Microbiological Research 297 (2025) 128187

Contents lists available at ScienceDirect

Microbiological Research

journal homepage: www.elsevier.com/locate/micres

# *Listeria monocytogenes* gut interactions and listeriosis: Gut modulation and pathogenicity

M. Oliveira, J. Barbosa, P. Teixeira *

*Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Rua de Diogo Botelho 1327, 4169-005, Porto, Portugal*

A R T I C L E I N F O

*Keywords:*
*Listeria monocytogenes*
Pathogenicity
Gastrointestinal tract
Microbiota interaction
Food safety

A B S T R A C T

Following ingestion via contaminated food, *Listeria monocytogenes* faces multiple hurdles through the human digestive system, thereby influencing its capacity to cause infection. This review provides a comprehensive overview of the multifaceted mechanisms employed by *L. monocytogenes* to overcome gastrointestinal hurdles and interact with the host's microbiota, facing chemical and physical barriers such as saliva, stomach acidity, bile salts and mechanical clearance. Proposed evasion strategies will be highlighted, exploring the bacteriocins produced by *L. monocytogenes*, such as the well-described bacteriocin Listeriolysin S (LLS), a bacteriocin that inhibits inflammogenic species – Lmo2776, and a phage tail-like bacteriocin, monocin. The competitive dynamic interactions within the gut microbiota, as well as the modulation of microbiota composition and immune responses, will also be explored. Finally, the adhesion and invasion of the intestinal epithelium by *L. monocytogenes* is described, exploring the mechanism of pathogenesis, biofilm and aggregation capacities and other virulence factors. Unlike previous reviews that may focus on individual aspects of *L. monocytogenes* pathogenicity, this review offers a holistic perspective on the bacterium's ability to persist and cause infection, integrating information about survival strategies, including bacteriocin production, immune modulation, and virulence factors. By connecting recent findings on microbial interactions and infection dynamics, this review incorporates recent developments in the field and connects various lines of research that explore both host and microbial factors influencing infection outcomes.

## 1. Introduction

The genus *Listeria* currently comprises twenty-seven species, two of which are pathogenic to humans: *Listeria monocytogenes* and *Listeria innocua*. These species can cause fatal listeriosis in humans, and other mammals, including cattle (Hafner et al., 2021). *Listeria innocua* is generally considered a non-pathogenic species (Drolia and Bhunia, 2019), sporadically identified in humans (Bagatella et al., 2022), but it was linked to one death (Osek and Wieczorek, 2022). *Listeria monocytogenes*, on the other hand, is the etiological agent of human listeriosis. In 2023, listeriosis was the fifth most reported zoonosis in humans in the European Union and the most severe zoonotic disease, with the highest percentage of hospitalisations among cases and the highest case fatality rate (ECDC, 2024; EFSA & ECDC, 2024). This life-threatening infection can affect healthy individuals, but the most serious situations occur in pregnant women, newborns, the elderly, and immunocompromised individuals (Radoshevich and Cossart, 2017; Swaminathan and Gerner-Smidt, 2007).

*Listeria monocytogenes* has a ubiquitous nature and great adaptability (Linke et al., 2014). It is commonly found in different ecological niches, including soil, stream water, sewage, and plants (McLauchlin et al., 2004) and is noteworthy for its persistence in food-manufacturing environments (Bland et al., 2022; Macleod et al., 2022; Vidovic et al., 2022; Zhu et al., 2022). Additionally, it exhibits remarkable environmental tolerance as a psychotropic organism, able to grow at temperatures ranging from −1.5–45 °C at high concentrations of salt (10.0 %, w/v), wide pH range (pH 4.4–9.4), low water activity (< 0.90), and in the presence or absence of oxygen (facultative anaerobic) (Bucur et al., 2018; Osek and Wieczorek, 2022; Ravindhiran et al., 2023). This raises major public health and food safety concerns, with consequent economic implications, and highlights the need for an effective response to the pertinence of this pathogen (EFSA & ECDC, 2024; Macleod et al., 2022).

As a saprophytic organism, *L. monocytogenes* can transition to an

* Corresponding author.
*E-mail address:* pcteixeira@ucp.pt (P. Teixeira).

https://doi.org/10.1016/j.micres.2025.128187
Received 25 February 2025; Received in revised form 16 April 2025; Accepted 17 April 2025
Available online 17 April 2025

infectious state upon ingestion, becoming a lethal intracellular pathogen (Bagatella et al., 2022; Davis et al., 2019; Herzog et al., 2023). Once inside the host, following the consumption of contaminated food, *L. monocytogenes* encounters multiple stressors within the gastrointestinal tract (GIT), including fluctuations in pH, bile salts, and oxygen availability (Davis et al., 2019). Conversely, the intestinal microbiota plays a protective role against various pathogens, including *L. monocytogenes,* through mechanisms beyond merely shaping host immunity (Chiu et al., 2017). Despite growing research efforts to elucidate the key factors underlying *L. monocytogenes* pathogenicity, its capacity to interact with and modulate the intestinal microbiota in its favor remains poorly understood (Bagatella et al., 2022; Davis et al., 2019; Herzog et al., 2023).

This review will explore the existing literature on the mechanisms employed by *L. monocytogenes* to overcome digestive barriers and the existing interactions between *L. monocytogenes* and the commensal microbiota. Therefore, this review is divided into two parts: i) the journey through the host's gastrointestinal tract and existent barriers: oral cavity, stomach, and intestine; and ii) proposed *L. monocytogenes* mechanisms to overcome digestion hurdles (e.g., acidic tolerance response; biofilm formation; aggregation; adhesion and invasion, intracellular survival; production of antimicrobial substances) and the interaction between *L. monocytogenes* and commensal microbes (e.g. modulation of host immune responses; competition for resources).

## 2. *Listeria monocytogenes* and its pathogenicity: the journey through the host's gastrointestinal tract

*Listeria monocytogenes* enters the host's gastrointestinal tract through the ingestion of contaminated food. Once inside the host, *L. monocytogenes* come upon digestion in the oral cavity and stomach (rapid digestion rate) and in the small intestine (ileum) (slow digestion rate) (Rinninella et al., 2019; Sensoy, 2021). In addition to overcoming chemical barriers like saliva components, stomach acidity, and bile salts in the small intestine, it must also navigate physical hurdles such as mechanical clearance and digestion, mucus layers, gastric and intestinal epithelial barriers, complex human microbiota, and the adaptive and innate immune response of the host (Becattini et al., 2017; Reinus and Simon, 2014). *Listeria monocytogenes* faces multiple obstacles as it travels through the human gastrointestinal tract, which can significantly affect its ability to cause an infection. However, there is still much to be learned about the mechanisms that *L. monocytogenes* employs to overcome these challenges and thrive in the gut. To better understand *L. monocytogenes* pathogenicity and its impact on the gut microbiota, the authors have chosen to present in this section a detailed account of the various environmental stressors faced by *L. monocytogenes* while traversing the gastrointestinal tract which includes the oral cavity, pharynx, esophagus, stomach, the gut itself, the small intestine, and the large intestine (Reinus and Simon, 2014; Smith and Morton, 2011).

Fig. 1 provides a brief overview of *L. monocytogenes'* journey and the different stressors it faces along the way. Despite the difficulties and hardships of traveling, enteric pathogens have evolved mechanisms that allow them to thrive and survive in harsh environmental conditions, improving their overall growth and survival capabilities.

Listeriosis is mainly acquired by the consumption of foods contaminated with *L. monocytogenes*. *Listeria monocytogenes* presents an amazing capacity to cross protective epithelial barriers, namely blood-brain, intestinal, and placental, and may manifest as brain inflammation and severe blood infection. Once it infects the host, *L. monocytogenes* crosses the intestinal epithelium via transcytosis and rapidly spreads through the lymphatic system or bloodstream to the mesenteric lymph nodes, spleen and the liver (Cossart and Toledo-Arana, 2008) *Listeria monocytogenes* faces multiple challenges in its journey through the human body.

### 2.1. Oral cavity barriers

*Listeria monocytogenes* is not commonly found in the oral microbiota,

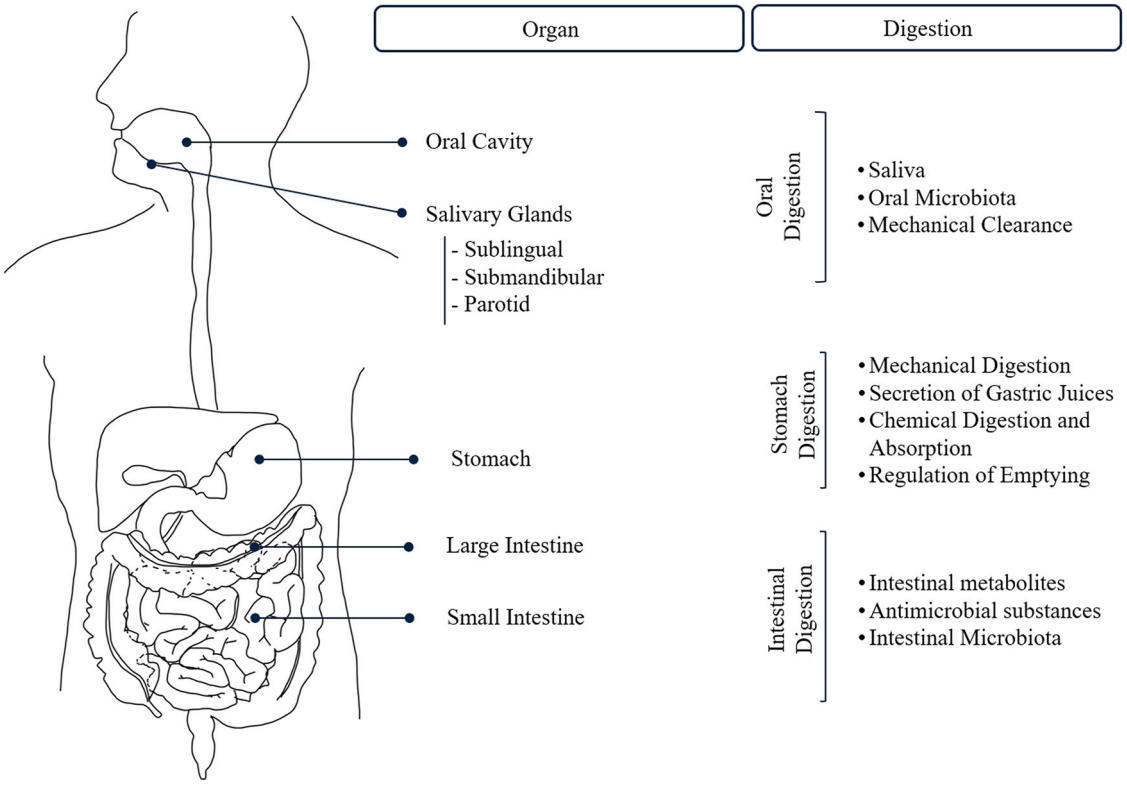


**Fig. 1.** Major hurdles encountered by *Listeria monocytogenes* when passing through the gastrointestinal tract: i) Oral digestion, ii) Stomach digestion, iii) Intestinal digestion.

but it can still find its way into the oral cavity through contaminated food or due to poor oral hygiene. Several barriers can prevent colonization by *L. monocytogenes*, such as salivary fluids, the presence of other microorganisms in the oral cavity, mechanical clearance, and the mucus layer, which enables the exchange of nutrients and provides lubrication as a physical barrier (Groeger and Meyle, 2019; Vila et al., 2019a) (refer to Table 1 for details). Additionally, it is important to note that the food consumed and its properties, such as acidity and buffer effect, can affect oral digestion, which, in turn, can act as a barrier against colonization by *L. monocytogenes* (Mennah-Govela et al., 2020).

Upon ingestion, the salivary fluid produced by the salivary glands (parotid, sublingual, and submandibular glands, as shown in Fig. 1) acts as a natural barrier against bacteria (Minekus et al., 2014). In addition to aiding in mastication and swallowing, saliva contains various components such as proteins, electrolytes, nitrogenous products, glucose, and enzymes that promote solubility, elasticity, and adhesiveness in the oral cavity (Sensoy, 2021). The focus shifts to how these pathogenic bacteria can potentially interact with or exploit the oral environment, particularly if there are breaches in the body's defenses. Pathogenic bacteria such as *L. monocytogenes* can gain access to the oral cavity by utilizing nutrients for growth and using the oral cavity environment to adhere to oral tissues, enabling easy colonization (Olsen, 2020; Pedersen and Belstrøm, 2019). Saliva plays an important role in protecting the oral cavity through its antibacterial components, including hydrogen peroxide, lactoferrin, lysozyme, and mucins. These substances collectively inhibit bacterial growth and promote microbial clearance (Reinus and Simon, 2014; Smith and Morton, 2011).

The oral microbiota, comprising over 700 bacterial species, is characterized by its diversity and functional specialization (Santacroce et al., 2023). Predominant genera such as *Streptococcus*, *Veillonella*, and *Selenomonas* contribute to microbial homeostasis through nutrient competition, production of antimicrobial substances, and biofilm formation (Lamont et al., 2018; Min et al., 2023). This intricate microbial ecosystem not only prevents colonization by harmful pathogens but also supports host immunity and overall oral health (Bowen et al., 2018; Vila et al., 2019b). Disruptions in this balance can lead to dysbiosis, increasing susceptibility to infections (Min et al., 2023).

Despite the protective mechanisms of saliva and the oral microbiota, *L. monocytogenes* can exploit breaches in these defenses. For instance, it resists lysozyme activity by regulating cell wall-modifying enzymes rather than acquiring new ones (Burke et al., 2014). However, hydrogen peroxide remains effective against *L. monocytogenes*, even penetrating its biofilms to inactivate the pathogen (Skowron et al., 2018). Interestingly, human lactoferrin has been found to facilitate hepatic colonization of *L. monocytogenes* under specific conditions (Lee et al., 2005), highlighting the complex interactions between host defenses and pathogenic mechanisms.

It is important to recognize that certain conditions, such as poor oral health, oral mucosal damage, or immunosuppression, may increase the likelihood of opportunistic pathogens breaching natural barriers and causing infections (Groeger and Meyle, 2019; Pedersen and Belstrøm, 2019). Furthermore, if *L. monocytogenes* enters the oral cavity through contaminated food, it can bypass some of these barriers and directly interact with the oral mucosa (D'orazio et al., 2014; Lammerding et al., 1992; Marco et al., 1997).

**Table 1**
Oral cavity barriers.

| Hurdles | Process |
|---|---|
| Saliva and Oral Microbiota | Saliva is essential in maintaining oral health. It contains antimicrobial components (proteins and peptides including mucins, lactoferrin, lactoperoxidase, lysozyme, histatins, statherin, and antibodies) that inhibit the growth of bacteria like *L. monocytogenes*. Furthermore, the complex oral microbiota plays an important role in maintaining oral health by competitively excluding potential pathogens and producing extracellular polymeric substances (EPSs) (Bowen et al., 2018; Lamont et al., 2018; Min et al., 2023; Reinus and Simon, 2014; Santacroce et al., 2023; Vila et al., 2019). |
| Mechanical Clearance | Chewing, swallowing, and salivary flow aid in clearing bacteria from the mouth by mechanically removing and flushing out bacteria. This reduces the likelihood of adherence and colonization by bacteria, including *L. monocytogenes* (Vila et al., 2019a). |
| Mucus Layer | The oral cavity's protective mucus layer serves as a physical barrier, trapping and eliminating bacteria to prevent microbial invasion. Despite the ability of *L. monocytogenes* to adhere to host cells, the mucus layer effectively hinders its access to the underlying tissues and interaction with the epithelial cells of the oral mucosa. This defense mechanism is crucial for maintaining oral health and preventing infections (Groeger and Meyle, 2019; Olsen, 2020). |

### 2.2. Passage through the stomach: survival and adaptability

When *L. monocytogenes* successfully survives oral digestion, it will face several barriers in the stomach that can affect its survival and ability to cause an infection. Harsh conditions like low pH, gastric motility, mucus layer, and gastric epithelial barrier (see Fig. 2) act as protective and physical barriers, making it difficult for the pathogen to establish an infection.

The stomach, a muscular organ located in the upper abdomen, plays a crucial role in the digestive system (Table 2).

Apart from breaking down food, processes occurring in the stomach also have the critical role of eliminating harmful microorganisms that could cause infection. The stomach has several complex mechanisms that act as barriers to prevent the spread of harmful bacteria, including *L. monocytogenes* (as shown in Fig. 2 below), and help to eliminate and expel them from the body. One of the most important mechanisms is the secretion of hydrochloric acid (HCl), which increases the stomach's acidity to a level that is lethal to most bacteria (Reinus and Simon, 2014; Smith and Morton, 2011). HCl disrupts and weakens the structural integrity of bacterial cells by denaturing proteins and interferes with various metabolic processes by acidifying the cytoplasm. Moreover, the disruption of the membrane function can cause the leakage of cellular components and, ultimately, cell death. The low pH facilitates the activation of pepsinogen, an inactive enzyme produced by the stomach's chief cells, converting it into its active form (pepsin). This enzyme can degrade bacterial proteins, further compromising the integrity of the bacteria (Caminero et al., 2023).

