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Colicins produced by *Escherichia coli*, a review

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ABSTRACT

Bacteria produce proteins called bacteriocins and can inhibit or even kill closely related species. Among the bacteriocins, Colicins are by far the most well-characterized group. They are generated by *Escherichia coli* and other Enterobacteriaceae family members, and they are effective against them. At least 34 Colicins have been identified, with 21 of them being more thoroughly studied, and they share not common set of properties. A group of carcinogenic bacteria generates colicin proteins under stressful conditions. The kind of stress that is causing the inductive activity must be specified. The release of colicins does not always result in the death of the cell that generates them.

Keywords: colicins, Enterobacteriaceae, *Escherichia coli*

INTRODUCTION

Colicins are a class of antimicrobial proteins that are produced by *Escherichia coli* with the purpose of suppressing the growth of other strains of *E. coli* and closely related bacterial species [1]. The proteins have undergone evolutionary changes in order to provide a competitive advantage to the host bacterium in its interactions with closely related bacterial species [2]. A lot of bacteria in the *Enterobacteriaceae* family can make colicins. In fact, tests have shown that about 30% of *E. coli* isolates can make at least one type of colicin [3].

The colicins produced by the colicinogenic bacteria are specially protected against unwanted environmental factors like high temperature and humidity. Furthermore, colicin gene clusters are plasmid-encoded [4,5]. Because of their wide range of action, colicins have been proposed for a variety of purposes. Among the applications of this kind are food preservatives, the management of diarrheal illnesses brought on by enteropathogenic bacteria, and others [5,6]. This study focuses on the most significant elements of these fascinating proteins known as colicins. The organization of all colicins is consistent with their mode of action. All colicin molecules have the same functional domain sequence, which runs from the N' (amino) to the C' (carboxy) terminus. With a molecular mass between 30 and 70 kDa, their structure consists of three distinct domains: (A) a domain responsible for the recognition of specific receptors, (B) a domain involved in translocation, and (C) a domain responsible for their lethal action [7,8].

The outer membrane of the bilayer, which contains lipopolysaccharide molecules on its outer surface and tiny holes, must be crossed by colicins in order for them to function. Then, the sensitive cells must absorb the colicins [7]. Therefore, colicins have developed a parasitic mechanism involving a complex system of many proteins that is used by a susceptible cell to carry out vital biological processes. The protein composition includes porins, including Omp F, Omp A, and Omp C, as well as vitamin B12 receptor (Btu B), siderophore receptor, nucleoside receptor (Tsx), and the multiprotein systems responsible for the transport and synthesis of these proteins [8]. The homologous Tonne and Tol translocation systems have been identified. TonB, ExbB, and ExbD, three proteins of the Tonne translocation system, reside near the *Escherichia coli* chromosome [9,10]. TolQ, TolR, TolA, TolB, and Pal are important parts of the Tol translocation system. These components are near the *Escherichia coli* chromosome [11].

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MOLECULAR INVESTIGATION OF THE COLICINOGENIC *ESCHERICHIA COLI*

Escherichia coli O157: H7 is commonly known as a foodborne bacterial that causes significant mortality worldwide [12]. The clinical manifestations associated with *E. coli* O157:H7 include a spectrum of symptoms, ranging from minor episodes of diarrhea to the development of hemolytic uremic syndrome (HUS). This condition may potentially lead to kidney diseases. The severity of these symptoms is contingent upon the immunological condition of the patient and the dose of bacterial infection [13,14]. Ruminants is the main reservoir of *Escherichia coli* O157:H7 [15]. The method for controlling *E. coli* O157:H7 is competitive elimination, which is defined as the employment of other probiotic bacteria to limit the pathogenic bacterium's development and colonization [16]. Using additional *Escherichia coli* that is not pathogens and generate colicins might be used to reduce *E. coli* O157:H7 [17].

The choice of host animal species may have an impact on the specific kind of colicin generated. In the case of bovine isolates, it is anticipated that they would exhibit a relatively low level of resistance to non-cattle sources. In a study conducted by [16,18], it was found that *Escherichia coli* O157:H7 can be effectively controlled through the use of a competitive-exclusion system involving colicinogenic *E. coli* isolates obtained from cattle. However, limited details were provided regarding the specific colicins produced by these isolates and the level of resistance exhibited by naturally occurring *E. coli* O157:H7 isolates [19].

