Adaptive Mechanisms of *Listeria monocytogenes* to Stressors: An Overview

B. A. Haruna¹*, A. S. Kumurya² and A. H. Musa¹

¹Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, University of Maiduguri, Nigeria.

²Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, Bayero University, Kano, Nigeria.

Authors’ contributions

This work was carried out in collaboration among all authors. Author BAH designed the study, wrote the protocol and wrote the first draft of the manuscript. Author ASK managed the analyses of the study. Author AHM managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/SAJRM/2019/v4i430111

Editor(s): (1) Dr. Eliton da Silva Vasconcelos, Department of Physiological Sciences, Federal University of Sao Carlos – UFSCar, Rod. Washington Luiz, Sao Carlos, Brazil.

Reviewers: (1) Dra. Claudia Maricel Mattana, National University of San Luis, Argentina.

(2) Felipe Silva de Miranda, State University of Santa Cruz, Brazil.

(3) Anahita Punj, Kaloji Narayana Rao University of Health Sciences, India.

Complete Peer review History: [http://www.sdiarticle4.com/review-history/50586](http://www.sdiarticle4.com/review-history/50586)

Received 01 July 2019
Accepted 06 September 2019
Published 20 September 2019

ABSTRACT

*Listeria monocytogenes* is a food borne pathogen which usually infects individuals with impaired cellular immunity and the healthy. Gastrointestinal tract (GIT) of the humans has lots of defensive mechanisms placed to prevent pathogens from establishing themselves and cause infectious diseases. Survival depends on the pathogen’s ability to overcome such preventive mechanism of the host. *Listeria monocytogenes* exhibits array of mechanisms that ensure its survival against these stressor. These stressors include gastric acid, bile salt, low oxygen tension, antimicrobial peptides e.t.c. Acid tolerance system (ATR), glutamate decarboxylase system (GAD), BilE system, MVs, oxygen sensors are used by *Listeria monocytogenes* to enhance its chances of survival within host. Our interest here is to look at such adaptive mesures with respect to the stressors encountered.

*Corresponding author: Email: hba92@ymail.com;*
Keywords: Glutamate decarboxylase system (GAD); Bile Expulsion (BilE); Membrane Vesicles (MVs); Acid Tolerance System (ATR); Listeria monocytogenes; stressors; Bile Salt Hydrolase (BSH).

1. INTRODUCTION

Listeria monocytogenes is a Gram-positive, facultative intracellular pathogen that infects human and animals through consumption of contaminated food [1]. This organism can invade intestinal epithelium and gain access to the lymphatic system and blood stream, eventually resulting in dissemination to the liver, spleen, and central nervous system [2]. It is one of the most virulent food borne pathogens and has high mortality rate especially among the immunocompromised and in those with impaired cell-mediated immunity (neonates, pregnant woman, elderly persons) causing septicemia, meningoencephalitis, still birth. L. monocytogenes can also induce febrile gastroenteritis in healthy individuals if it is ingested at high doses [3].

Despite its low incidence, listeriosis has a high mortality rate (30%), making it the most deadly foodborne disease in the United Kingdom and the United States, as it claims more lives than any other foodborne pathogen [4]. In Nigeria, few studies done regarding this pathogen especially in humans, there is inadequacy of data regarding listeriosis. It has developed many mechanisms that enable it to thrive and survive within GIT, multiplying and getting access to the human system. Adaptation to the GIT conditions such as acidity, osmolarity, oxygen tension, or the challenging effects of antimicrobial peptides and acidity, osmolarity, oxygen tension, or the challenging effects of antimicrobial peptides and bile is critical in order to survive. Interestingly, the more it is exposed to those challenges, the more it adapts to the environment which is achieved through expression of certain genes. The finding that the bacteria are able to colonize and persist in the gallbladder Moorhead and Dykes [5] suggests the occurrence of long-term and chronic infections and demonstrates the ability of pathogenic Listeria to survive within the various microenvironments of the gastrointestinal tract. The aim of this review is to discuss on the mechanisms employed by L. monocytogenes to cope with the harsh environment of the gastrointestinal tract.

