International Journal of Infection
ISSN 1972-6945 / 2022 vol. 6, ISSUE N. 2, May-August

ESCHERICHIA COLI RECEPTORS AND PATHOGENETIC MECHANISMS

Al. Caraffa[1] and R. Pellegrino[2*]

[1] School of Pharmacy, University of Camerino, Camerino, Italy;
[2] Physiatrist and Pain Therapist, Lecce, Italy.

Correspondence to:
Dr. Raffaello Pellegrino,
Physiatrist and Pain Therapist,
Lecce-Castromediano/Cavallino,
Via S. Pelico 34,
73100 Lecce, Italy.
e-mail: drpellegrino@yahoo.it

ABSTRACT

Escherichia coli (*E. coli*) is a group of bacteria found in humans and animals. Some strains can be highly pathogenic and cause severe immune and inflammatory reactions. *E. coli* is a member of the Enterobacteriaceae family and is a Gram-negative rod-shaped bacteria that has peritrichous flagella, which allow the bacteria to move. Pathogenic *E. coli* produces various toxins such as Shiga toxin (Stx) that disrupt normal cellular functions, inhibit protein synthesis, and cause cellular. Heat-labile (LT) and heat-stable (ST) enterotoxins are produced by enterotoxigenic *E. coli* (ETEC), and can cause intestinal ion alteration and diarrhea. Pathogenic *E. coli* is capable of injecting virulence factors directly into host cells and uses some antigens to carry out its pathogenic action. *E. coli* also uses immune mechanisms, such as alteration of surface antigens, to escape the immune response. Inhibition of *E. coli* and prevention with the use of vaccines or specific antibodies improves the infectious state and human health.

KEYWORDS: *Escherichia coli, Gram-negative bacterium, pathogenetic mechanism, E. Coli receptor, virulence*

INTRODUCTION

Escherichia coli (*E. coli*) is a diverse group of bacteria commonly found in the intestines of humans and animals. While most strains are harmless, some can cause serious food poisoning, infections, and diseases. *E. coli* is a Gram-negative bacterium that frequently exists in the lower intestine of warm-blooded organisms. This rod-shaped bacterium is a member of the Enterobacteriaceae family and is one of the most extensively studied prokaryotic model organisms in microbiology.

E. coli has specific morphological characteristics. It is a rod-shaped cylindrical bacillus and typically appears as short rods. It has a dimension of about 2 to 4 micrometers (µm) in length and 0.4 to 0.7 µm in diameter (1,2). In the laboratory, this Gram-negative bacillus does not retain the crystal violet stain used in the Gram stain procedure and appears red or pink under the microscope due to counterstaining, usually with safranin or fuchsin.

E. coli is usually found as single bacterium or in pairs. *E. coli* bacteria do not form clusters or chains, which distinguishes them from other types of bacteria. Many strains of *E. coli* possess peritrichous flagella, which are flagella distributed over the entire surface of the cell that allow the bacteria to move. Some strains of *E. coli* have a polysaccharide capsule surrounding the cell, which can help evade the host immune system and increase virulence (3). As a Gram-negative bacterium, *E. coli* has a characteristic cell wall structure consisting of a thin layer of peptidoglycan surrounded

Received: 02 May, 2022
Accepted: 12 August, 2022
1972-6945 (2022)
Copyright © by Biolife-Publisher
This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder. Unauthorized reproduction may result in financial and other penalties. Disclosure: all authors report no conflicts of interest relevant to this article.

by an outer membrane containing lipopolysaccharides (LPS) (4). The outer membrane also contains proteins, lipoproteins, and porins (5). *E. coli* does not form endospores, which are a type of dormant, hardy, non-reproductive structure that some bacteria produce to withstand unfavorable conditions (6). These morphological traits aid in the identification and study of *E. coli* in various microbiological and medical research contexts.

DISCUSSION

E. coli presents various molecular mechanisms and biochemical processes essential for its survival, growth, and pathogenicity. Of the molecular mechanisms of *E. coli*, DNA replication is important, which originates from the replication of the circular chromosome, a single origin of replication called oriC (7). *E. coli* primarily uses DNA polymerase III for chromosome replication, with DNA polymerase I involved in the removal of RNA primers and DNA repair (8). Transcription occurs through RNA polymerase which transcribes DNA into mRNA. Sigma factors are proteins that bind to RNA polymerase and direct it to specific promoters.

Translation occurs through ribosomes which translate mRNA into proteins. *E. coli* has 70S ribosomes, composed of 50S and 30S subunits (9). Gene regulation in *E. coli* occurs through the lac Operon which controls lactose metabolism and includes the lacZ, lacY, and lacA genes, regulated by the lac repressor and catabolite activator protein (CAP) (10).