The evaluation of evolutionary origins by phylogenetic analysis has proved useful in determining the pathogenicity characteristics of *Escherichia coli* isolates [20]. *E. coli* isolates can be assigned to one of the four major phylogenetic groups A, B1, B2, and D, which contain seven subgroups based on phylogenetic studies [21]. Previous research on the correlation between colicin production and virulence factors was restricted since it mostly examined UroPathogenic *Escherichia coli* (UPEC) isolates and found varying numbers of colicin and virulence genes [19].

MECHANISM OF ACTION

Colicins kill bacteria that are sensitive in three different ways. The process that most often leads to membrane depolarization is the creation of ion channels (pores) in the plasma membrane [5,7]. When the pores open, phosphate and sometimes K+ leave the cell, which lowers the amount of ATP in the cytoplasm [8].

Most colicins' translocation and ultimate contact with a cellular target are unknown, although the colicin A (pore-forming) and colicin E (nucleases) groups' mechanisms are better studied (Table 1). Inhibition of murein production and hydrolysis follows a mechanism that is very similar to that of beta-lactamic antibiotics and lysozyme activity [8,22].

Colicins are not as commonly found as other nucleases. They can work against genomic DNA (as a

TABLE 1. Colicin produced by *E. coli* types, mechanism of action and other features

Colicin type	Receptor/ Assisting protein	Translocation route	Mechanism of action	Colicin molecular weight
B	FepA	TonB/ExbB, D	pore formation	54.732
D	FepA	TonB/ExbB, D	translation block	74.688
El	BtuB/TolC	TolA, B,Q,R,	pore formation	52.279
E3	BtuB/OmpF	TolA, B,Q,R,	rRNA endonuclease	57.960
E4	BtuB/OmpF	TolA, B,Q,R,	rRNA endonuclease	ND
E5	BtuB/OmpF	TolA, B,Q,R,	translocation block	ND
E6	BtuB/OmpF	TolA, B,Q,R,	rRNA endonuclease	58.011
E7	BtuB/OmpF	TolA, B,Q,R,	DNA endonuclease	61.349
E8	BtuB/OmpF	TolA, B,Q,R,	DNA endonuclease	70.000
E9	BtuB/OmpF	TolA, B,Q,R,	DNA endonuclease	ND
G	Fiu	TonB/ExbB, D	membrane lysisND	5.500
H	Fiu	TonB/ExbB, D	membrane lysisND	100
Ia	Cir	TonB/ExbB, D	pore formation	69.406
M	FhuA	TonB/ExbB, D	Inhibition of murein synthesis	29.453
N	OmpF/OmpC, Phoe	TolA, Q,R,	pore formation	41.696
Q	Cir	TonB/ExbB, D	ND	ND
S4	SrfND/OmpF	TolA, B,Q,R,	pore formation	ND
5	Tsx/TolC	TonB/ExbB, D	pore formation	53.137
10	Tsx/TolC	TonB/ExbB, D	pore formation	53.342
V	Cir/TolC	CvaA, CvaB, CvaA	pore formation	9

general DNA endonuclease) or 16S-rRNA (as a selective endonuclease). The least commonly observed phenomenon involves the degradation process, which catalyzes the hydrolysis of the b-1,4 bond between N-acetyl glucosamine and N-acetylmuramic acid in the glycan backbone of the bacterial cell wall. Another method is the suppression of the production of wall peptidoglycan or murein, which results in the creation of spheroplasts and, ultimately, the death of the cell [5,23].

COLICIN SYNTHESIS, INDUCTION AND GENETIC FEATURES

Genes on Col plasmids regulate colicin production; these plasmids also have variable conjugative properties and can aid in the spread of antibiotic resistance and other virulence factors among *uropathogenic E. coli* strains [24,25]. The sizes of pCol plasmids exhibit significant variation, ranging from 6.6 Kb (pColE1) to 94 Kb (pColH). Nevertheless, it is worth noting that smaller plasmids measuring less than 5.5 Kb, as well as bigger plasmids exceeding 94 Kb, have also been identified [26]. Colicin is derived from a set of genes that consists of at least two and often three. One such gene is the colicin structure gene (pColE1 color cea). One more is the imm gene for the immune system protein. Finally, there's kil, short for lysis protein or bacteriocin release protein (BRP), a gene. Colicin production is stimulated by DNA-damaging chemicals or environmental conditions, including growing population density and nutritional deficiency [27].

