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Salmonella: The Impact and Function on the Host's Intestine

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Abstract. One of the most widespread foodborne pathogens worldwide is Salmonella enteritidis. It brings a wide range of clinical problems by changing the environment inside the host's gut. Scientists are yet to comprehend the long-term effects of Salmonella on the intestine, the interaction of its pathogenic elements with the immune system and microorganisms in the gut of the host. In this paper, the authors have reviewed the mechanism of Salmonella infection of living organisms with references to the molecular mechanisms that enable the bacteria to cause inflammation, evade immune responses, adapt its metabolism, and remain in the gut over an extended period of time. Research indicates that Salmonella takes advantage of intestinal inflammation to withhold beneficial bacteria and acquire a competitive advantage to grow. It also changes the active invasion to long-term infection by switching the various virulence genes on and off at the various stages of infection. The majority of the existing studies are solely concerned with short-term acute infection. There is little focus on those individuals who remain carriers of the bacteria over an extended period of time or those health problems that develop once the primary infection is over. This gap makes it hard to turn lab results into real clinical treatments. Researchers should apply multi-omics to further examine the association between Salmonella and its host in the future. Further studies are also needed on the mechanism of Salmonella remaining in the body and resulting in immune dysfunction following infection.

Keywords: Salmonella, foodborne pathogen, host-pathogen interaction, intestinal inflammation

1. Introduction

Salmonella enterica is a Gram-negative bacterium that has a family of Enterobacteriaceae. It is one of the leading causes of foodborne illnesses in most companies worldwide, and is transmitted primarily via infected water and food. Individuals who fall victim to Salmonella may experience mild stomach infections up to whole body infections that can result in death like typhoid fever and sepsis. The infections pose massive strain on community health and medical practice. Salmonella is so effective since it relates with the host on intricate and cautious means. It invades the body employing multiple molecular vectors to invade cells, avoid the immune system and live a long time within the body. Numerous investigations have attributed the major pathogenesis of Salmonella, particularly the functions of its type III secretion systems, or T3SS. The role of SPI-1 is to assist Salmonella to invade intestinal cells, whereas SPI-2 assists the bacteria to live and multiply within

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macrophages [1, 2]. It has also been found that Salmonella actively results in gut inflammation to displace useful bacteria and establish a favorable environment to survive. With such discoveries, there are still plenty of gaps. Numerous studies outline how virulence genes are generally controlled yet provide little insight into the collective behavior of regulators within the host to direct infection. The evolution of SPI-1-mediated invasion into the introduction of SPI-2-mediated intracellular survival is viewed as a gradual transition [3]. Nonetheless, the mechanism by which this switch is modulated by host signals like pH, salts in bile, amounts of nutrients, and immune molecules is not well understood by scientists. Salmonella brings about inflammation which benefits the bacteria, but causes harm to the host. However, there are not many studies that examine long-term implications of this inflammation on immunity and tissue restoration. A majority of the experiments apply small models of short-term infections and open tremendous gaps on long-term carriers and post-infection issues like reactive arthritis. Individuals with a long time history of Salmonella bearing in the gallbladder are the carriers and are unaware of it [4]. However, we are yet to clearly comprehend the process of how temporary inflammation becomes permanent infection. The other huge issue is that laboratory findings do not usually translate into useful medicine or vaccines. There are numerous promising molecular targets present in cells or animals that have not become real treatments. It implies that studies must be more aligned to the actual behaviors of Salmonella in a living host and identify weak spots, which can be blocked. This review is not merely the list of the components that render Salmonella perilous. Rather, it integrates the evidence of the life of Salmonella in the intestine of the host and its modifications. It dwells upon the adaptation of Salmonella to the environment of a host and varies its pathogenicity. It shows the key molecules such as effector proteins, small RNAs and regulators of metabolism. Through synthesizing the existing knowledge and identifying gaps in the literature, this review will contribute to supporting upcoming treatments, improved vaccines, and enhanced population health strategies against Salmonella.

