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A Brief Overview of *Escherichia coli* O157:H7 and Its Plasmid O157

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Abstract

Enterohemorrhagic *Escherichia coli* O157:H7 is a major foodborne pathogen causing severe disease in humans worldwide. Healthy cattle are a reservoir of *E. coli* O157:H7, and bovine food products and fresh produce contaminated with bovine waste are the most common sources for disease outbreaks in the United States. *E. coli* O157:H7 also survives well in the environment. The abilities to cause human disease, colonize the bovine gastrointestinal tract, and survive in the environment require that *E. coli* O157:H7 adapt to a wide variety of conditions. Three major virulence factors of *E. coli* O157:H7 have been identified including Shiga toxins, products of the pathogenicity island called the locus of enterocyte effacement, and products of the F-like plasmid pO157. Among these virulence factors, the role of pO157 is least understood. This review provides a board overview of *E. coli* O157:H7 with an emphasis on pO157.

Keywords

E. coli O157:H7; pO157

Escherichia coli O157:H7

Escherichia coli

Escherichia coli (*E. coli*) is a Gram-negative, rod-shaped, facultative anaerobic bacterium. This microorganism was first described by Theodor Escherich in 1885. Most *E. coli* strains harmlessly colonize the gastrointestinal tract of humans and animals as a normal flora. However, there are some strains that have evolved into pathogenic *E. coli* by acquiring virulence factors through plasmids, transposons, bacteriophages, and/or pathogenicity islands. These pathogenic *E. coli* can be categorized based on serogroups, pathogenicity mechanisms, clinical symptoms, or virulence factors [33, 47]. Among them, enterohemorrhagic *E. coli* (EHEC) is defined as pathogenic *E. coli* strains that produce Shiga toxins (Stxs) and cause hemorrhagic colitis (HC) and the life-threatening sequelae hemolytic uremic syndrome (HUS) in humans. Several serotypes in EHEC are frequently associated with human diseases such as O26:H11, O91:H21, O111:H8, O157:NM, and O157:H7 [44, 51]. *E. coli* O157:H7 is the most frequently isolated serotype of EHEC from ill persons in the United States, Japan, and the United Kingdom and it the focus of this review.

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History

EHEC serotype O157:H7 was first recognized in 1982 as a human pathogen associated with outbreaks of bloody diarrhea in Oregon and Michigan, U.S.A. [57, 71] and is also linked to sporadic cases of HUS in 1983 [34]. Since then, many outbreaks associated with EHEC have been reported in the United States and *E. coli* O157:H7 has become one of the most important foodborne pathogens.

Prevalence and Economic Cost

The Centers for Disease Control and Prevention (CDC) has estimated that *E. coli* O157:H7 infections cause 73,000 illnesses, 2,200 hospitalizations, and 60 deaths annually in the United States [43]. The outbreak surveillance data from CDC reported that *E. coli* O157:H7 infections are decreasing after the peak in 1999. However, large outbreaks and sporadic cases continue to occur. The annual cost of illness due to *E. coli* O157:H7 infections was 405 million dollars, including lost productivity, medical care, and premature deaths [21]. The high cost of illness requires additional efforts to control this pathogen.

Isolation and Identification

E. coli O157:H7 expresses somatic (O) antigen 157 and flagella (H) antigen 7. *E. coli* O157:H7 has unique features of delayed D-sorbitol fermentation (>24 h) and inability of producing β-glucuronidase, which can hydrolyze a synthetic molecule, 4-methyl-umbelliferyl-D-glucuronide (MUG) [68]. Thus, Sorbitol MacConkey (SMAC) agar supplemented with MUG has been used for detection of *E. coli* O157:H7. To increase the selectivity for *E. coli* O157:H7, cefixime, potassium tellurite, and vancomycin have been added to SMAC agar plates to inhibit other Gram-negative flora. The serotypes O157 and H7 can be further confirmed by a commercially available latex agglutination assay.

Genomic Organization

The chromosomal size of *E. coli* O157:H7 is 5.5 Mb. This genome includes a 4. 1 Mb backbone sequence conserved in all *E. coli* strains. The remaining are specific to *E. coli* O157:H7 [53]. Additionally, genome comparison of *E. coli* O157:H7 with nonpathogenic *E. coli* K12 shows that 0.53 Mb of DNA is missing for *E. coli* O157:H7, suggesting genomic reduction has also played a role in *E. coli* O157:H7 evolution [17, 53]. The majority of *E. coli* O157:H7-specific DNA sequences (1.4 Mb) are horizontally transferred foreign DNAs such as prophage and prophage-like elements. *E. coli* O157:H7 contains 463 phage-associated genes compared with only 29 in *E. coli* K-12 [72]. A change in G+C contents is one of the indications that a genomic region has been acquired by horizontal transfer, and Putonti *et al.* [55] estimated that at least 53 different species have contributed to these unique sequences in *E. coli* O157:H7. Virulence-associated genes between two sequenced *E. coli* O157:H7 strains are nearly identical (99%). Clearly, both the acquisition and loss of DNA have played an important role in the evolution of pathogenesis of *E. coli* O157:H7.

Evolution

Several comparative and epidemiological studies indicate that *E. coli* O157:H7 may have descended from the non-toxigenic and less virulent strain *E. coli* O55:H7 [72]. *E. coli* O15:H7 has emerged through four sequential events; (i) acquisition of an stx2-containing bacteriophage, (ii) acquisition of pO157 and the *rfb* region, (iii) acquisition of the stx1-containing bacteriophage, and (iv) loss of the ability to ferment D-sorbitol and loss of beta-glucuronidase (GUD) activity.

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Animal Reservoir

Cattle are the major reservoir of *E. coli* O157:H7 and this reservoir host is generally asymptomatic when carrying this microorganism. There are rare cases of diarrheal disease in young calves with this serotype. The proportion of cattle shedding at any one time varies. Sheep, goats, pigs, and turkeys have also been found to shed *E. coli* O157:H7 in their feces.

Molecular Subtyping

A variety of molecular subtyping methods have been developed to improve the understanding of the epidemiology of *E. coli* O157:H7 outbreaks. These methods include pulse-field gel electrophoresis (PFGE), restriction fragment length polymorphisms (RFLP), amplified fragment-length polymorphisms (AFLP), and phage typing [65, 73]. Among them, the PFGE method was standardized by CDC and has been applied successfully to discriminate outbreak-associated, sporadic, or unrelated infections since 1993 [3].

