Original Article

Understanding the Role of Internalin A and Internalin B in *Listeria Monocytogenes* Infection and Their Correlation with E-cad and C-met Receptors in the Intestine of Diarrhea Patients

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Abstract

Background: *Listeria monocytogenes* is a food-borne pathogen that may cause diarrhea in healthy people, meningitis in the immunocompromised, and abortion in pregnant women. *L. monocytogenes* uses surface proteins called internalin A (InlA) and internalin B (InlB) to invade human's intestinal epithelial cells. **Objective:** This study aimed to evaluate the role of InlA and InlB in *L. monocytogenes* infections and their correlation with E-cad and C-met receptors in diarrhea patients using the ligated rabbit intestinal loop model. **Materials and Methods:** Two intestinal loops in live rabbit were constructed surgically. The first intestinal loop was injected by 1 mL of 10^7 colony forming unit (CFU)/mL of *L. monocytogenes*, and the second intestinal loop was injected by 1 mL of phosphate-buffered saline as a control. **Results:** InlA was significantly expressed in *L. monocytogenes* injected into the rabbit intestinal loop (fold—3.966) compared to control (fold—1.002) (*P*-value 0.001). Also, the expression levels of InlA receptor, E-cad were significant in the rabbit intestinal tissue injected by *L. monocytogenes* (fold—4.022) compared to control (fold—1.0621) (*P*-value 0.003). Furthermore, InlB was significantly expressed in *L. monocytogenes* injected into the rabbit intestinal loop (fold—4.8835) compared to control (fold—1.0007) (*P* value 0.027). Also, the expression levels of InlB receptor, C-met were significant in the intestinal tissue injected by *L. monocytogenes* (fold—4.1341) compared to control (fold—1.0171) (*P* value 0.002). **Conclusion:** This study proposes a valuable strategy for understanding the host-pathogen interaction and the virulence of *L. monocytogenes* in the context of infection.

Keywords: Gene expression, internalins, intestinal receptors, *Listeria monocytogenes*

Introduction

Listeria monocytogenes is an intracellular Gram-positive food-born pathogen that belongs to the genus *Listeria* along with *L. ivanovii*, *L. innocua*, *L. welshimeri*, *L. selligeri*, and *L. grayi*.[1] Among these species, only *L. monocytogenes*, which infects both people and animals, and *L. ivanovii,* which infects ruminants are recognized as pathogens.[2] *L. monocytogenes* is a food-borne pathogen that may be found in a variety of foods, including vegetables, meat, milk, and dairy products. It is also extensively spread in the environment. Individuals who are infected with *L. monocytogenes* are at the risk of developing symptoms such as nausea, vomiting, and diarrhea. As this microbe can grow and live in unfavorable settings and at low pH levels, unlike other living microorganisms, it has recently gained significant attention from the public health community and the food sector.[3] The primary route through which pathogenic *L. monocytogenes* enter the host is via the gastrointestinal system.[4] *L. monocytogenes* pathogenicity relies on its ability to adhere and invade host cells, replicate and move within the host cells, and spread from cell to cell.[5] Each step requires the participation of virulence elements