2. RESPONSE TO ACIDS

Gastric acid represents the first stressor encountered during passage of Listeria monocytogenes in the GIT. The main constituent of gastric acid is hydrochloric acid produced by parietal cells (also called oxyntic cells) creating a pH of 1.5 to 3.5. In order to cause an infection, L. monocytogenes requires robust acid resistance mechanisms to overcome the acidic stress presented by fermented foods, gastric juice, volatile fatty acids in the intestine, and even the low pH of the macrophage phagosome [6].

It has been shown by [7,8] that the GAD system plays a vital role in adaptation to acidic environment in L. monocytogenes. The GAD system classically involves two proteins, a glutamate decarboxylase enzyme coupled to a glutamate/gamma-aminobutyrate antiporter, which results in the consumption of an intracellular proton for each glutamate entering the system. Some strains of L. monocytogenes (LO28) have three decarboxylases genes (gadD1, gadD2, and gadD3) with two antiporters (gadT1 and gadT2). These are organized in two pairs (gadD1T1 and gadD2T2) and a distinct gadD3. Now, to further elucidate the role of the system, Higuchi et al. [8] analysed 15 isogenic mutants and found that GadD2/T2 are primarily responsible for surviving severe acid challenge (pH 2.8) thus confirming previous observations from other researchers. They also established that GadD1 plays a major role in growth at mildly acidic pHs (pH 5.1) but failed to state the role of gadD3.

Paul et al. [9] and Karatzas et al. [10] hypothesised that GadD3 plays an important role in acid resistance by mediating the conversion of glutamate into GABA with concomitant consumption (removal) of protons in the cytoplasm.

Wemekamp-Kamphuis et al. [11] stated that several studies uncovered a link between the acid stress response of L. monocytogenes and nisin (bacteriocin) resistance [12,13,14]. GAD system seems to provide innate protection against nisin which is commonly seen among GAD Gram-positive microorganisms. In silico analyses reveal that GAD genes are present in the genomes of a variety of bacterial genera, including the Gram-positive food pathogens.

In addition, there are other mechanisms used by L. monocytogenes to cope with stress from acidic
environments. Regulation of protons movement across the cell membranes results pH homeostasis. In aerobic organisms it is coupled with electron transport chains while in anaerobic bacteria with H⁺-ATPase molecules, using energy generated from the hydrolysis of ATP molecules. L. monocytogenes being a facultative anaerobe is able to utilize both processes of pH homeostasis as demonstrated by Van et al. [15].

Interestingly, exposure to acidic stress confers resistant to various other stresses encountered by L. monocytogenes. Shabala et al. [16] and Phan-Thanh and Mahouin [17] showed that under acidic stress, various transcriptional regulators, GroEL protein, and ATP synthase are expressed in L. monocytogenes. Furthermore, Gahan et al. [18] demonstrated that adaptation to acid offers cross protection against heat, ethanol, oxidative, osmotic stresses and the bacteriocin nisin. And later in 2000, Shabala et al. [16] agreed to most of the findings of Gahan et al. [18].

Higuchi et al. [8] and Ferreira et al. [19] observed that survival of L. monocytogenes in the gastric fluid is partially due to the stress sigma factor σB. According to Kazmierczak et al. [20] sigma factor σB regulates the expression of the gadB and OpuC genes that encode glutamate decarboxylase and carnitine transporter respectively helping survival in acidic pH.

Lastly, histidine kinase and a response regulator that were identified in 1999 by Cotter et al. [21] were encoded by lisK and lisR genes respectively. Histidine kinase associated with membrane senses environmental changes, (low pH, oxidative stress e.t.c) and the alteration of gene expression is enabled by the response regulator according to Meenakshi et al. [22]. Low pH not only stimulates stress responses but also expression of virulence genes such as prfA. In 2013 Neuhaus et al. [23] showed that acid shock at low temperatures of 25°C may also induce prfA.

