphoglucomutase
			lmo1255 PTS trehalose transporter subunit IIBC
			lmo1254 alpha,alpha-phosphotrehalase
6	Amino sugar and nucleotide sugar metabolism (lmo00520)	9	lmo0105 chitinase B
			lmo0198 glmU; bifunctional N-acetylglucosamine-1-phosphate uridyltransferase/glucosamine-1-phosphate acetyltransferase

			lmo2801 N-acetylmannosamine-6-phosphate 2-epimerase
			lmo0956 N-acetylglucosamine-6P-phosphate deacetylase
			lmo0957 glucosamine-6-phosphate isomerase
			lmo0727 glucosamine--fructose-6-phosphate aminotransferase
			lmo0096 PTS mannose transporter subunit IIAB
			lmo0097 PTS mannose transporter subunit IIC
			lmo0098 PTS mannose transporter subunit IID
7	Pyruvate metabolism (lmo00620)	9	lmo2720 acetate-CoA ligase
			lmo1570 pykA; pyruvate kinase
			lmo1572 accA; acetyl-CoA carboxylase carboxyltransferase subunit alpha
			lmo1381 acylphosphatase
			lmo0722 pyruvate oxidase
			lmo0823 oxidoreductase
			lmo2168 glyoxalase
			lmo2167 hypothetical protein
			lmo1414 acetyl-CoA:acetyltransferase
8	Glyoxylate and dicarboxylate metabolism (lmo00630)	4	lmo2720 acetate-CoA ligase
			lmo1414 acetyl-CoA:acetyltransferase
			lmo2785 kat; catalase
			lmo2832 hypothetical protein

9	Propanoate metabolism (lmo00640)	4	lmo2720 acetate-CoA ligase
			lmo1572 accA; acetyl-CoA carboxylase carboxyltransferase subunit alpha
			lmo1414 acetyl-CoA:acetyltransferase
			lmo0823 oxidoreductase
10	Butanoate metabolism (lmo00650)	5	lmo1414 acetyl-CoA:acetyltransferase
			lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase
			lmo0913 succinate semialdehyde dehydrogenase
			lmo1984 ilvB; acetolactate synthase
11	C5-Branched dibasic acid metabolism (lmo00660)	1	lmo1984 ilvB; acetolactate synthase
	Energy metabolism		
12	Oxidative phosphorylation (lmo00190)	3	lmo2389 NADH dehydrogenase
			lmo2638 NADH dehydrogenase
			lmo2057 ctaB; protoheme IX farnesyltransferase
13	Methane metabolism (lmo00680)	1	lmo2720 acetate-CoA ligase
14	Nitrogen metabolism (lmo00910)	1	lmo0560 glutamate dehydrogenase
15	Sulfur metabolism (lmo00920)	1	lmo0223 cysK; cysteine synthase
	Lipid metabolism		
16	Fatty acid biosynthesis (lmo00061)	4	lmo1572 accA; acetyl-CoA carboxylase carboxyltransferase subunit alpha

			lmo2815 fabG; 3-ketoacyl-ACP reductase
			lmo2524 fabZ; (3R)-hydroxymyristoyl-ACP dehydratase
			lmo1688 enoyl-ACP reductase
17	Fatty acid degradation (lmo00071)	1	lmo1414 acetyl-CoA:acetyltransferase
18	Synthesis and degradation of ketone bodies (lmo00072)	1	lmo1414 acetyl-CoA:acetyltransferase
19	Secondary bile acid biosynthesis (lmo00121)	1	lmo2067 bile acid hydrolase
20	Glycerolipid metabolism (lmo00561)	4	lmo2832 hypothetical protein
			lmo2695 dihydroxyacetone kinase subunit DhaK
			lmo2696 dihydroxyacetone kinase
			lmo2697 PTS mannose transporter subunit IIA
21	Glycerophospholipid metabolism (lmo00564)	3	lmo1936 gpsA; NAD(P)H-dependent glycerol-3-phosphate dehydrogenase
			lmo1293 glpD; glycerol-3-phosphate dehydrogenase
			lmo0616 glycerophosphoryl diester phosphodiesterase
22	Arachidonic acid metabolism (lmo00590)	1	lmo0983 glutathione peroxidase
	Nucleotide metabolism		
23	Purine metabolism (lmo00230)	13	lmo1954 drm; phosphopentomutase
			lmo0199 prs; ribose-phosphate pyrophosphokinase
			lmo1775 purE; phosphoribosylaminoimidazole carboxylase catalytic subunit

			lmo1765 purH; bifunctional phosphoribosylaminoimidazolecarboxamide formyltransferase/IMP cyclohydrolase
			lmo1953 pnp; purine nucleoside phosphorylase
			lmo1856 deoD; purine nucleoside phosphorylase
			lmo1239 nucleoside-triphosphatase
			lmo1096 guaA; GMP synthase
			lmo1570 pykA; pyruvate kinase
			lmo2155 ribonucleotide-diphosphate reductase subunit alpha
			lmo2154 nrdF; ribonucleotide-diphosphate reductase subunit beta
			lmo0279 anaerobic ribonucleoside triphosphate reductase
			lmo0055 purA; adenylosuccinate synthetase
24	Pyrimidine metabolism (lmo00240)	15	lmo1835 carB; carbamoyl-phosphate synthetase
			lmo1833 pyrD; dihydroorotate dehydrogenase
			lmo1834 pyrDII; dihydroorotate dehydrogenase electron transfer subunit
			lmo1831 pyrE; orotate phosphoribosyltransferase
			lmo1832 pyrF; orotidine 5'-phosphate decarboxylase
			lmo1939 cmk; cytidylate kinase
			lmo2538 upp; uracil phosphoribosyltransferase
			lmo1993 pdp; pyrimidine-nucleoside phosphorylase