In metabolic processes, *E. coli* breaks down glucose through glycolysis to produce pyruvate, ATP, and NADH (11). The TCA cycle (Krebs Cycle) processes acetyl-CoA to produce ATP, NADH, and FADH2. Furthermore, *E. coli* can perform oxidative phosphorylation under aerobic conditions, using the electron transport chain to generate ATP (12). Under anaerobic conditions, *E. coli* can perform oxidative phosphorylation using the electron transport chain to generate ATP (13). Again, in anaerobic conditions, *E. coli* can ferment sugars, producing organic acids, alcohol, and gases as end products (14). *E. coli* synthesizes all 20 standard amino acids and nucleotides *de novo* (15). Furthermore, in cell wall synthesis, *E. coli* synthesizes peptidoglycan, an important component of its cell wall, which involves the assembly of N-acetylglucosamine and N-acetylmuramic acid (16).

E. coli acts through Tar and Tsr receptors, which sense chemical gradients in the environment and mediate chemotaxis, allowing bacteria to move toward attractants or away from repellents (17). The outer membrane receptors are porins such as OmpF and OmpC that form channels through which small molecules can diffuse (18). TonB-dependent receptors are FepA and FhuA receptors which are involved in the uptake of scarce resources such as iron by use of energy derived from the TonB complex (19). Regarding fimbrial adhesions, type 1 pili mediate adhesion to tissue and are important in the early stages of infection (20). The P Pili are involved in the attachment to the urinary tract epithelium, which is crucial for uropathogenic *E. coli* (UPEC) (21). Understanding these molecular mechanisms, biochemical processes, and receptor functions provides insights into how *E. coli* survives, adapts, and sometimes causes disease in host organisms.

E. Coli is broadly classified into six groups of pathogenic strains (Table I). Each pathogenic group has specific virulence factors that enable it to cause disease. These include adhesins, toxins, invasins, and secretion systems.

Table I. *The broadly classified pathogenic strains of Escherichia coli.*

• Enterotoxigenic *E. coli* (ETEC)	• Enterohemorrhagic *E. coli* (EHEC)
• Enteropathogenic *E. coli* (EPEC)	• Enteroaggregative *E. coli* (EAEC)
• Enteroinvasive *E. coli* (EIEC)	• Uropathogenic *E. coli* (UPEC)

Pathogenic *E. coli* produces various toxins, such as Shiga toxins (Stx), that disrupt normal cellular functions (22). These toxins produced by enterohemorrhagic *E. coli* (EHEC) inhibit protein synthesis, leading to cell death (23). Heat-labile (LT) and Heat-stable (ST) enterotoxins are produced by enterotoxigenic *E. coli* (ETEC), causing diarrhea by altering ion transport in the intestines (24).

Invasins are proteins that facilitate bacterial invasion of host cells. Invasion plasmid antigens (Ipa) are used by enteroinvasive *E. coli* (EIEC) to invade and multiply within intestinal cells (25). Pathogenic *E. coli* employs sophisticated secretion systems to inject virulence factors directly into host cells. The type III secretion system (T3SS) is used by enteropathogenic *E. coli* (EPEC) and EHEC to inject effector proteins into host cells, disrupting cellular processes and facilitating colonization (26).

ETEC adheres to the small intestine using colonization factor antigens (CFA) and produces enterotoxins (LT and ST) that stimulate fluid secretion, leading to diarrhea (27). The virulence factors are CFAs, LT, and ST. EPEC attaches to intestinal epithelial cells using bundle-forming pili (BFP) and forms characteristic attaching and effacing (A/E) lesions through the T3SS (28). Virulence factors are BFP, T3SS, Esp proteins. EHEC, in particular O157, adheres to the colon

using intiman and T3SS, producing Stx that cause severe damage to intestinal and renal cells (29). UPEC colonizes the urinary tract using P type 1 pili and fimbriae, producing hemolysin and cytotoxic necrotizing factor 1 (CNF1) to damage host cells (30). The genes encoding these virulence factors are often located on plasmids, which are extrachromosomal DNA elements that can be transferred between bacteria and contribute to the spread of virulence traits.

The *E. coli* pathogen interacts with host cells in several ways such as adhesion, invasion, toxin production, and immune evasion. In adhesion, initial attachment to the host cell surface is achieved by adhesins. Invasion intends the entry into host cells (e.g. EIEC). Toxin production refers to the disruption of host cellular functions. And immune evasion refers to the mechanisms used by the microorganism to avoid host immune responses, such as alteration of surface antigens (31).