The antibacterial colicin is normally only made in small amounts in *E. coli* cells that carry the Col plasmid. However, when these cells are exposed to DNA-damaging drugs like UV light or mitomycin C, a lot of it is made [28]. This is caused by the "SOS system of DNA repair" in bacteria [29], which turns on the RecA proteinase and turns off the Lex A protein. The Lex A protein is a regulator of several DNA repair genes and plasmid genes for colicin production. The majority of cells in the population have colicin synthesis turned off under normal, but unknown, circumstances; it only happens in a tiny percentage of cells due to an erratic activation of the "SOS system of DNA repair" [26]. Other methods of colicin production have been reported, including mRNA regulation via the "stringent response" and nonspecific catabolic suppression [30,31]. A protein called BRP, or lysis protein, must be produced and active in order for colonicin to be released into the extracellular medium [32]. The lytic protein, a small lipoprotein that facilitates endogenous outer membrane phospholipase A [33] is essential for cell envelope permeabilization (lysis) and producer bacterial mortality. Some colicin gene clusters, however, lack the kil (lysis protein) gene, and the mechanism by which these colicins are discharged into the extracellular environment remains unknown (Figure 1).

ECOLOGY OF COLICIN

Colicins are considered anticompetitor compounds from an ecological perspective [34]. Few things are known about the natural ecology of colicins and their function in the ecology of bacteria, despite the fact that research on colicins has produced a plethora of knowledge about molecular genetics, mechanism of action, and application [35]. One of the many ways that bacteria adapt to environmental stressors is by the synthesis of com-

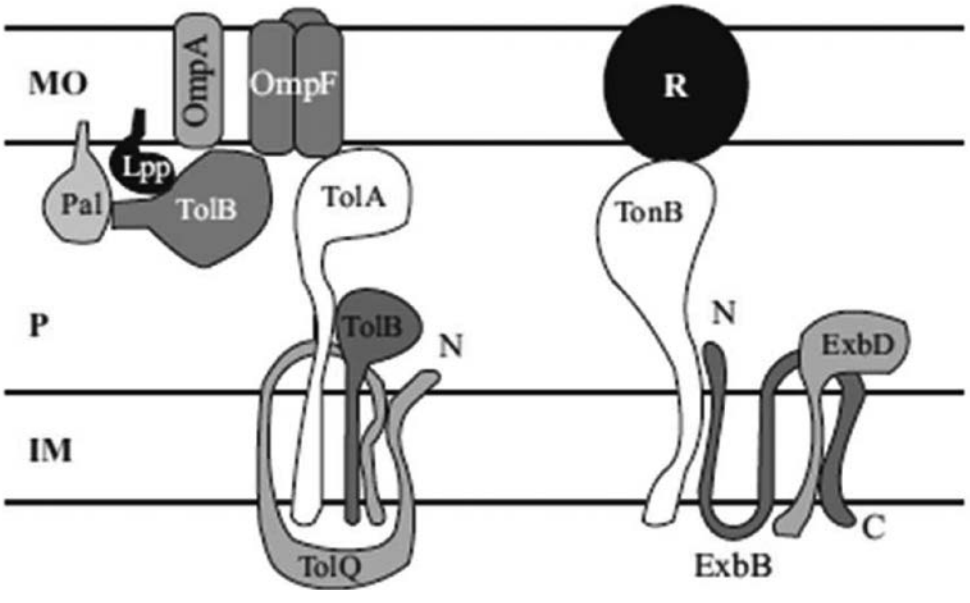

FIGURE 1. TonB and Tol-Pal translocation systems

OM; outer membrane, P; periplasmic space, IM; inner membrane, R; TonB-dependent receptor, C; C-terminus, N; N-terminus [8]

pounds with antimicrobial properties, including colicins [36]. It seems to be involved in interactions that are competitive among microbial community members [37]. Despite the fact that colicin production is ubiquitous, it is believed that colicins have a bigger role in intra-versus interspecies competitive interactions. This idea stems from data indicating that colicins produced by one species often do not work well against strains made by other species [38].