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that have been well studied and are known to subvert host cell activities. Internalins are proteins encoded by a group of genes linked to pathogenicity in a variety of *Listeria* species and were discovered in *L. monocytogenes* via the process of examining a collection of transposon-induced mutants for reduced invasiveness in Caco-2 cell monolayers.[6] Two listerial surface proteins mediate host cell-specific internalization, internalin A (InlA) and internalin B (InlB) are the most well-described internalins in terms of structure and function. The first molecule to be discovered that allowed *L. monocytogenes* to enter non-phagocytic cells, such as the human intestinal epithelium, was InlA.[7] InlA is necessary for adhering to and inducing uptake into epithelial cells. InlA contains 800 amino acids and separated to N-terminal half, which contains a single peptide and 15 leucine-rich repeats units (LRR) (A repeats), and to C-terminal half, which contains three longer repeat sequences (B repeats), a cell wall anchor with LPXTG motif tailed by a hydrophobic membrane-spanning region of approximately 20 amino acids. This structure is covalently connected to the peptidoglycan in Gram-positive bacteria, which attaches InlA to the bacterial cell membrane.[8] However, InlA uses eukaryotic cell surface receptor E-cadherin (E-cad) as a target.[9-11] E-cad is an adhesion glycoprotein that has five extracellular domains and a cytoplasmic tail, which serves as a receptor for InlA on host cells.[12] It was shown that *L. monocytogenes* enters polarized intestinal Caco-2 cells via the E-cad receptor on their basolateral surface. The E-cad receptor is not only found along the entire basolateral surface of intestinal epithelial cells, but it also accumulates at the junctions between these cells.[13] E-cad is also found on the surface of many other cells, such as dendritic cells, epithelial cells lining the choroid plexus, placental chorionic villi, and brain microvascular endothelial cells, which make them to be permissive to the InlA-mediated internalization of *L. monocytogenes*.[14]

Another surface-associated internalin family member is called InlB. Like InlA, InlB LRR region is required and sufficient to induce invasiveness.[15] There are 630 amino acids in InlB at its N-terminus, with seven LRR units.[16] The C-terminal of InlB lacks the LPXTG motif and the hydrophobic tail, but it has repetitions of GW sequence that contains around 80 amino acids in length. Recently, hepatocyte growth factor (HGF), commonly referred to as the scatter factor, has a high-affinity receptor called mesenchymal-epithelial transition (C-met). HGF is generated by fibroblasts, whereas C-met is expressed on endothelial and epithelial cells. Mature C-met consists of an a-subunit of 45 kDa and a b-subunit of 145 kDa that are connected by disulfide bonds.[17] C-met was shown to be a signaling receptor for inlB and acts as a ligand for HGF. It was shown that C-met is phosphorylated at its tyrosine residue upon interaction with InlB and the InlB-dependent entrance cannot be mediated in C-met -deficient cell lines, indicating a crucial function for this receptor in *L. monocytogenes* invasion.[18] However, in this study, we aimed to evaluate the significance of InlA and InlB in *L. monocytogenes* infection and their correlation with E-cad and C-met receptors in diarrhea patients using the rabbits small intestine-ligated loop model.

Materials and Methods

Bacterial strain and growth condition

Listeria monocytogenes used in this study was isolated from stool samples of diarrhea patients admitted in Al-Qasim General Hospital. *L. monocytogenes* was cultured on brain heart infusion (BHI) agar and broth at 30ºC to the optical density of 600 nm (optical density 600). *L. monocytogenes* was suspended in 1× phosphate-buffered saline (PBS) to 10^7 CFU/mL by spinning it at 8000 rpm for 10 min at room temperature.

Construction of rabbit intestinal ligated loop model

Five pathogen-free New Zealand white rabbits weighted 2.5 kg ± 10 g were used in this study. Animals were starved for 72 h before the construction of ligated intestinal loops. The rabbits were anesthetized with 10% ketamine (1.5 mL/kg) and xylazine (1 mL/kg).[19] When rabbits were completely anesthetized, a 3 cm incision near the intestinal site in its body wall was made. The lower part of rabbit's intestine was isolated, and two loops of about 3–4 cm each were constructed by double ligation. After the construction of intestinal loops, 1 mL of a 10^7 CFU/mL dosage of *L. monocytogenes* was inoculated into the first intestinal loop. The second intestinal loop was injected by 1 mL of (PBS) as a control. After the injection process, the lower intestine was placed back into the rabbit's body, and the rabbit's wall was sutured closed. The rabbits were then moved to their cage and remain for 8 h to allow the intestine to interact and respond to *L. monocytogenes*. After this time, the rabbits were sacrificed by intramuscular injection of 10 mL/kg of chloroform. All the experiments included in this study were performed in five replicates.