Additionally, the stomach contains mucus-producing cells that line its walls and form a protective layer that prevents the acid from damaging the stomach's tissues (Pelaseyed et al., 2014).

Moreover, the contractions of the stomach muscles, known as peristalsis, help to mix and grind the food, which further aids digestion and eliminates harmful microorganisms. The stomach also has a valve-like structure located at its lower end called the pyloric sphincter, which regulates the flow of food into the small intestine and prevents the backward flow of harmful bacteria. Thus, the stomach's complex mechanisms work together to ensure that harmful microorganisms are eliminated from the body and do not cause infections. Nevertheless, bacteria, including *L. monocytogenes*, have evolved a range of strategies to adapt and survive in harsh, stressful environments (Banerji et al., 2022; Cheng et al., 2017; Osek and Wieczorek, 2022).

The stomach helps mix and grind food, further supporting digestion and eliminating harmful microorganisms. It also contains a valve-like structure at its lower end, known as the pyloric sphincter, which regulates the flow of food into the small intestine and prevents the backward movement of harmful bacteria.

### 2.3. Navigating the gut: Listeria monocytogenes journey and intestinal hurdles

Once the partially digested food (chyme) enters the small intestine, most digestion and nutrient absorption occur. The small intestine further

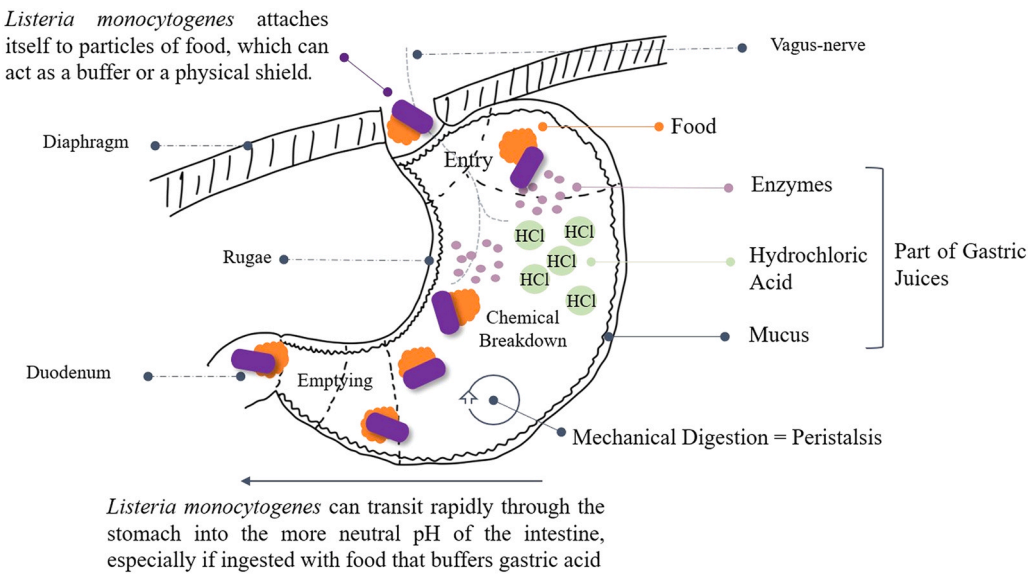


**Fig. 2.** Functional anatomy of the gastric mucosa (Samuelson, 2006; Toh and Alderuccio, 2007).

**Table 2**
Stomach mechanisms and functions.

| | Function |
|---|---|
| Stomach | The stomach is essential for digestion, acting as a temporary storage reservoir for food. As food travels down from the esophagus through the lower esophageal sphincter, the stomach expands to accommodate it. This enables the gradual breakdown of food into smaller pieces and its mixing with digestive juices before passing it on to the small intestine for further processing (Smith and Morton, 2011). |
| Mechanical Digestion | As food enters the stomach, its muscular walls undergo a rhythmic contraction and relaxation process known as peristalsis. This movement helps mix the food with digestive juices, breaking it down into smaller particles. The result is a semi-fluid mixture called chyme, which is formed due to the partially digested food (Sensoy, 2021). |
| Secretion of Gastric Juices | The stomach lining is a complex structure responsible for secreting a variety of gastric juices, which play a crucial role in digestion. These juices contain a mix of hydrochloric acid (HCl) and enzymes, including pepsin, which help to break down proteins. The acidic environment created by HCl helps to activate pepsin and "sterilize" any ingested food (Reinus and Simon, 2014; Smith and Morton, 2011). |
| Chemical Digestion and Absorption | As food enters the stomach, the enzymes present in the gastric juices work and begin breaking down the proteins into smaller peptides. However, it is worth noting that the stomach's acidic environment is not particularly conducive to the digestion of carbohydrates and fats, and therefore, their breakdown is limited at this stage (Boland, 2016). |
| Regulation of Emptying | The process of chyme release from the stomach to the small intestine is gradual and regulated by various factors, such as the consistency of the chyme and the presence of hormones and neural signals. The pyloric sphincter, a muscular valve at the stomach's exit, controls the rate at which the stomach empties ( Bredenoord et al., 2016). |

breaks down the chyme using pancreatic enzymes and bile, allowing the absorption of nutrients into the bloodstream (Dosch et al., 2019; Pandiri, 2013). The intestinal digestive system (see Fig. 3) is a complex microbiological machinery that plays a crucial role in breaking down food, absorbing nutrients, extracting water, and eliminating waste (Kiela and Ghishan, 2016; Song et al., 2023). The gut microbiome is crucial in supporting a healthy digestive system and overall well-being. Moreover, maintaining intestinal homeostasis is required to protect against pathogenic bacteria (Maloy and Powrie, 2011).

Several barriers influence the transit time of the small intestine. Produced by the liver and stored in the gallbladder, bile is a digestive fluid that aids in fat breakdown in the small intestine (Akritidou et al., 2022). Beyond its role in digestion, bile functions as a barrier to pathogens due to its bactericidal properties mainly targeting by disrupting bacterial membranes (Bustos et al., 2018). However, *L. monocytogenes* has developed mechanisms to resist bile stress, thereby facilitating its survival in the gastrointestinal tract. Notable adaptations include the synthesis of bile salt hydrolase (BSH), a detoxifying enzyme that neutralises bile acids, and the activation of stress response systems (Begley et al., 2005; Dussurget et al., 2002; Zhang et al., 2011). In the study conducted by Akritidou et al. (2022), it was hypothesised that the sensitivity of *L. monocytogenes* strains to bile salts could be a strain-specific trait, and dependent on the physiological state of the cells after exposure to low pH conditions, as the tolerance to bile salts in their study was lower than that found in previous studies.

Proteins and fats are digested by pancreatin, a digestive enzyme produced by the pancreas (Akritidou et al., 2022; Minekus et al., 2014). In the duodenum, situated between the stomach and the small intestine, partially digested food is further broken down by pancreatic juices. The bicarbonate-rich fluid and digestive enzymes released by the pancreas help to hydrolyze dietary macronutrients, such as protein, starch, and fat (Patricia and Dhamoon, 2022). Proteases are responsible for breaking down proteins (Minekus et al., 2014). Similarly, amylases are responsible for digesting starch, while lipases break down triglycerides and phospholipids (Brodkorb et al., 2019). All in all, the duodenum is a vital component of the digestive system, ensuring the body extracts nutrients from the food we consume. While these enzymes create a hostile environment for pathogens in general, *L. monocytogenes* has developed mechanisms to survive, including the upregulation of stress-related genes and modifying its membrane composition to resist enzymatic degradation (Carvalho et al., 2014).

In addition, the human intestine is home to a diverse community of microorganisms, known as the intestinal microbiota, which plays a vital role in the digestive process by helping to break down and ferment indigestible carbohydrates and other complex molecules (Thursby and Juge, 2017). This microbiota, along with digestive fluids like bile, acts as a natural defense against pathogens such as *L. monocytogenes* (Bustos et al., 2018). Gut microbiota species outcompete *L. monocytogenes* by

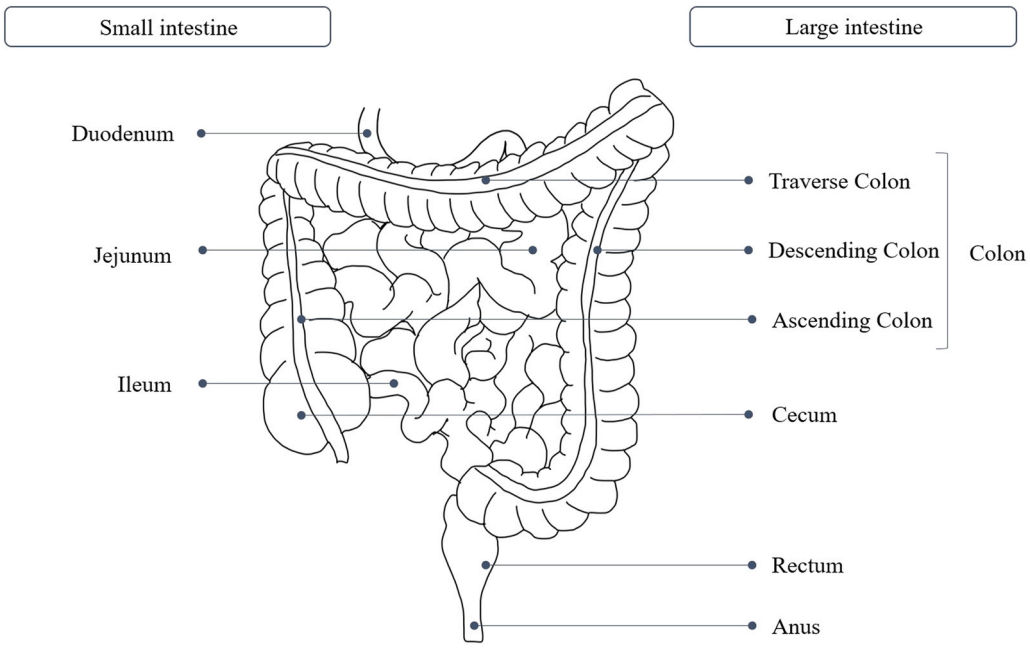


**Fig. 3.** Schematization of the intestinal anatomy.

producing antimicrobial peptides and altering local pH levels. For example, *Lactococcus lactis* produces nisin, inhibiting a broad spectrum of gram-positive bacteria including *L. monocytogenes* and *Staphylococcus aureus* (Asaduzzaman and Sonomoto, 2009; Wang et al., 2022a). Furthermore, the gut's physical and immune barriers, including the mucus layer and immune responses, help restrict *L. monocytogenes* colonization and invasion. As shown in Table 3, these hurdles work together to ensure effective digestion and nutrient absorption within the intestine.

## 3. Evasion strategies of *Listeria monocytogenes* in the digestive tract

As previously mentioned, *L. monocytogenes* can cause serious human infections, especially in individuals with weakened immune systems.

**Table 3**
Intestinal hurdles and their role.

| Hurdles | Process |
|---|---|
| **Bile** | Bile is a crucial fluid that supplies bile acids, lipids, and metabolites to the intestine. Also, with the help of lipases, it aids in breaking down fats in the small intestine. Bile is an essential part of the digestion of food. Additionally, bile exerts antimicrobial effects by disrupting bacterial membranes, contributing to intestinal defense against harmful microorganisms (Akritidou et al., 2022; Bustos et al., 2018; Reinus and Simon, 2014). |
| **Digestive Enzymes** | Food is broken down into smaller molecules during digestion with the aid of digestive enzymes. These enzymes, such as pancreatin, proteases and amylases, are crucial in breaking down nutrients like proteins, carbohydrates, and fats ( Brodkorb et al., 2019; Minekus et al., 2014; Patricia and Dhamoon, 2022) and can also exert antimicrobial activity by hydrolyzing key structural components such as proteins and lipids, thereby disrupting bacterial membranes and impairing ability to adhere or invade host tissues. |
| **Intestinal Microbiota** | A complex community of microorganisms, the human intestinal microbiota includes beneficial bacteria that can competitively inhibit or limit the growth and establishment of potential pathogens, like *L. monocytogenes*, by competing for nutrients and producing antimicrobial compounds (Chiu et al., 2017; Dey et al., 2022; Hooper and MacPherson, 2010; Thursby and Juge, 2017; H. Wang et al., 2022a). |

This pathogen has developed mechanisms to overcome the immune system's defenses and promote its survival and replication within the intestinal tract. It can adhere to and invade intestinal epithelial cells, modulate host immune responses, and manipulate host cell processes to create a conducive environment for its growth. Despite being an intracellular pathogen, it can transiently colonize the intestine in certain situations, such as when the barrier between epithelial cells and commensal or pathogenic microorganisms is compromised (Zhang et al., 2021), the intestinal microbiota is disrupted (Becattini et al., 2017), or the protective mucus layer is lost, or its secretion is impaired (Song et al., 2023). However, the exact mechanisms behind this interaction are still not fully understood, and several factors have been proposed to contribute to the ability of *L. monocytogenes* to persist and interact with the gut microbiota, such as acid tolerance response, biofilm formation, and antimicrobial secretion (Fulano et al., 2023; Kozak et al., 2018; Zhang et al., 2023). Factors such as coexisting microorganisms, the host's immune response, and the composition of the food matrix, as well as the presence of antibiotics in the host's system, may all play a role in determining the fate of *L. monocytogenes* during oral digestion (Akritidou et al., 2023a,b; Fuchisawa et al., 2022; Las Heras et al., 2019; Maury et al., 2019).

Foodborne pathogenic bacteria are generally sensitive to acidic conditions, which has been extensively studied by various researchers (Akritidou et al., 2022; Barbosa et al., 2012; Cunha et al., 2016; Formato et al., 2007; Kapetanakou et al., 2017; Martín et al., 2023; Ramalheira et al., 2010; Saklani-Jusforgues et al., 2000; Zhang, 2021). Certain strains of *L. monocytogenes* have developed unique mechanisms that allow them to survive and thrive in the harsh acidic conditions of the stomach. These mechanisms include the induction of acid tolerance responses (ATR), which enable the bacteria to withstand low pH conditions (Akritidou et al., 2022; Barretta et al., 2019; Fulano et al., 2023; Saklani-Jusforgues et al., 2000; Zhang et al., 2023; Zilelidou et al., 2020). Additionally, *L. monocytogenes* has the potential to transit through the stomach, attaching to food particles, which facilitates their passage (Fulano et al., 2023). It is worth noting that the severity and outcome of listeriosis can vary depending on several factors, such as the specific strain of *L. monocytogenes*, the dose of ingested bacteria, the immune status of the host, and other host-related factors (Fuchisawa et al., 2022; Jiang et al., 2010; Lammerding et al., 1992; Rahman et al., 2016, 2018; Zhang, 2021; Zilelidou et al., 2020). Studies have shown

that exposure to adverse conditions similar to the human gastrointestinal environment can affect the ability of *L. monocytogenes* to adapt and survive (Cheng et al., 2023; Pettersen et al., 2018; Ramalheira et al., 2010). Researchers have been studying the mechanisms behind this intricate capacity, including the effect of hypertonic solutions, pH changes, different bile salt concentrations, and digestive enzymes.

Cheng et al. (2023) showed that different subtypes of *L. monocytogenes* from both food and clinical sources have adaptive capacities to stressors such as acidity, heat, NaCl, and bile salt. When exposed to a simulated human gastrointestinal tract, the survival rates of the *L. monocytogenes* isolates were almost 100 %. Pettersen et al. (2018) found that the *L. monocytogenes* EGDe strain could easily invade *in vitro* HT-29 cells - which are often used to exhibit columnar epithelial cell characteristics - after passage through a harmonized standard *in vitro* digestion (Minekus et al., 2014). When compared to the EGDe strain, higher relative survival fractions were observed in isolates from three Scandinavian foodborne listeriosis outbreaks in the presence of low NaCl content before exposure to the *in vitro* digestion model (Pettersen et al., 2018), indicating that the effect is strain dependent. In a recent study by Akritidou et al. (2022), *L. monocytogenes* exhibited lower susceptibility to gastric acid than *Salmonella* Typhimurium. However, bile acids had a stronger bactericidal effect on *L. monocytogenes* than *S.* Typhimurium. This study further demonstrated that mild acidic shock could increase bile acid tolerance, leading to the emergence of cross-protection phenomena - when exposure to a sublethal level of one stressor increases resistance to another (Akritidou et al., 2022; Shah and Bergholz, 2020). *Listeria monocytogenes* can withstand acidic environments by adopting an acid-tolerant state, triggering specialized stress responses, and altering its cell membrane (Akritidou et al., 2022; Cheng et al., 2017). These adaptive mechanisms enable the bacterium to thrive in diverse conditions, such as the human digestive tract.