Infection

E. coli O157:H7 infection is a major public health concern in North America, Europe, and other areas of the world. Although the total case numbers of *E. coli* O157:H7 infections are lower than those of other enteric pathogens such as *Salmonella* or *Campylobacter* spp., the diseases caused by *E. coli* O157:H7 showed much higher hospitalization and fatality rates [43]. Human infection caused by *E. coli* O157:H7 can present a broad clinical spectrum ranging from asymptomatic cases to death. Most cases initiate with non-bloody diarrhea and self-resolve without further complication. However, some patients progress to bloody diarrhea or HC in 1–3 days. In 5–10% of HC patients, the disease can progress to the life-threatening sequelae, HUS or thrombocytopenic purpura (TTP) [1]. *E. coli* O157:H7 is the most common cause of HUS in the United States. Children and the elderly are at increased risk of severe clinical symptoms such as HUS.

Several strategies for therapy have been studied including the use of antibiotics and vaccination. However, there is no specific treatment for *E. coli* O157:H7 infection and the use of antibiotics may be contraindicated. Therefore, treatment is mainly supportive to limit the duration of symptoms and prevent systemic complications. Given this status, highly effective measures for prevention and control of *E. coli* O157:H7 infections are essential.

Transmission

In the United States, the most frequent route of transmission for *E. coli* O157:H7 infections is *via* consumption of contaminated food and water [56]. However, it can also be spread directly from person to person, particularly in child day-care facilities, and from animal to person. Infections have been documented from people visiting petting zoos, dairy farms, or camp grounds where cattle have previously grazed [28, 31]. Recently, potential airborne transmission has been reported in a contaminated building having an animal exhibit [70]. Of the 350 outbreaks reported to the CDC from 1982 to 2002, the determined transmission routes were foodborne (52%), unknown (21%), person-to-person (14%), waterborne (9%), and animal contact (3%) [56]. The model of transmission of *E. coli* O157:H7, which is updated from the diagram by Gansheroff and O'Brien [23] is shown in Fig. 1. These various transmission routes can be explained by the very low infectious dose (~50 CFU) of *E. coli* O157:H7.

Cattle are the natural reservoir of *E. coli* O157:H7. Between 1% and 50% of healthy cattle carry and shed *E. coli* O157:H7 in their feces at any given time [13, 18, 27]. Contaminated ground beef is the most common vehicle for *E. coli* O157:H7 outbreaks. Beef products may become contaminated during slaughter, and the process of grinding beef may transfer

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pathogens from the surface of the meat to the interior. Therefore, if ground beef is incompletely cooked, the bacteria can survive. In addition, there are a variety of contaminated food vehicles other than ground beef that have been linked to *E. coli* O157:H7 incidences, including unpasteurized milk, drinking water, salami, beef jerky, and fresh produce such as lettuce, radish sprouts, fresh spinach, and apple cider. The largest outbreak was traced to radish sprout contamination (1996) in Osaka, Japan, where 7,966 individuals were diagnosed with confirmed infections [45]. Epidemiological studies indicate that these food products seem to have been contaminated through bovine fecal materials. Therefore, prevention of *E. coli* O157:H7 in cattle can be one of the most important control methods. To control *E. coli* O157:H7 on the farm, the improvement of cattle management practices, the identification of inhibitory feeds, immunization, the utilization of feeding additives, and the use of probiotic cultures have been proposed.

Acid Resistance of *E. coli* O157:H7

Acid resistance (AR) is the ability of bacteria to protect themselves from extremely low pH (<pH 3.0). The low pH in the stomach (pH 1.5 to 3.0) is one of the first host defenses against foodborne enteric pathogens [54]. The ability to survive in the acidic environment of the stomach increases the chance of bacteria to colonize the intestines and cause infection. Acid resistance is associated with a lowering of the infectious dose of enteric pathogens [60]. The low infectious dose is one of the best known characteristics of *E. coli* O157:H7, making this bacterium highly infectious.

A variety of studies have reported the AR of *E. coli* O157:H7 strains [5, 12]. These studies have determined three efficient AR systems. The first AR system requires the alternative sigma factor RpoS and glucose repression. The *rpoS* mutant of *E. coli* O157:H7 was shed in lower numbers in experimentally infected mice and calves. The second AR system requires the addition of arginine during exposure of acidic condition. The arginine decarboxylase (*adiA*) and the regulator of *adiA* (*cysB*) were reported in this second AR system. The third AR system requires glutamate for protection at low pH condition. Essential components of this AR system include two isozymes of glutamate decarboxylase (*gadA* or *gadB)*, and a putative glutamate, γ-amino butyric acid antiporter (*gadC*). Whereas only one of the two glutamate decarboxylases is neededfor protection at pH 2.5, bothglutamate decarboxylase isozymes are required at pH 2.0. Previous results revealed that glutamate-dependent AR is the most effective protection at pH 2.0 in complex medium. *E. coli* O157:H7 possesses three overlapping AR systems, but the control and requirements for AR activity are different in each AR system.

Other than these three AR systems, several proteins involved in AR of *E. coli* O157:H7 have been identified. These proteins include chaperone HdeA, RNA polymerase-associated protein SspA, and DNA-binding protein Dps. Moreover, it was shown that alterations in the cell wall membrane or colonic acid production are associated with successful AR. Thus, *E. coli* O157:H7 utilizes different AR systems based on the type of acidic environment naturally encountered.

Colonization of Cattle

E. coli O157:H7 naturally colonizes the gastrointestinal tracts of cattle, and the lymphoid follicle-dense mucosa at the terminal rectum, called the rectoanal junction (RAJ) mucosa, is known as a principal site of colonization in cattle [39, 48].

Three distinct patterns of *E. coli* O157:H7 carriage in cattle have been described previously [14, 39, 58]. First, animals can be transiently culture positive for short durations of a few days and are considered passive shedders and are likely not colonized at the RAJ mucosa.

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Second, cattle can be colonized and shed the bacteria for an average of 1 month and typically not longer than 2 months. Third, a few rare animals are colonized for a long duration and shed the bacteria from 3 to 12 months or longer. This unique situation, in which a few animals develop long-duration colonization (>2 months) with *E. coli* O157:H7, is likely due to bacterial association at the RAJ mucosa; however, it may be due to unique colonization by the bacteria at a site(s) in addition to the RAJ mucosa.

Age, diet, and immunity of individual cattle could also potentially affect bacterial colonization. Cray and Moon [14] reported that calves shed *E. coli* O157:H7 longer than adult cattle given the same level of *E. coli* O157:H7 inoculums.

Reducing the level of carriage of *E. coli* O157:H7 in cattle, as a major source of *E. coli* O157:H7 infection, would play a key role in decreasing the risk of human infection. The understanding of colonization factors of *E. coli* O157:H7 will be necessary to develop effective strategies for reducing or preventing bovine carriage of *E. coli* O157:H7.