Total RNA extraction and cDNA synthesis

From sacrificed rabbits, the constructed intestinal loops were isolated and *L. monocytogenes* were collected from intestinal loops and directly placed in tubes containing RNA later also, the intestinal tissues were directly placed in liquid nitrogen. Then, RNA from collected *L. monocytogenes* was extracted using TriRNA Pure kit (Geneaid) according to the manufacturer's procedures in order to determine the expression level of InlA and InlB. Also, RNA extracted from *L. monocytogenes* was cultured on (BHI) agar as control. Furthermore, RNA from tissues injected with *L. monocytogenes* was extracted to determine the expression level of E-cad and C-met.

RNA from tissues injected with (PBS) was also extracted and used as a control. The RNA concentration and purity were measured using a Nano drop spectrophotometer (NanolytiK, Duesseldorf, Germany) and agarose gel electrophoresis. The RNAs were then converted into cDNA using reverse transcriptase (RT) PreMix kit (Bioneer) following the manufacturer's procedures.

Quantitative real-time PCR and data analysis

The relative expression levels of InlA, InlB, E-cad, and C-met were determined using Green starTM kit (Bioneer) on a Q3200 (Bio-Gener). The primers set were designed using Primer 3 software and made commercially (Scientific Researcher CO) [Table 1]. RT-qPCR reaction involved 20 µL of total volume containing (5 µL) of cDNA, (11 µL) of DDW, primers (1 µL each) and (2 µL) of SYBR Green MIX. The thermal cycling setup for all genes was 1 cycle at 95°C for 1 min, 40 cycles at 95°C for 5 s and at 55°C for 40 s and melting of one cycle at 95°C for 30 s and 60°C for 30 s. The relative expression level of InlA, InlB, E-cad and C-met was calculated using comparative ΔCt method (Livak method $2^{-\Delta\Delta CT}$).[20] 16s rRNA housekeeping gene was used to normalize the relative expression levels of InlA and InlB. Also, 18s rRNA housekeeping gene was used to normalize the relative expression levels of E-cad and C-met.

Statistical analysis

Statistical analysis was performed using statistical package for social sciences software (Armonk, New York: IBM SPSS, International Business Machines Corporation, version 26 and Microsoft Office Excel 2010). The two independent sample test was used to measure the differences between the expression levels of not only InlA and InlB in injected *L. monocytogenes* compared to *L. monocytogenes* cultured on (BHI) agar, but also E-cad and C-met receptors in intestinal loop injected by *L. monocytogenes* and in intestinal loop injected by (PBS). $P < 0.05$ was considered statistically significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number 935 in July 7, 2022 to get this approval.

Result

The RT-PCR technique was used to determine the expression levels of InlA, InlB, E-cad, and C-met after 8h post infection of rabbit's small intestine with *L. monocytogenes*. Results indicated that expression level of InlA was highly significant in *L. monocytogenes* injected into the intestinal loops with a fold change of (3.966) compared to expression level of InlA in *L. monocytogenes* cultured on (BHI) agar with a fold change of (1.002), (*P* value 0.001). Also, the expression level of E-cad was significantly high in the intestinal tissues injected by *L. monocytogenes* with a fold change of (4.022) compared to expression level of E-cad in the intestinal tissues injected by (PBS) with a fold change of 1.0621 (*P* value 0.003) [Table 2] [Figure 1] Furthermore, the expression level of InlB was significantly high in *L. monocytogenes* injected into the intestinal loops with a fold change of 4.8835 compared to expression levels of InlB in *L. monocytogenes* cultured on (BHI) agar with a fold change of 1.0007 (*P* value 0.027). Also, the expression level of C-met was highly significant in the intestinal tissues injected by *L. monocytogenes* with a fold change of 4.1341 compared to the intestinal tissues injected by (PBS) with a fold change of 1.0171 (*P* value 0.002) [Table 3] [Figure 2]

Discussion

The purpose of this study was to evaluate the role of InlA and InlB genes of *L. monocytogenes* and their correlation with