The high frequency of encounters with naturally occurring colicinogenic strains provides the strongest evidence for the ecological importance of the colicins [39]. It is often stated that 24-45% of Istrains exhibit colicinogeny [40]. The variables influencing the prevalence of colicinogeny in wild populations are not well understood [41,42]. However, Pugsley (Pugsley1984) discovered that more than 30% of the lactose-fermenting gram-negative bacteria from the River Seine made colicins that were effective against *E. coli* K12, which is a common strain used to test for colicins. It's interesting that 98% of these samples reacted to common antibiotics [39]. Studies show that pathogenic isolates are more likely to cause colicinogeny than commensal isolates, and human isolates (50%) are more likely than animal isolates (16%) [37,43]. Whether colicinogeny is a pathogen or a marker with additional virulence factors is unknown. However, P-fimbriae, alpha-haemolysin, and aerobactin synthesis are linked to specific colicins and may explain this association [44,45].

Colicinogenic bacteria, particularly those that generate colicin V (now microcin V), maybe more virulent due to these factors. Despite research showing its direct role in pathogenesis, colicin V does not seem to be a pathogenic determinant [46]. Šmarda and Obdrzálek [47] recently reported that 41% of E. coli strains isolated from healthy humans in the Czech population generate colicins. The same frequency of carcinogenic producers was found in the intestines of patients with salmonellosis or malignant colon tumors. The number of hemolytic uropathogenic strains found in these patients was only 22%. In the guts of people with Crohn's disease and ulcerative colitis, the numbers were 48% and 56%, respectively.

COLICINS EVOLUTION

Colicins have been used as a model to investigate the mechanisms of bacteriocin evolution and diversity due to the abundance of available data. Most of these investigations have examined colicin, immunity, and lysis gene and product DNA and protein sequences to imply evolutionary linkages and molecular diversity. The most intriguing conclusion to be drawn from the colicin protein's phylogenetic data is that this class of proteins is very diverse. Positive selection and recombination are the two alternative theoretical theories put out by Tan and Riley to account for the evolutionary diversity of colicins [48-50].

Positive selection has been hypothesized as a potential rationale for an atypical divergence trend seen in two distinct gene clusters (E3/E6 and E2/E9-nucleases). A large number of synonymous and nonsynonymous changes (which change the codon but not the exact amino acid) were found in the immunity binding region, the immunity gene, and the immunity component of the colicin gene. A diversification process was suggested to explain this occurrence. To begin, a point mutation develops in a colicin's immunity gene, conferring a broader immune role. Several other colicins are ineffective against these cells, as well as their DNA and their immediate ancestors. This colicin gene cluster will be selected for population preservation due to its superiority. A second mutation in the developed colicin gene may form a gene cluster that its predecessor cannot tolerate. This colicin gene cluster benefits a strain greatly and specifically. Positive selection will quickly introduce this “super killer”, and successive rounds of immunity function diversification will accumulate synonymous and nonsynonymous immunity component changes [51].

Increasing diversity via positive selection may be effective here. Thus, the process underlying the “super killer” appearance might be accountable for the highest expected degree of variety in a single species [52]: the 5% variation in IDNA. Protein sequence identity among pore-forming colicins is often around 40%, which the second scenario, recombination, may explain. Some study suggests that this group of colicins has reassembled gene sequences that code for certain functional domains to produce new colicins. These recombination processes occur inside and between pores-making colicin groups [51]. Based on DNA and protein sequence similarities, this colicin group is a diverse class of proteins with a common ancestor. Thus, pore-forming colicin diversification is the result of many recombination events that choose random functional domains and create novel colicin types [53].

CONCLUSION

Understanding colicine production is essential in the context of microbial ecology, bacterial competition, and potential applications in practical settings. Further research explores the characteristics, production mechanisms, and applications of colicins in gram-negative bacteria, emphasizing their significance in microbial interactions.