Environmental Survival

E. coli O157:H7 can survive and persist in numerous environments such as soil, water, and food as well as in animal reservoirs (Fig. 2). *E. coli* O157:H7 has been shown to survive for a year in manure-treated soil and for 21 months in raw manure that had not been composted [30]. Composting manure is effective in destroying *E. coli* O157:H7, if the temperature is maintained above 50°C for 6 days. *E. coli* O157:H7 can survive for a long time in water, especially at cold temperatures. Water trough sediments contaminated with bovine feces can serve as a long-term (>8 months) reservoir of *E. coli* O157:H7, and the surviving bacteria in contaminated troughs is a source of infection [38]. Barker *et al.* [2] showed that *E. coli* O157:H7 survives and replicates in *Acanthamoeba polyphaga. A. polyphaga* is a common environmental protozoan that is widely distributed in soil, water, and fecal slurry. Thus, it can be an efficient transmission vehicle of *E. coli* O157:H7 in these environments.

To survive in varied environments, *E. coli* O157:H7 requires the ability to adapt to variations or extreme changes in temperature, pH, and osmolarity conditions commonly encountered in nature. For example, the exopolysaccharide (EPS) production of *E. coli* O157:H7 is associated with heat and acid tolerance, and the alteration of lipid composition in membranes is induced by heat stress [77].

These environmental adaptations of *E. coli* O157:H7 play an important role in the persistence and dissemination of this microorganism on farms and the increasing transfer from cattle to cattle. In addition, the ability to survive outside the host reservoir increases the risk that the pathogen may contaminate crops and produce *via* bovine manure contamination, irrigation with contaminated water, or direct contact with infected animals [42].

Major Virulence Factors

Defining the virulence factors and mechanisms of *E. coli* O157:H7 pathogenesis has been a focus of numerous studies (Fig. 3). The production of Stxs is considered essential but not solely responsible for disease. In addition, *E. coli* O157:H7 associated with severe human disease must colonize the intestinal mucosa-and the possessing of pO157 also correlates with the ability to cause disease. Each of these aspects is described below.

Shiga Toxins (Stxs)

Stx is a potent cytotoxin and is bacteriophage-encoded. Stx is expanded from a single transcriptional unit and causes damage to a variety of cell types [29]. Stxs can be divided

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into two groups called Stx1 and Stx2 but do not generate cross-reactive antibodies that are 56% homologous in amino acid sequences. Stx1 is identical to Stx from *Shigella dysenteriae* I, but for a single amino acid difference. Virulent isolates of *E. coli* O157:H7 can express Stx1 only, Stx2 only, or both toxins. Stx2 is known to be more toxic and is more often associated with HC or HUS in human infections than are Stx1 strains [6, 50].

Stx has a conserved structure consisting of one enzymatically active A subunit (A1) and five identical receptor-binding B subunits (B5). The B5 subunit binds to the specific host receptors globotriaosylceramide (Gb3) or globotetraosylceramide (Gb4) [47]. After binding of Stx (A1B5) to the host cell, the A subunit is internalized to the cytoplasm. Al inhibits protein synthesis by the specific removal of a single adenine residue from the 28S rRNA of the 60S ribosomal subunit [59]. The detailed mechanisms of Stx translocation to various tissues are not fully understood.

The Locus of Enterocyte Effacement

E. coli O157:H7 colonizes the intestinal mucosa and induces a characteristic histopathological lesion referred to as attaching and effacing (A/E) lesions. The A/E lesion is characterized by effacement of microvilli and bacterial adherence to the epithelial cell membrane. Attached bacteria stimulate host cell actin polymerization accumulation, resulting in a raised attachment pedestal [11]. Genetic studies have shown that the genes responsible for A/E lesions map to a 13 region, which has been designated the locus of enterocyte effacement (LEE). The LEE of *E. coli* O157:H7 is conserved in EPEC as well, and it is well known that the presence of the LEE is strongly associated with disease [24]. The LEE of *E. coli* O157:H7 is 43 kb in size and contains an additional 7.5 kb prophage sequence compared with EPEC strains. The role of this additional sequence is not clearly defined. The LEE is composed of at least 41 different genes organized into three major regions; (i) a type III secretion system (TTSS) that exports effecter molecules; (ii) an adhesion called intimin and its translocated receptor, Tir, which is translocated into the host cell membrane by the TTSS; and (iii) several secreted proteins (Esp) as a part of TTSS, which are important in modification of host cell signal transduction during the formation of A/E lesions [15, 52]. Recently, non-LEE encoded effectors have also been identified, and the elucidation of their roles will further increase the understanding of the pathological phenomena in *E. coli* O157:H7 infections [16].

Plasmid O157 (pO157)

In addition to Stxs and the LEE, which both are chromosomally encoded, all clinical isolates of *E. coli* O157:H7 possess a putative virulence plasmid called pO157.

Plasmid O157 (pO157)

Plasmids

A plasmid is an extrachromosomal DNA that is capable of replicating independently of the chromosomal DNA. Plasmids are mobile elements that provide various host beneficial traits, such as resistance to antibiotics and heavy metals, production of toxins and other virulence factors, biotransformations of hydrocarbons, and symbiotic nitrogen fixation [22]. Plasmid-encoded genes are required for full pathogenesis in many enteropathogenic bacteria including *Shigella*, *Yersinia*, *Salmonella*, and *E. coli* species.

pO157

E. coli O157:H7 contains a highly conserved plasmid, named pO157. The pO157 is a nonconjugative F-like plasmid with a range size from 92 to 104 kb. The complete sequence of pO157 in two different outbreak isolates has been published [10, 41]. The pO157 shows a

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dynamic structure and includes different mobile genetic elements such as transposons, prophages, insertion sequences (IS), and parts of other plasmids. The heterogeneous composition of pO157 can delimit the co-responses to functional regions of pO157. Among them, IS or remnants of IS are frequently associated with the virulence-related segments, which are similar to compositions of the large virulence plasmid in *Shigella* spp. [10, 41]. These results indicate that the actual pO157 is formed by integration of fragments from evolutionally different species origins into an F-like plasmid, and thus virulence factors or putative virulence factors on the different segments of pO157 may be from different origins. The complete sequence of pO157 reveals 100 open reading frames (ORFs) [10]. Among them, 43 ORFs showed sufficient similarities to known proteins, suggesting functions, and 22 ORFs had no convincing similarity with any known proteins. Thirty-five proteins are presumably involved in the pathogenesis of *E. coli* O157:H7 infections, but of which only 19 genes have been previously characterized including a hemolysin (*ehxA*) [63], a catalase-peroxidase (*katP*) [9], a type II secretion system apparatus (*etp*) [62], a serine protease (*espP*) [8], a putative adhesin (*toxB*) [67], a zinc metalloprotease (s*tcE*) [37] and an *eae* conserved fragment (*ecf*) [75]. However, the biological significance of pO157 in pathogenesis is not fully understood.

Hemolysin (*ehx*)

Hemolysin was the first described virulence factor of pO157 [4, 61]. The hemolysin operon (*ehxCABD*) may be foreign in origin because it has a different G+C% and codon usage than the surrounding genetic contents. A 3.4-kb fragment encodes genes required for hemolysin synthesis and transport, and this region has been used as a diagnostic probe for *E. coli* O157:H7 and often EHEC isolates. Several studies showed that hemolysin is highly conserved among different serotypes of EHEC such as O157:H7, O111:H8, and O8:H19, but it is not known if these have identical biological activities [7].