Intestinal survival of *L. monocytogenes* is promoted by its evasive capabilities and other factors that potentiate replication within the intestinal environment. *Listeria monocytogenes* can adhere to and invade intestinal epithelial cells, modulate host immune responses, and alter host cell processes to establish a favorable environment for its growth. Additionally, *L. monocytogenes* can adapt to the intestinal environment and evade certain aspects of the immune response, including evasion from neutrophils and pattern recognition receptors (PRRs), and evasion from antigens and indole signaling that interferes with biofilm formation and other virulence traits of *L. monocytogenes* (Cornick et al., 2015; Groeger and Meyle, 2019; Rattanaphan et al., 2020; Witter et al., 2016). However, the host's immune system and the protective factors in the intestinal microbiota collectively act as barriers to limit the colonization and dissemination of *L. monocytogenes* in the human gut (Hooper and MacPherson, 2010; Round and Mazmanian, 2009).

Food manufacturing environments are highly susceptible to contamination, as some strains have evolved mechanisms to better adapt and persist. One such mechanism is biofilm formation (Ferreira et al., 2014; Fulano et al., 2023). This extracellular matrix comprises extracellular polymeric substances (EPS) that support microbial communities in their virulence (Karygianni et al., 2020). In the case of *L. monocytogenes*, exopolysaccharide synthesis aids in cell aggregation (Chen et al., 2014) and enhances tolerance to gastric acid, facilitating colonization of the small intestine (Fulano et al., 2023). Fulano et al. (2023) have also demonstrated that EPS-biofilm producer strains have an advantage in surviving not just at low pH levels but also during food storage. Notably, different strains exhibit significantly different biofilm formation abilities at various temperatures, indicating that environmental conditions can determine the level of biofilm production (Barbosa et al., 2013). This finding is particularly important in the context of food preparation, such as cheese ripening and meat preparation, where growth in different environmental conditions can have a significant impact (Maury et al., 2019).

The composition, structure, and buffering effect of food can also affect the behavior of foodborne pathogens during gastrointestinal digestion (Akritidou et al., 2023b; Barmpalia-Davis et al., 2009; Zhang et al., 2023). For instance, (Akritidou et al., 2023b) observed a higher buffering effect on protein than on fat, resulting in a stronger protective effect. Additionally, lower fat content has been associated with the development of stress-resistant pathogens, while higher fat content in food exerted a protective effect against gastric destruction in later gastric exposure (>60 min) (Barmpalia-Davis et al., 2009). Various strategies have been developed to prevent the unwanted growth of foodborne pathogens in food matrices. One such strategy is the usage of antimicrobials, either alone or in combination, during food storage (Kozak et al., 2018). Studies have shown that the inclusion of specific concentrations of food-grade chemicals is an effective way to control foodborne pathogens, such as *L. monocytogenes* and *Salmonella* spp. on slices of meat matrices during refrigeration storage (Luchansky et al., 2018; Porto-Fett et al., 2018). However, it has also been observed that exposure to antimicrobials can increase the resistance of *L. monocytogenes* to gastric fluid, thereby enhancing its survival (Stopforth et al., 2005).

### 3.1. *Bacteriocins: Listeria monocytogenes intricate tool for gastrointestinal residency*

The resilience of *L. monocytogenes* in the face of the complex and challenging conditions of the digestive system is a well-known fact. Numerous studies, as aforementioned, have highlighted the impact of pH, temperature, bile acids, and osmotic stresses on its survival (Akritidou et al., 2022, 2023b; Cheng et al., 2017; Fulano et al., 2023; Kapetanakou et al., 2017). During its transient colonization of the gut, *L. monocytogenes* uses mechanisms that contribute to its persistence and interaction with the gut microbiota. This review will highlight some of the evasion strategies employed by *L. monocytogenes*, including bacteriocin production, nutrient competition mechanisms and adhesion capacities. These strategies serve as effective mechanisms that allow the pathogen to navigate through the hostile environment of the digestive system.

Commensal microbes can act as a first-line defense against *L. monocytogenes* infection (Becattini et al., 2017). However, recent studies have suggested that certain *L. monocytogenes* strains produce and secrete bacteriocins, including Listeriolysin S produced by the F2365 strain and Lmo2776 bacteriocin produced by strain EGD-e, that can selectively target and eliminate specific gut microbes, thus promoting the colonization of the gut by *L. monocytogenes* (Quereda et al., 2016; Rolhion et al., 2019).

Bacteriocins are antimicrobial peptides or proteins active against other bacteria (Lee, 2020). These compounds can be structurally and functionally diverse (Sugrue et al., 2024). The mode of action of bacteriocin varies depending on the specific bacteriocin and its bacterial target, making them a potent antibacterial agent (Simons et al., 2020). In fact, bacteriocin production can be a characteristic of virulent strains (Hernández-González et al., 2021). At present, our knowledge of the mechanisms involved in the modulation of the intestinal microbiota by the action of bacteriocins produced by *L. monocytogenes* is still limited. However, a few studies have demonstrated the diversity of these proteinaceous substances that selectively deplete indigenous bacterial species or closely related bacteria to promote their colonization (Lee, 2020) while avoiding excessive inflammation of the human gut and inhibition of the human microbiota (Rolhion et al., 2019). Bacteriocins with such properties include the intensely investigated bacteriocins listeriolysin S (LLS) and Lmo2776, as well as much less studied monocins.

Listeriolysin S (LLS) belongs to the family of thiazole/oxazole-modified microcins (TOMMs) (Meza-Torres et al., 2021). It behaves as a bacteriocin, having cytotoxic functions and hemolyzing activity (Bryant and Stevens, 2015; Cotter et al., 2008). It has been identified in various gram-positive pathogens and shows high genetic similarity to streptolysin S (SLS), a major virulence factor of *Streptococcus pyogenes*

(Reglinski and Sriskandan, 2014). Phylogenetic placement demonstrated that LLS-like toxins were found in *L. innocua*. *Enterococcus durans* and *Enterococcus caccae* also present toxins homologous to LLS (Mohammadzadeh et al., 2019). A study by Quereda et al. (2018) used chicken embryo models to explore the role of LLS in virulence. They found that LLS is a bacteriocin that contributes to virulence, specifically in the gut. It was also shown that virulence was minimal when the infection models avoided the intestinal route since the chicken embryos were infected via the allantoic cavity and not fed contaminated food. In a previous study, Quereda et al. (2017) confirmed that the major role of LLS as a bacteriocin in the intestine is during oral or intravenous infection of mice. In fact, in a mammalian model, LLS showed bactericidal activity against the indigenous gut microbiota but did not target eukaryotic host cells, targeting only prokaryotic cells *in vitro* and *in vivo* and it was involved in internal organ infections during systemic infection (Quereda et al., 2017, 2018).

LLS, produced locally in the gut, has been found to modify the structure of the host gut microbiota, which facilitates intestinal colonization by *L. monocytogenes* (Herzog et al., 2023; Quereda et al., 2016, 2017). LLS works by inducing membrane permeabilization and depolarization of target bacteria, thus promoting the progression of the infection (Meza-Torres et al., 2021). In a study by Mohammadzadeh et al. (2019), the interplay between LLS-producing (serotype 4b, lineage I) and non-LLS-producing (1/2a, NCTC7973) strains was investigated when cocultured with *Lactiplantibacillus plantarum*. *Lactiplantibacillus plantarum* is a bacterium that not only takes part in the human gut microbiota but also has probiotic properties. The study revealed that *Lpb. plantarum* was able to inhibit the growth of the co-cultured non-LLS-producing strain. However, when cocultured with the LLS-producing strain, the inhibitory effect of *Lpb. plantarum in vitro* was significantly reduced. Meza-Torres et al. (2021) studied the molecular mechanisms of action of LLS on target bacteria. It was found that LLS acts by forming pores in the membranes of target cells, resulting in cell lysis and death. The effect of cell disruption was demonstrated by Quereda et al. (2017), where the highest disruption of cell wall integrity of *Lactococcus lactis* was observed after 6 hours of coculture with an LLS-producing strain.

The LLS operon encodes eight structural genes that are required for the ability to invade and persist in the gut, including the *llsA* gene, which encodes the toxic component and structural peptide, and the *llsB* gene, which may be involved in post-translational modification of LLS (S. Lee, 2020; Mohammadzadeh et al., 2019). The deletion of these genes (ΔllsA and ΔllsB mutants), compared to the wild-type (WT) strain, demonstrated a significant decrease in viable *L. monocytogenes* cells in deep organs (liver and spleen) (Cotter et al., 2008). Furthermore, ΔllsA and ΔllsB strains have been found to reduce *L. monocytogenes* infection and reduce bacterial loads in the intestinal content (Quereda et al., 2016, 2018), indicating that LLS is necessary for virulence. An advantage of LLS is its contact-dependent activity. This means that LLS is metabolically active in the presence of LLS-resistant pathogenic bacteria that could benefit from the presence of LLS (Meza-Torres et al., 2021).

Another *L. monocytogenes* bacteriocin discovered, known as Lmo2776, is present in both lineage I (involved in clinical cases) and lineage II strains (e.g., EGD-e strain) and can be expressed under laboratory conditions. This bacteriocin selectively reduces the population levels of Bacteroidetes and increase levels of Firmicutes in the gut microbiota, preventing excessive inflammation (Rolhion et al., 2019). The Lmo2776 operon consists of two other genes - *lmo2774* and *lmo2775* - which are involved in immunity and transport, respectively (Lee, 2020). Lmo2776 is closely related to Lactococcin 972 (Lcn972), a class IIa bacteriocin produced by *Lact. Lactis* (Rolhion et al., 2019), which was recently discovered in *Bifidobacterium longum* subsp. *infantis* (Yu et al., 2023). Lmo2776 has been found to inhibit certain species that constitute the human gut microbiota, such as the inflammogenic species *Prevotella copri*, and inhibit the genera *Allobaculum* and *Alloprevotella* (Rolhion et al., 2019). *Prevotella copri* has the ability to induce mucus degradation (Wright et al., 2000) and reduce the mucosal immune response, thereby allowing better accessibility to *L. monocytogenes* infection. The exacerbation of bacterial infection allows impaired virulence and infection. Contrary to LLS, Lmo2776 limits *L. monocytogenes* infection. Moreover, besides *P. copri*, Lmo2776 also kills *B. subtilis* (one of the target members of the lactococcin 972 – Lcn972 – family of bacteriocins, which share between 38 % and 47 % overall amino acid sequence similarity with Lmo2776) demonstrating that this bacteriocin does not contribute to *L. monocytogenes* pathogenicity inside the host. Although only a few studies have been carried out to unveil the mechanisms of this bacteriocin, it remains a necessary discovery. However, the Lmo2776 peptide is capable of inhibiting *P. copri* and *B. subtilis* (Lee, 2020; Rolhion et al., 2019).

Studies have shed light on monocins, a type of phage tail-like structures produced by *L. monocytogenes* that are believed to play an important role as evasive strategies in complex environments. Monocins constitute a diverse group of high-molecular-weight bacteriocins that have been found in some *L. monocytogenes* strains. Some strains contain a monocin locus with 17 genes, while others harbor shorter versions of three to six genes (Argov et al., 2019). These structures were first reported in 1992, displaying similar activity to bacteriocins identified in some strains of *Enterococcus* and *Streptococcus* (Argov et al., 2019; Curtis and Mitchell, 1992).

A study conducted by Zink et al. (1995) revealed an evolutionary link between monocins and bacteriophages. DNA sequence homologies indicated a parallel coevolution with *L. monocytogenes* bacteriophages. *Listeria monocytogenes* exhibited close association with monocins wherein incomplete prophage DNA was present in the *L. monocytogenes* chromosome. However, these monocins integrated incompletely assembled phage particles from cryptic prophages that may have integrated phage lysin. In the same study, Zink et al. (1995) found that a monocin-producing strain harbored a lysin gene capable of killing *L. monocytogenes* cells. Later, Argov et al. (2019) analyzed a strain harboring two phage elements (active prophage and monocin), which triggered bacterial lysis under the stress conditions of the mammalian niche. It was found that the monocin locus encodes phage-tail-like bacteriocins responsible for regulating the active prophage. The active prophage, in turn, generates infectious virions that promote the virulence of its host. Pasechnek et al. (2020) demonstrated that prophages and monocins are active participants in the *L. monocytogenes* phage-host system and are synchronously regulated, promoting cooperation in virulence activity.

Monocins were found to be independent of the prophage and are involved in intraspecies antagonism, killing other related species (*L. innocua*, and *L. welshimeri*) but not the parental strain (Argov et al., 2019; Curtis and Mitchell, 1992). While it may seem altruistic, since cells must sacrifice themselves to release bacteriocins for the benefit of others, providing sister cells a competitive advantage, these monocins are active against other species and genera (Lee et al., 2016), which will promote *L. monocytogenes* colonization.

The intricate mechanisms that govern the regulatory pathways are still not examined in detail, as the link between the prophage and monocins encountered in various *L. monocytogenes* strains and their metabolic factors remains largely unexplored. Although it has been proposed that the cooperation between these entities is driven by their adaptation to catabolic pathways and their dual functions as phage regulators under coculture growth conditions, it has also been hypothesized that the lysogeny pathway is upregulated in response to complex environments (Anas and Schmitz-Esser, 2020; Azulay et al., 2022; Gkerekou et al., 2023; Pasechnek et al., 2020). Further research is required to determine whether both prophages and monocins interact with each other and potentially provide bacterial fitness to the host, thereby necessitating a comprehensive understanding of the concomitant regulation involved. The partial monocin locus present within *Listeria* species is currently being used for bacterial typing, which could aid in discovering new species, such as the recently proposed *Listeria*

*swaminathanii* (Hudson et al., 2022). All in all, the activity of monocin may provide competitive advantages in *L. monocytogenes* stress survival, similar to LLS.

While the subject is still in its infancy, research on *Listeria* bacteriocins has revealed significant variations between them and their potential impact. These findings highlight the complex relationship between commensal bacteria and pathogens, underscoring the importance of further research in this field.

### 3.2. *Listeria monocytogenes: competitive dynamics within the gut microbiota*

After traversing the upper gastrointestinal tract, *L. monocytogenes* faces its biggest challenge - the densely populated microbial habitat ($10^{11}$ to $10^{12}$ cells/ml) of the gut (Rinninella et al., 2019). To establish infection, *L. monocytogenes* must outcompete resident microbes for nutrients and adhesion sites while evading the host immune response. The pathogen employs several virulence factors, such as listeriolysin O and internalins, that facilitate translocation across the epithelial barrier (Zhang et al., 2021). Importantly, *L. monocytogenes* actively manipulates the gut environment by inducing a local inflammatory response. This inflammation not only disrupts the balance of commensal bacteria diminishing beneficial bacteria like *Bifidobacteria* and butyrate producers (Alam et al., 2021; Amiri et al., 2022; Witter et al., 2016) but also liberates nutrients (e.g., sugars and iron) that the pathogen can exploit more efficiently than many resident microbes (Becattini et al., 2017; Guo et al., 2023; Hafner et al., 2021).

Among the resident gut microbes, *Akkermansia muciniphila* plays an important role in maintaining the mucosal barrier through its ability to degrade mucin and produce short-chain fatty acids (Belzer and De Vos, 2012; Keane et al., 2023; Santacruz et al., 2010). Studies have shown that both high-fat diets and ageing reduce the abundance of *A. muciniphila*, which is associated with diminished mucosal integrity and increased susceptibility to infection (Alam et al., 2021; Solar et al., 2019). During *L. monocytogenes* infection, the observed low levels of *A. muciniphila* may further compromise barrier functions, facilitating pathogen adhesion to mucin and promoting systemic dissemination to organs such as the liver, spleen, and mesenteric lymph nodes (Kim et al., 2021; Zhang et al., 2021).

Beyond exploiting host-induced inflammation, *L. monocytogenes* may also engage in direct antagonism with other gut microbes. Although several commensal bacteria (e.g., those belonging to the genera *Ligilactobacillus*, *Enterococcus*, and *Lactococcus*) produce bacteriocins that inhibit *L. monocytogenes* (Barrett et al., 2007; Castellano et al., 2018; Corr et al., 2007; Golmoradi et al., 2022; Hanchi et al., 2018; Lakshminarayanan et al., 2013; Martín et al., 2022), the balance between these inhibitory effects and the pathogen's countermeasures plays a key role in its dynamic competition within the gut. Moreover, studies comparing carriers and non-carriers of *L. monocytogenes* have demonstrated that carriers often exhibit lower microbiota diversity, a factor that correlates with increased pathogen colonization (Hafner et al., 2021).