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REFERENCES

1. Jeziorowski A, Gordon DM. Evolution of microcin V and Colicin Ia plasmids in Escherichia coli. *J Bacteriol.* 2007;189:7045-52. doi: 10.1128/jb.00243-07
2. Inglis RF, Bayramoglu B, Gillor O, Ackermann M. The role of bacteriocins as selfish genetic elements. *Biol Lett.* 2013;9:20121173. doi: 10.1098%2Frsbl.2012.1173
3. Diez-Gonzalez F. Applications of bacteriocins in livestock. *Curr Issues Intest Microbiol.* 2007;8:15-23. https://pubmed.ncbi.nlm.nih.gov/17489435/
4. Riley MA, Gordon DM. The ecology and evolution of bacteriocins. *J Ind Microbiol.* 1996;17(3-4):151-8. doi: 10.1007/BF01574688
5. Smarda J, Smajs D. Colicins-exocellular lethal proteins of Escherichia coli. *Folia Microbiol* (Praha). 1998;43(6):563-82. doi: 10.1007/BF02816372
6. Murinda SE, Roberts RF, Wilson RA. Evaluation of colicins for inhibitory activity against diarrheagenic Escherichia coli strains, including serotype O157:H7. *Appl Environ Microbiol.* 1996 Sep;62(9):3196-202. doi: 10.1128/aem.62.9.3196-3202.1996
7. Benedetti H, Frenette M, Baty D, Knibiehler M, Pattus F, Lazdunski C. Individual domains of colicins confer specificity in colicin uptake, in pore-properties and in immunity requirement. *J Mol Biol.* 1991 Feb 5;217(3):429-39. doi: 10.1016/0022-2836(91)90747-t. PMID: 1704440.
8. Lazdunski CJ, Bouveret E, Rigal A, Journet L, Lloubès R, Bénédetti H. Colicin import into Escherichia coli cells. *J Bacteriol.* 1998 Oct;180(19):4993-5002. doi: 10.1128/JB.180.19.4993-5002.1998
9. Ahmer BM, Thomas MG, Larsen RA, Postle K. Characterization of the exbBD operon of Escherichia coli and the role of ExbB and ExbD in TonB function and stability. *J Bacteriol.* 1995 Aug;177(16):4742-7. doi: 10.1128/jb.177.16.4742-4747.1995
10. Vianney A, Lewin TM, Beyer WF Jr, Lazzaroni JC, Portalier R, Webster RE. Membrane topology and mutational analysis of the TolQ protein of Escherichia coli required for the uptake of macromolecules and cell envelope integrity. *J Bacteriol.* 1994 Feb;176(3):822-9. doi: 10.1128/jb.176.3.822-829.1994
11. Postle K. TonB protein and energy transduction between membranes. *J Bioenerg Biomembr.* 1993 Dec;25(6):591-601. doi: 10.1007/BF00770246
12. Abdissa R, Haile W, Fite AT, Beyi AF, Agga GE, Edao BM et al. Prevalence of Escherichia coli O157: H7 in beef cattle at slaughter and beef carcasses at retail shops in Ethiopia. *BMC Infect Dis.* 2017;17:277. doi: 10.1186/s12879-017-2372-2
13. Ferens WA, Hovde CJ. Escherichia coli O157:H7: animal reservoir and sources of human infection. *Foodborne Pathog Dis.* 2011;8:465-87. doi: 10.1089/fpd.2010.0673
14. Rahal EA, Kazzi N, Nassar FJ, Matar GM. Escherichia coli O157:H7—clinical aspects and novel treatment approaches. *Front Cell Infect Microbiol.* 2012;2:138. doi: 10.3389/fcimb.2012.00138
15. Elder RO, Keen JE, Siragusa GR, Barkocy-Gallagher GA, Koohmaraie M, Laegreid WW. Correlation of enterohemorrhagic Escherichia coli O157 prevalence in feces, hides, and carcasses of beef cattle during processing. *Proc Natl Acad Sci.* 2000;97:2999-3003. doi: 10.1073/pnas.97.7.2999
16. Schamberger GP, Diez-Gonzalez F. Assessment of resistance to Colicinogenic Escherichia coli by E. coli O157:H7 strains. *J Appl Microbiol.* 2005;98:245-52. doi: 10.1111/j.1365-2672.2004.02452.x
17. Schamberger GP, Diez-Gonzalez F. Characterization of Colicinogenic Escherichia coli strains inhibitory to enterohemorrhagic Escherichia coli. *J Food Prot.* 2004;67:486-92. doi: 10.4315/0362-028x-67.3.486
18. Zhao T, Doyle MP, Harmon BG, Brown CA, Mueller POE, Parks AH. Reduction of carriage of enterohemorrhagic Escherichia coli O157:H7 in cattle by inoculation with probiotic bacteria. *J Clin Microbiol.* 1998;36:641-7. doi: 10.1128/jcm.36.3.641-647.1998
19. Micenková L, Bosák J, Štaudová B, Kohoutová D, Čejková D, Woznicová V, et al. Microcin determinants are associated with B2 phylogroup of human fecal Escherichia coli isolates. *Microbiology.* 2016;5:490-8. doi: 10.1002/mbo3.345