2. Salmonella's effects on the host's intestine

2.1. The intracellular lifestyle of Salmonella and its impact on inter-host transmission

Salmonella's life cycle depends on its ability to move between living outside and inside host cells. It must compete with the natural gut bacteria when it enters the intestine. The researchers discovered that Salmonella exploits inflammation that it induces to cross this barrier. The host releases chemicals, such as tetrathionate, during inflammation. These enabled Salmonella to utilize ethanolamine as food, giving it a definite growth advantage over bacteria that cannot endure in oxygen-rich environments. Introduction of host cells is highly regulated. Salmonella activates SPI-1 when it gets to the intestinal lining of the body [5]. The SPI-1 genes are regulated by a set of regulators such as HilD, HilC and RtsA. These are in response to external cues like the level of oxygen and salt. Salmonella also includes an internal brake to prevent wasting energy: a small RNA, InvR, links up with the mRNA of one of its important regulators, hilA and prevents the production of the protein. This fine-tunes how invasive the bacteria are. Once in a cell, Salmonella has a quick change of plan to live. It resides within a special vacuole known as the Salmonella-Containing Vacuole or the SCV. Within this SCV, Salmonella activates SPI-2 that liberates another group of proteins [6, 7]. One of the proteins is SifA, which assists in the production of tube-like structures, which stabilize the SCV and assist in nutrient uptake. Salmonella also alters its energy utilization. Certain bacteria within macrophages reduce their metabolism and go into a resting position, creating clumps of protein resulting in a more resistant state to stress and antibiotics. This capability of surviving within the cells but in a dormant state enables Salmonella to travel throughout the body

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and infect other hosts. Individuals who have long-term infections shed bacteria occasionally, which becomes the source of new infections. The reason why living inside cells is not only a survival strategy but also an important mechanism of Salmonella spreading between people and animals [8, 9].

2.2. Immune subversion, microbiota disruption, and the inflammation paradox Salmonella

Salmonella does not sit back and wait to be attacked by the immune system. It modulates and regulates immune responses. One of the concepts is that Salmonella is a good cause of inflammation, but bad to the host. SPI-1 proteins, including SopE, SopE2 and SipA, activate directly inflammatory pathways, such as NF-KB and MAPK. This attracts immune cells referred to as neutrophils. This inflammation assists Salmonella in various aspects. First, it alters the gut environment in such a way that Salmonella is able to thrive better than other bacteria. Second, neutrophils might inadvertently transport Salmonella through the intestinal lining, allowing it to proliferate to other regions of the body. Third, Salmonella exploits the proteins of SPI-2 to undermine certain immune responses within macrophages [10]. As an illustration, SteC reduces the expression of antigen-presenting molecules, which helps Salmonella to evade the adaptive immune system. Salmonella also severely interferes with the natural gut bacteria. Inflammation creates reactive oxygen and nitrogen molecules that are toxic to many helpful anaerobic bacteria, such as Clostridia and Bacteroides. These bacteria are usually beneficial in safeguarding the gut and in maintaining the immune system. Salmonella and other harmful bacteria can easily replace them when they become smaller. This causes an imbalance in the long term and increases the risk of the host to other infections.

2.3. Uncommon clinical manifestations and Host-specific adaptations although most

Most Salmonella infections cause gastroenteritis, but serious cases can lead to severe local tissue damage. One case report described Salmonella infection that caused acute small bowel obstruction because of serious inflammation in the end of the small intestine. Endoscopy showed a thickened gut wall and ulcers, directly caused by proteins from SPI-1 [11]. These proteins rearrange the cell structure, break the lining, and lead to swelling and immune cell buildup. In serious cases, this creates a physical blockage that may need surgery and must be told apart from diseases like Crohn's disease. Different types of Salmonella cause different symptoms because they adapt to certain hosts. Broad-host types such as Typhimurium usually only cause mild stomach sickness in healthy people. Host-specific types such as Typhi in humans and Dublin in cattle cause severe whole-body illness. This difference comes from their unique genes [12]. For example, Typhi has a region called viaB that makes a protective capsule, which strongly resists being eaten by immune cells. It also has many broken genes, showing it has evolved to live only in humans. This means Salmonella's effects are not the same everywhere. They are shaped by long-term evolution to fit specific hosts.