			lmo0279 anaerobic ribonucleoside triphosphate reductase
			lmo2155 ribonucleotide-diphosphate reductase subunit alpha
			lmo2154 nrdF; ribonucleotide-diphosphate reductase subunit beta
			lmo1953 pnp; purine nucleoside phosphorylase
			lmo1856 deoD; purine nucleoside phosphorylase
			lmo2544 thymidine kinase
			lmo2340 hypothetical protein
	Amino acid metabolism		
25	Alanine, aspartate and glutamate metabolism (lmo00250)	8	lmo1940 asparaginase
			lmo0055 purA; adenylosuccinate synthetase
			lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase
			lmo0913 succinate semialdehyde dehydrogenase
			lmo0560 glutamate dehydrogenase
			lmo1835 carB; carbamoyl-phosphate synthetase
			lmo0727 glucosamine--fructose-6-phosphate aminotransferase
26	Glycine, serine and threonine metabolism (lmo00260)	6	lmo2547 hom; homoserine dehydrogenase
			lmo2545 thrB; homoserine kinase
			lmo2546 thrC; threonine synthase

			lmo2832 hypothetical protein
			lmo1627 trpA; tryptophan synthase subunit alpha
			lmo1628 trpB; tryptophan synthase subunit beta
27	Cysteine and methionine metabolism (lmo00270)	3	lmo0223 cysK; cysteine synthase
			lmo2547 hom; homoserine dehydrogenase
			lmo2770 bifunctional glutamate--cysteine ligase/glutathione synthetase
28	Valine, leucine and isoleucine degradation (lmo00280)	1	lmo1414 acetyl-CoA:acetyltransferase
29	Valine, leucine and isoleucine biosynthesis (lmo00290)	1	lmo1984 ilvB; acetolactate synthase
30	Lysine biosynthesis (lmo00300)	6	lmo2547 hom; homoserine dehydrogenase
			lmo1588 argD; acetylornithine aminotransferase
			lmo0265 succinyl-diaminopimelate desuccinylase
			lmo1952 lysA; diaminopimelate decarboxylase
			lmo1012 N-acyl-L-amino acid amidohydrolase
			lmo0856 murF; UDP-N-acetylmuramoylalanyl-D-glutamyl-2,6-diamino pimelate-D-alanyl-D-alanyl ligase
31	Lysine degradation (lmo00310)	2	lmo1414 acetyl-CoA:acetyltransferase
			lmo0913 succinate semialdehyde dehydrogenase
32	Arginine biosynthesis (lmo00220)	2	lmo0560 glutamate dehydrogenase

			lmo1588 argD; acetylornithine aminotransferase
33	Tyrosine metabolism (lmo00350)	1	lmo0913 succinate semialdehyde dehydrogenase
34	Tryptophan metabolism (lmo00380)	2	lmo1414 acetyl-CoA:acetyltransferase
			lmo2785 kat; catalase
35	Phenylalanine, tyrosine and tryptophan biosynthesis (lmo00400)	2	lmo1627 trpA; tryptophan synthase subunit alpha
			lmo1628 trpB; tryptophan synthase subunit beta
	Metabolism of other amino acids		
36	beta-Alanine metabolism (lmo00410)	4	lmo1900 panD; aspartate alpha-decarboxylase
			lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase
			lmo1901 panC; pantoate--beta-alanine ligase
37	Taurine and hypotaurine metabolism (lmo00430)	2	lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase
38	Selenocompound metabolism (lmo00450)	2	lmo2478 trxB; thioredoxin reductase
			lmo0177 metS; methionyl-tRNA synthetase
39	Cyanoamino acid metabolism (lmo00460)	2	lmo0372 beta-glucosidase
			lmo1940 asparaginase
40	D-Alanine metabolism (lmo00473)	2	lmo0974 dltA; D-alanine--poly(phosphoribitol) ligase subunit 1
			lmo0972 dltC; D-alanine--poly(phosphoribitol) ligase subunit 2

41	Glutathione metabolism (lmo00480)	6	lmo2770 bifunctional glutamate--cysteine ligase/glutathione synthetase
			lmo0906 glutathione reductase
			lmo1433 glutathione reductase
			lmo1376 6-phosphogluconate dehydrogenase
			lmo1978 glucose-6-phosphate 1-dehydrogenase
			lmo0983 glutathione peroxidase
	Glycan biosynthesis and metabolism		
42	Peptidoglycan biosynthesis (lmo00550)	2	lmo0856 murF; UDP-N-acetylmuramoylalanyl-D-glutamyl-2,6-diamino pimelate-D-alanyl-D-alanyl ligase
			lmo2229 penicillin-binding protein
	Metabolism of cofactors and vitamins		
43	Thiamine metabolism (lmo00730)	3	lmo1593 iron-sulfur cofactor synthesis protein NifS
			lmo1592 thiamine biosynthesis protein ThiI
			lmo1365 tktB; 1-deoxy-D-xylulose-5-phosphate synthase
44	Riboflavin metabolism (lmo00740)	2	lmo2263 hypothetical protein
			lmo1329 ribC; riboflavin kinase
45	Vitamin B6 metabolism (lmo00750)	2	lmo0662 thiD; phosphomethylpyrimidine kinase
			lmo2546 thrC; threonine synthase
46	Nicotinate and nicotinamide metabolism (lmo00760)	5	lmo1953 pnp; purine nucleoside phosphorylase
			lmo1856 deoD; purine nucleoside phosphorylase