3. RESPONSE TO BILE

Bile or gall is a dark green to yellowish brown fluid, produced by the liver of most vertebrates that aids the digestion of lipids in the small intestine. Bile acids (BA), major components of bile, are synthesized from cholesterol and conjugated to either glycine or taurine in the liver, stored in gallbladder before secretion into the duodenum via the common bile duct [24]. BA is biological detergents that facilitate the emulsification and solubilization of dietary lipids and fat-soluble vitamins, favouring its absorption by enterocytes. Although the major fraction of BAs are actively reabsorbed by enterocytes and sent back to the liver (enterohepatic circulation), a small fraction is modified by the indigenous microbiota [25]. The composition of hepatic bile is 97% water, 0.7% bile salts, [26] 0.2% bilirubin, 0.51% fats (cholesterol, fatty acids, and lecithin) and 200 meq/l inorganic salts [27]. The salts are amphipathic molecules that have been shown to possess antimicrobial properties; bile salts have been shown to degrade viral and bacterial membranes containing lipids and also induce DNA damage [28,29].

L. monocytogenes possesses numerous mechanisms which allow for resistance against bile; the bile salt hydrolase bsh [29,30], the general stress response sigma factor sigB [31,29] the bile exclusion system bile [32] and virulence regulator prfA [30].

Dec conjugation (bile salt) is catalyzed by bile salt hydrolase (BSH) enzymes, which hydrolyze the amide bond and liberate the glycine/taurine moiety from the steroid core. The resulting acids are termed unconjugated or deconjugated bile acids hence inactivating the potent salt. Deletion of the bsh gene invariably reduces the ability of L. monocytogenes to cause systemic infections as stated by [29,30]. Several previous works also suggest that BSH activity could play a role in bile tolerance in some Gram-positive bacteria and would be part of a cell detoxification strategy [33,34]. In fact, free BA produced by BSH activity have decreased solubility, precipitate at intestinal pH (decreased mainly by the activity of lactic acid bacteria) and leave the GIT in the faeces. In addition, the diminished detergent activity may be less toxic to bacteria in the intestine [25]. In Listeria, BSH levels increased under certain conditions such as low oxygen tensions prevalent in the host during infection [30].

Also heat shock proteins DnaK, GroEL and GroES were seen to be responses related against bile and other several stimuli in many bacteria genera as shown by [35,36].

Ferreira et al. [19] has shown that sigma factor sigB is involved in regulating gene expression for osmolyte transporters (OpuC) and regulates processes needed for survival in
response to stresses of oxidation, reduced pH, and starvation. It also serve as a positive regulator of factor A which activates major virulence factors. A connection between sigB and the genes expression related to bile resistance such as bteI and bsh have been shown by Sue et al. [37]. The bile exclusion system, (BteI) serves to prevent bile from entering the cell as bile is toxic to most pathogens. Salt stress response related proteins such as RecA and UvrA were also identified in molecular vesicles (MVs) from salt stressed L. monocytogenes. RecA is an important factor in DNA repair. It contributes to acid and bile salt stress as well as adhesion and invasion of L. monocytogenes to Caco-2 intestinal epithelial cells [38]. Nucleotide-excision repair protein UvrA is also required for acid and bile resistance of L. monocytogenes [39]. Another finding also shows that MVs contrary to the above function also confer and aid host cell survival. According to So-Hyun et al. [40], MVs of L. monocytogenes can increase host cell viability, but not cell death, which may due to the fact that MVs secreted from extracellular L. monocytogenes can secure important niche for bacterial invasion.

