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# COMPARATIVE GENOMICS, PHYLOGENETIC, AND FUNCTIONAL ANALYSES OF *YERSINIA ENTEROCOLITICA*, A GASTROINTESTINAL PATHOGEN, WITH OTHER SOIL-BORNE BACTERIA CAUSING DISEASES

*Yersinia enterocolitica is a harmful bacterium transmitted through contaminated food, causing gastrointestinal illness and lymph node inflammation. The rise of drug-resistant strains of Y. enterocolitica poses a serious public health threat, necessitating research on its ecology, related species, and unique genes linked to virulence and antibiotic resistance. This study identified eight microorganisms similar to Y. enterocolitica and conducted a pan-genomic analysis, revealing specific genes exclusive to Y. enterocolitica. Enrichment analysis of these genes unveiled their involvement in antibiotic synthesis pathways, such as siderophore production, osmoregulated periplasmic glucan activation, and antibiotic resistance. These pathways, including biofilm formation and increased antibiotic tolerance, are vital for Yersinia's virulence. Furthermore, specific genes related to glutamate metabolism, nitrogen regulation, motility, purine, and pyrimidine synthesis may contribute to Y. enterocolitica's pathogenicity, growth, and virulence factor production. Phylogenetic analysis demonstrated the evolutionary relationship between Y. enterocolitica and similar species like Escherichia coli, Campylobacter jejuni, and Salmonella enterica, stressing the need to monitor Y. enterocolitica in slaughterhouses due to animal carriers. The study's findings shed light on the ecological factors and genetic mechanisms driving Y. enterocolitica's pathogenicity and antibiotic resistance. Targeting genes involved in purine and pyrimidine synthesis, such as ushA, cpdB, and deoB, could be potential strategies for controlling pathogenicity and antimicrobial resistance. Understanding the relationships and genetic interactions between Y. enterocolitica and related microorganisms is crucial for developing effective surveillance and management approaches in the future.*

***Keywords:*** *Yersinia enterocolitica, food-borne pathogen, antibiotic resistance, pan-genomic analysis, ecology.*

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*Yersinia enterocolitica* (*Y. enterocolitica*) is a gram-negative, coccoid-shaped, facultatively anaerobic, non-capsulated, and non-sporing bacteria, which have a width of 0.5—0.8 μm and length of 1—3 μm. They have a single circular chromosome, 4,552,107 base pairs (bp) in length, and a *Yersinia* virulence plasmid (pYV), 69,704 bp long [1]. The genus *Yersinia* spp. belongs to the *Enterobacteriaceae* family and includes 18 species, of which 3 species, i.e., *Y. enterocolitica, Y. pseudotuberculosis,* and *Y. pestis,* cause infection in humans and animals [2]. *Y. enterocolitica* was categorized into two subspecies based on 16s rRNA gene type: *Y. enterocolitica* subsp. *enterocolitica* and *Y. enterocolitica* subsp. *palaearctica* [3]. The primary origin of *Y. enterocolitica* is animal-source food like pork and its raw or undercooked meat products. It is also found in environmental sources such as soil and water [4]. It is a psychrophilic [5], heat-sensitive bacterium, and becomes inactive when food products like meat and milk are pasteurized at 60 °C for 1—3 minutes [6]. The infectious dose of *Y. enterocolitica* is $10^4$—$10^6$ colony-forming units (CFU) $mL^{-1}$ for humans [7].

*Y. enterocolitica* is a heterogeneous bacterium categorized into six biotypes (1A, 1B, 2, 3, 4, and 5) and 70 different serotypes based on biochemical and immunological tests, respectively. Biotypes and serotypes play a role in the pathogenicity of microorganisms. Biotype 1A is non-pathogenic, 1B is highly pathogenic, and biotypes 2—5 are moderately pathogenic. Strains with biotype-serotype combinations such as 1B/O:8, 2/O:5,27, 2/O:9, 3/O:3, and 4/O:3 are the most common cause of human illness. Biotypes 2 and 4 are often isolated from yersiniosis patients [8, 9].