CONCLUSIONS

The molecular aspects of *E. coli* pathogenesis have crucial clinical implications. Diagnosis occurs through molecular techniques, such as PCR and sequencing, that can identify specific virulence genes. Targeting specific virulence factors (e.g., anti-adhesive therapies, neutralizing toxins) can improve treatment outcomes, while prevention is achieved through the use of vaccines targeting the main virulence factors for some *E. coli* pathotypes.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Shiomi D, Mori H, Niki H. Genetic mechanism regulating bacterial cell shape and metabolism. *Communicative & Integrative Biology*. 2009;2(3):219-220. doi:https://doi.org/10.4161/cib.2.3.7930
2. Yuge S, Akiyama M, Komatsu T. An *Escherichia coli* trap in human serum albumin microtubes [published correction appears in Chem Commun (Camb). 2014 Aug 28;50(67):9608]. *Chemical communications (Cambridge, England)*. 2014;50(68):9640-9643. doi:10.1039/c4cc03632h
3. Sande C, Whitfield C. Capsules and Extracellular Polysaccharides in *Escherichia coli* and Salmonella. Slauch JM, ed. *EcoSal Plus*. 2021;9(2). doi:https://doi.org/10.1128/ecosalplus.esp-0033-2020
4. Silhavy TJ, Kahne D, Walker S. The bacterial cell envelope. *Cold Spring Harbor Perspectives in Biology*. 2010;2(5). doi:https://doi.org/10.1101/cshperspect.a000414
5. Konovalova A, Perlman DH, Cowles CE, Silhavy TJ. Transmembrane domain of surface-exposed outer membrane lipoprotein RcsF is threaded through the lumen of β-barrel proteins. *Proceedings of the National Academy of Sciences of the United States of America*. 2014;111(41):E4350-4358. doi:https://doi.org/10.1073/pnas.1417138111
6. Tenaillon O, Skurnik D, Picard B, Denamur E. The Population Genetics of Commensal *Escherichia Coli*. *Nature Reviews Microbiology*. 2010;8(3):207-217. doi:https://doi.org/10.1038/nrmicro2298
7. Wolański M, Donczew R, Zawilak-Pawlik A, Zakrzewska-Czerwińska J. oriC-encoded instructions for the initiation of bacterial chromosome replication. *Frontiers in microbiology*. 2015;5:735. doi:10.3389/fmicb.2014.00735
8. Fijalkowska IJ, Schaaper RM, Jonczyk P. DNA replication fidelity in *Escherichia coli*: a multi-DNA polymerase affair. *FEMS Microbiology Reviews*. 2012;36(6):1105-1121. doi:https://doi.org/10.1111/j.1574-6976.2012.00338.x
9. Stark H, Mueller F, Orlova EV, et al. The 70S *Escherichia coli* ribosome at 23 å resolution: fitting the ribosomal RNA. *Structure*. 1995;3(8):815-821. doi:https://doi.org/10.1016/s0969-2126(01)00216-7
10. Santillán M, Mackey MC. Quantitative approaches to the study of bistability in the lac operon of *Escherichia coli*. *Journal of The Royal Society Interface*. 2008;5(suppl_1). doi:https://doi.org/10.1098/rsif.2008.0086.focus
11. Hollinshead WD, Rodriguez S, Martin HG, et al. Examining *Escherichia coli* glycolytic pathways, catabolite repression, and metabolite channeling using Δpfk mutants. *Biotechnology for Biofuels*. 2016;9(1). doi:https://doi.org/10.1186/s13068-016-0630-y