It has been also described that multidrug resistance (MDR) transporters belonging to the ATP binding cassette or the major facilitator superfamily could play an important role in the bile resistance phenotypes in Gram-negative and Gram-positive bacteria [41]. This is elucidated and explicated in Listeria monocytogenes by Quillin et al. [42] which identified a TetR-type regulator [renamed bile-regulated transcription factor A (BrtA)] that senses bile and regulates expression of two multidrug resistance (MDR) efflux pumps (MdrM and MdrT) that mediate bile tolerance and liver/gall bladder colonization [43]. This finding may be particularly relevant given the broader role of MdrM/T in mediating secretion of cyclic-di-AMP, a signaling molecule that triggers STING-dependent production of interferon-beta and promotes in vivo survival of the Listeria monocytogenes [44].

4. RESPONSE TO OXYGEN TENSION

Carbon dioxide is known to inhibit the growth of most bacteria [45] and found as an acid reaction byproduct in the stomach with the amount produced differs from individual to individual.

Anaerobiosis might be an environmental signal, which triggers the first colonisation of L. monocytogenes within the intestine during in vivo growth. Furthermore, Jydegaard-Axelsens et al. [46] observed an increased gene expression essential for survival in acidic conditions and also increased branch-chain fatty acids in the cell membrane when L. monocytogenes is cultured in elevated carbon dioxide and anaerobic conditions. It is obvious that gene expression changed for invasion-associated internalin proteins (InIA and LmaA) that are involved in attachment and invasion of the host cells in preference to escape the acidic environment.

L. monocytogenes being a facultative anaerobe, capable to undergo aerobic respiration, fermentation, and anaerobic respiration, however, this is still dependent upon oxygen availability. This environmental sensing is typically controlled by a two-component signal transduction system which consists of a membrane bound sensor and a cytoplasmic response regulator [47]. Few researches have been done to show the connection between anaerobiosis and increased survival in the presence of stressors in Listeria monocytogenes, but a lot is known about Gram-positive organisms.

In various Gram-positive bacteria, such as Staphylococcus aureus, Bacillus subtilis and Mycobacterium tuberculosis, two-component systems have been shown to regulate metabolism and the expression of virulence factors in response to decreased oxygen concentrations [48,49,50]. For instance, the SrrAB two-component system of S. aureus is involved in the activation of stress response proteins, specifically those involved in DNA repair, the oxidative stress response and the alternative sigma factor, SigB, in oxygen limited environments [51].

The two-component system ResDE of B. subtilis, homologous to SrrAB in S. aureus, has been shown to regulate virulence factors, sporulation, and fermentation in B. subtilis [49,50]. A homolog to resD has been characterized in L. monocytogenes [52]. ResD was found to influence the activity of prfA in L. monocytogenes, which in turn alters the expression of several virulence genes, including inlA [53]. This point that ResD is an important element in the virulence factors regulation and stress responses under low-oxygen conditions.

A recent genomic study identified DosP in L. monocytogenes, which is similar to the histidine
kinase found in *M. tuberculosis*, suggesting that *L. monocytogenes* belong to the category of Gram-positives that possess an oxygen sensor [54,55]. This suggests that there is a link in the organisms' ability to detect oxygen levels among Gram-positive bacteria.

Wright et al. [56] recently showed a potential link between oxygen availability and bile resistance by observing several strains of *L. monocytogenes* growth in 0%, 1%, 5% and 10% porcine bile. This shows that resistance to bile increases under anaerobic conditions as compared to aerobic for virulent strains F2365, 10403S and EGD-e but not for avirulent strain HCC23. A comprehensive total proteomic study to identify mechanisms (metabolism and stress response) found that proteins associated with the cell envelope, membrane bioenergetics, cell division, and dehydrogenases involved in NADH:NAD⁺ alteration were increased under anaerobic conditions. It is possible that these proteins may play a role in bile resistance during anaerobic growth, despite oxygen sensor which may regulate these mechanisms has not been uncovered.