Table 1: Gene ID and primers used for RT-qPCR in this study

Gene		The sequence of primers (5'-3')	Gene ID	Amplicon length
InlA	F	CGCTTCAGGCGGATAGATTAG	985151	108
	R	GTGGCGTTATGTCCGTAAGT		
InlB	F	GGGAATGCAGGCATCTACAA	986892	110
	R	CCATTTCGGGCTTCTCTATCAA		
16S rRNA	F	GGTGGAGCATGTGGTTTAATTC	X56153.1	320
	R	TTCGCGACCCTTTGTACTATC		
E-cad	F	CTGTCTCTCAGTCCCTCTACTT	100356548	124
	R	GATACTGTCACCAGGTCCTTTC		
C-met	F	CGAGGTCCTTAACCAACTACAA	100126565	112
	R	CAATGTCCTTCTCCACCCTATC		
18S rRNA	F	CTGAGAAACGGCTACCACATC	NR-033238.1	107
	R	GCCTCGAAAGAGTCCTGTATTG		

Table 2: Genes expression change of InlA and E-cad receptor

Target gene	Control fold change	Infected fold change	*T* test	*P* value
InlA	0.998615	5.456591	6.333	<0.001
	1.041022	4.65248		
	1.077733	3.429504		
	1.019598	3.2898		
	0.875391	3.006323		
Mean ± SE	1.0025 ± 0.034357	3.9669 ± 0.447753		
SD	0.07682	1.04393		
E-Cadherin	0.695441	5.11949	4.147	0.003
	0.618138	5.486933		
	1.244874	4.809877		
	1.219255	2.339175		
	1.53262	2.355446		
Mean ± SE	1.0025 ± 0.174791	4.0222 ± 0.692119		
SD	0.07682	1.54762		