Catalase-Peroxidase (*katP*)

A gene for a catalase-peroxidase activity (*katP*) was identified from pO157 [9]. This gene is 2.2 kb in size and is highly homologous to the bacterial bifunctional catalase-peroxidase. The KatP enzyme activity of *E. coli* O157:H7 was shown in both cytoplasm and periplasm fractions. The N-terminal signal sequence suggests that this enzyme is transported through the cytoplasmic membrane. The *katP* gene was found in all *E. coli* O157:H7 strains but is not found in EPEC, ETEC, EIEC, and EAggEC strains. This enzyme may help *E. coli* O157:H7 colonize host intestines by reducing oxidative stress and using the by-product oxygen in diminished or deprived oxygen conditions of the host intestine.

Type II Secretion System (T2SS) (*etp*)

The pO157 encodes 13 ORFs named *etpC* to *etpO*, which show high similarities to T2SS of Gram-negative bacteria [62]. These genes are located adjacent to the hemolysin locus. An IS911-like insertion element was found to be located far from the *etp* and *ehx* genes. Similar to the *katP* gene, *etp* genes were also found in all *E. coli* O157:H7 strains, some in non-O157 EHEC strains, and not found in EPEC, ETEC, EIEC, and EAggEC strains. This T2SS is similar to the pullulanase secretion pathway (*pulO*) of *Klebsiella oxytoca*, but its function has not been identified.

Serine Protease (*espP*)

EspP is the pO157-encoded type V secreted serine protease and is known to cleave pepsin A and human coagulation factor V [8]. This extracellular enzyme is similar to several secreted or surface-bound proteins, including PssA in EHEC O26:H-, EspC in EPEC, and IgA1 protease in *Neisseria* species [69]. Recently, Dziva *et al.* [19] reported that EspP influences

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the intestinal colonization of calves and adherence to bovine primary intestinal epithelial cells. Moreover, degradation of human coagulation factor V *via* EspP could contribute to the mucosal hemorrhage observed in HC patients.

Metalloprotease (*stcE*)

A metalloprotease, StcE, is encoded on pO157 and specifically cleaves the C1 esterase inhibitor [37]. The C1 esterase inhibitor is a host regulator of multiple proteolytic cascades related to inflammation pathways, such as the classical complement, intrinsic coagulation, and contact activation. StcE is secreted through T2SS encoded on pO157 and is regulated by the LEE-encoded regulator (*ler*) [20, 37]. Grys *et al.* [25] demonstrated that StcE can contribute to intimate adherence of *E. coli* O157:H7 to Hep2 cells *in vitro*. The *stcE* gene was found all in *E. coli* O157:H7, some in EPEC serotype O55:H7, and it is not found in other diarrheagenic *E. coli*.

Putative Adhesion (*toxB*)

The *toxB* gene is encoded on a sequence 9.5 kb in size, and its predicted product shows 20% similarity with toxin B of *Clostridium difficile* [41]. Recent studies showed that ToxB contributes to the adherence of *E. coli* O157:H7 to Caco-2 cells through the increased secretion of TTSS [67]. Moreover, a sequence comparison revealed that ToxB shares 28% of amino acids identity and 47% of similarity to the predicted product of *efa-1*/*lifA*, another virulence gene frequently found on the chromosome of EPEC and non-O157 EHEC isolates [46]. The presence of the *efa-1*/ *lifA* gene is known to inhibit the activation of human and murine gastrointestinal lymphocytes, and therefore ToxB might be involved in inhibiting host lymphocytes [36]. However, a mutation of the *toxB* and *efa-1* genes did not influence intestinal colonization in calves or sheep [66].

Eae Gene-Positive Conserved Fragments (*ecf*)

Recently, we reported that pO157 encoded the *ecf* operon (*ecf1–4*) that is temperature regulated by an intrinsically curved DNA [76]. *ecf1* and *ecf2* encode a putative polysaccharide deacetylase and an LPS α-1, 7-*N*-acetylglucosamine transferase, respectively, and both are unique to pO157 [32]. *ecf3* shows similarity to the putative outermembrane protein in *E. coli* K1, associated with bacterial invasion [49]. *ecf4*, also named *msbB2*, encodes the second copy of a lipid A myristoyl transferase [35, 76]. The double mutant carrying deletions in the *ecf4* and its chromosomal copy *lpxM* of *E. coli* O157:H7 had an altered lipid A structure and membrane fatty acid composition, and showed decreased persistence in bovine gastrointestinal tracts [76]. However, a single mutant of *ecf4* did not show significant difference compared with wild-type *E. coli* O157:H7.

Pathogenesis of pO157

After the first report that pO157 was required for the expression of fimbriae and adhesion to epithelial cells, several studies reported conflicting results on the role of pO157 in adherence to epithelial cells (Table 1) [74]. *In vivo* studies of pO157, using animal models including the mouse, rabbit, and gnobiotic piglet, also showed conflicting results. However, the *in vivo* studies have limitations because there is no suitable animal model reproducing all aspects of the disease. Therefore, the precise role of pO157 in the pathogenesis of *E. coli* O157:H7 still needs to be defined.

Recently, we showed that the pO157 affects the efficiency of *E. coli* O157:H7 colonization of healthy cattle and survival in acidic conditions [40, 64]. An isogenic ΔpO157 *E. coli* O157:H7 mutant is more resistant to acidic synthetic bovine gastric fluid and bile than wild type [40]. This enhanced acid resistance in the ΔpO157 mutant is due to increased glutamate

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decarboxylase (GAD) expression. The mechanism of *gad* regulation by the pO157 is not known, but is likely due to pO157 regulation of chromosomal genes. *In vivo*, the ΔpO157 mutant survives passage through the bovine gastrointestinal tracts better than wild type, but does not colonize the bovine RAJ mucosa well as wild type [40, 64].

pO157-Like Plasmids in EHEC

Large plasmids resembling pO157 are found in most non-O157 EHEC isolates, but not all isolates from humans, and the size is varied from 70 to 200 kb [26]. These plasmids usually carry the hemolysin operon (*ehx*), but the *etpC-O*, *katP*, and *espP* genes are found in less than 50% of the isolates [11]. Some of these EHEC–hemolysin plasmids are reported to be involved in adhesion, but some are not. Epidemiological evidence suggests a stronger correlation of the presence of this EHEC–hemolysin plasmid with the development of HUS rather than diarrhea. In addition to pO157 or EHEC–hemolysin plasmids, a number of other plasmids ranging in size from 2 to 87 kb have been reported in *E. coli* O157:H7 isolates. However, no correlation has been seen with possession of any of these plasmids and clinical disease.