Host factors, including diet, ageing, and antibiotic use, further modulate these interactions. High dietary fat intake and ageing have been shown to alter the ratio of Firmicutes to Bacteroidetes and reduce levels of protective commensals, thereby enhancing *L. monocytogenes* colonization (Alam et al., 2021; Las Heras et al., 2019). Additionally, antibiotic treatment can disrupt the gut microbial balance, weakening colonization resistance and facilitating the pathogen's survival and expansion in the large intestine, the major replication site for *L. monocytogenes* (Becattini et al., 2017; Birg et al., 2019; Chiu et al., 2017; Ducarmon et al., 2019).

### 3.3. *Listeria monocytogenes intestinal epithelial adhesion and invasion: virulence traits and pathogenicity*

After passing through the dense diverse gut microbiota community, *L. monocytogenes* intracellular pathogenesis involves bacterial translocation across the intestinal barrier to enter the systemic circulation, eventually accessing distant organs. *Listeria monocytogenes* employ various mechanisms, such as aggregation and motility, to navigate the complex host gut environment (Ji et al., 2023; Travier et al., 2013). Additionally, by expressing virulence traits, *L. monocytogenes* can survive and thrive in the gastrointestinal tract. It employs sophisticated mechanisms to cross the gut epithelial barrier, breach other barriers such as fetoplacental and blood-brain and interact with the host's gut epithelial barriers using various virulence factors (Meireles et al., 2024; Osek and Wieczorek, 2022). The ability of *L. monocytogenes* to adhere to and invade host cells involves multiple stages. Table 4 briefly highlights a few examples of these mechanisms.

During the infection process, *L. monocytogenes* employs mechanisms that enable it to move from one infected host cell to another, allowing it to avoid exposure to the extracellular environment, evading the host immune system, and propagating within the host. The process of cell-to-cell spread in *L. monocytogenes* infection involves several steps, including entry and phagocytosis facilitated internalin expression), escape from the phagosome mediated by LLO and phospholipases, intracellular motility by formation of Actin Tails, and invasion of neighboring cells (refer to Fig. 4 for a detailed schematic of the intracellular pathogenesis cycle).

The transition of *L. monocytogenes* from a saprophytic lifestyle (e.g., soil, plants, water) to its infectious life (warm-blooded hosts) involves several altered gene expressions contributing to its lethal intracellular pathogenicity. When exposed to environmental stressors (e.g., temperature, pH, humidity) or gastrointestinal-like stressors (e.g., enzyme activity, gastric acidity, gastric mucus, gastric juices, intestinal mucus layer, host-released metabolites microbiota), this bacterium can use evasive strategies as aforementioned. The expression of *L. monocytogenes* virulence properties is a survival strategy that can be potentiated under stress conditions. Detailed reviews provide a comprehensive understanding of *L. monocytogenes* evasion strategies and the expression of virulence genes (Baümler and Sperandio, 2016; Drolia and Bhunia, 2019; Osek and Wieczorek, 2022; Quereda et al., 2021; Ravindhiran et al., 2023).

One such survival strategy involves the formation of biofilm and/or aggregates. It is hypothesized that the ability of *L. monocytogenes* to form biofilm and aggregation in the gut environment can shape the intestinal microbiota. Biofilm formation is not limited to food processing environments (food-contact surfaces); it is also enhanced after exposure to the host's gastrointestinal stress conditions, such as simulated gastric and intestinal fluids (Bai et al., 2021; Barbosa et al., 2013). Biofilms are composed of an extracellular matrix containing polysaccharides, extracellular DNA, and other inorganic molecules, along with microbial cells (Coenye, 2022). This structured microbial community, or suspended aggregates, favor bacterial survival by facilitating colonization, absorption of nutrients, and communication between members (Liu et al., 2023).

The endogenous bacteria in the microbial community of the intestinal microbiota can adopt a sessile lifestyle, forming surface-attached communities or aggregates of bacteria that adhere to the epithelial cells in the gastrointestinal tract (Ellermann and Sartor, 2018). A layer of mucus covers these cells, physically preventing underlying luminal commensal microbiota and pathogenic bacteria from accessing the mucosal surface (see Fig. 5). Research has shown that in mouse models inoculated with the *L. monocytogenes* EGDe strain, histological and immunohistological analysis of the villous intestine demonstrated that Peyer's patches (10–20 times higher than in the villous intestine) are preferential sites for *L. monocytogenes* replication and aggregates of bacteria are present in the mucus (Pron et al., 1998).

**Table 4**
*Listeria monocytogenes* adhesion and invasion mechanisms involved in its virulence.

| Virulence Determinant | Functions |
|---|---|
| Internalin (InlA and InlB) | InlA and InlB are surface proteins facilitating *L. monocytogenes* adherence to and invasion of the host epithelial cells in the gut. InlA binds specifically to E-cadherin on intestinal cells, facilitating transcytosis, while InlB binds to host receptor Met, aiding in the bacterial cell surface internalization (Camargo et al., 2022; Drolia and Bhunia, 2019; Lamond et al., 2021; Mathipa et al., 2019; Schiavano et al., 2023). |
| PrfA (Positive Regulatory Factor A) | PrfA is a transcription factor that regulates the expression of several virulence genes, including *actA* and *hyl*. Under specific conditions, PrfA activates the expression of these genes and is enhanced in the intracellular niche. It is also necessary for cell infection *in vitro* (Jiang et al., 2010; Price et al., 2018; Quereda et al., 2018, 2021). |
| ActA (Actin Assembly-Inducing Protein) | ActA, a PrfA-regulated gene product, is a crucial virulence factor enabling *L. monocytogenes* to move within and between host cells by inducing actin polymerization, facilitating intracellular motility and cell-to-cell spread. When PrfA is fully active, ActA is expressed. ActA is essential for bacterial aggregation, biofilm formation and transmission between the host and environment (Osek and Wieczorek, 2022; Quereda et al., 2018; Travier et al., 2013). |
| Phospholipases | *Listeria monocytogenes* produces phospholipases, such as PlcA and PlcB, which contribute to the breakdown of host cell membranes and facilitate the release of the pathogen into the cytoplasm. Although poorly expressed it plays a major role in cell infection *in vitro* (Lam et al., 2011; Quereda et al., 2018). |
| Metal Transporters | *Listeria monocytogenes* encodes various transporters for acquiring essential micronutrients such as zinc, iron, and manganese, which play a crucial role for its growth and survival in the host environment. Metals display an important role as structure and catalytic cofactors, enabling bacteria to survive in environments with metal deficiencies (Corbett et al., 2012; Murdoch and Skaar, 2022). |
| Autolysin (Ami) | Autolysin is downregulated and an adhesion-related gene involved in cell wall degradation and colonization of host tissue and contributes to the escape of *L. monocytogenes* from the host cell during cell-to-cell spread (Jiang et al., 2010). |
| Table 4. Listeria *monocytogenes* adhesion and invasion mechanisms involved in its virulence (continuation) | |
| Listeriolysin O (LLO) | While not strictly considered a bacteriocin, Listeriolysin O (LLO) is a potent virulence factor produced by *L. monocytogenes*, possessing the ability to evade host vacuole, thereby hindering its survival (Radoshevich and Cossart, 2017). LLO is encoded in LIPI-1 (Quereda et al., 2021) and is a cholesterol-dependent porogenic toxin encoded by the *hyl* gene (PrfA regulates *plcA* and *hyl* promoters) (Liu et al., 2023; Quereda et al., 2018; Wang et al., 2022b). LLO acts by perforating the phagosomal membrane, such as in liver granuloma macrophages (Birmingham et al., 2008), and also suppresses reactive oxygen species (Lam et al., 2011). Additionally, LLO can lyse host cell membranes, facilitating the escape of *L. monocytogenes* from phagosomes (mediated by LLO and PlcB), and contributing to its intracellular survival and pathogenesis (Rinehart et al., 2020). |
| Stress Survival Islet | Stress survival islets encode stress response genes such as those for acid, osmotic, and bile stress (referred to as stress survival islet−1; SSI−1) as well as oxidative and acid stresses (stress survival islet−2; SSI−2). Genomic islands may enhance the ability of *L. monocytogenes* to survive and invade harsh conditions in the gastrointestinal tract (Lakicevic et al., 2021; Wiktorczyk-Kapischke et al., 2023). |
| Sigma B (SigB / σB) | The stress response factor, Sigma B, has been identified in bacteria among phylum Firmicutes, such as *Listeria*, *Bacillus*, and *Staphylococcus*. Sigma B controls the general stress response (e.g., regulates InlA expression) and contributes to the capacity of *L. monocytogenes* to withstand and adjust to various environmental stresses, including those encountered in the gut (Guerreiro et al., 2020; Kazmierczak et al., 2003; McGann et al., 2007; Sibanda and Buys, 2022). |

If a dense microbial community resembling a biofilm embedded in the mucus layer (Duncan et al., 2021) can functionally shape the mucosal barrier, it is possible that *L. monocytogenes* is able to evade such immune barriers and modulate the intestinal microbiota by forming aggregates or biofilm-like structures.

Mucins (Muc2) are actively broken down by members of the gut microbiota, which are part of the mucus-associated biofilm-like community. These mucin-degrading bacteria embedded in the mucus layer are diverse, harboring various phyla with the exception of the phylum Proteobacteria (as per the research conducted by Duncan et al. (2021). The study also found that antibiotics led to an increase in Proteobacteria and a decrease in Firmicutes. However, the stability of the biofilm-like structure depended on the type of antibiotic used, and the usage of an antibiotic that targeted commensals belonging to class Clostridia (which is essential for the integrity of this gram-positive commensal bacteria) completely collapsed the biofilm-like structure. As *L. monocytogenes*, belonging to the Firmicutes phylum, is taxonomically related to Clostridia, and this specialized community enriches bacteria belonging to anaerobic bacteria, it is plausible that *L. monocytogenes* can form aggregation-like structures that can modulate the mucosal barrier (Becattini et al., 2017; Duncan et al., 2021).

Additionally, *L. monocytogenes* can easily bind to Muc2 cells, and the absence of this major constituent of the mucus layer (Muc22/2$^{-/-}$) in an orogastric challenge in mice models showed heightened susceptibility to *L. monocytogenes* (Zhang et al., 2021). Compared to wild-type mice, this infection model demonstrated higher mortality than intraperitoneally *L. monocytogenes* administration in which burdens were equivalent to WT and Muc22/2$^{-/-}$ animals (Zhang et al., 2021). Furthermore, exposure to simulated gastrointestinal stress conditions showed that planktonic cells had higher adhesion, invasion and transepithelial translocation through Caco-2 cells than the corresponding biofilm-isolated cells (Bai et al., 2021). However, exposure to gastrointestinal conditions increased virulence attributes in *L. monocytogenes* sessile cells, although less virulent than the planktonic cells (Bai et al., 2021).

In infected *Cornu aspersum* maxima snails, the hypervirulent strain activity was associated with increased tolerance to mucus barriers and cell surface properties, such as autoaggregation and biofilm formation that modulate cell populations and functions (Dushku et al., 2020). These findings suggest that virulence traits may not be the only properties linked to gut microbiota and immune modulation.

The survival ability of *L. monocytogenes* within and outside the host is largely attributed to virulent gene expression. A study by Popowska et al. (2017) revealed that a class I internalin (InlL), which is encoded by the *lmo2026* gene, exhibits adhesion domains that enable the binding of mucin, thereby enhancing the colonization ability of *L. monocytogenes*. The regulatory proteins PrfA and SigB, as well as the virulence proteins LAP, InlA, and LLO, are pivotal for extraintestinal tissue invasion. These protein and regulatory genes are expressed in both sessile and planktonic lifestyles (Bai et al., 2021), and contribute to biofilm development, which is regulated by quorum-sensing (QS), a bacterial communication system found in forming biofilms in several bacterial species, including *Salmonella* spp., *E. coli*, and *Pseudomonas aeruginosa* (Duncan et al., 2021; Lee and Wang, 2020). This mechanism regulates gene expression as a stress response system (Banerji et al., 2022). In mice, sessile *L. monocytogenes* strains have been shown to have delayed invasion and affected tissue distribution, possibly due to the reduced expression of ActA, PrfA, and SigB-regulated proteins (Bai et al., 2021). The adaptability of *L. monocytogenes* to transitions in new environments may be linked to its ability to acquire indole signaling from the mammalian gut microbiota, where indole served as a metabolite. Quorum-sensing signal molecules, such as indole-treated cells, can downregulate transcript levels of virulence-associated and regulatory genes necessary for biofilm formation (Rattanaphan et al., 2020). These findings suggest that *L. monocytogenes* can transiently switch from a sessile to a planktonic lifestyle upon encountering harsh conditions to adapt better and colonize the intestinal environment. In line with this, a study by Price et al. (2018) on an outbreak associated with whole cantaloupe demonstrated that *L. monocytogenes* mutant strains (2011L-2858, serotype 1/2b) harboring a single insertion in *prfA*, encoding PrfA, exhibited significantly reduced biofilm formation. Inactivation of the *prf*A gene also

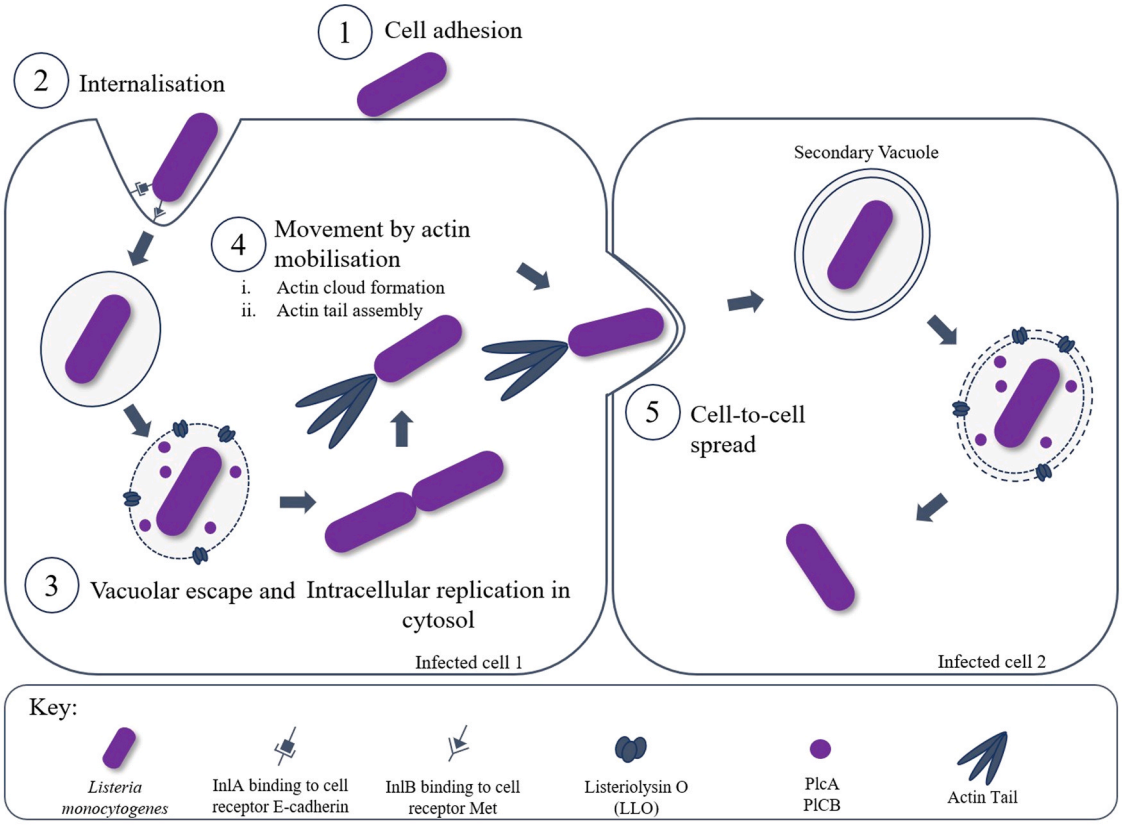


**Fig. 4.** *Listeria monocytogenes* adhesion and invasion in the non-phagocytic host's cell. The process of pathogenesis occurs as follows: it begins with the 1 – Internalization. *Listeria*'s cell adheres to the host cell surface via *Listeria* adhesion protein (LAP); 2 – Phagocytosis. It enters the host cell by the interaction of surface internalins InlA and InlB with the host receptors E-cadherin and Met, respectively. Phagocytosis occurs via a zipper mechanism engulfing the bacterium; 3 - Vacuolar escape by expression of pore-forming Listeriolysin O and phospholipase C (PLC; synthesized by metalloproteases, Mpl), which disrupt the phagosomal membrane; 4 - Replication in the cytosol; 5 – *Listeria monocytogenes* exploits the host cell's actin (actin-based motility system) to promote locomotion. Formation of "actin tails" by actin polymerization allows the bacteria to propel across the cytoplasm until it reaches the host cell periphery; 5 – Promotion of cell-to-cell spread. Paracellular translocation and intracellular persistence. When it reaches the host cell's plasma membrane it induces membrane protrusions, and ultimately comes into contact with the neighboring cell, leading to the spread of the infection from one host cell to another. Disruption of the double-membrane vacuole by secretion of toxins. Start of the new infection cycle and dissemination within intestinal tissue and potentially reaching other organs (Ireton et al., 2021; Luque-Sastre et al., 2018; Ravindhiran et al., 2023; Stavru et al., 2011).

resulted in reduced aggregation of *L. monocytogenes*. These findings highlight the crucial role of virulence factors, serotype, and their potential link between biofilm formation, aggregation and incidence of *L. monocytogenes* disease.