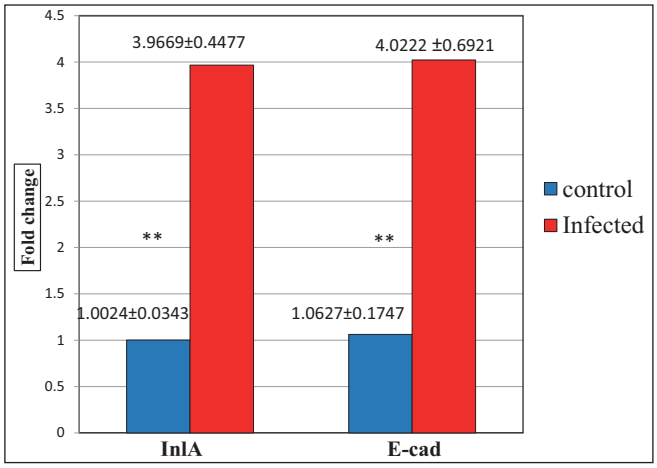

Figure 1: Genes expression change of InlA and E-cad receptors

E-cad and C-met receptors in diarrhea patients using the rabbits intestinal ligated loop model. The rabbits intestinal ligated loop model is often used in research to characterize human diseases and infections. The ligated intestinal loop has been proven to be a useful model to study bacterial gastrointestinal diseases and it often leads to more accurate descriptions of human conditions.[21] However, in previous studies, a serious systemic infection called listeriosis is brought on by the food-borne bacterial pathogen *L. monocytogenes*.[22,23] In the intestine, *L. monocytogenes* may use its surface protein InlA to interact with the hosts via the InlA specific receptor's E-cadherin (E-cad) in order to translocate across the intestinal epithelium via goblet cells, in which E-cad may reach luminally.[24] The present study showed that InlA was significantly expressed in *L. monocytogenes* injected into the intestinal loops with a fold change of 3.966 compared to expression level of InlA in *L. monocytogenes* cultured on (BHI) agar with a fold change of 1.002 (*P* value <0.001). Also, E-cad was significantly expressed in the rabbit intestinal tissues injected by *L. monocytogenes* with a fold change of 4.022 compared to the expression level of E-cad in the intestinal tissues injected by PBS with a fold change of 1.0621, (*P* value 0.003). In the context of *Listeria* infection, the significantly elevated level of InlA production in this study indicated its important role in bacterial invasion. Also, there was a clear correlation with its specific receptor E-cad as it was significantly expressed. InlA binds to E-cad, a host cell receptor, facilitating the entrance of *L. monocytogenes* into epithelial cells in the intestinal lining. E-cad is a type of cell adhesion molecule that has a precarious role in maintaining tissue integrity and cell-to-cell interactions. It is typically expressed on the surface of cells and are involved in cell adhesion, migration, and signaling.[25] According to earlier research, *Listeria* can bind with E-cad receptor which is present at the apical surface of enterocytes.[26] In our study, the significant expression of InlA and E-cad compared to controls showed a clear connection to many studies demonstrating that *L. monocytogenes* can interact with E-cad on the surface of host cells, such as intestinal epithelial cells, to aid the organism's invasion into the tissue of the hosts. By attaching to E-cad on the surface of the cells with the help of the protein internalin, *Listeria* is able to enter host cells and evade the immune system response of the host. Because of the connection between *Listeria* and E-cad, the host's reaction to the infection may result in an increase of E-cad expression in host tissues.[27] Our result also agreed with,[27] which reported that the specificity of the contractions between InlA and E-cad, the signaling cascade that is, triggered when InlA engages with E-cad, and the function of InlA and E-cad in the breaching of host defenses and the spread of infection. Our finding suggests that *L. monocytogenes* can induce an increase in InlA expression in the rabbits intestinal tissue, which may contribute to the ability of the bacterium to invade and persist in the host.

Furthermore, it was previously reported that InlB is another virulence gene enabling *L. monocytogenes* to

Table 3: Genes expression change of InlB and C-met receptor

Target gene	Control fold change	Infected fold change	*T* test	*P* value
InlB	0.998615	5.456591	6.333	< 0.001
	1.033831	4.65248		
	1.012555	3.429504		
	1.02669	3.2898		
	0.93174	3.006323		
Mean ± SE	1.0007 ± 0.018267	4.8835 ± 1.438809		
SD	0.04085	3.21727		
C-met	0.79996	4.588428	4.474	0.002
	0.887611	5.381469		
	1.085229	5.68831		
	0.957935	2.358713		
	1.354725	10.8238		
Mean ± SE	1.0171 ± 0.096449	4.1341 ± 0.689983		
SD	0.21567	1.54285		