			lmo1093 nadE; NAD synthetase
			lmo2571 nicotinamidase
			lmo0913 succinate semialdehyde dehydrogenase
47	Pantothenate and CoA biosynthesis (lmo00770)	4	lmo1984 ilvB; acetolactate synthase
			lmo1902 panB; 3-methyl-2-oxobutanoate hydroxymethyltransferase
			lmo1901 panC; pantoate--beta-alanine ligase
			lmo1900 panD; aspartate alpha-decarboxylase
48	Biotin metabolism (lmo00780)	2	lmo2815 fabG; 3-ketoacyl-ACP reductase
			lmo2524 fabZ; (3R)-hydroxymyristoyl-ACP dehydratase
49	Lipoic acid metabolism (lmo00785)	1	lmo0931 lipoate protein ligase A
50	Folate biosynthesis (lmo00790)	4	lmo0225 folA; dihydroneopterin aldolase
			lmo0226 folK; 7,8-dihydro-6-hydroxymethylpterin pyrophosphokinase
			lmo0224 sul; dihydropteroate synthases
			lmo1038 hypothetical protein
51	One carbon pool by folate (lmo00670)	2	lmo1877 formyl-tetrahydrofolate synthetase
			lmo1765 purH; bifunctional phosphoribosylaminoimidazolecarboxamide formyltransferase/IMP cyclohydrolase
52	Porphyrin and chlorophyll metabolism (lmo00860)	11	lmo1557 hemA; glutamyl-tRNA reductase

			lmo1553 hemL; glutamate-1-semialdehyde aminotransferase
			lmo1554 hemB; delta-aminolevulinic acid dehydratase
			lmo1556 hemC; porphobilinogen deaminase
			lmo1555 hemD; uroporphyrinogen-III synthase
			lmo2212 hemE; uroporphyrinogen decarboxylase
			lmo2211 hemH; ferrochelatase
			lmo2113 heme peroxidase
			lmo2057 ctaB; protoheme IX farnesyltransferase
			lmo1209 hypothetical protein
			lmo1208 cbiP; cobyric acid synthase CbiP
53	Ubiquinone and other terpenoid-quinone biosynthesis (lmo00130)	5	lmo1676 menF; menaquinone-specific isochorismate synthase
			lmo1675 menD; 2-succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylate synthase
			lmo1674 prolyl aminopetidase
			lmo1672 menE; O-succinylbenzoic acid--CoA ligase
			lmo1673 menB; naphthoate synthase
	Metabolism of terpenoids and polyketides		
54	Terpenoid backbone biosynthesis (lmo00900)	4	lmo1365 tktB; 1-deoxy-D-xylulose-5-phosphate synthase
			lmo1414 acetyl-CoA:acetyltransferase
			lmo0825 3-hydroxy-3-methylglutaryl-CoA reductase
			lmo1383 isopentenyl pyrophosphate isomerase

55	Biosynthesis of siderophore group nonribosomal peptides (lmo01053)	1	lmo1676 menF; menaquinone-specific isochorismate synthase
	Biosynthesis of other secondary metabolites		
56	Prodigiosin biosynthesis (lmo00333)	1	lmo2815 fabG; 3-ketoacyl-ACP reductase
	Xenobiotics biodegradation and metabolism		
57	Benzoate degradation (lmo00362)	1	lmo1414 acetyl-CoA:acetyltransferase
58	Aminobenzoate degradation (lmo00627)	2	lmo1381 acylphosphatase lmo2401 hypothetical protein
	Genetic Information Processing		
	Transcription		
59	RNA polymerase (lmo03020)	1	lmo2606 rpoA; DNA-directed RNA polymerase subunit alpha
	Translation		
60	Ribosome (lmo03010)	11	lmo2615 rpsE; 30S ribosomal protein S5 lmo1797 rpsP; 30S ribosomal protein S16 lmo0249 rplA; 50S ribosomal protein L1 lmo0251 rplL; 50S ribosomal protein L7/L12 lmo0250 rplJ; 50S ribosomal protein L10 lmo0248 rplK; 50S ribosomal protein L11 lmo2613 rplO; 50S ribosomal protein L15 lmo2616 rplR; 50S ribosomal protein L18 lmo0211 ctc; 50S ribosomal protein L25

			lmo2614 rpmD; 50S ribosomal protein L30
			lmo0486 rpmF; 50S ribosomal protein L32
61	Aminoacyl-tRNA biosynthesis (lmo00970)	6	lmo1755 gatA; aspartyl/glutamyl-tRNA amidotransferase subunit A
			lmo1754 gatB; aspartyl/glutamyl-tRNA amidotransferase subunit B
			lmo1504 alaS; alanyl-tRNA synthetase
			lmo2747 serS; seryl-tRNA synthetase
			lmo0177 metS; methionyl-tRNA synthetase
			lmo2198 trpS; tryptophanyl-tRNA synthetase
	Folding, sorting and degradation		
62	Protein export (lmo03060)	6	lmo2612 secY; preprotein translocase subunit SecY
			lmo1529 hypothetical protein
			lmo2854 sporulation protein SpoJ
			lmo1269 type I signal peptidase
			lmo1270 type I signal peptidase
			lmo1844 lspA; lipoprotein signal peptidase
63	Sulfur relay system (lmo04122)	2	lmo1593 iron-sulfur cofactor synthesis protein NifS
			lmo1592 thiamine biosynthesis protein ThiI
64	RNA degradation (lmo03018)	2	lmo0866 ATP-dependent RNA helicase
			lmo1942 recS; ATP-dependent DNA helicase
	Replication and repair		