Some structures, such as plasmid and chromosomes, play an important role in the virulence of *Y. enterocolitica* infections and are known as virulent markers or virulent determinants. The most recognized and significant virulence indicator of *Y. enterocolitica* is the *Yersinia* virulence plasmid (pYV), which typically ranges in size from 64 to 75 kb. Several genes that are directly responsible for the pathogenicity of *Y. enterocolitica* are located within the pYV, such as *yadA* encoding the *Yersinia* adhesin (YadA) or the *yop* virulon encoding *Yersinia* outer membrane proteins (Yops). The genes present in these proteins allow bacteria to invade a susceptible organism, establish colonization, evade the immune response, and thrive even in unfavourable environments [10, 11].

*Y. enterocolitica* is frequently isolated from soil, water, and animals and can cause contamination in foods of all types [12]. It shares ecology with other bacteria such as *Escherichia coli* and is found in tropical and subtropical soils [13], *Campylobacter jejuni* is found in soil, roots, and shoots and causes gastroenteritis [14], *Salmonella enterica* causes contamination through the soil on which the plant is growing [15], *Staphylococcus aureus* is found in soil, water, and air and causes staphylococcal food poisoning [16], *Clostridium perfringens* is found frequently in soil, feces, and normal intestinal flora [17], *Bacillus cereus* is found in soil, vegetation, and food and causes intestinal illness with nausea, vomiting, and diarrhea; the soil is also the main habitat of *Listeria monocytogenes* and plays a pivotal role in the transmission of these bacteria from soil to plants and animals [18], and *C. botulinum* exists in soil, river, and sea and produces toxins in food.

Similar to the previously mentioned bacteria, *Y. enterocolitica* causes a foodborne zoonotic disease called yersiniosis, which is the 3rd most significant disease in Europe, with 6823 confirmed human cases in 2017, as stated in the latest report of the European Food Safety Authority (EFSA). As it is a zoonotic disease, which means it is transmissible from animals to humans, the human-to-human transmission is scarce. However, some reports have shown that it can be transmitted by infected food handlers, contaminated food, and healthcare-associated

infections (HAI) and causes the highest mortality cases through infected blood [19]. The main clinical implications of yersiniosis include gastroenteritis. The incubation time is 3 to 7 days, and the symptoms generally disappear within 14—21 days.

*Y. enterocolitica* is highly susceptible to many antibiotics, except for penicillin, ampicillin, and first-generation cephalosporins [20]. Different strains of *Y. enterocolitica* are widely recognized to possess resistance to β-lactam antibiotics, including ampicillin and cephalothin. The level and range of resistance are determined by the varying expression and effectiveness of two separate β-lactamases encoded in the chromosomal DNA [21].

Due to the increase in resistance of *Y. enterocolitica* to several antibiotics, it is necessary to compare its genome, study and analyze its ecology and interaction with the previously mentioned soil-based bacteria, and identify essential genes involved in its growth, development, and virulence. Hence, this study aims to find closely related species of *Y. enterocolitica* and shortlisted species through a phylogenetic analysis of the 16S rRNA gene sequence, its unique genes, perform its functional enrichment analysis, and hence, shortlist genes that could be a target for fighting pathogenicity and antimicrobial resistance. The insights of the study will lead to the identification and potential function of unique genes, the specific adaptation of *Y. enterocolitica* to its environment, the identification of virulence factors that are similar among species and the ones that are unique to *Y. enterocolitica*, and the prediction of the mechanism by which the bacterial strain can cause diseases and finally understand the potential risks associated with its presence in the soil and food processing units.

**Methodology.** ***Identification of microorganisms with ecological similarities.*** A comprehensive review of the existing scientific literature was conducted through the PubMed repository (https://pubmed.ncbi.nlm.nih.gov/ ) at the National Center for Biotechnology Information (NCBI) to identify microorganisms with ecological characteristics similar to *Y. enterocolitica*, specifically those that are soil-borne and possess pathogenicity [22].