Vázquez-Boland et al. [57] observed a significant difference in the bacterial loads in liver of the treated animals with high anaerobic dose of *Listeria monocytogenes*. The pathogen disseminates to the secondary target organs, including the brain and the uterus after invasion of the liver. In the treatment group, there were high loads of the pathogen in the GIT and feces, which may prime the bacteria to survive the GI tract stressors and cross to the liver. They further revealed that exposure of *L. monocytogenes* to anaerobic conditions prior to infection, such as what occurs within a food processing environment or packaging, enhances the probability of the pathogen to resist the stressors encountered within the GI tract.

### 5. CONCLUSION

Many mechanisms are used by *L. monocytogenes* to overcome stressors encountered within the GIT. As mentioned in this paper, GAD system, protons movements across membrane, BiE exclusion, BSH, MVs, anaerobiosis e.t.c are some of the mechanisms employed in adapting to environmental stresses. Extra-intestinal conditions such as pH and packaging of the food also aid in the adaptation to the GIT stressors. Listeriosis is few incases, but it high mortality rate (30%) makes it the most dangerous food borne pathogen. Employment of several adaptive mechanisms used for its survival present an additional challenge which may increase the cases and mortality rates in near future, if more effective measures are not taken.

There are need for further studies so as to determine if GAD genes contribute to the tolerance of nisin, whether MVs aid in host cell survival, to expantiate and confirm on the role of Gad3 and how SigB makes *L. monocytogenes* vulnerable to stresses under aerobic conditions. The fact that prfA is stimulated by low pH and heat shock at low temperature need more details from further experiments.

### ACKNOWLEDGEMENT

My appreciation goes to miss Ruma Bag of Science Domain International for the encouragement and motivation and Alhaji Haruna Musa of Medical Laboratory Science Department, University of Maiduguri for his tireless effort and support.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

### REFERENCES

1. Schlech WF. Foodborne Listeriosis. Clin. Infect. Dis. 2000;31:770–775.
2. Begley M, Gahan CG, Hill C. The interaction between bacteria and bile. FEMS Microbiol. Rev. 2005;29:625–651.
3. Dalton CB, Austin CC, Sobel J, Hayes PS, Bibb WF, Graves LM, et al. An outbreak of gastroenteritis and fever due to *Listeria monocytogenes* in milk, N. Engl. J. Med. 1997;336:100–105.
4. Mook P, Grant KA, Little CL, Kafatos G, Gillespie IA. Emergence of pregnancy-related listeriosis amongst ethnic minorities in England and Wales. Euro Surveill. 2010;15:19610.
5. Moorhead SM, Dykes GA. The role of the sig B gene in the general stress response of *Listeria monocytogenes* varies between a strain of serotype 1/2a and a strain of serotype 4c. Curr Microbiol. 2003;46:0461–0466.
6. Begley M, Kerr C, Hill C. Exposure to bile influences biofilm formation by
Listeria monocytogenes. Gut Pathog. 2009;1:11. DOI: 10.1186/1757-4749-1-11

7. Jeroen Koomea, Heidy MW, den Bestena, Karin I. Metselaarasa, Marcel H. Tempelaarasa, Lucas M. Wijnandsb, Marcel H. Ziwieteringa, Tjakkoo Abeee. Gene profiling-based phenotyping for identification of cellular parameters that contribute to fitness, stress-tolerance and virulence of Listeria monocytogenes variants. International Journal of Food Microbiology. 2018;283:14–21.

8. Higuchi T, Hayashi H, Abe K. Exchange of glutamate and aminobutyrate in a Lactobacillus strain. Appl. Environ. Microbiol. 1997;179:3362–3364.

9. Paul D. Cotter, Sheila Ryan, Cormac G. M. Gahan, Colin Hill presence of GadD1 glutamate decarboxylase in selected Listeria monocytogenes strains is associated with an ability to grow at low pH. Applied and Environmental Microbiology. 2005;71:2832–2839.