Concluding Remarks

This review focuses on the serotype *E. coli* O157:H7 and its 92-kb plasmid. *E. coli* O157:H7 causes severe human disease worldwide. Three major virulence factors include Shiga toxins, products of the pathogenicity island called the locus of enterocyte effacement, and products of the F-like plasmid pO157. This pathogen survives well in diverse environments, from its silent reservoir in healthy cattle to the farm environment. Genes encoded on the pO157 influence bacterial adherence to eukaryotic cells, colonization of cattle, and acid resistance. Further study to understand the mechanisms of *E. coli* O157:H7 pathogenesis and persistence in the environment will lead to effective interventions to prevent human disease.

References

1. Banatvala N, Griffin PM, Greene KD, Barrett TJ, Bibb WF, Green JH, Wells JG. The United States National Prospective Hemolytic Uremic Syndrome Study: Microbiologic, serologic, clinical, and epidemiologic findings. J Infect Dis. 2001; 183:1063–1070. [PubMed: 11237831]
2. Barker J, Humphrey TJ, Brown MW. Survival of *Escherichia coli* O157 in a soil protozoan: Implications for disease. FEMS Microbiol Lett. 1999; 173:291–295. [PubMed: 10227158]
3. Barrett TJ, Lior H, Green JH, Khakhria R, Wells JG, Bell BP, Greene KD, Lewis J, Griffin PM. Laboratory investigation of a multistate food-borne outbreak of *Escherichia coli* O157:H7 by using pulsed-field gel electrophoresis and phage typing. J Clin Microbiol. 1994; 32:3013–3017. [PubMed: 7883892]
4. Bauer ME, Welch RA. Characterization of an RTX toxin from enterohemorrhagic *Escherichia coli* O157:H7. Infect Immun. 1996; 64:167–175. [PubMed: 8557336]
5. Benjamin MM, Datta AR. Acid tolerance of enterohemorrhagic *Escherichia coli*. Appl Environ Microbiol. 1995; 61:1669–1672. [PubMed: 7747983]
6. Boerlin P, McEwen SA, Boerlin-Petzold F, Wilson JB, Johnson RP, Gyles CL. Associations between virulence factors of Shiga toxin-producing *Escherichia coli* and disease in humans. J Clin Microbiol. 1999; 37:497–503. [PubMed: 9986802]
7. Brashears MM, Galyean ML, Loneragan GH, Mann JE, Killinger-Mann K. Prevalence of *Escherichia coli* O157:H7 and performance by beef feedlot cattle given *Lactobacillus* direct-fed microbials. J Food Prot. 2003; 66:748–754. [PubMed: 12747680]
8. Brunder W, Schmidt H, Karch H. EspP, a novel extracellular serine protease of enterohaemorrhagic *Escherichia coli* O157:H7 cleaves human coagulation factor V. Mol Microbiol. 1997; 24:767–778. [PubMed: 9194704]

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9. Brunder W, Schmidt H, Karch H. KatP, a novel catalase-peroxidase encoded by the large plasmid of enterohaemorrhagic *Escherichia coli* 0157:H7. Microbiology. 1996; 142:3305–3315. [PubMed: 8969527]
10. Burland V, Shao Y, Perna NT, Plunkett G, Sofia HJ, Blattner FR. The complete DNA sequence and analysis of the large virulence plasmid of *Escherichia coli* O157:H7. Nucl Acids Res. 1998; 26:4196–4204. [PubMed: 9722640]
11. Caprioli A, Morabito S, Brugère H, Oswald E. Enterohaemorrhagic *Escherichia coli*: Emerging issues on virulence and modes of transmission. Vet Res. 2005; 36:289–311. [PubMed: 15845227]
12. Castanie-Cornet MP, Penfound TA, Smith D, Elliott JF, Foster JW. Control of acid resistance in *Escherichia coli*. J Bacteriol. 1999; 181:3525–3535. [PubMed: 10348866]
13. Cho S, Bender JB, Diez-Gonzalez F, Fossler CP, Hedberg CW, Kaneene JB, Ruegg PL, Warnick LD, Wells SJ. Prevalence and characterization of *Escherichia coli* O157 isolates from Minnesota dairy farms and county fairs. J Food Prot. 2006; 69:252–259. [PubMed: 16496562]
14. Cray WC Jr, Moon HW. Experimental infection of calves and adult cattle with *Escherichia coli* O157:H7. Appl Environ Microbiol. 1995; 61:1586–1590. [PubMed: 7747972]
15. Delahay RM, Frankel G, Knutton S. Intimate interactions of enteropathogenic *Escherichia coli* at the host cell surface. Curr Opin Infect Dis. 2001; 14:559–565. [PubMed: 11964876]
16. Deng W, Puente JL, Gruenheid S, Li Y, Vallance BA, Vázquez A, et al. Dissecting virulence: Systematic and functional analyses of a pathogenicity island. Proc Natl Acad Sci USA. 2004; 101:3597–3602. [PubMed: 14988506]
17. Dobrindt U, Agerer F, Michaelis K, Janka A, Buchrieser C, Samuelson M, et al. Analysis of genome plasticity in pathogenic and commensal *Escherichia coli* isolates by use of DNA arrays. J Bacteriol. 2003; 185:1831–1840. [PubMed: 12618447]
18. Dunn JR, Keen JE, Thompson RA. Prevalence of Shiga-toxigenic *Escherichia coli* O157:H7 in adult dairy cattle. J Am Vet Med Assoc. 2004; 224:1151–1158. [PubMed: 15074864]
19. Dziva F, Mahajan A, Cameron P, Currie C, McKendrick IJ, Wallis TS, Smith DGE, Stevens MP. EspP, a type V-secreted serine protease of enterohaemorrhagic *Escherichia coli* O157:H7, influences intestinal colonization of calves and adherence to bovine primary intestinal epithelial cells. FEMS Microbiol Lett. 2007; 271:258–264. [PubMed: 17451446]
20. Elliott SJ, Sperandio V, Giron JA, Shin S, Mellies JL, Wainwright L, Hutcheson SW, McDaniel TK, Kaper JB. The locus of enterocyte effacement (LEE)-encoded regulator controls expression of both LEE- and non-LEE-encoded virulence factors in enteropathogenic and enterohemorrhagic *Escherichia coli*. Infect Immun. 2000; 68:6115–6126. [PubMed: 11035714]
21. Frenzen PD, Drake A, Angulo FJ. Economic cost of illness due to *Escherichia coli* O157 infections in the United States. J Food Prot. 2005; 68:2623–2630. [PubMed: 16355834]
22. Frost LS, Leplae R, Summers AO, Toussaint A. Mobile genetic elements: The agents of open source evolution. Nat Rev Microbiol. 2005; 3:722–732. [PubMed: 16138100]
23. Gansheroff LJ, O'Brien AD. *Escherichia coli* O157:H7 in beef cattle presented for slaughter in the US: Higher prevalence rates than previously estimated. Proc Natl Acad Sci USA. 2000; 97:2959–2961. [PubMed: 10737775]
24. Griffin PM, Tauxe RV. The epidemiology of infections caused by *Escherichia coli* O157:H7, other enterohemorrhagic *E. coli*, and the associated hemolytic uremic syndrome. Epidemiol Rev. 1991; 13:60–98. [PubMed: 1765120]
25. Grys TE, Siegel MB, Lathem WW, Welch RA. The StcE protease contributes to intimate adherence of enterohemorrhagic *Escherichia coli* O157:H7 to host cells. Infect Immun. 2005; 73:1295–1303. [PubMed: 15731026]
26. Hales BA, Hart CA, Batt RM, Saunders JR. The large plasmids found in enterohemorrhagic and enteropathogenic *Escherichia coli* constitute a related series of transfer-defective Inc F-IIA replicons. Plasmid. 1992; 28:183–193. [PubMed: 1461937]
27. Hancock DD, Besser TE, Rice DH, Herriott DE, Tarr PI. A longitudinal study of *Escherichia coli* O157 in fourteen cattle herds. Epidemiol Infect. 1997; 118:193–195. [PubMed: 9129597]
28. Heuvelink AE, van Heerwaarden C, Zwartkruis-Nahuis JT, van Oosterom R, Edink K, van Duynhoven YT, de Boer E. *Escherichia coli* O157 infection associated with a petting zoo. Epidemiol Infect. 2002; 129:295–302. [PubMed: 12403105]