65	DNA replication (lmo03030)	1	lmo0162 DNA polymerase III subunit delta'
66	Base excision repair (lmo03410)	2	lmo1689 A/G-specific adenine glycosylase
			lmo1782 3'-exo-deoxyribonuclease
67	Nucleotide excision repair (lmo03420)	1	lmo1234 uvrC; excinuclease ABC subunit C
68	Mismatch repair (lmo03430)	1	lmo0162 DNA polymerase III subunit delta'
69	Homologous recombination (lmo03440)	1	lmo0162 DNA polymerase III subunit delta'
	Environmental Information Processing		
	Membrane transport		
70	ABC transporters (lmo02010)	35	lmo1040 molybdenum ABC transporter permease
			lmo1039 ABC transporter ATP-binding protein
			lmo0810 spermidine/putrescine ABC transporter substrate-binding protein
			lmo0809 spermidine/putrescine ABC transporter permease
			lmo0808 spermidine/putrescine ABC transporter permease
			lmo0807 spermidine/putrescine ABC transporter ATP-binding protein
			lmo1016 gbuC; glycine/betaine ABC transporter substrate-binding protein
			lmo1015 gbuB; glycine/betaine ABC transporter permease
			lmo1014 gbuA; glycine/betaine ABC transporter ATP-binding protein
			lmo1426 opuCC; glycine/betaine ABC transporter substrate-binding protein

	lmo1425 opuCD; glycine/betaine ABC transporter permease
	lmo0278 sugar ABC transporter ATP-binding protein
	lmo1388 tcsA; CD4+ T cell-stimulating antigen, lipoprotein
	lmo1390 ABC transporter permease
	lmo1391 sugar ABC transporter permease
	lmo1389 sugar ABC transporter ATP-binding protein
	lmo2495 phosphate ABC transporter ATP-binding protein
	lmo0847 glutamine ABC transporter
	lmo0848 amino acid ABC transporter ATP-binding protein
	lmo2251 amino acid ABC transporter ATP-binding protein
	lmo2196 hypothetical protein
	lmo2195 peptide ABC transporter permease
	lmo2194 peptide ABC transporter permease
	lmo2193 peptide ABC transporter ATP-binding protein
	lmo2192 peptide ABC transporter ATP-binding protein
	lmo1847 metal ABC transporter
	lmo0153 zinc ABC transporter substrate-binding protein
	lmo1671 ABC transporter
	lmo1446 zurM; metal (zinc) transport protein (ABC transporter, permease)
	lmo1447 zurA; metal (zinc) transport protein (ABC transporter, ATP-binding protein)

			lmo2506 ftsX; cell division protein FtsX
			lmo2507 ftsE; cell division protein FtsE
			lmo1652 ABC transporter ATP-binding protein
			lmo1651 ABC transporter ATP-binding protein
			lmo2752 ABC transporter ATP-binding protein
71	Phosphotransferase system (PTS) (lmo02060)	13	lmo0027 PTS beta-glucoside transporter subunit IIABC
			lmo1255 PTS trehalose transporter subunit IIBC
			lmo2799 PTS mannitol transporter subunit IIBC
			lmo2685 PTS cellbiose transporter subunit IIA
			lmo1095 PTS cellbiose transporter subunit IIB
			lmo2683 PTS cellbiose transporter subunit IIB
			lmo2708 PTS cellbiose transporter subunit IIC
			lmo0373 PTS beta-glucoside transporter subunit IIC
			lmo0096 PTS mannose transporter subunit IIAB
			lmo0097 PTS mannose transporter subunit IIC
			lmo0098 PTS mannose transporter subunit IID
			lmo2665 PTS galacticol transporter subunit IIC
			lmo2335 fruA; PTS fructose transporter subunit IIABC
72	Bacterial secretion system (lmo03070)	3	lmo2612 secY; preprotein translocase subunit SecY
			lmo1529 hypothetical protein
			lmo2854 sporulation protein SpoJ

	Signal transduction		
73	Two-component system (lmo02020)	15	lmo0292 heat-shock protein htrA serine protease
			lmo0690 flaA; flagellin
			lmo0685 flagellar motor protein MotA
			lmo0288 two-component sensor histidine kinase
			lmo0974 dltA; D-alanine--poly(phosphoribitol) ligase subunit 1
			lmo0973 dltB; DltB protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid
			lmo0972 dltC; D-alanine--poly(phosphoribitol) ligase subunit 2
			lmo0971 dltD; DltD protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid
			lmo0051 response regulator
			lmo2515 two-component response regulator DegU
			lmo1414 acetyl-CoA:acetyltransferase
			lmo0683 chemotaxis protein CheR
			lmo0692 cheA; two-component sensor histidine kinase CheA
			lmo0691 cheY; chemotaxis response regulator CheY
			lmo0689 chemotaxis protein CheV
	Cellular Processes		
	Cellular community - prokaryotes		
74	Quorum sensing (lmo02024)	20	lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase

			lmo2362 amino acid antiporter
			lmo0051 response regulator
			lmo2196 hypothetical protein
			lmo2195 peptide ABC transporter permease
			lmo2194 peptide ABC transporter permease
			lmo2193 peptide ABC transporter ATP-binding protein
			lmo2192 peptide ABC transporter ATP-binding protein
			lmo2569 peptide ABC transporter substrate-binding protein
			lmo0135 peptide ABC transporter substrate-binding protein
			lmo0152 peptide ABC transporter substrate-binding protein
			lmo0136 peptide ABC transporter permease
			lmo0137 peptide ABC transporter permease
			lmo0539 tagatose 1
			lmo2854 sporulation protein SpoJ
			lmo2270 comK'; competence protein ComK
			lmo2612 secY; preprotein translocase subunit SecY
			lmo1529 hypothetical protein
			lmo2515 two-component response regulator DegU
	Cell motility		
75	Bacterial chemotaxis (lmo02030)	11	lmo0692 cheA; two-component sensor histidine kinase CheA
			lmo0691 cheY; chemotaxis response regulator CheY