10. Karatzas KA, Brennan O, Heavin S, Morrissey J, O’Byrne CP. Intracellular accumulation of high levels of gamma-aminobutyrate by Listeria monocytogenes 10403S in response to low pH: uncoupling of gamma-aminobutyrate synthesis from efflux in a chemically defined medium. Appl. Environ. Microbiol. 2010;76:3529–3537. DOI: 10.1128/AEM.03063-09

11. Wemekamp-Kamphuis HH, Wouters JA, de Leeuw PPLA, Hain T, Chakraborty T, Abee T. Identification of sigma factor B-controlled genes and their impact on acid stress, high hydrostatic pressure, and freeze survival in Listeria monocytogenes. Appl. Microbiol. 2004;70:3457–3466.

12. Mair’e Begley, Colin Hill and Cormac G. M. Gahan. Bile Salt Hydrolase Activity in Probiotics Applied and Environmental Microbiology. 2006;72:1729–1738.

13. Bonnet M, Rafi MM, Chikindas ML, Montville TJ. Bioenergetic mechanism for nisin resistance, induced by the acid tolerance response of Listeria monocytogenes. Appl. Environ. Microbiol. 2006;72:2556–2563.

14. McEntire JC, Carman GM, Montville TJ. Increased ATPase activity is responsible for acid sensitivity of nisin-resistant Listeria monocytogenes ATCC 700302. Appl. Environ. Microbiol. 2004;70:2717–2721.

15. Van Schalk W, Gahan CG, Hill C. Acid-adapted Listeria monocytogenes displays enhanced tolerance against the lantibiotics nisin and lacticin. J. Food Prot. 1999; 62:536–539.

16. Shabala L, Budde B, Ross T, Siegumfeldt H, McMeekin T. Responses of Listeria monocytogenes to acid stress and glucose availability monitored by measurements of intracellular pH and viable counts. Int. J. Food Microbiol. 2002;75(1–2): 89–97.

17. Phan-Thanh L, Mahouin F. A proteomic approach to study the acid response in Listeria monocytogenes. Electrophoresis. 1999:20(11):2214–2224.

18. Gahan CG, O’Driscoll B, Hill C. Acid adaptation of Listeria monocytogenes can enhance survival in acidic foods and during milk fermentation. Applied and Environmental Microbiology. 1996;62(9): 3128–3132.

19. Ferreira A, Sue D, O’Byrne CP, Boor KJ. Role of Listeria monocytogenes sigma (B) in survival of lethal acidic conditions and in the acquired acid tolerance response. Appl. Environ. Microbiol. 2003;69(5):2692–2698.

20. Kazmierczak MJ, Mithoe SC, Boor KJ, Wiedmann M. Listeria monocytogenes σB regulates stress response and virulence functions. J. Bacteriol. 2003;185:5722–5734.

21. Cotter PD, Gahan CGM, Hill C. Analysis of the role of the Listeria monocytogenes F0F1-ATPase operon in the acid tolerance response. Int. J. Food Microbiol. 2000;60:137–146.

22. Meenakshi Thakur, Rajesh Kumar Asrani, Vikram Patial. Listeria monocytogenes: A food-borne pathogen. Copyright © Elsevier Inc. All rights reserved. Chapter 6. 2006;157.

23. Neuhaus K, Satorhelyi P, Schauer K, Scherer S, Fuchs T. Acid shock of Listeria monocytogenes at low environmental temperatures induces prFA, epithelial cell invasion, and lethality towards Caenorhabditis elegans. BMC Genom. 2013;14:285.