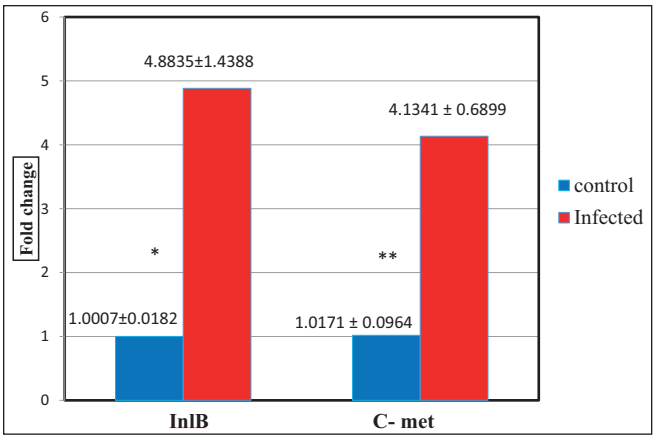

Figure 2: Genes expression change of InlB and C-met receptor

invade the host cells. Through its interaction with its cognate receptor C-met on the surface of the host cell, InlB facilitates bacterial entrance into non-phagocytic cells.[28] The present study showed that InlB was significantly expressed in *L. monocytogenes* injected into the intestinal loops with a fold change of (4.8835) compared to expression level of IntB in *L. monocytogenes* cultured on (BHI) agar with a fold change of (1.0007) (*P* value 0.027). Also, C-met was significantly expressed in the intestinal tissues injected by *L. monocytogenes* with a fold change of 4.1341 compared to the expression levels of C-met in the intestinal tissues injected by (PBS) with a fold change of 1.0171, (*P* value 0.002). Our result indicated that InlB plays a significant role in the invasion of *L. monocytogenes* to the rabbit's intestinal tissues. Also, the increased level of C-met expression in the intestinal tissues injected by *L. monocytogenes* showed a strong correlation with InlB level of expression. This result is consistent with the study conducted by,[29] which reported that InlB locally activates C-met to accelerate junctional endocytosis and bacterial invasion to the intestine. The elevated expression levels of C-met receptors in the rabbit intestinal tissues injected by *L. monocytogenes* are consistent with the previous study conducted by,[30] which revealed that C-met enhances host responses to bacterial infections. In addition, our result is consistent with the previous study done by,[31] which found that C-met has a significant role in enhancing host responses to bacterial infections. C-met is tyrosine kinase receptor, which has very important function in the cell migration and growth during the embryogenesis process. It also participated in the invasion of cells by bacterial pathogen.[32] The present result demonstrated that there is a direct positive correlation between InlB and the C-met receptor. Our result agreed with previously reported study showed that that InlB can directly interact with C-met receptor in order to promote the internalization of pathogen in many mammalian cells.[33]

It has been reported that InlA and InlB may get activated during infection of the gastrointestinal tract, in which the InlB is the immediate downstream of InlA and is translated bicistronically with InlA,[6] whereas, other studies showed that both InlB and InlA function synergistically during the invasion of epithelial cells through an unknown mechanism.[27,34] In our study, the elevated expression levels of InlA and InlB genes in *L. monocytogenes* injected in the rabbit intestinal tissues could indicate increased virulence of our inoculate, leading to enhance its invasion and colonization to the intestinal tissues, which agrees with previous studies that shows the importance of these genes in the pathogenesis of *L. monocytogenes* infections.[35-37] However, our findings also suggest that InlA and InlB play crucial roles in *L. monocytogenes* ability to penetrate and cause inflammation in the intestines. A study in mice showed that InlA expression markedly improved bacterial dispersion to the mesenteric lymph nodes and increased bacterial persistence in the underlying lamina propria.[36]

A study conducted in animal model showed that bacteria can successfully invade the intestinal barrier via InlA.[23] When bacteria are in the intestinal lumen, the InlAB operon is activated, and expression of InlB increases intestinal epithelial cell invasion when InlA-E-cad connections are active.[34]

Conclusion

The current study concludes that InlA and InlB genes are virulence factors that enable *L. monocytogenes* to invade host cells. Also, E-cad and C-met are host cell receptors facilitating bacterial entry. Moreover, the high levels of InlA and InlB gene expression within *L. monocytogenes* play a role in the invasion and colonization of this bacterium to the intestine of diarrhea patients and successfully cause infection. Further research is needed to fully understand the molecular mechanisms underlying the interaction between internalines (InlA, InlB) in *L. monocytogenes* and their receptors E-cad and C-met in diarrhea patient's intestinal tissues during infection.

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Conflicts of interest

There are no conflicts of interest.