			lmo0689 chemotaxis protein CheV
			lmo0683 chemotaxis protein CheR
			lmo0714 fliG; flagellar motor switch protein FliG
			lmo0699 fliM; flagellar motor switch protein FliM
			lmo0693 flagellar motor switch protein FliY
			lmo0700 flagellar motor switch protein FliY
			lmo0698 flagellar motor switch protein
			lmo0685 flagellar motor protein MotA
			lmo0686 motB; flagellar motor rotation MotB
76	Flagellar assembly (lmo02040)	26	lmo0690 flaA; flagellin
			lmo0707 fliD; flagellar capping protein FliD
			lmo0706 flgL; flagellar hook-associated protein FlgL
			lmo0705 flgK; flagellar hook-associated protein FlgK
			lmo0696 flgD; flagellar basal body rod modification protein
			lmo0697 flgE; flagellar hook protein FlgE
			lmo0682 flgG; flagellar basal body rod protein FlgG
			lmo0710 flgB; flagellar basal-body rod protein FlgB
			lmo0711 flgC; flagellar basal body rod protein FlgC
			lmo0712 fliE; flagellar hook-basal body protein FliE
			lmo0713 fliF; flagellar MS-ring protein FliF
			lmo0714 fliG; flagellar motor switch protein FliG

			lmo0699 fliM; flagellar motor switch protein FliM
			lmo0693 flagellar motor switch protein FliY
			lmo0700 flagellar motor switch protein FliY
			lmo0698 flagellar motor switch protein
			lmo0680 flhA; flagellar biosynthesis protein FlhA
			lmo0679 flhB; flagellar biosynthesis protein FlhB
			lmo0715 fliH; flagellar assembly protein H
			lmo0716 fliI; flagellum-specific ATP synthase
			lmo0676 fliP; flagellar biosynthesis protein FliP
			lmo0677 fliQ; flagellar biosynthesis protein FliQ
			lmo0678 fliR; flagellar biosynthesis protein FliR
			lmo0685 flagellar motor protein MotA
			lmo0686 motB; flagellar motor rotation MotB
			lmo0708 flagellar protein
	Organismal Systems		
	Immune system		
77	NOD-like receptor signaling pathway (lmo04621)	3	lmo1233 trxA; thioredoxin
			lmo2152 thioredoxin
			lmo0690 flaA; flagellin
	Human Diseases		

	Infectious disease: bacterial		
78	Bacterial invasion of epithelial cells (lmo05100)	2	lmo0433 inlA; internalin A
			lmo0434 inlB; internalin B
	Drug resistance: antimicrobial		
79	beta-Lactam resistance (lmo01501)	6	lmo2196 hypothetical protein
			lmo2195 peptide ABC transporter permease
			lmo2194 peptide ABC transporter permease
			lmo2193 peptide ABC transporter ATP-binding protein
			lmo2192 peptide ABC transporter ATP-binding protein
			lmo2229 penicillin-binding protein
80	Vancomycin resistance (lmo01502)	1	lmo0856 murF; UDP-N-acetylmuramoylalanyl-D-glutamyl-2,6-diamino
81	Cationic antimicrobial peptide (CAMP) resistance (lmo01503)	5	lmo0292 heat-shock protein htrA serine protease
			lmo0974 dltA; D-alanine--poly(phosphoribitol) ligase subunit 1
			lmo0973 dltB; DltB protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid
			lmo0972 dltC; D-alanine--poly(phosphoribitol) ligase subunit 2
			lmo0971 dltD; DltD protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid

Table A-7 KEGG pathway analysis for DEGs of *Listeria monocytogenes* R2-499 during organic acid habituation compared to pH control.

No.	Pathway	DEGs count	Gene symbol/Description
	Metabolic		
	Carbohydrate metabolism		
1	Glycolysis / Gluconeogenesis (lmo00010)	3	lmo1570 pykA; pyruvate kinase
			lmo2720 acetate-CoA ligase
			lmo1017 PTS glucose transporter subunit IIA
2	Citrate cycle (TCA cycle) (lmo00020)	1	lmo1641 citB; aconitate hydratase
3	Pentose phosphate pathway (lmo00030)	2	lmo0558 hypothetical protein
			lmo1376 6-phosphogluconate dehydrogenase
4	Fructose and mannose metabolism (lmo00051)	4	lmo0096 PTS mannose transporter subunit IIAB
			lmo0097 PTS mannose transporter subunit IIC
			lmo0098 PTS mannose transporter subunit IID
			lmo2799 PTS mannitol transporter subunit IIBC
5	Galactose metabolism (lmo00052)	1	lmo0539 tagatose 1
6	Starch and sucrose metabolism (lmo00500)	6	lmo2685 PTS cellbiose transporter subunit IIA
			lmo2683 PTS cellbiose transporter subunit IIB
			lmo2684 PTS cellbiose transporter subunit IIC
			lmo1017 PTS glucose transporter subunit IIA

			lmo1255 PTS trehalose transporter subunit IIBC
			lmo1254 alpha,alpha-phosphotrehalase
7	Amino sugar and nucleotide sugar metabolism (lmo00520)	7	lmo0105 chitinase B
			lmo1017 PTS glucose transporter subunit IIA
			lmo2801 N-acetylmannosamine-6-phosphate 2-epimerase
			lmo0956 N-acetylglucosamine-6P-phosphate deacetylase
			lmo0096 PTS mannose transporter subunit IIAB
			lmo0097 PTS mannose transporter subunit IIC
			lmo0098 PTS mannose transporter subunit IID
8	Pyruvate metabolism (lmo00620)	6	lmo2720 acetate-CoA ligase
			lmo1570 pykA; pyruvate kinase
			lmo0722 pyruvate oxidase
			lmo0823 oxidoreductase
			lmo2168 glyoxalase
			lmo2167 hypothetical protein
9	Glyoxylate and dicarboxylate metabolism (lmo00630)	2	lmo2720 acetate-CoA ligase
			lmo1641 citB; aconitate hydratase
10	Propanoate metabolism (lmo00640)	2	lmo2720 acetate-CoA ligase
			lmo0823 oxidoreductase