***Annotating genome assemblies.*** To perform a comparative genome analysis of the shortlisted microorganisms, the genome repository (https://www.ncbi.nlm.nih.gov/genome) at the NCBI database (https://www.ncbi.nlm.nih.gov/) was accessed to acquire the genomic data in FASTA (.fna) format. The genome FASTA sequences of the selected microorganism shown in Table 2 were then annotated using the Prokka base, and genome-annotated files (.gff) were generated for each genome. Prokka (version 1.14.6) is an open-source tool that is widely used for the annotation of microbial genomes [23] and can be accessed through the provided GitHub repository (https://github.com/tseemann/prokka).

***Pan genome analysis.*** To identify the core and accessory genes of the shortlisted bacterial species, the genome annotated files (.gff) generated in the previous step were used to perform a pan-genome analysis using the Roary tool (version 3.11.2, http://sanger-pathogens.github.io/Roary/). It is a high-speed, standalone pan-genome pipeline that takes annotated assemblies, generates a large-scale pan-genome, and identifies core and accessory genes [24]. The analysis resulted in the identification of core and accessory genes.

***Identification of unique genes of Y. enterocolitica.*** To filter out the unique genes of *Y. enterocolitica*, a custom Python script was conditioned to identify only the unique genes specific to *Y. enterocolitica* from the generated output in the previous step. The list of unique genes was evaluated for hypothetical and known proteins. The known proteins were shortlisted for further analysis.

***Pathways analysis of the unique genes of Y. enterocolitica.*** Furthermore, the enrichment

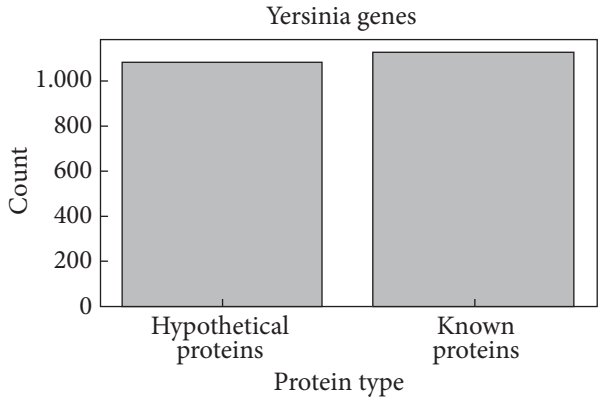


***Fig. 1.*** A bar plot illustrating hypothetical and known proteins found in *Y. enterocolitica.* The x-axis represents the type of proteins in *Y. enterocolitica,* and the y-axis shows the count value

analysis was performed on the shortlisted genes using the KEGG Orthology-Based Annotation System (KOBAS) tool (version 3.0), and a bar plot was generated for the enriched pathways. KOBAS (http://kobas.cbi.pku.edu.cn/) annotates sequences with KEGG Orthology terms and identifies the significantly enhanced pathways among the queried sequences [25].

***Evolutionary relationships and similarities among microorganisms.*** To identify the evolutionary relationship and similarity in characteristics among the microorganisms mentioned above, we selected the 16S rRNA gene as a marker gene. We retrieved its FASTA sequence for each of the bacteria through NCBI.

*Table 1.* **List of top 8 microorganisms with characteristics and pathological properties similar to *Y. enterocolitica's***

| No. | Bacteria | Disease | References |
|---|---|---|---|
| 1 | *Clostridium botulinum* | Botulism | [30] |
| 2 | *Clostridium perfringens* | Food poisoning | [31] |
| 3 | *Bacillus cereus* | Gastroenteritis | [31] |
| 4 | *Listeria monocytogenes* | Gastroenteritis | [31] |
| 5 | *Escherichia coli* | Urinary tract infections | [32] |
| 6 | *Campylobacter jejuni* | Food poisoning | [33] |
| 7 | *Salmonella enterica* | Salmonellosis | [33] |
| 8 | *Staphylococcus aureus* | Food poisoning | [33] |

The 16S rRNA gene is a component of the ribosome found in prokaryotes (bacteria and archaea), and it plays a crucial role in protein synthesis. This gene is highly conserved across different species, but it also contains variable regions that allow for differentiation between closely related organisms [26]. Due to its conserved and variable regions, the 16S rRNA gene has become a widely used tool in phylogenetic and evolutionary studies. Evolutionary relationships can be inferred by comparing the sequences of the 16S rRNA gene among different organisms, and phylogenetic trees can be constructed. This gene serves as a molecular clock, providing insights into the divergence and relatedness of various microbial species over the evolutionary time [27].