20. Chandran A, Mazumder A. Prevalence of diarrhea-associated virulence genes and genetic diversity in Escherichia coli isolates from fecal material of various animal hosts. *Appl Environ Microbiol.* 2013;79:7371-80. doi: 10.1128/aem.02653-13
21. Clermont O, Bonacorsi S, Bingen E. Rapid and simple determination of the Escherichia coli phylogenetic group. *Appl Environ Microbiol.* 2000;66:4555-8. doi: 10.1128/aem.66.10.4555-4558.2000
22. Cramer WA, Lindeberg M, Taylor R. The best offense is a good defense. *Nat Struct Biol.* 1999 Apr;6(4):295-7. doi: 10.1038/7520
23. Konisky J. Colicins and others bacteriocins with established modes of action. *Ann Rev Microbiol.* 1982;36:125-144. doi: 10.1146/annurev.mi.36.100182.001013
24. Clowes RC. Colicin factors and epissomes. Genet Res Cambr. 1963;4:162-165.
25. Fredericq P, Betz-Bareau M. Transfert génétique de la propriété colicinogène chez E. coli [Genetic transfer of colicinogenic property in E. coli]. *C R Seances Soc Biol Fil.* 1953 Jun;147(11-12):1110-2. Undetermined Language. PMID: 13116607.
26. Smarda J, Smajs D. Colicins - exocellular lethal proteins of Escherichia coli. *Folia Microbiol (Praha).* 1998;43(6):563-82. doi: 10.1007/BF02816372
27. Ozeki H, Stocker BA, De Margerie H. Production of colicine by single bacteria. *Nature.* 1959 Aug 1;184:337-9. doi: 10.1038/184337a0. PMID: 14429601.
28. James R, Kleanthous C, Moore GR. The biology of E colicins: paradigms and paradoxes. *Microbiology* (Reading). 1996 Jul;142 (Pt 7):1569-80. doi: 10.1099/13500872-142-7-1569
29. Lu FM, Chak KF. Two overlapping SOS-boxes in ColE operons are responsible for the viability of cells harboring the Col plasmid. *Mol Gen Genet.* 1996 Jun 24;251(4):407-11. doi: 10.1007/BF02172368
30. Lotz W. Effect of guanosine tetraphosphate on in vitro protein synthesis directed by E1 and E3 colicinogenic factors. *J Bacteriol.* 1978 Aug;135(2):707-12. doi: 10.1128/jb.135.2.707-712.1978
31. Salles B, Weisemann JM, Weinstock GM. Temporal control of colicin E1 induction. *J Bacteriol.* 1987 Nov;169(11):5028-34. doi: 10.1128/jb.169.11.5028-5034.1987
32. van der Wal FJ, Luirink J, Oudega B. Bacteriocin release proteins: mode of action, structure, and biotechnological application. *FEMS Microbiol Rev.* 1995 Dec;17(4):381-99. doi: 10.1111/j.1574-6976.1995.tb00221.x
33. Dekker N, Tommassen J, Verheij HM. Bacteriocin release protein triggers dimerization of outer membrane phospholipase A in vivo. *J Bacteriol.* 1999 May;181(10):3281-3. doi: 10.1128/JB.181.10.3281-3283.1999
34. Dykes GA. Bacteriocins: ecological and evolutionary significance. *Trends Ecol Evol.* 1995 May;10(5):186-9. doi: 10.1016/s0169-5347(00)89049-7
35. Dykes GA, Hastings JW. Selection and fitness in bacteriocin-producing bacteria. *Proc Biol Sci.* 1997 May 22;264(1382):683-7. doi: 10.1098/rspb.1997.0097
36. Campbell A. Evolutionary significance of accessory DNA elements in bacteria. *Ann Rev Microbiol.* 1981;35:55-83. doi: 10.1146/annurev.mi.35.100181.000415
37. Riley MA, Wertz JE. Bacteriocins: evolution, ecology, and application. *Ann Rev Microbiol.* 2002;56:117-37. doi: 10.1146/annurev.micro.56.012302.161024. Epub 2002 Jan 30.
38. Frank S. Spatial polymorphism of bacteriocins and other allelopathic traits. *Evol Ecol.* 1994;8: 369-386. https://link.springer.com/article/10.1007/BF01238189
39. Pugsley AP, Schwartz M. Colicin E2 release: lysis, leakage or secretion? Possible role of a phospholipase. *EMBO J.* 1984 Oct;3(10):2393-7. doi: 10.1002/j.1460-2075.1984.tb02145.x
40. Brandis H, Šmarda J. Bacteriocine und bacteriocinnähnliche Substanzen. Gustav Fisher Verlag, Jena, 1971.
41. Hardy KG. Colicinogeny and related phenomena. *Bacteriol Rev.* 1975 Dec;39(4):464-515. doi: 10.1128/br.39.4.464-515.1975
42. Šmajs D. The morphology of bacterial cell in inhibition zones produced by colicins. *Scripta Med.* 1995;68:171-80. https://www.muni.cz/en/research/publications/194143
43. Waters VL, Crosa JH. Colicin V virulence plasmids. *Microbiol Rev.* 1991 Sep;55(3):437-50. doi: 10.1128/mr.55.3.437-450.1991
44. Dobrindt U, Blum-Oehler G, Hartsch T, Gottschalk G, Ron EZ, Fünfstück R, Hacker J. S-Fimbria-encoding determinant sfa(I) is located on