11	Butanoate metabolism (lmo00650)	4	lmo2363 glutamate decarboxylase lmo2434 glutamate decarboxylase lmo0913 succinate semialdehyde dehydrogenase lmo1992 alpha-acetolactate decarboxylase
12	C5-Branched dibasic acid metabolism (lmo00660)	1	lmo1992 alpha-acetolactate decarboxylase
	Energy metabolism		
13	Oxidative phosphorylation (lmo00190)	1	lmo2389 NADH dehydrogenase
14	Methane metabolism (lmo00680)	1	lmo2720 acetate-CoA ligase
	Lipid metabolism		
15	Fatty acid biosynthesis (lmo00061)	2	lmo2202 3-oxoacyl-ACP synthase lmo2815 fabG; 3-ketoacyl-ACP reductase
16	Glycerolipid metabolism (lmo00561)	3	lmo2695 dihydroxyacetone kinase subunit DhaK lmo2696 dihydroxyacetone kinase lmo2697 PTS mannose transporter subunit IIA
17	Glycerophospholipid metabolism (lmo00564)	1	lmo1293 glpD; glycerol-3-phosphate dehydrogenase
18	Arachidonic acid metabolism (lmo00590)	1	lmo0983 glutathione peroxidase
	Nucleotide metabolism		
19	Purine metabolism (lmo00230)	4	lmo1570 pykA; pyruvate kinase lmo2155 ribonucleotide-diphosphate reductase subunit alpha lmo2154 nrdF; ribonucleotide-diphosphate reductase subunit beta

			lmo0802 hypothetical protein
20	Pyrimidine metabolism (lmo00240)	3	lmo1993 pdp; pyrimidine-nucleoside phosphorylase
			lmo2155 ribonucleotide-diphosphate reductase subunit alpha
			lmo2154 nrdF; ribonucleotide-diphosphate reductase subunit beta
	Amino acid metabolism		
21	Alanine, aspartate and glutamate metabolism (lmo00250)	3	lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase
			lmo0913 succinate semialdehyde dehydrogenase
22	Cysteine and methionine metabolism (lmo00270)	1	lmo2770 bifunctional glutamate--cysteine ligase/glutathione synthetase
23	Lysine degradation (lmo00310)	1	lmo0913 succinate semialdehyde dehydrogenase
24	Tyrosine metabolism (lmo00350)	1	lmo0913 succinate semialdehyde dehydrogenase
	Metabolism of other amino acids		
25	beta-Alanine metabolism (lmo00410)	4	lmo1900 panD; aspartate alpha-decarboxylase
			lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase
			lmo1901 panC; pantoate--beta-alanine ligase
26	Taurine and hypotaurine metabolism (lmo00430)	2	lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase

27	D-Alanine metabolism (lmo00473)	2	lmo0974 dltA; D-alanine--poly(phosphoribitol) ligase subunit 1
			lmo0972 dltC; D-alanine--poly(phosphoribitol) ligase subunit 2
28	Glutathione metabolism (lmo00480)	3	lmo2770 bifunctional glutamate--cysteine ligase/glutathione synthetase
			lmo1376 6-phosphogluconate dehydrogenase
			lmo0983 glutathione peroxidase
	Metabolism of cofactors and vitamins		
29	Riboflavin metabolism (lmo00740)	1	lmo2263 hypothetical protein
30	Nicotinate and nicotinamide metabolism (lmo00760)	1	lmo0913 succinate semialdehyde dehydrogenase
31	Pantothenate and CoA biosynthesis (lmo00770)	3	lmo1900 panD; aspartate alpha-decarboxylase
			lmo1902 panB; 3-methyl-2-oxobutanoate hydroxymethyltransferase
			lmo1901 panC; pantoate--beta-alanine ligase
32	Biotin metabolism (lmo00780)	1	lmo2815 fabG; 3-ketoacyl-ACP reductase
33	Porphyrin and chlorophyll metabolism (lmo00860)	8	lmo1557 hemA; glutamyl-tRNA reductase
			lmo1553 hemL; glutamate-1-semialdehyde aminotransferase
			lmo1554 hemB; delta-aminolevulinic acid dehydratase
			lmo1556 hemC; porphobilinogen deaminase
			lmo2212 hemE; uroporphyrinogen decarboxylase
			lmo2211 hemH; ferrochelatase

			lmo2113 heme peroxidase
			lmo1209 hypothetical protein
34	Ubiquinone and other terpenoid-quinone biosynthesis (lmo00130)	4	lmo1676 menF; menaquinone-specific isochorismate synthase
			lmo1675 menD; 2-succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylate synthase
			lmo1672 menE; O-succinylbenzoic acid--CoA ligase
			lmo1673 menB; naphthoate synthase
	Metabolism of terpenoids and polyketides		
35	Terpenoid backbone biosynthesis (lmo00900)	1	lmo1383 isopentenyl pyrophosphate isomerase
36	Biosynthesis of siderophore group nonribosomal peptides (lmo01053)	1	lmo1676 menF; menaquinone-specific isochorismate synthase
	Biosynthesis of other secondary metabolites		
37	Prodigiosin biosynthesis (lmo00333)	1	lmo2815 fabG; 3-ketoacyl-ACP reductase
	Genetic Information Processing		
	Translation		
38	Ribosome (lmo03010)	1	lmo0211 ctc; 50S ribosomal protein L25
	Folding, sorting and degradation		
39	Protein export (lmo03060)	1	lmo0361 membrane protein
	Replication and repair		
40	Base excision repair (lmo03410)	1	lmo1782 3'-exo-deoxyribonuclease
	Environmental Information Processing		