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29. Jacewicz MS, Acheson DW, Binion DG, West GA, Lincicome LL, Fiocchi C, Keusch GT. Responses of human intestinal microvascular endothelial cells to Shiga toxins 1 and 2 and pathogenesis of hemorrhagic colitis. Infect Immun. 1999; 67:1439–1444. [PubMed: 10024592]
30. Jiang X, Morgan J, Doyle MP. Fate of *Escherichia coli* O157:H7 in manure-amended soil. Appl Environ Microbiol. 2002; 68:2605–2609. [PubMed: 11976144]
31. Johnson, RP.; Wilson, JB.; Michel, P.; Rahn, K.; Renwick, SA.; Gyles, CL.; Spika, JS. Human infection with verotoxigenic *Escherichia coli* associated with exposure to farms and rural environments. In: Stewart, CS.; Flints, HJ., editors. Escherichia coli O157 in Farm Animals. CABI Publishing; Wallingford, U.K: 1999. p. 147-168.
32. Kaniuk NA, Vinogradov E, Li J, Monteiro MA, Whitfield C. Chromosomal and plasmid-encoded enzymes are required for assembly of the R 3-type core oligosaccharide in the lipopolysaccharide of *Escherichia coli* O157:H7. J Biol Chem. 2004; 279:31237–31250. [PubMed: 15155763]
33. Kaper JB, Nataro JP, Mobley HL. Pathogenic *Escherichia coli*. Nat Rev Microbiol. 2004; 2:123–140. [PubMed: 15040260]
34. Karmali MA, Steele BT, Petric M, Lim C. Sporadic cases of haemolytic–uraemic syndrome associated with faecal cytotoxin and cytotoxin-producing *Escherichia coli* in stools. Lancet. 1983; 1:619–620. [PubMed: 6131302]
35. Kim SH, Jia W, Bishop RE, Gyles C. An msbB homologue carried in plasmid pO157 encodes an acyltransferase involved in lipid A biosynthesis in *Escherichia coli* O157:H7. Infect Immun. 2004; 72:1174–1180. [PubMed: 14742570]
36. Klapproth JMA I, Scaletsky CA, McNamara BP, Lai LC, Malstrom C, James SP, Donnenberg MS. A large toxin from pathogenic *Escherichia coli* strains that inhibits lymphocyte activation. Infect Immun. 2000; 68:2148–2155. [PubMed: 10722613]
37. Lathem WW, Grys TE, Witowski SE, Torres AG, Kaper JB, Tarr PI, Welch RA. StcE, a metalloprotease secreted by *Escherichia coli* O157:H7, specifically cleaves C1 esterase inhibitor. Mol Microbiol. 2002; 45:277–288. [PubMed: 12123444]
38. LeJeune JT, Besser TE, Hancock DD. Cattle water troughs as reservoirs of *Escherichia coli* O157. Appl Environ Microbiol. 2001; 67:3053–3057. [PubMed: 11425721]
39. Lim JY, Li J, Sheng H, Besser TE, Potter K, Hovde CJ. *Escherichia coli* O157:H7 colonization at the rectoanal junction of long-duration culture-positive cattle. Appl Environ Microbiol. 2007; 73:1380–1382. [PubMed: 17189448]
40. Lim JY, Sheng H, Seo KS, Park YH, Hovde CJ. Characterization of an *Escherichia coli* O157:H7 Plasmid O157 deletion mutant and its survival and persistence in cattle. Appl Environ Microbiol. 2007; 73:2037–2047. [PubMed: 17277224]
41. Makino K, Ishii K, Yasunaga T, Hattori M, Yokoyama K, Yutsudo CH, et al. Complete nucleotide sequences of 93-kb and 3.3-kb plasmids of an enterohemorrhagic *Escherichia coli* O157:H7 derived from Sakai outbreak. DNA Res. 1998; 5:1–9. [PubMed: 9628576]
42. Maule A. Survival of verocytotoxigenic *Escherichia coli* O157 in soil, water and on surfaces. Symp Ser Soc Appl Microbiol. 2000; 29:71S–78S.
43. Mead PS, Slutsker L, Dietz V, McCaig LF, Bresee JS, Shapiro C, Griffin PM, Tauxe RV. Food-related illness and death in the United States. Emerg Infect Dis. 1999; 5:607–625. [PubMed: 10511517]
44. Melton-Celsa AR, Darnell SC, O'Brien AD. Activation of Shiga-like toxins by mouse and human intestinal mucus correlates with virulence of enterohemorrhagic *Escherichia coli* O91:H21 isolates in orally infected, streptomycin-treated mice. Infect Immun. 1996; 64:1569–1576. [PubMed: 8613362]
45. Michino H, Araki K, Minami S, Takaya S, Sakai N, Miyazaki M, Ono A, Yanagawa H. Massive outbreak of *Escherichia coli* O157:H7 infection in school children in Sakai City, Japan, associated with consumption of white radish sprouts. Am J Epidemiol. 1999; 150:787–796. [PubMed: 10522649]
46. Morabito S, Tozzoli R, Oswald E, Caprioli A. A mosaic pathogenicity island made up of the locus of enterocyte effacement and a pathogenicity island of *Escherichia coli* O157:H7 is frequently present in attaching and effacing *E. coli*. Infect Immun. 2003; 71:3343–3348. [PubMed: 12761117]