PrfA is a master regulator for numerous virulence genes, including *actA* and *hyl*. These genes are essential for aggregation and biofilm formation (Bai et al., 2021) and also contribute to actin polymerization that further potentiates motility and cell-to-cell spread (Travier et al., 2013). This author also found that this virulence factor mediates aggregation via direct ActA-ActA interactions and correlates with elevated gut colonization and fecal shedding (Travier et al., 2013). Interestingly, *L. monocytogenes* aggregates were observed within the cecum and colon lumens, suggesting mucus may favor *L. monocytogenes* aggregate formation. Additionally, it is plausible that low levels of extracellular PrfA would be an advantage to flagellum-propelled *L. monocytogenes* bacteria for cell adhesion, intracellular invasion, and biofilm formation (Lemon et al., 2010).

It is also worth noting that the effectiveness of *L. monocytogenes* infection can be affected by factors such as food components, acidity, or antimicrobial substances. For instance, the expression of the *inl*A gene can be downregulated or upregulated in response to the presence of bacteriocins and pH 4.5 or sucrose, respectively, which are correlated with biofilm formation (Winkelströter and De Martinis, 2013).

To put it simply, the ability of *L. monocytogenes* to form aggregates or biofilm and its motility plays a crucial role in its ability to evade and persist within the harsh conditions of the intestinal tract.

## 4. Conclusions and perspectives

The presence of *L. monocytogenes* can cause a change in the composition of the gut microbiota, either directly through mechanisms such as the production of bacteriocins, competition for nutrients, or evasion of the immune response, or indirectly through factors such as the host's age or dietary habits. By analyzing the topological properties of microbiota and the genetic makeup of *L. monocytogenes*, it is feasible to ascertain the significance of *L. monocytogenes* in shaping and influencing the long-term dynamics of the gut microbiome.

Although substantial progress has been made in understanding the relationships between *L. monocytogenes*, gut microbiota, and the host gastrointestinal tract, many questions remain unanswered that need to be addressed. Determining the exact molecular mechanisms underlying the interaction between commensal gut bacteria and *L. monocytogenes* should be the main goal of future research. For example, investigating how particular microbiota compositions either promote or inhibit *L. monocytogenes* colonization may reveal important information about protective microbial communities or vulnerabilities associated with dysbiosis. Furthermore, considering the significance of foodborne transmission pathways, the role of diet, and its impact on microbiota dynamics during *L. monocytogenes* infections are still poorly understood.

A deeper understanding of host-pathogen-microbiome interactions

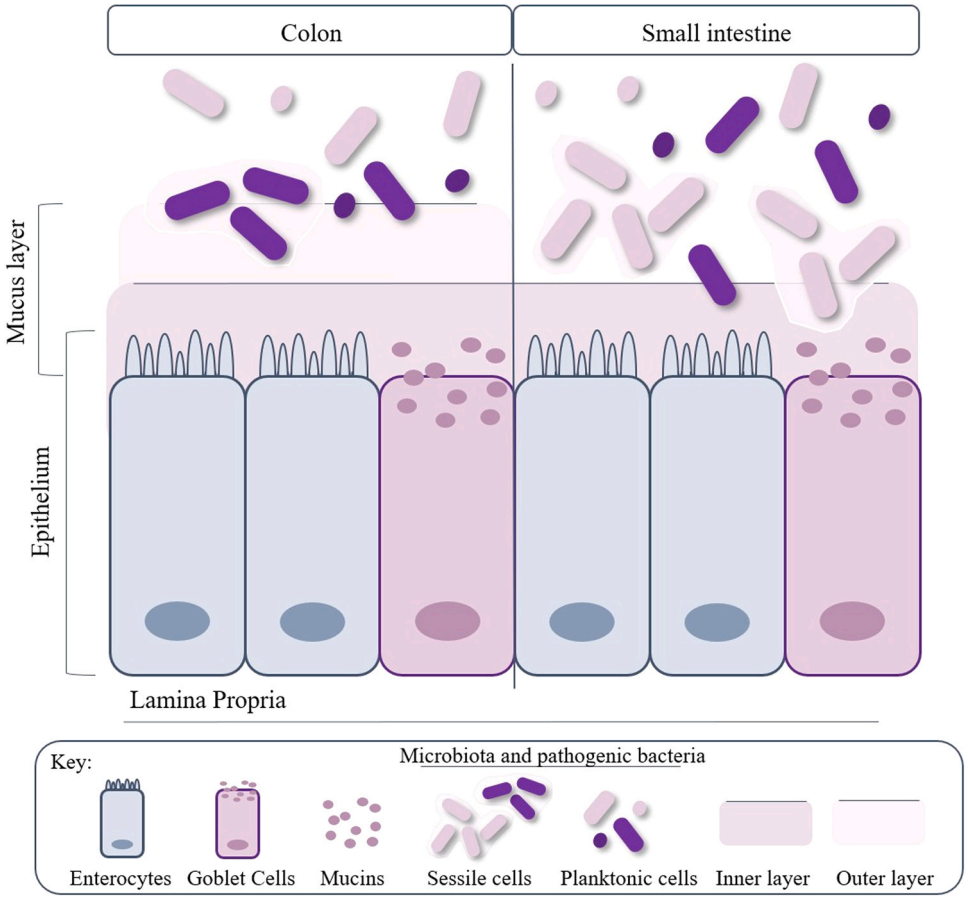


**Fig. 5.** The intestinal mucus layer has a varied structure depending on the region of the intestinal tract. It is mainly composed of a thick coated mucus layer, which has a two-layer firm inner layer and a loose outer layer mucin in the distal colon, or a thin, porous mucus layer in the small intestine. The mucosal immune system also includes host secretions, a single layer of epithelial and goblet cells (the latter responsible for renewing of mucus by secreting mucins), antimicrobial peptides (secreted by Paneth cells in the small intestine), and soluble IgA antibodies. These components play a crucial role in maintaining the health of the gut and protecting against infections (Ellermann and Sartor, 2018; Seo et al., 2021; Zhang et al., 2021).

may be possible using technological innovations like multi-omics techniques (e.g., metagenomics, transcriptomics, and metabolomics). These instruments may aid in the identification of important metabolic processes or microbial metabolites that influence the pathogenicity and survival of *L. monocytogenes*. Furthermore, creating physiologically accurate *in vitro* gut models—such as organoids or gut-on-a-chip systems—offers intriguing chances to investigate *L. monocytogenes* behavior under carefully monitored circumstances that closely resemble the intricate human gastrointestinal environment.

Future clinical approaches to prevent or lessen *L. monocytogenes* infections might involve probiotics or microbiome-based treatments. Novel, non-antibiotic interventions may be made possible by understanding the interactions between *L. monocytogenes* and particular probiotics or engineered bacteria. The need to investigate alternative antimicrobial agents, such as phage therapies, bacteriocins, or other antimicrobial peptides, is also underscored by the growing concern over antibiotic resistance in *L. monocytogenes*. These agents may provide targeted approaches to inhibit the pathogen while maintaining the integrity of the gut microbiota.

## CRediT authorship contribution statement

**M. Oliveira:** Conceptualization, Methodology, Formal analysis, Investigation, Writing-Original Draft, Writing-Review & Editing, Visualization. **J. Barbosa:** Conceptualization, Wrting - Review & Editing, Supervision. **P.Teixeira:** Conceptualization, Writing -Review & Editing, Supervision, Funding acquisition.

## Declaration of Competing Interest

The authors declare that they have no competing interests.

## Acknowledgements

This work was supported by National Funds from FCT - Fundação para a Ciência e a Tecnologia through project GenoPheno-Traits4Persitence - Genomic and phenotypic traits contributing to persistence of *Listeria monocytogenes* in food processing environment (PTDC/BAA-AGR/4194/2021); https://doi.org/10.54499/PTDC/BAA-AGR/4194/2021. The authors would like to thank the scientific collaboration under the Fundação para a Ciência e a Tecnologia (FCT) project UIDP/00329/2020. Financial support for author Mónica Oliveira was provided by the doctoral fellowships 2021.08345.BD.

## Data availability

No data was used for the research described in the article.

## References

Akritidou, T., Akkermans, S., Gaspari, S., Azraini, N.D., Smet, C., Van de Wiele, T., Van Impe, J.F.M., 2022. Effect of gastric pH and bile acids on the survival of *Listeria monocytogenes* and *Salmonella* Typhimurium during simulated gastrointestinal digestion. Innov. Food Sci. Emerg. Technol. 82, 103161. https://doi.org/10.1016/J.IFSET.2022.103161.

Akritidou, T., Akkermans, S., Smet, C., de Mey, F., Van Impe, J.F.M., 2023a. Influence of hurdle technology on foodborne pathogen survival in the human gastrointestinal tract. Microorganisms 11 (2), 405. https://doi.org/10.3390/microorganisms11020405.

Akritidou, T., Akkermans, S., Smet, C., Delens, V., Van Impe, J.F.M., 2023b. Effect of food structure and buffering capacity on pathogen survival during in vitro digestion. Food Res. Int. 164, 112305. https://doi.org/10.1016/J.FOODRES.2022.112305.

Alam, M.S., Gangiredla, J., Hasan, N.A., Barnaba, T., Tartera, C., 2021. Aging-induced dysbiosis of gut microbiota as a risk factor for increased *Listeria monocytogenes* infection. Front. Immunol. 12. https://doi.org/10.3389/fimmu.2021.672353.

Amiri, P., Hosseini, S.A., Ghaffari, S., Tutunchi, H., Ghaffari, S., Mosharkesh, E., Asghari, S., Roshanravan, N., 2022. Role of butyrate, a gut microbiota derived metabolite, in cardiovascular diseases: a comprehensive narrative review. Front. Pharmacol. 12, 837509. https://doi.org/10.3389/fphar.2021.837509.

Anas, J.M., Schmitz-Esser, S., 2020. The transcriptome of *Listeria monocytogenes* during co-cultivation with cheese rind bacteria suggests adaptation by induction of ethanolamine and 1,2-propanediol catabolism pathway genes. PLoS ONE 15 (7 July). https://doi.org/10.1371/journal.pone.0233945.

Argov, T., Sapir, S.R., Pasechnek, A., Azulay, G., Stadnyuk, O., Rabinovich, L., Sigal, N., Borovok, I., Herskovits, A.A., 2019. Coordination of cohabiting phage elements supports bacteria–phage cooperation. Nat. Commun. 2019 10 (1), 1–14. https://doi.org/10.1038/s41467-019-13296-x.

Asaduzzaman, S.M., Sonomoto, K., 2009. Lantibiotics: diverse activities and unique modes of action. J. Biosci. Bioeng. 107 (5), 475–487. https://doi.org/10.1016/J.JBIOSC.2009.01.003.

Azulay, G., Pasechnek, A., Stadnyuk, O., Borovok, I., Sigal, N., Correspondence, A.A.H., Ran-Sapir, S., Fleisacher, A.M., Herskovits, A.A., 2022. A dual-function phage regulator controls the response of cohabiting phage elements via regulation of the bacterial SOS response. Cell Rep. 39. https://doi.org/10.1016/j.celrep.2022.110723.

Bagatella, S., Tavares-Gomes, L., Oevermann, A., 2022. *Listeria monocytogenes* at the interface between ruminants and humans: a comparative pathology and pathogenesis review. Vet. Pathol. 59 (2), 186–210. https://doi.org/10.1177/03009858211052659.

Bai, X., Liu, D., Xu, L., Tenguria, S., Drolia, R., Gallina, N.L.F., Cox, A.D., Koo, O.K., Bhunia, A.K., 2021. Biofilm-isolated *Listeria monocytogenes* exhibits reduced systemic dissemination at the early (12–24 h) stage of infection in a mouse model. NPJ Biofilms Micro 7 (1). https://doi.org/10.1038/S41522-021-00189-5.

Banerji, R., Karkee, A., Kanojiya, P., Patil, A., Saroj, S.D., 2022. Bacterial communication in the regulation of stress response in *Listeria monocytogenes*. LWT 154, 112703. https://doi.org/10.1016/J.LWT.2021.112703.

Barbosa, J., Borges, S., Camilo, R., Magalhães, R., Ferreira, V., Santos, I., Silva, J., Almeida, G., Teixeira, P., 2013. Biofilm formation among clinical and food isolates of *Listeria monocytogenes*. Int. J. Microbiol. 2013, 524975. https://doi.org/10.1155/2013/524975.

Barbosa, J., Borges, S., Magalhães, R., Ferreira, V., Santos, I., Silva, J., Almeida, G., Gibbs, P., Teixeira, P., 2012. Behaviour of *Listeria monocytogenes* isolates through gastro-intestinal tract passage simulation, before and after two sub-lethal stresses. Food Microbiol. 30 (1), 24–28. https://doi.org/10.1016/J.FM.2011.10.001.

Barmpalia-Davis, I.M., Geornaras, I., Kendall, P.A., Sofos, J.N., 2009. Effect of fat content on survival of *Listeria monocytogenes* during simulated digestion of inoculated beef frankfurters stored at 7 ºC. Food Microbiol. 26 (5), 483–490. https://doi.org/10.1016/J.FM.2009.02.011.

Barrett, E., Hayes, M., O'Connor, P., Gardiner, G., Fitzgerald, G.F., Stanton, C., Ross, R.P., Hill, C., 2007. Salivaricin p, one of a family of two-component antilisterial bacteriocins produced by intestinal isolates of *Lactobacillus salivarius*. Appl. Environ. Microbiol. 73 (11), 3719–3723. https://doi.org/10.1128/AEM.00666-06.

Barretta, C., Verruck, S., Maran, B.M., Maurício, L. dos S., Miotto, M., Vieira, C.R.W., Prudencio, E.S., 2019. *Listeria monocytogenes* survival in raw Atlantic salmon (*Salmo salar*) fillet under in vitro simulated gastrointestinal conditions by culture, qPCR and PMA-qPCR detection methods. LWT 107, 132–137. https://doi.org/10.1016/J.LWT.2019.03.015.

Baümler, A.J., Sperandio, V., 2016. Interactions between the microbiota and pathogenic bacteria in the gut. Nature 535 (7610), 85. https://doi.org/10.1038/NATURE18849.

Becattini, S., Littmann, E.R., Carter, R.A., Kim, S.G., Morjaria, S.M., Ling, L., Gyaltshen, Y., Fontana, E., Taur, Y., Leiner, I.M., Pamer, E.G., 2017. Commensal microbes provide first line defense against *Listeria monocytogenes* infection. J. Exp. Med. 214 (7), 1973–1989. https://doi.org/10.1084/jem.20170495.

Begley, M., Sleator, R.D., Gahan, C.G.M., Hill, C., 2005. Contribution of three bile-associated loci, *bsh*, *pva*, and *btlB*, to gastrointestinal persistence and bile tolerance of *Listeria monocytogenes*. Infect. Immun. 73 (2), 894. https://doi.org/10.1128/IAI.73.2.894-904.2005.

Belzer, C., De Vos, W.M., 2012. Microbes inside—from diversity to function: the case of *Akkermansia*. ISME J. 6 (8), 1449–1458. https://doi.org/10.1038/ismej.2012.6.

Birg, A., Ritz, N.L., Lin, H.C., 2019. The unknown effect of antibiotic-induced dysbiosis on the gut microbiota. Micro Metab. Diagn. Ther. Other Strateg. Appl. 195–200. https://doi.org/10.1016/B978-0-12-815249-2.00020-8.

Birmingham, C.L., Canadien, V., Kaniuk, N.A., Steinberg, B.E., Higgins, D.E., Brumell, J. H., 2008. Listeriolysin O allows *Listeria monocytogenes* replication in macrophage vacuoles. Nature 451 (7176), 350–354. https://doi.org/10.1038/nature06479.

Bland, R., Brown, S.R.B., Waite-Cusic, J., Kovacevic, J., 2022. Probing antimicrobial resistance and sanitizer tolerance themes and their implications for the food industry through the *Listeria monocytogenes* lens. Compr. Rev. Food Sci. Food Saf. 21 (2), 1777–1802. https://doi.org/10.1111/1541-4337.12910.