24. Li T, Chiang JY. Bile acids as metabolic regulators. Current opinion in Lucas M. Wijnandsb, Marcel H. Ziwieteringa, Tjakkoo Abeee. Gene profiling-based phenotyping for identification of cellular parameters that contribute to fitness, stress-tolerance and virulence of Listeria monocytogenes.
variants. International Journal of Food Microbiology. 2015;283:14-21.
25. Chand D, Avinash VS, Yadav Y, Pundle AV, Suresh CG, Ramasamy S. Molecular features of bile salt hydrolases and relevance in human health. Biochimica et Biophysica Acta. 2017; 1861(1 Pt A):2981-2991. DOI: 10.1016/j.bbagen.2016.09.024
26. Barrett E, Gran's review of medical physiology 24th ed. New York: McGraw-Hill medical. 2012;512.
27. Guyton and Hall. Textbook of medical physiology. U.S. Saunders Elsevier. 2011;784.
28. Bernstein C, Bernstein H, Payne CM, Beard SE, Schneider J. Bile Salt Activation of Stress Response Promoters in Escherichia coli. Curr. Microbiol. 1999; 39:68–72.
29. Begley M, Gahan CG, Hill C. The interaction between bacteria and bile. FEMS Microbiol. Rev. 2005;29:625–651.
30. Dussurget O, Cabanes D, Dehoux P, Lecuit M, Buchrieser C, Glaser P, Cossart P. Listeria monocytogenes bile salt hydrolase is a PrfA-regulated virulence factor involved in the intestinal and hepatic phases of listeriosis. Mol. Microbiol. 2002; 45:1095–1106.
31. Dowd GC, Joyce SA, Hill C, Gahan CG. Investigation of the mechanisms by which Listeria monocytogenes grows in porcine gallbladder bile. Infect. Immun. 2011;79:369–379.
32. Sleator RD, Wemekamp-Kampshuis HH, Gahan CG, Abeeb T, Hill C. A PrfA-regulated bile exclusion system (BilE) is a novel virulence factor in Listeria monocytogenes. Mol. Microbiol. 2005;55:1183–1195.
33. Begley M, Hill C, Ross RP. Tolerance of Listeria monocytogenes to cell envelope-acting antimicrobial agents is dependent on SigB. Appl. Environ. Microbiol. 2006; 72:2231–2234.
34. Grill JP, Cayuela C, Antoine JM, Schneider F. Isolation and characterization of a Lactobacillus amylovorus mutant depleted in conjugated bile salt hydrolase activity: Relation between activity and bile salt resistance. J. Appl. Microbiol. 2000;89: 553–563.
35. Ruiz L, Hidalgo C, Blanco-Miguez A, Lourenço A, Sánchez B, Margolles A. Tackling probiotic and gut microbiota functionality through proteomics. Journal of Proteomics. 2016;147:28-39.
36. Siciliano RA, Mazzeo MF. Molecular mechanisms of probiotic action: A proteomic perspective. Current Opinion in Microbiology. 2012;15(3):390-396.
37. Sue D, Fink D, Wiedmann M, Boor KJ. B-dependent gene induction and expression in Listeria monocytogenes during osmotic and acid stress conditions simulating the intestinal environment. Microbiology. 2004;150:3843–3855.
38. Van der Veen S, Abeeb T. Mixed species biofilms of Listeria monocytogenes and Lactobacillus plantarum show enhanced resistance to benzalkonium chloride and peracetic acid. International Journal of Food Microbiology. 2011;144(3):421-431.
39. Kim SH, Gorski L, Reynolds J, Orozo E, Fielding S, Park YH, et al. Role of uvrA in the growth and survival of Listeria monocytogenes under UV radiation and acid and bile stress. J. Food Prot. 2006;69:3031–3036.
40. So-Hyun Juna, Taewon Leeb, Je-Chul Leea, Ji-Hyun Shin. Different epithelial cell response to membrane vesicles produced by Listeria monocytogenes cultured with or without salt stress. Microbial Pathogenesis. 2019;131:103554.
41. Šárka H, Milada P, Kateřina D. Importance of microbial defence systems to bile salts and mechanisms of serum cholesterol reduction. Biotechnology Advances; 2017.
42. Quillin SJ, Schwartz KT, Leber JH. The novel Listeria monocytogenes bile sensor BrtA controls expression of the cholic acid efflux pump MdrT. Mol. Microbiol. 2011;81:129–142. DOI: 10.1111/j.1365-2958.2011.07683.x
43. Davis ML, Ricke SC, Donaldson JR. Establishment of Listeria monocytogenes in the gastrointestinal tract. Microorganisms. 2019;7(3):75. DOI:10.3390/microorganisms7030075
44. Crimmins GT, Herskovits AA, Rehder K, Sivick KE, Lauer P, Dubensky TW, et al. Listeria monocytogenes multidrug resistance transporters activate a cytosolic surveillance pathway of innate immunity. Proc. Natl. Acad. Sci. U.S.A. 2008;105:10191–10196. DOI: 10.1073/pnas.0804170105
45. Gill CO, Tan KH. Effect of carbon dioxide on growth of meat spoilage bacteria. Appl. Environ. Microbiol. 1980;39:317–319.