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47. Nataro JP, Kaper JB. Diarrheagenic *Escherichia coli*. Clin Microbiol Rev. 1998; 11:142–201. [PubMed: 9457432]
48. Naylor SW, Low JC, Besser TE, Mahajan A, Gunn GJ, Pearce MC, McKendrick IJ, Smith DGE, Gally DL. Lymphoid follicle-dense mucosa at the terminal rectum is the principal site of colonization of enterohemorrhagic *Escherichia coli* O157:H7 in the bovine host. Infect Immun. 2003; 71:1505–1512. [PubMed: 12595469]
49. Orndorff PE, Wang Y, Huang SH, Wass CA, Stins MF, Kim KS. The gene locus *yijP* contributes to *Escherichia coli* K1 invasion of brain microvascular endothelial cells. Infect Immun. 1999; 67:4751–4756. [PubMed: 10456927]
50. Ostroff SM, Tarr PI, Neill MA, Lewis JH, Hargrett-Bean N, Kobayashi JM. Toxin genotypes and plasmid profiles as determinants of systemic sequelae in *Escherichia coli* O157:H7 infections. J Infect Dis. 1989; 160:994–998. [PubMed: 2685131]
51. Paton AW, Paton JC. Direct detection of Shiga toxigenic *Escherichia coli* strains belonging to serogroups O111, O157, and O113 by multiplex PCR. J Clin Microbiol. 1999; 37:3362–3365. [PubMed: 10488207]
52. Perna NT, Mayhew GF, Posfai G, Elliott S, Donnenberg MS, Kaper JB, Blattner FR. Molecular evolution of a pathogenicity island from enterohemorrhagic *Escherichia coli* O157:H7. Infect Immun. 1998; 66:3810–3817. [PubMed: 9673266]
53. Perna NT, Plunkett G, Burland V, Mau B, Glasner JD, Rose DJ, et al. Genome sequence of enterohaemorrhagic *Escherichia coli* O157:H7. Nature. 2001; 409:529–533. [PubMed: 11206551]
54. Peterson WL, Mackowiak PA, Barnett CC, Marling-Cason M, Haley ML. The human gastric bactericidal barrier: Mechanisms of action, relative antibacterial activity, and dietary influences. J Infect Dis. 1989; 159:979–983. [PubMed: 2651535]
55. Putonti C, Luo Y, Katili C, Chumakov S, Fox GE, Graur D, Fofanov Y. A computational tool for the genomic identification of regions of unusual compositional properties and its utilization in the detection of horizontally transferred sequences. Mol Biol Evol. 2006; 23:1863–1868. [PubMed: 16829541]
56. Rangel JM, Sparling PH, Crowe C, Griffin PM, Swerdlow DL. Epidemiology of *Escherichia coli* O157:H7 outbreaks, United States, 1982–2002. Emerg Infect Dis. 2005; 11:603–609. [PubMed: 15829201]
57. Riley LW, Remis RS, Helgerson SD, McGee HB, Wells JG, Davis BR, et al. Hemorrhagic colitis associated with a rare *Escherichia coli* serotype. N Engl J Med. 1983; 308:681–685. [PubMed: 6338386]
58. Sanderson MW, Besser TE, Gay JM, Gay CC, Hancock DD. Fecal *Escherichia coli* O157:H7 shedding patterns of orally inoculated calves. Vet Microbiol. 1999; 69:199–205. [PubMed: 10512044]
59. Saxena SK, O'Brien AD, Ackerman EJ. Shiga toxin, Shiga-like toxin II variant, and ricin are all single-site RNA *N*-glycosidases of 28S RNA when microinjected into *Xenopus* oocytes. J Biol Chem. 1989; 264:596–601. [PubMed: 2642481]
60. Schlech WF III, Chase DP, Badley A. A model of food-borne *Listeria monocytogenes* infection in the Sprague–Dawley rat using gastric inoculation: Development and effect of gastric acidity on infective dose. Int J Food Microbiol. 1993; 18:15–24. [PubMed: 8466809]
61. Schmidt H, Beutin L, Karch H. Molecular analysis of the plasmid-encoded hemolysin of *Escherichia coli* O157:H7 strain EDL 933. Infect Immun. 1995; 63:1055–1061. [PubMed: 7868227]
62. Schmidt H, Henkel B, Karch H. A gene cluster closely related to type II secretion pathway operons of Gram-negative bacteria is located on the large plasmid of enterohemorrhagic *Escherichia coli* O157 strains. FEMS Microbiol Lett. 1997; 148:265–272. [PubMed: 9084155]
63. Schmidt H, Karch H, Beutin L. The large-sized plasmids of enterohemorrhagic *Escherichia coli* O157 strains encode hemolysins which are presumably members of the *E. coli* alpha-hemolysin family. FEMS Microbiol Lett. 1994; 117:189–196. [PubMed: 8181722]
64. Sheng H, Lim JY, Knecht HJ, Li J, Hovde CJ. Role of *Escherichia coli* O157:H7 virulence factors in colonization at the bovine terminal rectal mucosa. Infect Immun. 2006; 74:4685–4693. [PubMed: 16861656]