Boland, M., 2016. Human digestion – a processing perspective. J. Sci. Food Agric. 96 (7), 2275–2283. https://doi.org/10.1002/JSFA.7601.

Bowen, W.H., Burne, R.A., Wu, H., Koo, H., 2018. Oral biofilms: pathogens, matrix, and polymicrobial interactions in microenvironments. Trends Microbiol. 26 (3), 229–242. https://doi.org/10.1016/J.TIM.2017.09.008.

Bredenoord, A.J., Smout, A., Tack, J., 2016. A Guide to Gastrointestinal Motility Disorders. Springer. https://doi.org/10.1007/978-3-319-26938-2.

Brodkorb, A., Egger, L., Alminger, M., Alvito, P., Assunção, R., Ballance, S., Bohn, T., Bourlieu-Lacanal, C., Boutrou, R., Carrière, F., Clemente, A., Corredig, M., Dupont, D., Dufour, C., Edwards, C., Golding, M., Karakaya, S., Kirkhus, B., Le Feunteun, S., Recio, I., 2019. INFOGEST static in vitro simulation of gastrointestinal food digestion. Nat. Protoc. 14 (4), 991–1014. https://doi.org/10.1038/s41596-018-0119-1.

Bryant, A.E., Stevens, D.L., 2015. *Streptococcus pyogenes*. Mandel, Douglas, Bennett'S. Princ. Pract. Infect. Dis., 2, 2285–2299.e4. https://doi.org/10.1016/B978-1-4557-4801-3.00199-5.

Bucur, F.I., Grigore-Gurgu, L., Crauwels, P., Riedel, C.U., Nicolau, A.I., 2018. Resistance of *Listeria monocytogenes* to stress conditions encountered in food and food processing environments. Front. Microbiol. 9, 2700. https://doi.org/10.3389/fmicb.2018.02700.

Burke, T.P., Loukitcheva, A., Zemansky, J., Wheeler, R., Boneca, I.G., Portnoy, D.A., 2014. *Listeria monocytogenes* is resistant to lysozyme through the regulation, not the acquisition, of cell wall-modifying enzymes. J. Bacteriol. 196 (21), 3756. https://doi.org/10.1128/JB.02053-14.

Bustos, A.Y., Font de Valdez, G., Fadda, S., Taranto, M.P., 2018. New insights into bacterial bile resistance mechanisms: the role of bile salt hydrolase and its impact on human health. Food Res. Int. 112, 250–262. https://doi.org/10.1016/J.FOODRES.2018.06.035.

Camargo, A.C., McFarland, A.P., Woodward, J.J., Nero, L.A., 2022. The magnitude of cell invasion and cell-to-cell spread of *Listeria monocytogenes* is correlated with serotype-specific traits. Int. J. Food Microbiol. 382, 109906. https://doi.org/10.1016/J.IJFOODMICRO.2022.109906.

Caminero, A., Guzman, M., Libertucci, J., Lomax, A.E., 2023. The emerging roles of bacterial proteases in intestinal diseases. Gut Microbes 15 (1). https://doi.org/10.1080/19490976.2023.2181922.

Carvalho, F., Sousa, S., Cabanes, D., 2014. How *Listeria monocytogenes* organizes its surface for virulence. Front. Cell. Infect. Microbiol. 4, 82128. https://doi.org/10.3389/FCIMB.2014.00048/PDF.

Castellano, P., Pérez Ibarreche, M., Longo Borges, L., Niño Arias, F.C., Ross, G.R., De Martinis, E.C.P., 2018. *Lactobacillus* spp. impair the ability of *Listeria monocytogenes* FBUNT to adhere to and invade Caco-2 cells. Biotechnol. Lett. 40 (8), 1237–1244. https://doi.org/10.1007/S10529-018-2572-X/FIGURES/4.

Chen, L.H., Köseoğlu, V.K., Güvener, Z.T., Myers-Morales, T., Reed, J.M., D'Orazio, S.E. F., Miller, K.W., Gomelsky, M., 2014. Cyclic di-GMP-dependent signaling pathways in the pathogenic Firmicute *Listeria monocytogenes*. PLoS Pathog. 10 (8), e1004301. https://doi.org/10.1371/JOURNAL.PPAT.1004301.

Cheng, C., Dong, Z., Han, X., Sun, J., Wang, H., Jiang, L., Yang, Y., Ma, T., Chen, Z., Yu, J., Fang, W., Song, H., 2017. *Listeria monocytogenes* 10403S arginine repressor ArgR finely tunes arginine metabolism regulation under acidic conditions. Front. Microbiol. 8, 246956. https://doi.org/10.3389/FMICB.2017.00145/BIBTEX.

Cheng, Wang, X., Liu, Y., Qin, X., Li, Z., Dong, Q., 2023. Growth and survival characteristics of *Listeria monocytogenes* of different sources and subtypes. LWT 184, 115114. https://doi.org/10.1016/J.LWT.2023.115114.

Chiu, L., Bazin, T., Truchetet, M.E., Schaeverbeke, T., Delhaes, L., Pradeu, T., 2017. Protective microbiota: From localized to long-reaching co-immunity. Front. Immunol. 8, 1678. https://doi.org/10.3389/FIMMU.2017.01678/BIBTEX.

Coenye, T., 2022. Biofilms. Reference Module in Life Sciences. Elsevier. https://doi.org/10.1016/B978-0-12-822563-9.00068-8.

Corbett, D., Wang, J., Schuler, S., Gloria, L.C., Glenn, S., Brough, D., Andrew, P.W., Cavet, J.S., Roberts, I.S., 2012. Two zinc uptake systems contribute to the full virulence of *Listeria monocytogenes* during growth in vitro and in vivo. Infect. Immun. 80 (1), 14. https://doi.org/10.1128/IAI.05904-11.

Cornick, S., Tawiah, A., Chadee, K., 2015. Roles and regulation of the mucus barrier in the gut. Tissue Barriers 3 (1–2). https://doi.org/10.4161/21688370.2014.982426.

Corr, S.C., Li, Y., Riedel, C.U., O'Toole, P.W., Hill, C., Gahan, C.G.M., 2007. Bacteriocin production as a mechanism for the antiinfective activity of *Lactobacillus salivarius* UCC118. Proc. Natl. Acad. Sci. USA 104 (18), 7617–7621. https://doi.org/10.1073/PNAS.0700440104.

Cossart, P., Toledo-Arana, A., 2008. *Listeria monocytogenes*, a unique model in infection biology: an overview. Microbes Infect. 10 (9), 1041–1050. https://doi.org/10.1016/J.MICINF.2008.07.043.

Cotter, P.D., Draper, L.A., Lawton, E.M., Daly, K.M., Groeger, D.S., Casey, P.G., Ross, R. P., Hill, C., 2008. Listeriolysin S, a novel peptide haemolysin associated with a subset of lineage I *Listeria monocytogenes*. PLoS Pathog. 4 (9), e1000144. https://doi.org/10.1371/journal.ppat.1000144.

Cunha, S., Komora, N., Magalhães, R., Almeida, G., Ferreira, V., Teixeira, P., 2016. Characterization of clinical and food *Listeria monocytogenes* isolates with different antibiotic resistance patterns through simulated gastrointestinal tract conditions and environmental stresses. Microb. Risk Anal. 1, 40–46. https://doi.org/10.1016/J.MRAN.2015.08.001.

Curtis, G.D.W., Mitchell, R.G., 1992. Bacteriocin (monocin) interactions among *Listeria monocytogenes* strains. Int. J. Food Microbiol. 16 (4), 283–292. https://doi.org/10.1016/0168-1605(92)90030-7.

D'orazio, S.E.F., Seveau, S.M., Bauer, M.E., Bakardjiev, A., 2014. Animal models for oral transmission of *Listeria monocytogenes*. Front. Cell. Infect. Microbiol. 4 (15). https://doi.org/10.3389/fcimb.2014.00015.

Davis, M.L., Ricke, S.C., Donaldson, J.R., 2019. Establishment of *Listeria monocytogenes* in the gastrointestinal tract. Microorganisms 7 (3), 75. https://doi.org/10.3390/microorganisms7030075.

Dey, P., Saumya, Chaudhuri, R., 2022. The opportunistic nature of gut commensal microbiota. Crit. Rev. Microbiol. 49 (6), 739–763. https://doi.org/10.1080/1040841X.2022.2133987.

Dosch, A.R., Imagawa, D.K., Jutric, Z., 2019. Bile Metabolism and lithogenesis: an update. Surg. Clin. North Am. 99 (2), 215–229. https://doi.org/10.1016/J.SUC.2018.12.003.

Drolia, R., Bhunia, A.K., 2019. Crossing the intestinal barrier via *Listeria* adhesion protein and Internalin A. Trends Microbiol. 27 (5), 408–425. https://doi.org/10.1016/j.tim.2018.12.007.

Ducarmon, Q.R., Zwittink, R.D., Hornung, B.V.H., van Schaik, W., Young, V.B., Kuijper, E.J., 2019. Gut microbiota and colonization resistance against bacterial enteric infection. Microbiol. Mol. Biol. Rev. 83 (3). https://doi.org/10.1128/MMBR.00007-19.

Duncan, K., Carey-Ewend, K., Vaishnava, S., 2021. Spatial analysis of gut microbiome reveals a distinct ecological niche associated with the mucus layer. Gut Microbes 13 (1). https://doi.org/10.1080/19490976.2021.1874815.

Dushku, E., Kotzamanidis, C., Avgousti, K., Zdragas, A., Vafeas, G., Giantzi, V., Staikou, A., Yiangou, M., 2020. *Listeria monocytogenes* induced dysbiosis in snails and rebiosis achieved by administration of the gut commensal *Lactobacillus plantarum* Sgs14 strain. Fish. Shellfish Immunol. 104, 337–346. https://doi.org/10.1016/J.FSI.2020.04.041.

Dussurget, O., Cabanes, D., Dehoux, P., Lecuit, M., Buchrieser, C., Glaser, P., Cossart, P., 2002. *Listeria monocytogenes* bile salt hydrolase is a PrfA-regulated virulence factor involved in the intestinal and hepatic phases of listeriosis. Mol. Microbiol. 45 (4), 1095–1106. https://doi.org/10.1046/J.1365-2958.2002.03080.X.

ECDC 2024. European Centre for Disease Prevention and Control, 2024. Listeriosis. In: ECDC, Annual epidemiological report for 2022. ECDC, Stockholm.

EFSA & ECDC, 2024. The European Union One Health 2023 Zoonoses Report. EFSA J. 22 (21), e9106. https://doi.org/10.2903/j.efsa.2024.9106.

Ellermann, M., Sartor, R.B., 2018. Intestinal bacterial biofilms modulate mucosal immune responses. J. Immunol. Sci. 2 (2), 13. https://doi.org/10.29245/2578-3009/2018/2.1122.

Ferreira, V., Wiedmann, M., Teixeira, P., Stasiewicz, M.J., 2014. *Listeria monocytogenes* persistence in food-associated environments: epidemiology, strain characteristics, and implications for public health. J. Food Prot. 77 (1), 150–170. https://doi.org/10.4315/0362-028X.JFP-13-150.

Formato, G., Georgaras, I., Barmpalia, I.M., Skandamis, P.N., Belk, K.E., Scanga, J.A., Kendall, P.A., Smith, G.C., Sofos, J.N., 2007. Effect of acid adaptation on growth during storage at 10 degrees C and resistance to simulated gastric fluid of *Listeria monocytogenes* inoculated onto bologna formulated with or without antimicrobials. J. Food Prot. 70 (1), 65–69. https://doi.org/10.4315/0362-028X-70.1.65.

Fuchisawa, Y., Abe, H., Koyama, K., Koseki, S., 2022. Competitive growth kinetics of *Campylobacter jejuni*, *Escherichia coli* O157:H7 and *Listeria monocytogenes* with enteric microflora in a small-intestine model. J. Appl. Microbiol. 132 (2), 1467–1478. https://doi.org/10.1111/JAM.15294.

Fulano, A.M., Elbakush, A.M., Chen, L.H., Gomelsky, M., 2023. The *Listeria monocytogenes* exopolysaccharide significantly enhances colonization and survival on fresh produce. Front. Microbiol. 14. https://doi.org/10.3389/fmicb.2023.1126940.

Gkerekou, M.A., Kaparakou, E.H., Tarantilis, P.A., Skandamis, P.N., 2023. Studying the metabolic factors that may impact the growth of co-cultured *Listeria monocytogenes* strains at low temperature. Food Res. Int. 171, 113056. https://doi.org/10.1016/j.foodres.2023.113056.

Golmoradi, R., Asgharzadeh, S., Darbandi, A., Aliramezani, A., Masjedian Jazi, F., 2022. Characterization of bacteriocins produced by *Lactobacillus* species against adhesion and invasion of *Listeria monocytogenes* isolated from different samples. Microb. Pathog. 162, 105307. https://doi.org/10.1016/J.MICPATH.2021.105307.

Groeger, S., Meyle, J., 2019. Oral mucosal epithelial cells. Front. Immunol. 10, 423006. https://doi.org/10.3389/FIMMU.2019.00208/BIBTEX.

Guerreiro, D.N., Arcari, T., O'Byrne, C.P., 2020. The σB-mediated general stress response of *Listeria monocytogenes*: life and death decision making in a pathogen. Front. Microbiol. 11, 556640. https://doi.org/10.3389/FMICB.2020.01505/BIBTEX.

Guo, L., Yin, X., Liu, Q., 2023. Fecal microbiota transplantation reduces mouse mortality from *Listeria monocytogenes* infection. Microb. Pathog. 178. https://doi.org/10.1016/j.micpath.2023.106036.

Hafner, L., Pichon, M., Burucoa, C., Nusser, S.H.A., Moura, A., Garcia-Garcera, M., Lecuit, M., 2021. *Listeria monocytogenes* faecal carriage is common and depends on the gut microbiota. Nat. Commun. 12 (1). https://doi.org/10.1038/s41467-021-27069-y.

Hanchi, H., Mottawea, W., Sebei, K., Hammami, R., 2018. The genus *Enterococcus*: between probiotic potential and safety concerns—an update. Front. Microbiol. 9 (AUG), 1791. https://doi.org/10.3389/FMICB.2018.01791.

Hernández-González, J.C., Martínez-Tapia, A., Lazcano-Hernández, G., García-Pérez, B. E., Castrejón-Jiménez, N.S., 2021. Bacteriocins from lactic acid bacteria. A powerful alternative as Antimicrobials, Probiotics, and Immunomodulators in Veterinary Medicine. Anim.: Open Access J. MDPI 11 (4), 979. https://doi.org/10.3390/ANI11040979.

Herzog, M.K.M., Cazzaniga, M., Peters, A., Shayya, N., Beldi, L., Hapfelmeier, S., Heimesaat, M.M., Bereswill, S., Frankel, G., Gahan, C.G.M., Hardt, W.D., 2023. Mouse models for bacterial enteropathogen infections: insights into the role of colonization resistance. Gut Microbes 15 (1), 2172667. https://doi.org/10.1080/19490976.2023.2172667.

Hooper, L.V., MacPherson, A.J., 2010. Immune adaptations that maintain homeostasis with the intestinal microbiota. Nat. Rev. Immunol. 10, 159–169. https://doi.org/10.1038/nri2710.

Hudson, L.K., Chaggar, H.K., Schamp, C.N., Claxton, M.L., Bryan, D.W., Peters, T.L., Song, Y., Carlin, C.R., Den Bakker, H.C., Denes, T.G., 2022. Phenotypic characterization and analysis of complete genomes of two distinct strains of the proposed species "*L. swaminathanii*. Sci. Rep. 12, 9137. https://doi.org/10.1038/s41598-022-13119-y.

Ireton, K., Mortuza, R., Gyanwali, G.C., Gianfelice, A., Hussain, M., 2021. Role of internalin proteins in the pathogenesis of *Listeria monocytogenes*. Mol. Microbiol. 116 (6), 1407–1419. https://doi.org/10.1111/MMI.14836.

Ji, C., Li, N., Jiao, J., Sun, Y., Zuo, Y., Huang, X., Huang, X., Li, Z., Li, Y., Leng, Q., Cai, X., Meng, Q., Qiao, J., 2023. A small regulatory RNA, Rli82, is involved in the motility and pathogenicity of *Listeria monocytogenes*. Jundishapur J. Microbiol. 2023 16 (9), 139707. https://doi.org/10.5812/JJM-139707.

Jiang, L., Olesen, I., Andersen, T., Fang, W., Jespersen, L., 2010. Survival of *Listeria monocytogenes* in simulated gastrointestinal system and transcriptional profiling of stress-and adhesion-related genes. Foodborne Pathog. Dis. 7 (3), 267–274. https://doi.org/10.1089/fpd.2009.0361.