	Membrane transport		
41	ABC transporters (lmo02010)	20	lmo0810 spermidine/putrescine ABC transporter substrate-binding protein
			lmo0809 spermidine/putrescine ABC transporter permease
			lmo0808 spermidine/putrescine ABC transporter permease
			lmo0807 spermidine/putrescine ABC transporter ATP-binding protein
			lmo0278 sugar ABC transporter ATP-binding protein
			lmo1388 tcsA; CD4+ T cell-stimulating antigen, lipoprotein
			lmo1390 ABC transporter permease
			lmo1391 sugar ABC transporter permease
			lmo1389 sugar ABC transporter ATP-binding protein
			lmo0847 glutamine ABC transporter
			lmo0848 amino acid ABC transporter ATP-binding protein
			lmo2196 hypothetical protein
			lmo2195 peptide ABC transporter permease
			lmo2194 peptide ABC transporter permease
			lmo2193 peptide ABC transporter ATP-binding protein
			lmo0153 zinc ABC transporter substrate-binding protein
			lmo1671 ABC transporter
			lmo0154 zinc ABC transporter ATP-binding protein
			lmo1652 ABC transporter ATP-binding protein

			lmo1651 ABC transporter ATP-binding protein
42	Phosphotransferase system (PTS) (lmo02060)	13	lmo1017 PTS glucose transporter subunit IIA
			lmo0027 PTS beta-glucoside transporter subunit IIABC
			lmo2772 PTS beta-glucoside transporter subunit IIABC
			lmo1255 PTS trehalose transporter subunit IIBC
			lmo2799 PTS mannitol transporter subunit IIBC
			lmo2685 PTS cellbiose transporter subunit IIA
			lmo2683 PTS cellbiose transporter subunit IIB
			lmo2684 PTS cellbiose transporter subunit IIC
			lmo0096 PTS mannose transporter subunit IIAB
			lmo0097 PTS mannose transporter subunit IIC
			lmo0098 PTS mannose transporter subunit IID
			lmo2001 PTS mannose transporter subunit IIC
			lmo2000 PTS mannose transporter subunit IID
43	Bacterial secretion system (lmo03070)	1	lmo0361 membrane protein
	Signal transduction		
44	Two-component system (lmo02020)	10	lmo0292 heat-shock protein htrA serine protease
			lmo0685 flagellar motor protein MotA
			lmo0974 dltA; D-alanine--poly(phosphoribitol) ligase subunit 1
			lmo0973 dltB; DltB protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid
			lmo0972 dltC; D-alanine--poly(phosphoribitol) ligase subunit 2

			lmo0971 dltD; DltD protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid
			lmo0683 chemotaxis protein CheR
			lmo0692 cheA; tquorwo-component sensor histidine kinase CheA
			lmo0691 cheY; chemotaxis response regulator CheY
			lmo0689 chemotaxis protein CheV
	Cellular Processes		
	Cellular community - prokaryotes		
45	Quorum sensing (lmo02024)	10	lmo2363 glutamate decarboxylase
			lmo2434 glutamate decarboxylase
			lmo2362 amino acid antiporter
			lmo0448 amino acid antiporter
			lmo2196 hypothetical protein
			lmo2195 peptide ABC transporter permease
			lmo2194 peptide ABC transporter permease
			lmo2193 peptide ABC transporter ATP-binding protein
			lmo2569 peptide ABC transporter substrate-binding protein
			lmo0539 tagatose 1
	Cell motility		
46	Bacterial chemotaxis (lmo02030)	11	lmo0692 cheA; two-component sensor histidine kinase CheA
			lmo0691 cheY; chemotaxis response regulator CheY

			lmo0689 chemotaxis protein CheV
			lmo0683 chemotaxis protein CheR
			lmo0714 fliG; flagellar motor switch protein FliG
			lmo0699 fliM; flagellar motor switch protein FliM
			lmo0693 flagellar motor switch protein FliY
			lmo0700 flagellar motor switch protein FliY
			lmo0698 flagellar motor switch protein
			lmo0685 flagellar motor protein MotA
			lmo0686 motB; flagellar motor rotation MotB
47	Flagellar assembly (lmo02040)	25	lmo0707 fliD; flagellar capping protein FliD
			lmo0706 flgL; flagellar hook-associated protein FlgL
			lmo0705 flgK; flagellar hook-associated protein FlgK
			lmo0696 flgD; flagellar basal body rod modification protein
			lmo0697 flgE; flagellar hook protein FlgE
			lmo0682 flgG; flagellar basal body rod protein FlgG
			lmo0710 flgB; flagellar basal-body rod protein FlgB
			lmo0711 flgC; flagellar basal body rod protein FlgC
			lmo0712 fliE; flagellar hook-basal body protein FliE
			lmo0713 fliF; flagellar MS-ring protein FliF
			lmo0714 fliG; flagellar motor switch protein FliG
			lmo0699 fliM; flagellar motor switch protein FliM

			lmo0693 flagellar motor switch protein FliY
			lmo0700 flagellar motor switch protein FliY
			lmo0698 flagellar motor switch protein
			lmo0680 flhA; flagellar biosynthesis protein FlhA
			lmo0679 flhB; flagellar biosynthesis protein FlhB
			lmo0715 fliH; flagellar assembly protein H
			lmo0716 fliI; flagellum-specific ATP synthase
			lmo0676 fliP; flagellar biosynthesis protein FliP
			lmo0677 fliQ; flagellar biosynthesis protein FliQ
			lmo0678 fliR; flagellar biosynthesis protein FliR
			lmo0685 flagellar motor protein MotA
			lmo0686 motB; flagellar motor rotation MotB
			lmo0708 flagellar protein
	Organismal Systems		
	Immune system		
48	NOD-like receptor signaling pathway (lmo04621)	2	lmo1233 trxA; thioredoxin
			lmo2152 thioredoxin
	Human Diseases		
	Infectious disease: bacterial		
49	Bacterial invasion of epithelial cells (lmo05100)	2	lmo0433 inlA; internalin A

			lmo0434 inlB; internalin B
	Drug resistance: antimicrobial		
50	beta-Lactam resistance (lmo01501)	4	lmo2196 hypothetical protein
			lmo2195 peptide ABC transporter permease
			lmo2194 peptide ABC transporter permease
			lmo2193 peptide ABC transporter ATP-binding protein
51	Cationic antimicrobial peptide (CAMP) resistance (lmo01503)	5	lmo0292 heat-shock protein htrA serine protease
			lmo0974 dltA; D-alanine--poly(phosphoribitol) ligase subunit 1
			lmo0973 dltB; DltB protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid
			lmo0972 dltC; D-alanine--poly(phosphoribitol) ligase subunit 2
			lmo0971 dltD; DltD protein for D-alanine esterification of lipoteichoic acid and wall teichoic acid