References

1. Ryser ET, Marth EH. The genus *Listeria* and *Listeria monocytogenes*: Phylogenetic position, taxonomy, and identification. In: Listeria, Listeriosis, and Food Safety. CRC Press; 2007. p. 19–38.
2. Guillet C, Join-Lambert O, Le Monnier A, Leclercq A, Mechaï F, Mamzer-Bruneel M-F, *et al*. Human listeriosis caused by *Listeria ivanovii*. Emerg Infect Dis 2010;16:136-8.
3. Lopez-Valladares G, Danielsson-Tham M-L, Tham W. Implicated food products for listeriosis and changes in serovars of *Listeria monocytogenes* affecting humans in recent decades. Foodborne Pathog Dis 2018;15:387-97.
4. Cunha S, Komora N, Magalhães R, Almeida G, Ferreira V, Teixeira P. Characterization of clinical and food *Listeria monocytogenes* isolates with different antibiotic resistance patterns through simulated gastrointestinal tract conditions and environmental stresses. Microbial Risk Anal 2016;1:40-6.
5. Akgul A, Al-Janabi N, Das B, Lawrence M, Karsi A. Small molecules targeting LapB protein prevent *Listeria* attachment to catfish muscle. PLoS ONE 2017;12:e0189809.
6. Gaillard J-L, Berche P, Frehel C, Gouln E, Cossart P. Entry of *L. monocytogenes* into cells is mediated by internalin, a repeat protein reminiscent of surface antigens from gram-positive cocci. Cell 1991;65:1127-41.
7. Schubert WD, Urbanke C, Ziehm T, Beier V, Machner MP, Domann E, *et al*. Structure of internalin, a major invasion protein of *Listeria monocytogenes*, in complex with its human receptor E-cadherin. Cell 2002;111:825-36.
8. Camejo A, Carvalho F, Reis O, Leitão E, Sousa S, Cabanes D. The arsenal of virulence factors deployed by *Listeria monocytogenes* to promote its cell infection cycle. Virulence 2011;2:379-94.
9. Hayder SA, Raziq AH. The correlation of E-cadherin expression with the modified Gleason score and the grade group of prostatic adenocarcinoma. Med J Babylon 2021;18:103.
10. Abdullah RA, Abdulrahman IS. Circulating cell adhesion molecules level in type 2 diabetes mellitus and its correlation with glycemic control and metabolic syndrome: A case-control study. Med J Babylon 2023;20:64-70.
11. Lecuit M, Ohayon H, Braun L, Mengaud J, Cossart P. Internalin of *Listeria monocytogenes* with an intact leucine-rich repeat region is sufficient to promote internalization. Infect Immun 1997;65:5309-19.
12. Yap AS, Niessen CM, Gumbiner BM. The juxtamembrane region of the cadherin cytoplasmic tail supports lateral clustering, adhesive strengthening, and interaction with p120ctn. J Cell Biol 1998;141:779-89.
13. Temm-Grove CJ, Jockusch BM, Rohde M, Niebuhr K, Chakraborty T, Wehland J. Exploitation of microfilament proteins by *Listeria monocytogenes*: Microvillus-like composition of the comet tails and vectorial spreading in polarized epithelial sheets. J Cell Sci 1994;107:2951-60.
14. Mengaud J, Ohayon H, Gounon P, Mège R-M, Cossart P. E-cadherin is the receptor for internalin, a surface protein required for entry of *L. monocytogenes* into epithelial cells. Cell 1996;84:923-32.
15. Braun L, Ohayon H, Cossart P. The InlB protein of *Listeria monocytogenes* is sufficient to promote entry into mammalian cells. Mol Microbiol 1998;27:1077-87.
16. Dramsi S, Biswas I, Maguin E, Braun L, Mastroeni P, Cossart P. Entry of *Listeria monocytogenes* into hepatocytes requires expression of inIB, a surface protein of the internalin multigene family. Mol Microbiol 1995;16:251-61.
17. Birchmeier C, Gherardi E. Developmental roles of HGF/SF and its receptor, the c-Met tyrosine kinase. Trends Cell Biol 1998;8:404-10.
18. Shen Y, Naujokas M, Park M, Ireton K. InlB-dependent internalization of Listeria is mediated by the Met receptor tyrosine kinase. Cell 2000;103:501-10.
19. Khalef AK. Immunomolecular and histological changes induced by Listeria monocytogenes using intestinal loop model. MSc Thesis. College of Biotechnology, AL-Qasim Green University; 2022.
20. Farhan SS, Tahmasebi P, Al-Dahmoshi HOM, Gatea HS. Gene expression of TNF-α among Iraqi COVID-19 patients with a different severity status. Med J Babylon 2023;20:91.
21. Jiminez JA, Uwiera TC, Douglas Inglis G, Uwiera RRE. Animal models to study acute and chronic intestinal inflammation in mammals. Gut Pathog 2015;7:1-31.
22. Lecuit M. *Listeria monocytogenes*, a model in infection biology. Cell Microbiol 2020;22:e13186.
23. Lecuit M, Vandormael-Pournin S, Lefort J, Huerre M, Gounon P, Dupuy C, *et al*. A transgenic model for listeriosis: Role of internalin in crossing the intestinal barrier. Science (New York, NY) 2001;292:1722-5.
24. Nikitas G, Deschamps C, Disson O, Niault T, Cossart P, Lecuit M. Transcytosis of *Listeria monocytogenes* across the intestinal barrier upon specific targeting of goblet cell accessible E-cadherin. J Exp Med 2011;208:2263-77.
25. Maître J-L, Heisenberg C-P. Three functions of cadherins in cell adhesion. Curr Biol 2013;23:R626-33.
26. Pentecost M, Otto G, Theriot JA, Amieva MR. *Listeria monocytogenes* invades the epithelial junctions at sites of cell extrusion. PLoS Pathog 2006;2:e3.
27. Bonazzi M, Lecuit M, Cossart P. *Listeria monocytogenes* internalin and E-cadherin: From bench to bedside. Cold Spring Harb Perspect Biol 2009;1:a003087.
28. Kenzel J, Brüggemann DA, Funke SA. Selection of *Listeria monocytogenes* InlA-binding peptides using phage display—Novel compounds for diagnostic applications? Appl Microbiol 2022;2:921-33.
29. Pentecost M, Kumaran J, Ghosh P, Amieva MR. *Listeria monocytogenes* internalin B activates junctional endocytosis to accelerate intestinal invasion. PLoS Pathog 2010;6:e1000900.
30. Quereda JJ, Morón-García A, Palacios-Gorba C, Dessaux C, García-del Portillo F, Pucciarelli MG, *et al*. Pathogenicity and

