# Microbe Profile

MICROBIOLOGY

**MICROBE PROFILE**

Gally and Stevens, *Microbiology* 2017;163:1–3

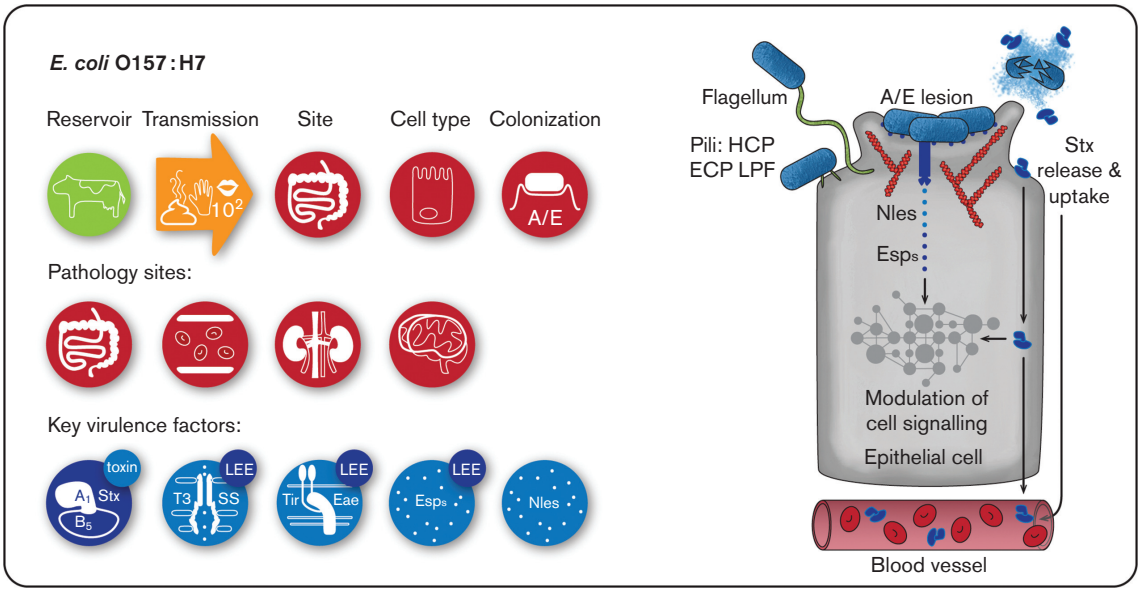
DOI 10.1099/mic.0.000387

MICROBIOLOGY SOCIETY

OPEN MICROBIOLOGY

# Microbe Profile: *Escherichia coli* O157 : H7 – notorious relative of the microbiologist's workhorse

David L. Gally* and Mark P. Stevens




**Graphical abstract**

Summary of enterohaemorrhagic *Escherichia coli* O157 pathogenesis using basic symbols. The right-hand illustration shows enterohaemorrhagic *E. coli* interactions with an epithelial cell.

**Abstract**

*Escherichia coli* O157 : H7 is a zoonotic diarrhoeal pathogen of worldwide importance. It belongs to a subset of Shiga toxin-producing *E. coli* that can form attaching and effacing lesions on intestinal epithelia via the action of a type 3 secretion system that injects bacterial effectors into enterocytes. Infections in humans often arise from contaminated food or direct environmental exposure and can involve life-threatening Shiga toxin-dependent sequelae. In the three decades since *E. coli* O157 : H7 was first recognized intensive research has helped to unravel the basis of pathogenesis, but few effective options for prevention and treatment of infections exist.

Received 25 May 2016; Accepted 28 October 2016

**Author affiliation:** The Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Midlothian EH25 9RG, UK.
***Correspondence:** David L. Gally, david.gally@roslin.ed.ac.uk

**Keywords:** *E. coli* O157; Shiga toxin; type 3 secretion; cattle; bacteriophage.

**Abbreviations:** A/E, attaching and effacing; ECP, *E. coli* common pilus; EHEC, enterohaemorrhagic *E. coli*; Esp, *E. coli* secreted protein; HCP, Haemorrhagic coli pilus; LEE, locus of enterocyte effacement; LPF, long polar fimbriae; Nle, non LEE-encoded effector; Stx, Shiga toxin; T3SS, type 3 secretion system.

## TAXONOMY

Domain *Bacteria*, phylum *Proteobacteria*, class *Gammaproteobacteria*, order *Enterobacteriales*, family *Enterobacteriaceae*, genus *Escherichia*, species *E. coli*, serotype O157 : H7.