CURRICULUM VITAE

MINGHAO LI

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EDUCATION

Utah State University (USU) Logan, USA
Doctor of Philosophy, Nutrition and Food Science May. 2020
GPA: 3.89

Wageningen University (WUR) Wageningen, NL
Master of Science, Food Technology Sept. 2014
GPA: 3.60

Hunan Agricultural University (HAU) Hunan, CN
Bachelor of Engineering, Food Science and Engineering July 2011
GPA: 3.41

RESEARCH UNDERTAKINGS

Utah State University Logan, USA
Graduate Research Assistant May. 2015 – Present

- **Exploring the connection between acid exposure and virulence in *Listeria monocytogenes* (PhD dissertation)**
  - Project supported by BUILD Dairy program, Western Dairy Center, USU
  - Investigated the molecular basis and potential consequences of induced acid and bile resistance in acid habituated *Listeria* strains

Wageningen University Wageningen, NL
Graduate Research Assistant Sept. 2012 – Sept. 2014

- **Population dynamics of Ur strains in dairy starter (Master thesis)**
  - Project supported by TIFN, the Netherlands
  - Investigated compositional changes in Ur starter culture observed during experimental evolution
- **Enzymatic solutions for whey-derived food ingredients**
  - Project supported by DSM, the Netherlands
  - Provided enzymatic modification of whey protein for specific food ingredient
- **Quality and microbial safety of reduced sodium-salt sauerkraut**
  - Monitored fermentation process in reduced sodium salt sauerkraut

- Investigated the mechanism of texture loss in low sodium sauerkraut
- Investigated microbial safety in reduced sodium salt sauerkraut

Utah State University Logan, USA
Graduate Research Assistant Aug. 2013 – Feb. 2014

- **Effects of consuming a bioactive yogurt supplemented with milk fat globule membrane on endotoxemia and markers of metabolic syndrome**
  - Project supported by Dairy Research Institute (DRI), the United State
  - Characterization and comparison between yogurt with milk fat globule membrane (MFGM) and normal yogurt
  - Investigated healthy properties of MFGM in overweight subjects

National Vegetable Processing Technology R & D Center Hunan, CN
Junior Researcher July 2011 – July 2012

- **Processing method of high-calcium flavor noodles**
  - Developed the processing method of a novel flavor noodles supplemented with high-calcium animal parts
  - Characterization of high-calcium flavor noodles

Hunan Agricultural University Hunan, CN
Undergraduate Research Assistant Sept. 2007 – July 2011

- **Research on techniques of soy sauce fermented with salted chili juice (Bachelor thesis)**
  - Project supported by the Department of Agriculture, China
  - Designed and optimized fermentation conditions for soy sauce fermented with salted chili juice
  - Characterization and comparison between soy sauce with salted chili juice and normal soy sauce

PROFESSIONAL EXPERIENCES

IFT Student Association USA
Pacific Northwest Area Meeting Chair 2017 – 2018

- IFTSA area meeting; College Bowl

Changsha Tantanxiang Seasoning Food Co., Ltd Changsha, CN
Summer Undergraduate Researcher June 2009 – Sept. 2009

- R&D Staff; Quality manager

Changsha Yalin Food Co., Ltd Changsha, CN
Summer Undergraduate Researcher June 2008 – Sept. 2008

- R&D Staff; Quality manager

PUBLICATIONS AND PATENTS

>> Journals

Ward, R. E., Benninghoff, A. D., Healy, B. J., **Li, M.**, Vagu, B., & Hintze, K. J. (2017). Consumption of the total Western diet differentially affects the response to green tea in rodent models of chronic disease compared to the AIN93G diet. Molecular nutrition & food research, 61(4).

Spus, M., **Li, M.**, Alexeeva, S., Wolkers-Rooijackers, J. C. M., Zwietering, M. H., Abee, T., & Smid, E. J. (2015). Strain diversity and phage resistance in complex dairy starter cultures. Journal of dairy science, 98(8), 5173-5182.

M. Li, X. Hu and Y. Xia (2011). "The analysis and comparison of flavor compounds between soy sauce fermented with salted chili juice and normal soy sauce." Food & Machinery 27(5): 58-62

M. Li, X. Hu, L. Pang and Y. Xia (2011). "Fermentation techniques of soy sauce with salted chili juice." China Brewing 237(12): 30-33

>> Patents

Method for processing high-calcium noodles with flavor poultry skeleton soup
Inventors: B. Xia, L. Pang, **M. Li**. Publication number: CN102160622 B

Method for processing high-calcium noodles with livestock bone paste
Inventors: L. Pang, B. Xia, **M. Li**. Publication number: CN102160621 B

Method for processing high-calcium noodles with fish head soup
Inventors: B. Xia, L. Pang, **M. Li**. Publication number: CN102160620 B

>> Books

Approaching Science, Editor, Central People University Press 2008.5

SELECTED HONORS & AWARDS

IMPA Product Development Competition 1st Prize	Aug. 2018
Excellent Bachelor Thesis, HAU	June 2011
Third-Class Scholarship Reward, HAU	Sept. 2010
Outstanding Student Union Leader, HAU	Oct. 2009
Outstanding Student Leader of Youth League, HAU	May 2009

RESEARCH AREAS

- Food microbiology and fermentation
- Food safety