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65. Shima K, Yoshii N, Akiba M, Nishimura K, Nakazawa M, Yamasaki S. Comparison of PCR–RFLP and PFGE for determining the clonality of enterohemorrhagic *Escherichia coli* strains. FEMS Microbiol Lett. 2006; 257:124–131. [PubMed: 16553842]
66. Stevens MP, Roe AJ, Vlisidou I, Van Diemen PM, La Ragione RM, Best A, Woodward MJ, Gally DL, Wallis TS. Mutation of *toxB* and a truncated version of the *efa*-1 gene in *Escherichia coli* O157:H7 influences the expression and secretion of locus of enterocyte effacement-encoded proteins but not intestinal colonization in calves or sheep. Infect Immun. 2004; 72:5402–5411. [PubMed: 15322038]
67. Tatsuno I, Horie M, Abe H, Miki T, Makino K, Shinagawa H, Taguchi H, Kamiya S, Hayashi T. *toxB* gene on pO157 of enterohemorrhagic *Escherichia coli* O157:H7 is required for full epithelial cell adherence phenotype. Infect Immun. 2001; 69:6660–6669. [PubMed: 11598035]
68. Thompson JS, Hodge DS, Borczyk AA. Rapid biochemical test to identify verocytotoxin-positive strains of *Escherichia coli* serotype O157. J Clin Microbiol. 1990; 28:2165–2168. [PubMed: 2229338]
69. van Diemen PM, Dziva F, Stevens MP, Wallis TS. Identification of enterohemorrhagic *Escherichia coli* O26:H-genes required for intestinal colonization in calves. Infect Immun. 2005; 73:1735–1743. [PubMed: 15731074]
70. Varma JK, Greene KD, Reller ME, DeLong SM, Trottier J, Nowicki SF, et al. An outbreak of *Escherichia coli* O157 infection following exposure to a contaminated building. JAMA. 2003; 290:2709–2712. [PubMed: 14645313]
71. Wells JG, Davis BR, Wachsmuth IK, Riley LW, Remis RS, Sokolow R, Morris GK. Laboratory investigation of hemorrhagic colitis outbreaks associated with a rare *Escherichia coli* serotype. J Clin Microbiol. 1983; 18:512–520. [PubMed: 6355145]
72. Wick LM, Qi W, Lacher DW, Whittam TS. Evolution of genomic content in the stepwise emergence of *Escherichia coli* O157:H7. J Bacteriol. 2005; 187:1783–1791. [PubMed: 15716450]
73. Willshaw GA, Smith HR, Cheasty T, Wall PG, Rowe B. Vero cytotoxin-producing *Escherichia coli* O157 outbreaks in England and Wales, 1995: Phenotypic methods and genotypic subtyping. Emerg Infect Dis. 1997; 3:561–565. [PubMed: 9366610]
74. Yoon JW, Hovde CJ. All blood, no stool: Enterohemorrhagic *Escherichia coli* O157:H7 infection. J Vet Sci. 2008; 9:219–231. [PubMed: 18716441]
75. Yoon JW, Lim JY, Park YH, Hovde CJ. Involvement of the *Escherichia coli* O157:H7(pO157) *ecf* operon and lipid A myristoyl transferase activity in bacterial survival in the bovine gastrointestinal tract and bacterial persistence in farm water troughs. Infect Immun. 2005; 73:2367–2378. [PubMed: 15784583]
76. Yoon JW, Minnich SA, Ahn JS, Park YH, Paszczynski A, Hovde CJ. Thermoregulation of the *Escherichia coli* O157:H7 pO157 *ecf* operon and lipid A myristoyl transferase activity involves intrinsically curved DNA. Mol Microbiol. 2004; 51:419–435. [PubMed: 14756783]
77. Yuk HG, Marshall DL. Adaptation of *Escherichia coli* O157:H7 to pH alters membrane lipid composition, verotoxin secretion, and resistance to simulated gastric fluid acid. Appl Environ Microbiol. 2004; 70:3500–3505. [PubMed: 15184149]

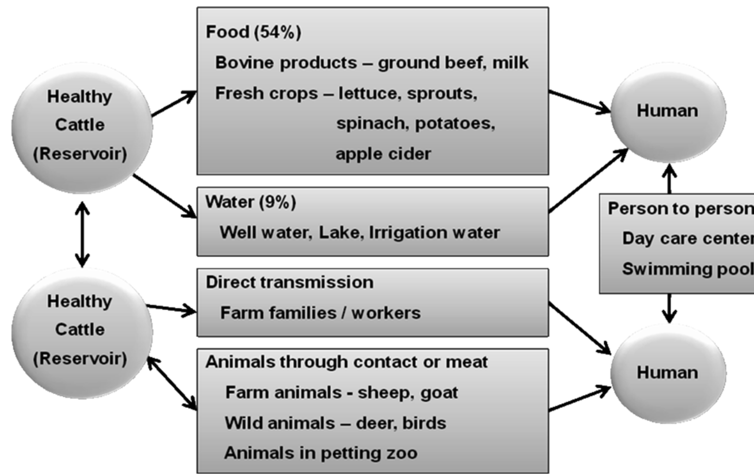

Fig. 1.

Transmission of *E. coli* O157:H7.

Healthy cattle are the major reservoirs of *E. coli* O157:H7 and carry this microorganism transiently without symptoms. Contaminated bovine products and crops are predominant sources for human infections.

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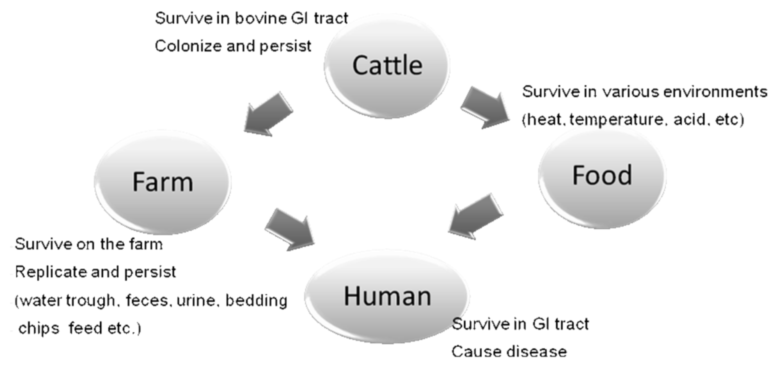

Fig. 2.

Ecological scheme of *E. coli* O157:H7.

GI tract, gastrointestinal tract.

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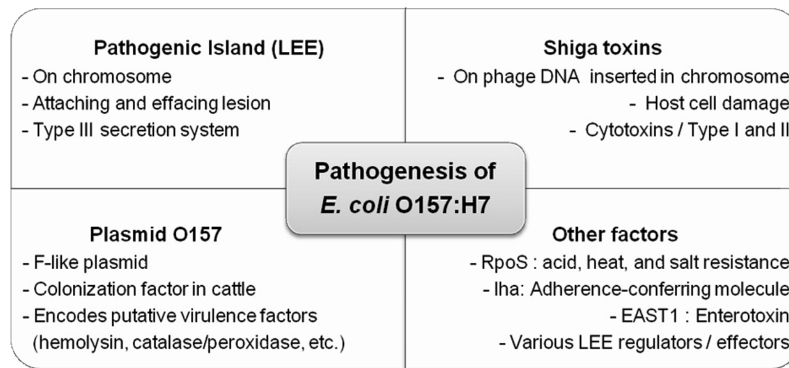

Fig. 3.
Virulence factors of *E. coli* O157:H7.

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Table 1

Summary of studies on pO157 pathogenesis *in vitro* and *in vivo*.

	Year	Target	Pathogenesis	Effect
In vitro	1987	Whole plasmid	Expression of fimbriae Adherence to epithelial cells	Yes
	1990	Whole plasmid	Adherence to epithelial cells	Yes
	1993	Whole plasmid	Production of pilli Adherence to epithelial cells	No
	2001	*toxB* gene on pO157	Adherence to epithelial cells	Yes
	2005	*stcE* gene on pO157	Adherence to epithelial cells	Yes
	2007	*espP* gene on pO157	Adherence to bovine primary intestinal epithelial cells	Yes
In vivo	1987	Whole plasmid	Attaching and effacing lesion in gnotobiotic piglets	No
	1990	Whole plasmid	Colonization of mouse	No
	1993	Whole plasmid	Clinical symptoms in rabbit	No
	2006	Whole plasmid	Colonization of cattle	Yes
	2007	Whole plasmid	Colonization of cattle	Yes
	2007	*espP* gene on pO157	Colonization of calves	Yes