## PROPERTIES

*E. coli* O157 : H7 is a chemoorganotrophic facultative anaerobe with both respiratory and fermentative metabolism identified by biochemical tests and selective/chromogenic media. Cells are Gram-negative straight rods about 1 µm×2–6 µm and typically motile via peritrichous flagella. The enterohaemorrhagic *E. coli* (EHEC) pathotype describes strains that can express a type 3 secretion system (T3SS) and produce Shiga toxin subtypes (Stx 1a, 2a, 2c, etc.), although the original definition also required an association with human disease [1]. Different EHEC serotypes are associated with severe human disease but O157 : H7 is the most prevalent in North and South America and the UK.

## GENOME

EDL933 was the first O157 strain to be sequenced with a 5.4 Mb chromosome encoding 1.34 Mb (1387 genes) in 177 'O-islands' which were not present in the laboratory-adapted *E. coli* K-12 strain MG1655, although the strains share 4.1 Mb of highly homologous DNA [2]. The majority of *E. coli* O157 : H7 isolates also contain a 92 kb plasmid. Lambdoid bacteriophages, integrative elements and plasmids have introduced the same or similar genes into diverse serotypes that have distinct evolutionary histories, indicating parallel evolution of EHEC by independent acquisition of mobile elements. Sequencing of *E. coli* O157 : H7 catalysed our understanding of the vast diversity that can exist in the 'accessory genome', with just 39.2 % of non-redundant proteins shared by EDL933, MG1655 and uropathogenic *E. coli* CFT703. The most recent evidence, based on analysis of over 1000 *E. coli* O157 : H7 genomes, is that the more recent acquisition of Stx2a prophages was critical to emergence of EHEC O157 : H7 as a life-threatening zoonotic pathogen in the last few decades [3]. Machine-learning approaches applied to whole-genome sequences indicate that only a minority of *E. coli* O157 : H7 isolates may have zoonotic potential with prophage variation being critical to this capacity [4].

## PHYLOGENY

Evidence supports evolution of *E. coli* O157 : H7 from a non-toxigenic EPEC O55 : H7 by acquisition of Stx2c-encoding prophage followed by the pO157 plasmid and the switch to the O157 somatic antigen via recombination. There was divergence from this $\beta$-glucuronidase-positive last common ancestor approximately 400 years ago with the common ancestor of the current diversity appearing an estimated 175 years ago. There are considered to be three main lineages of EHEC O157 : H7, viz. I, I/II and II. The common ancestor was lineage II, $\beta$-glucuronidase negative and sorbitol non-fermenting. Lineage I split from this approximately 125 years ago and lineage I/II approximately 95 years ago [3, 5].

## KEY FEATURES AND DISCOVERIES

In 1983, Karmali *et al.* noted that Stx-producing *E. coli* may be a common cause of haemorrhagic colitis preceding haemolytic uraemic syndrome [6]. Stx is produced and released following induction of the bacterial SOS response which induces activation of the integrated Stx-encoding prophage(s). As specific classes of antibiotics can induce this response, there is debate over their use to treat EHEC infections. Stxs share their catalytic mechanism with ricin with an A subunit that arrests translation by depurination of 28S rRNA as well as five B subunits involved in cell binding and trafficking. Globotriaosylceramide (Gb3/CD77) toxin receptors are present on the surface of endothelial cells throughout the human body, particularly capillaries in the kidneys and brain. For intestinal colonization, *E. coli* O157 : H7 forms 'attaching and effacing' lesions on intestinal epithelia in a manner dependent on the T3SS encoded by the locus of enterocyte effacement. Attaching and effacing lesions are characterized by intimate bacterial adherence to the apical surface of enterocytes on actin-rich 'pedestals' and destruction of proximal microvilli (Graphical abstract figure). Remarkably, intimate adherence is facilitated by injection of Tir, which serves as a receptor for the bacterial outer membrane protein intimin [7]. Prototype *E. coli* O157 : H7 strains inject around 40 'effector' proteins, expressed from the locus of enterocyte effacement and assorted prophage regions, into enterocytes to subvert cellular responses [8].