virulence of *Listeria monocytogenes*: A trip from environmental to medical microbiology. Virulence 2021;12:2509-45.
31. Bleymüller WM, Lämmermann N, Ebbes M, Maynard D, Geerds C, Niemann HH. MET-activating residues in the B-repeat of the *Listeria monocytogenes* invasion protein InlB. J Biol Chem 2016;291:25567-77.
32. Trusolino L, Comoglio PM. Scatter-factor and semaphorin receptors: Cell signalling for invasive growth. Nat Rev Cancer 2002;2:289-300.
33. Pizarro-Cerdá J, Kühbacher A, Cossart P. Entry of *Listeria monocytogenes* in mammalian epithelial cells: An updated view. Cold Spring Harb Perspect Med 2012;2:a010009.
34. Disson O, Grayo S, Huillet E, Nikitas G, Langa-Vives F, Dussurget O, *et al*. Conjugated action of two species-specific invasion proteins for fetoplacental listeriosis. Nature 2008;455:1114-8.
35. Tamburro M, Sammarco ML, Ammendolia MG, Fanelli I, Minelli F, Ripabelli G. Evaluation of transcription levels of inlA, inlB, hly, bsh and prfA genes in *Listeria monocytogenes* strains using quantitative reverse-transcription PCR and ability of invasion into human CaCo-2 cells. FEMS Microbiol Lett 2015;362:fnv018.
36. Bou Ghanem EN, Jones GS, Myers-Morales T, Patil PD, Hidayatullah AN, D'Orazio SEF. InlA promotes dissemination of *Listeria monocytogenes* to the mesenteric lymph nodes during food borne infection of mice. PLoS Pathog 2012;8:e1003015.
37. Werbrouck H, Grijspeerdt K, Botteldoorn N, Van Pamel E, Rijpens N, Van Damme J, *et al*. Differential inlA and inlB expression and interaction with human intestinal and liver cells by *Listeria monocytogenes* strains of different origins. Appl Environ Microbiol 2006;72:3862-71.