46. Jydegaard-Axelsen AM, Hoiby PE, Holmstrom K, Russell N, Knochel S. CO2 - and anaerobiosis-induced changes in physiology and gene expression of different Listeria monocytogenes strains. Appl. Environ. Microbiol. 2004;70:4111–4117.

47. Stock AM, Robinson VL, Goudreau PN. Two-component signal transduction. Annu. Rev. Biochem. 2000;69:183. DOI: 10.1146/annurev.biochem.69.1.183

48. Throup JP, Lunsford RD, Lonsdale JT, Bryant AP, McDevitt D, Rosenberg M, Burnham MK. The srhSR gene pair from Staphylococcus aureus: Genomic and proteomic approaches to the identification and characterization of gene function. Biochemistry. 2001,40:10392–10401.

49. Yarwood JM, McCormick JK, Schlievert PM. Identification of a novel two-component regulatory system that acts in Global regulation of virulence factors of Staphylococcus aureus. J. Bacteriol. 2001;183:1113–1123. DOI: 10.1128/JB.183.4.1113-1123.2001

50. Nakano MM, Dailly YP, Zuber P, Clark DP. Characterization of anaerobic fermentative growth of Bacillus subtilis: Identification of fermentation end products and genes required for growth. J. Bacteriol. 1997;179:6749–6755.

51. Kinkel TL, Roux CM, Dunman PM, Fang FC. The Staphylococcus aureus SrrAB two-component system promotes resistance to Nitrosative Stress and Hypoxia. mBio. 2013;4:696-13.

52. Morgan L. Davis, Steven C. Ricke, Janet R. Donaldson. Establishment of Listeria monocytogenes in the gastrointestinal tract. Microorganisms. 2019;7(3):75.

53. Larsen MH, Kallipolitis BH, Christiansen JK, Olsen JE, Ingmer H. The response regulator ResD modulates virulence gene expression in response to carbohydrates in Listeria monocytogenes. Mol. Microbiol. 2006;61:1622–1635.

54. Chiara M, D’Erchia AM, Manzari C, Minotto A, Montagna C, Addante N, Santagada G, Latorre L, Pesole G, Horner DS. Draft genome sequences of six Listeria monocytogenes strains isolated from dairy products from a processing plant in Southern Italy. Genome Announc. 2014; 2:e00282-14.

55. Holch A, Webb K, Lukjancenko O, Ussery D, Rosenthal BM, Gram L. Genome sequencing identifies two nearly unchanged strains of persistent Listeria monocytogenes isolated at two different fish processing plants sampled 6 years apart. Appl. Environ. Microbiol. 2013;79:2944–2951.

56. Wright ML, Pendarvis K, Nanduri B, Edelmann MJ, Jenkins HN, Reddy JS, Wilson JG, Ding X, Broadway PR, Ammari MG. The effect of oxygen on bile resistance in Listeria monocytogenes. J. Proteom. Bioinform. 2016;9:107–119.

57. Vázquez-Boland JA, Kuhn M, Berche P, Chakraborty T, Domínguez-Bernal G, Goebel W, Kreft J. Listeria pathogenesis and molecular virulence determinants. Clinical Microbiology Reviews. 2001;14(3):584–640. DOI:10.1128/CMR.14.3.584-640

© 2019 Haruna et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdlarticle4.com/review-history/50586