Kapetanakou, A.E., Gkerekou, M.A., Vitzilaiou, E.S., Skandamis, P.N., 2017. Assessing the capacity of growth, survival, and acid adaptive response of *Listeria monocytogenes* during storage of various cheeses and subsequent simulated gastric digestion. Int. J. Food Microbiol. 246, 50–63. https://doi.org/10.1016/J.IJFOODMICRO.2017.01.015.

Karygianni, L., Ren, Z., Koo, H., Thurnheer, T., 2020. Biofilm matrixome: extracellular components in structured microbial communities. Trends Microbiol. 28 (8), 668–681. https://doi.org/10.1016/J.TIM.2020.03.016.

Kazmierczak, M.J., Mithoe, S.C., Boor, K.J., Wiedmann, M., 2003. *Listeria monocytogenes* σB regulates stress response and virulence functions. J. Bacteriol. 185 (19), 5722. https://doi.org/10.1128/JB.185.19.5722-5734.2003.

Keane, J.M., Las Heras, V., Pinheiro, J., FitzGerald, J.A., Núñez-Sánchez, M.A., Hueston, C.M., O'Mahony, L., Cotter, P.D., Hill, C., Melgar, S., Gahan, C.G.M., 2023. *Akkermansia muciniphila* reduces susceptibility to *Listeria monocytogenes* infection in mice fed a high-fat diet. Gut Microbes 15 (1). https://doi.org/10.1080/19490976.2023.2229948.

Kiela, P.R., Ghishan, F.K., 2016. Physiology of intestinal absorption and secretion. Best. Pract. Res. Clin. Gastroenterol. 30 (2), 145–159. https://doi.org/10.1016/J.BPG.2016.02.007.

Kim, S., Shin, Y.-C., Kim, T.-Y., Kim, Y., Lee, Y.-S., Lee, S.-H., Kim, M.-N., Kim, K.S., Kweon, M.-N., 2021. Mucin degrader *Akkermansia muciniphila* accelerates intestinal stem cell-mediated epithelial development. Gut Microbes 13. https://doi.org/10.1080/19490976.2021.1892441.

Kozak, S.M., Bobak, Y., D'Amico, D.J., 2018. Efficacy of antimicrobials applied individually and in combination for controlling *Listeria monocytogenes* as surface contaminants on queso fresco. J. Food Prot. 81 (1), 46–53. https://doi.org/10.4315/0362-028X.JFP-17-279.

Lakicevic, B.Z., Den Besten, H.M.W., De Biase, D., 2021. Landscape of stress response and virulence genes among *Listeria monocytogenes* strains. Front. Microbiol. 12. https://doi.org/10.3389/FMICB.2021.738470.

Lakshminarayanan, B., Guinane, C.M., O'Connor, P.M., Coakley, M., Hill, C., Stanton, C., O'Toole, P.W., Ross, R.P., 2013. Isolation and characterization of bacteriocin-producing bacteria from the intestinal microbiota of elderly Irish subjects. J. Appl. Microbiol. 114 (3), 886–898. https://doi.org/10.1111/jam.12085.

Lam, G.Y., Fattouh, R., Muise, A.M., Grinstein, S., Higgins, D.E., Brumell, J.H., 2011. Listeriolysin O suppresses phospholipase C-mediated activation of the microbicidal NADPH oxidase to promote *Listeria monocytogenes* infection. Cell Host Microbe 10 (6), 627–634. https://doi.org/10.1016/J.CHOM.2011.11.005.

Lammerding, A.M., Glass, K.A., Gendron-Fitzpatrick, A., Doyle, M.P., 1992. Determination of virulence of different strains of *Listeria monocytogenes* and *Listeria innocua* by oral inoculation of pregnant mice. Appl. Environ. Microbiol. 58 (12), 3991–4000. https://doi.org/10.1128/aem.58.12.3991-4000.1992.

Lamond, N.M., McMullen, P.D., Paramasvaran, D., Visvahabrathy, L., Eallonardo, S.J., Maheswhari, A., Freitag, N.E., 2021. Cardiotropic isolates of *Listeria monocytogenes* with enhanced vertical transmission dependent upon the bacterial surface protein InlB. Infect. Immun. 89 (2), e00321-20. https://doi.org/10.1128/IAI.00321-20.

Lamont, R.J., Koo, H., Hajishengallis, G., 2018. The oral microbiota: dynamic communities and host interactions. Nat. Rev. Microbiol. 16 (12), 745. https://doi.org/10.1038/S41579-018-0089-X.

Las Heras, V., Clooney, A.G., Ryan, F.J., Cabrera-Rubio, R., Casey, P.G., Hueston, C.M., Pinheiro, J., Rudkin, J.K., Melgar, S., Cotter, P.D., Hill, C., Gahan, C.G.M., 2019. Short-term consumption of a high-fat diet increases host susceptibility to *Listeria monocytogenes* infection. Microbiome 7 (1), 7. https://doi.org/10.1186/s40168-019-0621-x.

Lee, S., 2020. Bacteriocins of *Listeria monocytogenes* and their potential as a virulence factor. Toxins 12 (2), 1–13. https://doi.org/10.3390/toxins12020103.

Lee, Chakraborty, U., Gebhart, D., Govoni, G.R., Zhou, Z.H., Scholl, D., 2016. F-type bacteriocins of *Listeria monocytogenes*: a new class of phage tail-like structures reveals broad parallel coevolution between tailed bacteriophages and high-molecular-weight bacteriocins. J. Bacteriol. 198 (20), 2784–2793. https://doi.org/10.1128/JB.00489-16.

Lee, H.Y., Park, J.H., Seok, S.H., Baek, M.W., Kim, D.J., Lee, B.H., Kang, P.D., Kim, Y.S., Park, J.H., 2005. Potential antimicrobial effects of human lactoferrin against oral infection with *Listeria monocytogenes* in mice. J. Med. Microbiol. 54 (Pt 11), 1049–1054. https://doi.org/10.1099/JMM.0.45918-0.

Lee, Y.J., Wang, C., 2020. Links between S-adenosylmethionine and Agr-based quorum sensing for biofilm development in *Listeria monocytogenes* EGD-e. MicrobiologyOpen 9 (5). https://doi.org/10.1002/MBO3.1015.

Lemon, K.P., Freitag, N.E., Kolter, R., 2010. The virulence regulator PrfA promotes biofilm formation by *Listeria monocytogenes*. J. Bacteriol. 192 (15), 3969–3976. https://doi.org/10.1128/JB.00179-10.

Linke, K., Rückerl, I., Brugger, K., Karpiskova, R., Walland, J., Muri-Klinger, S., Tichy, A., Wagner, M., Stessl, B., 2014. Reservoirs of *Listeria* species in three environmental ecosystems. Appl. Environ. Microbiol. 80 (18), 5583. https://doi.org/10.1128/AEM.01018-14.

Liu, M., Lv, Q., Xu, J., Liu, B., Zhou, Y., Zhang, S., Shen, X., Wang, L., 2023. Isoflavone glucoside genistin, an inhibitor targeting Sortase A and Listeriolysin O, attenuates the virulence of *Listeria monocytogenes* in vivo and in vitro. Biochem. Pharmacol. 209, 115447. https://doi.org/10.1016/J.BCP.2023.115447.

Luchansky, J.B., Campano, S.G., Rieker, M., Mahoney, C., Vinyard, B.T., Shane, L.E., Shoyer, B.A., Osoria, M., Porto-Fett, A.C.S., 2018. Viability of *Listeria monocytogenes* and *Salmonella* spp. on slices of a German-style bologna containing blends of organic acid salts during storage at 4 or 12 °C. J. Food Prot. 86, 100019. https://doi.org/10.1016/j.jfp.2022.100019.

Luque-Sastre, L., Arroyo, C., Fox, E.M., McMahon, B.J., Bai, L., Li, F., Fanning, S., 2018. Antimicrobial resistance in *Listeria* species. Microbiol. Spectr. 6 (4). https://doi.org/10.1128/MICROBIOLSPEC.ARBA-0031-2017.

Macleod, J., Beeton, M.L., Blaxland, J., 2022. An Exploration of *Listeria monocytogenes*, its influence on the UK food industry and future public health strategies. Foods 11, 1456. https://doi.org/10.3390/foods11101456.

Maloy, K.J., Powrie, F., 2011. Intestinal homeostasis and its breakdown in inflammatory bowel disease. Nature 2011 474 (7351), 298–306. https://doi.org/10.1038/nature10208.

Marco, A.J., Altimira, J., Prats, N., López, S., Dominguez, L., Domingo, M., Briones, V., 1997. Penetration of *Listeria monocytogenes* in mice infected by the oral route. Microb. Pathog. 23 (5), 255–263. https://doi.org/10.1006/MPAT.1997.0144.

Martín, I., Córdoba, J.J., Rodríguez, A., 2023. Effect of acidic conditions on the growth and expression of two virulence genes of *Listeria monocytogenes* serotype 4b. Res. Microbiol., 104042 https://doi.org/10.1016/J.RESMIC.2023.104042.

Martín, I., Rodríguez, A., Delgado, J., Córdoba, J.J., 2022. Strategies for biocontrol of *Listeria monocytogenes* using lactic acid bacteria and their metabolites in ready-to-eat meat- and dairy-ripened products. Foods 11, *542*. https://doi.org/10.3390/FOODS11040542.

Mathipa, M.G., Bhunia, A.K., Thantsha, M.S., 2019. Internalin AB-expressing recombinant *Lactobacillus casei* protects Caco-2 cells from *Listeria monocytogenes*-induced damages under simulated intestinal conditions. PloS One 14 (7). https://doi.org/10.1371/JOURNAL.PONE.0220321.

Maury, M.M., Bracq-Dieye, H., Huang, L., Vales, G., Lavina, M., Thouvenot, P., Disson, O., Leclercq, A., Brisse, S., Lecuit, M., 2019. Hypervirulent *Listeria monocytogenes* clones' adaption to mammalian gut accounts for their association with dairy products. Nat. Commun. 10 (1), 1–13. https://doi.org/10.1038/s41467-019-10380-0.

McGann, P., Wiedmann, M., Boor, K.J., 2007. The alternative Sigma Factor σB and the virulence gene regulator PrfA both regulate transcription of *Listeria monocytogenes* internalins. Appl. Environ. Microbiol. 73 (9), 2919. https://doi.org/10.1128/AEM.02664-06.

McLauchlin, J., Mitchell, R.T., Smerdon, W.J., Jewell, K., 2004. *Listeria monocytogenes* and listeriosis: A review of hazard characterisation for use in microbiological risk assessment of foods. Int. J. Food Microbiol. 92 (1), 15–33. https://doi.org/10.1016/S0168-1605(03)00326-X.

Meireles, D., Pombinho, R., Cabanes, D., 2024. Signals behind *Listeria monocytogenes* virulence mechanisms. Gut Microbes 16 (1). https://doi.org/10.1080/19490976.2024.2369564.

Mennah-Govela, Y.A., Cai, H., Chu, J., Kim, K., Maborang, M.K., Sun, W., Bornhorst, G. M., 2020. Buffering capacity of commercially available foods is influenced by composition and initial properties in the context of gastric digestion. Food Funct. 11 (3), 2255–2267. https://doi.org/10.1039/C9FO03033F.

Meza-Torres, J., Lelek, M., Quereda, J.J., Sachse, M., Manina, G., Ershov, D., Tinevez, J. Y., Radoshevich, L., Maudet, C., Chaze, T., Gianetto, Q.G., Matondo, M., Lecuit, M., Martin-Verstraete, I., Zimmer, C., Bierne, H., Dussurget, O., Cossart, P., Pizarro-Cerdá, J., 2021. Listeriolysin S: a bacteriocin from *Listeria monocytogenes* that induces membrane permeabilization in a contact-dependent manner. Proc. Natl. Acad. Sci. USA 118 (40), e2108155118. https://doi.org/10.1073/pnas.2108155118.

Min, Z., Yang, L., Hu, Y., Huang, R., 2023. Oral microbiota dysbiosis accelerates the development and onset of mucositis and oral ulcers. Front. Microbiol. 14, 1061032. https://doi.org/10.3389/FMICB.2023.1061032.

Minekus, M., Alminger, M., Alvito, P., Ballance, S., Bohn, T., Bourlieu, C., Carrière, F., Boutrou, R., Corredig, M., Dupont, D., Dufour, C., Egger, L., Golding, M., Karakaya, S., Kirkhus, B., Le Feunteun, S., Lesmes, U., MacIerzanka, A., MacKie, A., Brodkorb, A., 2014. A standardised static in vitro digestion method suitable for food-an international consensus. Food Funct. 5 (6), 1113–1124. https://doi.org/10.1039/c3fo60702j.

Mohammadzadeh, R., Azadegan, A., Kalani, B.S., 2019. Listeriolysin S may inhibit the anti-listerial properties of *Lactobacillus plantarum*. Microb. Pathog. 137, 103744. https://doi.org/10.1016/J.MICPATH.2019.103744.

Murdoch, C.C., Skaar, E.P., 2022. Nutritional immunity: the battle for nutrient metals at the host–pathogen interface. Nat. Rev. Microbiol. 20 (11), 657–670. https://doi.org/10.1038/s41579-022-00745-6.

Olsen, I., 2020. Mucus is more than just a physical barrier for trapping oral microorganisms. J. Oral. Microbiol. 12 (1). https://doi.org/10.1080/20002297.2020.1788352.

Osek, J., Wieczorek, K., 2022. *Listeria monocytogenes*—How this pathogen uses its virulence mechanisms to infect the hosts. Pathogens 11 (12). https://doi.org/10.3390/pathogens11121491.

Pandiri, A.R., 2013. Overview of exocrine pancreatic pathobiology. Toxicol. Pathol. 42 (1), 207. https://doi.org/10.1177/0192623313509907.

Pasechnek, A., Rabinovich, L., Stadnyuk, O., Azulay, G., Mioduser, J., Argov, T., Borovok, I., Sigal, N., Herskovits, A.A., 2020. Active lysogeny in *Listeria monocytogenes* is a bacteria-phage adaptive response in the mammalian environment. Cell Rep. 32 (4). https://doi.org/10.1016/J.CELREP.2020.107956.

Patricia, J.J., Dhamoon, A.S., 2022. Physiol. Dig. StatPearls. ⟨https://www.ncbi.nlm.nih.gov/books/NBK544242/⟩.

Pedersen, A.M., Belstrøm, D., 2019. The role of natural salivary defences in maintaining a healthy oral microbiota. J. Dent. 80, S3–S12. https://doi.org/10.1016/J.JDENT.2018.08.010.

Pelaseyed, T., Bergström, J.H., Gustafsson, J.K., Ermund, A., Birchenough, G.M.H., Schütte, A., van der Post, S., Svensson, F., Rodríguez-Piñeiro, A.M., Nyström, E.E.L., Wising, C., Johansson, M.E.V., Hansson, G.C., 2014. The mucus and mucins of the goblet cells and enterocytes provide the first defense line of the gastrointestinal tract and interact with the immune system. Immunol. Rev. 260 (1), 8. https://doi.org/10.1111/IMR.12182.

Pettersen, K.S., Skjerdal, T., Wasteson, Y., Lindbäck, T., Vegarud, G., Comi, I., Aspholm, M., 2018. Survival of *Listeria monocytogenes* during in vitro gastrointestinal digestion after exposure to 5 and 0.5% sodium chloride. Food Microbiol. 77, 78–84. https://doi.org/10.1016/j.fm.2018.08.010.

Popowska, M., Krawczyk-Balska, A., Ostrowski, R., Desvaux, M., 2017. InlL from *Listeria monocytogenes* is involved in biofilm formation and adhesion to mucin. Front. Microbiol. 8. https://doi.org/10.3389/fmicb.2017.00660.

Porto-Fett, A.C.S., Campano, S.G., Rieker, M., Stahler, L.J., Mcgeary, L., Shane, L.E., Shoyer, B.A., Osoria, M., Luchansky, J.B., 2018. Behavior of *Listeria monocytogenes* on mortadella formulated using a natural, clean-label antimicrobial agent during extended storage at 4 or 128 ºC. J. Food Prot. 81 (5), 769–775. https://doi.org/10.4315/0362-028X.JFP-17-400.

Price, R., Jayeola, V., Niedermeyer, J., Parsons, C., Kathariou, S., 2018. The *Listeria monocytogenes* key virulence determinants *hly* and *prfA* are involved in biofilm formation and aggregation but not colonization of fresh produce. Pathogens 7 (1), 18. https://doi.org/10.3390/pathogens7010018.

Pron, B., Boumaila, C., Jaubert, F., Sarnacki, S., Monnet, J.-P., Berche, P., Gaillard, J.-L., 1998. Comprehensive study of the intestinal stage of listeriosis in a rat ligated ileal loop system. Infect. Immun. 66 (2), 747–755. https://doi.org/10.1128/IAI.66.2.747-755.1998.