12. Erhardt H, Dempwolff F, Pfreundschuh M, et al. Organization of the *Escherichia coli* aerobic enzyme complexes of oxidative phosphorylation in dynamic domains within the cytoplasmic membrane. *MicrobiologyOpen*. 2014;3(3):316-326. doi:https://doi.org/10.1002/mbo3.163
13. Zhang W, Chen X, Sun W, Nie T, Quanquin N, Sun Y. *Escherichia coli* Increases its ATP Concentration in Weakly Acidic Environments Principally through the Glycolytic Pathway. *Genes*. 2020;11(9):991. doi:https://doi.org/10.3390/genes11090991
14. Förster AH, Gescher J. Metabolic Engineering of *Escherichia coli* for Production of Mixed-Acid Fermentation End Products. *Frontiers in Bioengineering and Biotechnology*. 2014;2(16). doi:https://doi.org/10.3389/fbioe.2014.00016
15. Price MN, Zane GM, Kuehl JV, et al. Filling gaps in bacterial amino acid biosynthesis pathways with high-throughput genetics. Casadesús J, ed. *PLOS Genetics*. 2018;14(1):e1007147. doi:https://doi.org/10.1371/journal.pgen.1007147
16. Heijenoort J v. Formation of the glycan chains in the synthesis of bacterial peptidoglycan. *Glycobiology*. 2001;11(3):25R36R. doi:https://doi.org/10.1093/glycob/11.3.25r
17. Hu B, Tu Y. Precision Sensing by Two Opposing Gradient Sensors: How Does *Escherichia coli* Find its Preferred pH Level? *Biophysical Journal*. 2013;105(1):276-285. doi:https://doi.org/10.1016/j.bpj.2013.04.054
18. Masi M, Pagès JM. Structure, Function and Regulation of Outer Membrane Proteins Involved in Drug Transport in Enterobactericeae: the OmpF/C – TolC Case. *The Open Microbiology Journal*. 2013;7(1):22-33. doi:https://doi.org/10.2174/1874285801307010022
19. Ogierman M, Braun V. Interactions between the Outer Membrane Ferric Citrate Transporter FecA and TonB: Studies of the FecA TonB Box. *Journal of Bacteriology*. 2003;185(6):1870-1885. doi:https://doi.org/10.1128/jb.185.6.1870-1885.2003
20. Melican K, Sandoval RM, Kader A, et al. Uropathogenic *Escherichia coli* P and Type 1 fimbriae act in synergy in a living host to facilitate renal colonization leading to nephron obstruction. *PLoS pathogens*. 2011;7(2):e1001298. doi:10.1371/journal.ppat.1001298
21. Bien J, Sokolova O, Bozko P. Role of Uropathogenic *Escherichia coli* Virulence Factors in Development of Urinary Tract Infection and Kidney Damage. *International journal of nephrology*. 2012;2012:681473. doi:10.1155/2012/681473
22. Paton JC, Paton AW. Pathogenesis and diagnosis of Shiga toxin-producing *Escherichia coli* infections. *Clinical microbiology reviews*. 1998;11(3):450-479. doi:10.1128/CMR.11.3.450
23. Pacheco AR, Sperandio V. Shiga toxin in enterohemorrhagic *E.coli*: regulation and novel anti-virulence strategies. *Frontiers in cellular and infection microbiology*. 2012;2:81. doi:10.3389/fcimb.2012.00081
24. Zhang W, Berberov EM, Freeling J, He D, Moxley RA, Francis DH. Significance of Heat-Stable and Heat-Labile Enterotoxins in Porcine Colibacillosis in an Additive Model for Pathogenicity Studies. *Infection and Immunity*. 2006;74(6):3107-3114. doi:https://doi.org/10.1128/iai.01338-05
25. Michelacci V, Prosseda G, Maugliani A, et al. Characterization of an emergent clone of enteroinvasive *Escherichia coli* circulating in Europe. *Clinical Microbiology and Infection*. 2016;22(3):287.e11-287.e19. doi:https://doi.org/10.1016/j.cmi.2015.10.025
26. Gaytán MO, Martínez-Santos VI, Soto E, González-Pedrajo B. Type Three Secretion System in Attaching and Effacing Pathogens. *Frontiers in Cellular and Infection Microbiology*. 2016;6. doi:https://doi.org/10.3389/fcimb.2016.00129
27. Fleckenstein JM, Hardwidge PR, Munson GP, Rasko DA, Sommerfelt H, Steinsland H. Molecular mechanisms of enterotoxigenic *Escherichia coli* infection. *Microbes and infection / Institut Pasteur*. 2010;12(2):89-98. doi:10.1016/j.micinf.2009.10.002
28. Saldaña Z, Erdem AL, Schüller S, et al. The *Escherichia coli* common pilus and the bundle-forming pilus act in concert during the formation of localized adherence by enteropathogenic *E. coli*. *Journal of bacteriology*. 2009;191(11):3451-3461. doi:10.1128/JB.01539-08
29. Golan L, Gonen E, Yagel S, Rosenshine I, Shpigel NY. Enterohemorrhagic *Escherichia coli* induce attaching and effacing lesions and hemorrhagic colitis in human and bovine intestinal xenograft models. *Disease Models & Mechanisms*. 2010;4(1):86-94. doi:https://doi.org/10.1242/dmm.005777
30. Garcia TA, Ventura CL, Smith MA, Merrell DS, O'Brien AD. Cytotoxic Necrotizing Factor 1 and Hemolysin from Uropathogenic *Escherichia coli* Elicit Different Host Responses in the Murine Bladder. McCormick BA, ed. *Infection and Immunity*. 2012;81(1):99-109. doi: https://doi.org/10.1128/iai.00605-12

31. Abreu AG, Barbosa AS. How *Escherichia coli* Circumvent Complement-Mediated Killing. *Frontiers in Immunology*. 2017;8(452). doi:https://doi.org/10.3389/fimmu.2017.00452