Ruminants are a key reservoir of *E. coli* O157 : H7. Colonization of cattle is generally asymptomatic, as Gb3 is not expressed on the surface of bovine endothelial cells. The bacteria primarily colonize follicle-associated epithelium of the terminal rectum and super-shedding animals are responsible for the majority of on-farm transmission and the threat of zoonosis [9]. The primary role of Stxs in reservoir hosts or the environment remains to be determined but may include killing of grazing protozoa, immune modulation and enhancement of bacterial adherence. Selection of *E. coli* O157 : H7 in the bovine host may be towards innate and adaptive immune silencing mechanisms that promote persistence and transmission, whereas these mechanisms may have different outcomes in humans as an incidental host leading to life-threatening pathology.

Control measures have focused on the ruminant reservoir, including vaccines based on secreted proteins or an extract of iron-limited *E. coli* O157 : H7, but to date these have not received sufficient uptake. Treatment in humans remains largely supportive, with Stx-specific neutralizing antibody and receptor mimics showing promise for control of systemic sequelae in animal models. A serious outbreak in 2011 caused by an Stx2-producing *E. coli* O104 : H4 hybrid with features of EHEC and enteroaggregative *E. coli* serves to highlight the dynamic evolution of Stx-producing *E. coli*

and compels us to look beyond *E. coli* O157 : H7 for future threats.

## KEY QUESTIONS

- What is the purpose of Stx in the environment and/or ruminant host? Ultimately, the selective pressure maintaining Stx also drives the evolution of EHEC strains and so this knowledge is critical.
- What factors influence the zoonotic potential of EHEC strains and disease severity? Despite the common presence of Stx-encoding *E. coli* in ruminants and the environment, why do only a small subset of strains actually cause serious human disease?
- What processes lead to the genetic convergence of multiple lambdoid prophages encoding both effector proteins and Stx in strains with a T3SS, and how likely are similar convergences with pathogenic potential?
- How do you generate an effective immune response against an organism that manipulates host responses to remain 'under the radar'?
- What level of reduction of shedding in cattle is required to reduce incidence of human disease? If only a small subset of strains cause human disease, would widely applied cattle-based interventions ever represent a cost-effective method of controlling human infections?

Funding information
The authors received strategic institute core support from the BBSRC (BB/J004227/1).

Acknowledgements
We acknowledge Dr Eliza Wolfson (http://lizawolfson.co.uk) for production of the graphical summary.

Conflicts of interest
The authors declare that there are no conflicts of interest.

References
1. Nataro JP, Kaper JB. Diarrheagenic *Escherichia coli*. *Clin Microbiol Rev* 1998;11:142–201.
2. Perna NT, Plunkett G, Burland V, Mau B, Glasner JD *et al.* Genome sequence of enterohaemorrhagic *Escherichia coli* O157 : H7. *Nature* 2001;409:529–533.
3. Dallman TJ, Allison L, Gally DL, Wain J, Ashton PM *et al.* Applying phylogenomics to understand the emergence of Shiga-toxin-producing *Escherichia coli* O157 : H7 strains causing severe human disease in the UK. *Microb Genom* 2015;1:13.
4. Lupolova N, Dallman TJ, Matthews L, Bono JL, Gally DL. Support vector machine applied to predict the zoonotic potential of *E. coli* O157 cattle isolates. *Proc Natl Acad Sci USA* 2016;113:11312–11317.
5. Feng P, Lampel KA, Karch H, Whittam TS. Genotypic and phenotypic changes in the emergence of *Escherichia coli* O157 : H7. *J Infect Dis* 1998;177:1750–1753.
6. Karmali MA, Petric M, Steele BT, Lim C. Sporadic cases of haemolytic-uraemic syndrome associated with faecal cytotoxin and cytotoxin-producing *Escherichia coli* in stools. *Lancet* 1983;321:619–620.
7. Kenny B, Devinney R, Stein M, Reinscheid DJ, Frey EA *et al.* Enteropathogenic *E. coli* (EPEC) transfers its receptor for intimate adherence into mammalian cells. *Cell* 1997;91:511–520.
8. Tobe T, Beatson SA, Taniguchi H, Abe H, Bailey CM *et al.* An extensive repertoire of type III secretion effectors in *Escherichia coli* O157 and the role of lambdoid phages in their dissemination. *Proc Natl Acad Sci USA* 2006;103:14941–14946.
9. Matthews L, Low JC, Gally DL, Pearce MC, Mellor DJ *et al.* Heterogeneous shedding of *Escherichia coli* O157 in cattle and its implications for control. *Proc Natl Acad Sci USA* 2006;103:547–552.

Edited by: T. Parish