Quereda, Andersson, C., Cossart, P., Johansson, J., Pizarro-Cerdá, J., 2018. Role in virulence of phospholipases, listeriolysin O and listeriolysin S from epidemic *Listeria monocytogenes* using the chicken embryo infection model. Vet. Res. 49 (1), 1–9. https://doi.org/10.1186/s13567-017-0496-4.

Quereda, Dussurget, O., Nahori, M.A., Ghozlane, A., Volant, S., Dillies, M.A., Regnault, B., Kennedy, S., Mondot, S., Villoing, B., Cossart, P., Pizarro-Cerda, J., 2016. Bacteriocin from epidemic *Listeria* strains alters the host intestinal microbiota to favor infection. Proc. Natl. Acad. Sci. USA 113 (20), 5706–5711. https://doi.org/10.1073/pnas.1523899113.

Quereda, Morón-García, A., Palacios-Gorba, C., Dessaux, C., García-del Portillo, F., Pucciarelli, M.G., Ortega, A.D., 2021. Pathogenicity and virulence of *Listeria monocytogenes*: a trip from environmental to medical microbiology. Virulence 12 (1), 2509–2545. https://doi.org/10.1080/21505594.2021.1975526.

Quereda, Nahori, M.A., Meza-Torres, J., Sachse, M., Titos-Jiménez, P., Gomez-Laguna, J., Dussurget, O., Cossart, P., Pizarro-Cerdá, J., 2017. Listeriolysin S is a streptolysin S-like virulence factor that targets exclusively prokaryotic cells in vivo. MBio 8 (2). https://doi.org/10.1128/mBio.00259-17.

Radoshevich, L., Cossart, P., 2017. *Listeria monocytogenes*: towards a complete picture of its physiology and pathogenesis. Nat. Rev. Microbiol. 16 (1), 32–46. https://doi.org/10.1038/nrmicro.2017.126.

Rahman, S.M.A., Munther, D., Fazil, A., Smith, B., Wu, J., 2016. Unraveling the dose-response puzzle of L. monocytogenes: a mechanistic approach. Infect. Dis. Model. 1 (1), 101–114. https://doi.org/10.1016/J.IDM.2016.09.001.

Rahman, S.M.A., Munther, D., Fazil, A., Smith, B., Wu, J., 2018. Advancing risk assessment: mechanistic dose-response modelling of *Listeria monocytogenes* infection in human populations. R. Soc. Open Sci. 5 (8). https://doi.org/10.1098/RSOS.180343.

Ramalheira, R., Almeida, M., Azeredo, J., Brandão, T.R., Almeida, G., Silva, J., Teixeira, P., 2010. Survival of clinical and food isolates of *Listeria monocytogenes* through simulated gastrointestinal tract conditions. Foodborne Pathog. Dis. 7 (2), 121–128. https://doi.org/10.1089/fpd.2009.0319.

Rattanaphan, P., Mittraparp-Arthorn, P., Srinoun, K., Vuddhakul, V., Tansila, N., 2020. Indole signaling decreases biofilm formation and related virulence of *Listeria monocytogenes*. FEMS Microbiol. Lett. 367 (14), 116. https://doi.org/10.1093/FEMSLE/FNAA116.

Ravindhiran, R., Sivarajan, K., Sekar, J.N., Murugesan, R., Dhandapani, K., 2023. *Listeria monocytogenes* an emerging pathogen: a comprehensive overview on listeriosis, virulence determinants, detection, and anti-listerial interventions. Microb. Ecol. 86 (4), 2231–2251. https://doi.org/10.1007/s00248-023-02269-9.

Reglinski, M., Sriskandan, S., 2014. Streptococcus pyogenes. Mol. Med. Microbiol. 675–716. https://doi.org/10.1016/B978-0-12-397169-2.00038-X.

Reinus, J.F., Simon, D., 2014. Gastrointestinal Anatomy and Physiology: The Essentials. Wiley-Blackwell.

Rinehart, E., Chapman, J., Sun, Y., 2020. The production of Listeriolysin O and subsequent intracellular infections by *Listeria monocytogenes* are regulated by

exogenous short chain fatty acid mixtures. Toxins 12, 218. https://doi.org/10.3390/TOXINS12040218.
Rinninella, E., Raoul, P., Cintoni, M., Franceschi, F., Miggiano, G.A.D., Gasbarrini, A., Mele, M.C., 2019. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms 7 (1). https://doi.org/10.3390/microorganisms7010014.
Rolhion, N., Chassaing, B., Nahori, M.-A., de Bodt, J., Moura, A., Lecuit, M., Dussurget, O., Bérard, M., Marzorati, M., Fehlner-Peach, H., Littman, D.R., Gewirtz, A.T., Van de Wiele, T., Cossart, P., 2019. A *Listeria monocytogenes* bacteriocin can target the commensal *Prevotella copri* and modulate intestinal infection. Cell Host Microbe 26 (5), 691–701.e5. https://doi.org/10.1016/j.chom.2019.10.016.
Round, J.L., Mazmanian, S.K., 2009. The gut microbiota shapes intestinal immune responses during health and disease. Nat. Rev. Immunol. 2009 9 (5), 313–323. https://doi.org/10.1038/nri2515.
Saklani-Jusforgues, H., Fontan, E., Goossens, P.L., 2000. Effect of acid-adaptation on *Listeria monocytogenes* survival and translocation in a murine intragastric infection model. FEMS Microbiol. Lett. 193, 155–159. https://doi.org/10.1111/j.1574-6968.2000.tb09418.x.
Samuelson, L.C., 2006. Genetically engineered mouse models of gastric physiology. In: Physiology of the Gastrointestinal Tract, 2. Elsevier, pp. 1293–1312. https://doi.org/10.1016/B978-012088394-3/50054-4.
Santacroce, L., Passarelli, P.C., Azzolino, D., Bottalico, L., Charitos, I.A., Cazzolla, A.P., Colella, M., Topi, S., Godoy, F.G., D'Addona, A., 2023. Oral microbiota in human health and disease: a perspective. Exp. Biol. Med. 248 (15), 1288. https://doi.org/10.1177/15353702231187645.
Santacruz, A., Collado, M.C., García-Valdés, L., Segura, M.T., Martín-Lagos, J.A., Anjos, T., Martí-Romero, M., Lopez, R.M., Florido, J., Campoy, C., Sanz, Y., 2010. Gut microbiota composition is associated with body weight, weight gain and biochemical parameters in pregnant women. Br. J. Nutr. 104 (1), 83–92. https://doi.org/10.1017/S0007114510000176.
Schiavano, G.F., Guidi, F., Pomilio, F., Brandi, G., Salini, R., Amagliani, G., Centorotola, G., Palma, F., Felici, M., Lorenzetti, C., Blasi, G., 2023. *Listeria monocytogenes* strains persisting in a meat processing plant in central Italy: use of whole genome sequencing and in vitro adhesion and invasion assays to decipher their virulence potential. Microorganisms 11 (7). https://doi.org/10.3390/microorganisms11071659.
Sensoy, I., 2021. A review on the food digestion in the digestive tract and the used in vitro models. Curr. Res. Food Sci. 4, 308. https://doi.org/10.1016/J.CRFS.2021.04.004.
Seo, K., Seo, J., Yeun, J., Choi, H., Kim, Y.I., Chang, S.Y., 2021. The role of mucosal barriers in human gut health. Arch. Pharm. Res. 2021 44 (4), 325–341. https://doi.org/10.1007/S12272-021-01327-5.
Shah, M.K., Bergholz, T.M., 2020. Variation in growth and evaluation of cross-protection in *Listeria monocytogenes* under salt and bile stress. J. Appl. Microbiol. 129 (2), 367–377. https://doi.org/10.1111/JAM.14607.
Sibanda, T., Buys, E.M., 2022. *Listeria monocytogenes* pathogenesis: the role of stress adaptation. Microorganisms 10, 1522. https://doi.org/10.3390/microorganisms10081522.
Simons, A., Alhanout, K., Duval, R.E., 2020. Bacteriocins, antimicrobial peptides from bacterial origin: overview of their biology and their impact against multidrug-resistant bacteria. Microorganisms 8 (5), 639. https://doi.org/10.3390/microorganisms8050639.
Skowron, K., Hulisz, K., Gryń, G., Olszewska, H., Wiktorczyk, N., Paluszak, Z., 2018. Comparison of selected disinfectants efficiency against *Listeria monocytogenes* biofilm formed on various surfaces. Int. Microbiol. 21 (1–2), 23–33. https://doi.org/10.1007/S10123-018-0002-5.
Smith, M.E., Morton, D.G., 2011. In: Smith, M.E., Morton, D.G. (Eds.), The Digestive System: Systems of the Body Series, 2nd ed. Elsevier Health Sciences.
Solar, C., Escalona, A., Garrido, D., 2019. The gut microbiome after bariatric surgery. Micro Metab. Diagn., Ther., Other Strateg. Appl. 235–242. https://doi.org/10.1016/B978-0-12-815249-2.00024-5.
Song, C., Chai, Z., Chen, S., Zhang, H., Zhang, X., Zhou, Y., 2023. Intestinal mucus components and secretion mechanisms: what we do and do not know. Exp. Mol. Med. 55 (4), 681–691. https://doi.org/10.1038/s12276-023-00960-y.
Stavru, F., Archambaud, C., Cossart, P., 2011. Cell biology and immunology of *Listeria monocytogenes* infections: novel insights. Immunol. Rev. 240 (1), 160–184. https://doi.org/10.1111/J.1600-065X.2010.00993.X.
Stopforth, J.D., Yoon, Y., Barmpalia, I.M., Samelis, J., Skandamis, P.N., Sofos, J.N., 2005. Reduction of *Listeria monocytogenes* populations during exposure to a simulated gastric fluid following storage of inoculated frankfurters formulated and treated with preservatives. Int. J. Food Microbiol. 99 (3), 309–319. https://doi.org/10.1016/J.IJFOODMICRO.2004.08.022.
Sugrue, I., Ross, R.P., Hill, C., 2024. Bacteriocin diversity, function, discovery and application as antimicrobials. Nat. Rev. Microbiol. 22 (9), 556–571. https://doi.org/10.1038/s41579-024-01045-x.
Swaminathan, B., Gerner-Smidt, P., 2007. The epidemiology of human listeriosis. Microbes Infect. 9, 1236–1243. https://doi.org/10.1016/j.micinf.2007.05.011.
Thursby, E., Juge, N., 2017. Introduction to the human gut microbiota. Biochem. J. 474 (11), 1823. https://doi.org/10.1042/BCJ20160510.
Toh, B.-H., Alderuccio, F., 2007. Parietal cell and intrinsic factor autoantibodies. Autoantibodies. Elsevier, pp. 479–486. https://doi.org/10.1016/B978-044452763-9/50064-0.
Travier, L., Guadagnini, S., Gouin, E., Dufour, A., Chenal-Francisque, V., Cossart, P., Olivo-Marin, J.C., Ghigo, J.M., Disson, O., Lecuit, M., 2013. ActA promotes *Listeria monocytogenes* aggregation, intestinal colonization and carriage. PLOS Pathog. 9 (1), e1003131. https://doi.org/10.1371/JOURNAL.PPAT.1003131.
Vidovic, S., Paturi, G., Gupta, S., Fletcher, G.C., 2022. Lifestyle of *Listeria monocytogenes* and food safety: emerging listericidal technologies in the food industry. Crit. Rev. Food Sci. Nutr. 64 (7), 1817–1835. https://doi.org/10.1080/10408398.2022.2119205.
Vila, T., Rizk, A.M., Sultan, A.S., Jabra-Rizk, M.A., 2019a. The power of saliva: antimicrobial and beyond. PLoS Pathog. 15 (11). https://doi.org/10.1371/JOURNAL.PPAT.1008058.
Vila, T., Rizk, A.M., Sultan, A.S., Jabra-Rizk, M.A., 2019b. The power of saliva: antimicrobial and beyond. PLoS Pathog. 15 (11), e1008058. https://doi.org/10.1371/JOURNAL.PPAT.1008058.
Wang, H., Li, J., Wu, G., Zhang, F., Yin, J., He, Y., 2022a. The effect of intrinsic factors and mechanisms in shaping human gut microbiota. Med. Microecol. 12, 100054. https://doi.org/10.1016/J.MEDMIC.2022.100054.
Wang, T., Liu, B., Zhang, C., Fang, T., Ding, Y., Song, G., Zhang, S., Shi, L., Deng, X., Wang, J., 2022b. Kaempferol-driven inhibition of Listeriolysin O pore formation and inflammation suppresses *Listeria monocytogenes* infection. Microbiol. Spectr. 10, e01810-22. https://doi.org/10.1128/spectrum.01810-22.
Wiktorczyk-Kapischke, N., Skowron, K., Wałecka-Zacharska, E., 2023. Genomic and pathogenicity islands of *Listeria monocytogenes*—overview of selected aspects. Front. Mol. Biosci. 10. https://doi.org/10.3389/FMOLB.2023.1161486.
Winkelströter, L.K., De Martinis, E.C.P., 2013. Effect of bacteriocins and conditions that mimic food and digestive tract on biofilm formation, in vitro invasion of eukaryotic cells and internalin gene expression by *Listeria monocytogenes*. Probiot. Antimicrob. Proteins 5 (3), 153–164. https://doi.org/10.1007/S12602-013-9135-1/TABLES/8.
Witter, A.R., Okunnu, B.M., Berg, R.E., 2016. The essential role of neutrophils during infection with the intracellular bacterial pathogen *Listeria monocytogenes*. J. Immunol. 197 (5), 1557. https://doi.org/10.4049/JIMMUNOL.1600599.
Wright, D.P., Rosendale, D.I., Roberton, A.M., 2000. *Prevotella* enzymes involved in mucin oligosaccharide degradation and evidence for a small operon of genes expressed during growth on mucin. FEMS Microbiol. Lett. 190 (1), 73–79. https://doi.org/10.1111/J.1574-6968.2000.TB09265.X.
Yu, D., Pei, Z., Chen, Y., Wang, H., Xiao, Y., Zhang, H., Chen, W., Lu, W., 2023. *Bifidobacterium longum* subsp. *infantis* as widespread bacteriocin gene clusters carrier stands out among the *Bifidobacterium*. Appl. Environ. Microbiol. 89, e00979-23. https://doi.org/10.1128/aem.00979-23.
Zhang, L.(2021). Studies on the Survival of Listeria monocytogenes in Filtered Fluid Milk Products Under Simulated Human Gastric Conditions (SHIME®) and on the Viable but Non-culturable State of the Organism, [University of Guelph].⟨https://hdl.handle.net/10214/26341⟩.
Zhang, Q., Feng, Y., Deng, L., Feng, F., Wang, L., Zhou, Q., Luo, Q., 2011. SigB plays a major role in *Listeria monocytogenes* tolerance to bile stress. Int. J. Food Microbiol. 145 (1), 238–243. https://doi.org/10.1016/J.IJFOODMICRO.2010.12.028.
Zhang, Parreira, V.R., Rahman, A., Smith, B.A., Munther, D.S., Farber, J.M., 2023. Survival and predictive modeling of *Listeria monocytogenes* under simulated human gastric conditions in the presence of bovine milk products. Int. J. Food Microbiol. 396, 110201. https://doi.org/10.1016/j.ijfoodmicro.2023.110201.
Zhang, Sasabe, J., Hullahalli, K., Sit, B., Waldor, M.K., 2021. Increased *Listeria monocytogenes* dissemination and altered population dynamics in Muc2-deficient mice. Infect. Immun. 89 (4). https://doi.org/10.1128/IAI.00667-20.
Zhu, T., Yang, C., Bao, X., Chen, F., Guo, X., 2022. Strategies for controlling biofilm formation in food industry. Grain and Oil Science and Technology. KeAi Communications Co, pp. 179–186. https://doi.org/10.1016/j.gaost.2022.06.003, 5.
Zilelidou, E.A., Milina, V., Paramithiotis, S., Zoumpopoulou, G., Poimenidou, S.V., Mavrogonatou, E., Kletsas, D., Papadimitriou, K., Tsakalidou, E., Skandamis, P.N., Dudley, E.G., 2020. Differential modulation of *Listeria monocytogenes* fitness, in vitro virulence, and transcription of virulence-associated genes in response to the presence of different microorganisms. Appl. Environ. Microbiol. 86, e01165-20. https://doi.org/10.1128/AEM.01165-20.
Zink, R., Loessner, M.J., Scherer, S., 1995. Characterization of cryptic prophages (monocins) in Listeria and sequence analysis of a holinlendolysin gene. Microbiology 141, 2577–2584. https://doi.org/10.1099/13500872-141-10-2577.