pathogenicity island III(536) of uropathogenic Escherichia coli strain 536. *Infect Immun.* 2001 Jul;69(7):4248-56. doi: 10.1128/IAI.69.7.4248-4256.2001
45. Moss JE, Cardozo TJ, Zychlinsky A, Groisman EA. The selC-associated SHI-2 pathogenicity island of Shigella flexneri. *Mol Microbiol.* 1999 Jul;33(1):74-83. doi: 10.1046/j.1365-2958.1999.01449.x
46. Wooley RE, Nolan LK, Brown J, Gibbs PS, Bounous DI. Phenotypic expression of recombinant plasmids pKT107 and pHK11 in an avirulent avian Escherichia coli. *Avian Dis.* 1994 Jan-Mar;38(1):127-34.
47. Smarda J, Obdrzálek V. Incidence of colicinogenic strains among human Escherichia coli. *J Basic Microbiol.* 2001;41(6):367-74. doi: 10.1002/1521-4028(200112)41:6<367::AID-JOBM367>3.0.CO;2-X
48. Feldgarden M, Golden S, Wilson H, Riley MA. Can phage defence maintain colicin plasmids in Escherichia coli? *Microbiology* (Reading). 1995 Nov;141(Pt 11):2977-84. doi: 10.1099/13500872-141-11-2977
49. Riley MA, Tan Y, Wang J. Nucleotide polymorphism in colicin E1 and Ia plasmids from natural isolates of Escherichia coli. *Proc Natl Acad Sci U S A.* 1994 Nov 8;91(23):11276-80. doi: 10.1073/pnas.91.23.11276
50. Tan Y, Riley MA. Rapid invasion by colicinogenic Escherichia coli with novel immunity functions. *Microbiology* (Reading). 1996 Aug;142(Pt 8):2175-80. doi: 10.1099/13500872-142-8-2175
51. Riley MA. Molecular mechanisms of bacteriocin evolution. *Annu Rev Genet.* 1998;32:255-78. doi: 10.1146/annurev.genet.32.1.255
52. Morell V. Bacteria diversify through warfare. *Science.* 1997 Oct 24;278(5338):575. doi: 10.1126/science.278.5338.575a
53. Riley MA, Gordon DM. A survey of Col plasmids in natural isolates of Escherichia coli and an investigation into the stability of Col-plasmid lineages. *J Gen Microbiol.* 1992 Jul;138(7):1345-52. doi: 10.1099/00221287-138-7-1345