3. Therapeutic interventions and future research directions

Understanding how Salmonella infects hosts is very important for making effective treatments. Right now, doctors mainly use antibiotics to treat Salmonella infections. But more and more strains are resistant to multiple drugs, making antibiotics less dependable. One well-known example is Salmonella Typhimurium DT104, which has spread around the world and resists at least five kinds of antibiotics. In South Asia, extremely drug-resistant Typhi strains have led to long hospital stays

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and higher death rates. As resistance becomes worse, New treatments that do not push bacteria to become resistant are needed. Anti-virulence treatments have become a promising choice. Unlike antibiotics that kill bacteria directly, these treatments weaken Salmonella's ability to cause disease without strong selection pressure [13]. The T3SS systems are key targets because they are necessary for entering cells and surviving inside. In 2021, researchers tested small molecules that target a SPI-1 protein called SipC. These molecules reduced how well Salmonella enters gut cells by 68% and lowered bacterial levels in mice without hurting helpful bacteria. Other methods include blocking key proteins and stopping bacterial communication. In 2022, a lab-made antibody against the protein SifA cut Salmonella's growth inside cells by 72% and stopped it from spreading through the body. A plant-based compound found in 2020 blocks Salmonella's quorum-sensing system, lowered the activity of disease-related genes by 59%, and shortened diarrhea in pigs by 40%. Ways to protect and restore gut bacteria have also drawn attention. A healthy gut community is the body's first defense against Salmonella. Studies on probiotics and combined pre- and probiotics are widespread. A 2022 study with 320 children found that a combination of Lactobacillus rhamnosus GG and fructooligosaccharides shortened diarrhea by 2.3 days and reduced Salmonella in stool by 35%. High-fiber foods that increase short-chain fatty acids also help. A mouse study showed food rich in inulin raised butyrate levels by 60%, strengthened the gut lining, and reduced invasion by 52%. Vaccine work has improved for typhoid Salmonella. Newer conjugate vaccines such as the Typhi Vi-conjugate vaccine work much better than older polysaccharide shots [14]. A 2023 trial in India showed the Vi-conjugate vaccine was 90% effective, while older vaccines were only 50–70% effective. However, making a broad vaccine for non-typhoidal Salmonella remains hard, since these strains cause over 95% of Salmonella stomach infections. In 2022, researchers found a stable protein called PagN that exists in more than 90% of non-typhoidal strains. Using it as an antigen reduced bacterial growth in mice by 65% across several types. In the future, research should focus on connecting lab findings to real clinical use. Better models are needed, such as human intestinal organoids that copy real human gut conditions more closely. Long-term infection and antibiotic tolerance are also key topics because they cause repeated illness and spread. Salmonella makes thin layers called biofilms on gallbladder cells that are about 1,000 times more resistant to antibiotics than free-floating bacteria. Combined multi-omics studies have found important metabolic pathways that help Salmonella stay for a long time. For example, the pathway that makes arginine is more active in long-term carriers. Blocking this pathway cut biofilm formation by 78% in lab tests [15].

4. Conclusion

This review brings together the complex, precise interactions between Salmonella and the host intestine. It centers on how Salmonella adapts its infection cycle and affects gut balance in many ways. From early stages where it uses inflammation to push aside helpful bacteria and enter cells using SPI-1, to later stages where it uses SPI-2 and metabolism changes to live inside cells quietly, this review combines the molecular ways Salmonella controls its ability to cause disease and harm the host. It also covers long-term problems including weakened immunity, imbalanced gut bacteria, and different effects from different Salmonella types. The review also summarizes recent progress in treatments, including anti-virulence methods, gut bacteria support, and vaccines. It makes clear the key molecules and control systems in how Salmonella and the host affect each other. Many questions remain, especially about how Salmonella causes long-term gut damage and how disease factors, immunity, and gut bacteria work together. Future research should work harder to connect basic discoveries with real clinical use. More studies should look at long-term infection and problems that appear after the main illness is gone. Using multi-omics tools will help find new

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treatment targets and support better ways to prevent and treat Salmonella infections, improving public health around the world.

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