To perform the alignment of the 16S rRNA gene sequences, we used Multiple Sequence Comparison by Log-Expectation (MUSCLE) method [30] in Molecular Evolutionary Genetic Analysis (MEGA) software (v. 11.0) and built a Neighbor-Joining tree. It is a fast and efficient method for inferring phylogenetic trees. We built the tree using the Bootstrap method, and the iterations were set to a limit of 1000. It performs replicates of the phylogenetic analysis and generates consensus trees with bootstrap values given to the branches. It merges the clusters or nodes based on pairwise distances. The node represents the common ancestor of the merged clusters [29].

**Results.** ***Identification of microorganisms sharing similar ecological characteristics to Y. enterocolitica.*** A total of 8 microorganisms were found to be reported in the literature that have similar ecology, i.e. soil, and are involved in the prevalence of diseases such as gastroenteritis and resistance to antibiotics such as ampicillin and cephalothin. The list of these bacteria is shown in Table 1.

***Identification of core and accessory genes of Y. enterocolitica using comparative genomic analysis approach.*** The annotated genome assemblies were built in Prokka, and the pan-genome analysis was performed using Roary, which generated 30.937 core and accessory genes.

A distinct set of 2.207 genes exclusive to *Y. enterocolitica* was determined upon gene filtering. The genes were then evaluated, resulting in 1.128 known proteins and 1.079 hypothetical proteins, and a bar plot was generated, as shown in Fig. 1. The hypothetical proteins were filtered out, and the known proteins were further analyzed.

***Functional enrichment analysis.*** To identify the pathways in which the unique genes of *Y. enterocolitica* are involved, we performed a KEGG pathway analysis using the KOBAS tool (Fig. 2). The analysis of the KEGG pathway revealed a significant enrichment of genes associated with the production of secondary metabolites and metabolic pathways in *Y. enterocolitica.* Notably, genes such as ushA, tal, glgC, hemN, leuC, pssA, gcvT, acs, ubiF, putA, speF, asnB, and ilvB were found to be significantly enriched in the biosynthesis of secondary metabolites. Similarly, genes such as galU, glmU, glmS, gcvT, acs, tal, putA, speF, and ilvB were significantly enriched in the biosynthesis of antibiotics. Additionally, genes such as ushA, cpdB, deoB, and cyaB were involved in the synthesis of purine and pyrimidine, which can secrete virulence factors; speF, astD, putA, astE, and aguA were involved in the metabolism of arginine and proline; galE, lacZ, and galU were involved in the galactose metabolism, and asnB, gabD, putA, and glmS genes were involved in glutamate metabolism.

***Evolutionary relationship among soil-borne pathogens.*** We observed a phylogenetic relationship among the species based on the nucleotide sequence of the conserved gene, i.e. 16S rRNA, as listed in Table 2, performed phylogenetic analysis and constructed a Neighbor-Joining tree, shown in Fig. 3. The microorganisms depicted on the same node have similar characteristics, while the ones far distanced from each other represent variability in characteristics. It was observed that *Y. enterocolitica* was closely associated with the two species, i.e. *S. enterica* and *E. coli,* which were connected to a clade. Moreover, *Y. enterocolitica* also showed closeness to *C. jejuni, C. botulinum,* and *C. perfringens* branched from a common node. Among these species, *L. monocytogenes* was out-grouped as it was far distanced in the phylogenetic tree, which shows that it exhibits relatively different characteristics as compared to *Y. enterocolitica*.

**Discussion.** *Y. enterocolitica*, a zoonotic foodborne pathogen, contaminates food products, and its symptoms vary from a mild and temporary form of gastroenteritis to the development of acute mesenteric lymphadenitis [34]. In the last decade, the multi-drug resistance of *Y. enterocolitica* strains has increased due to the use of antibiotics in livestock production. Therefore, conducting a comparative genomic, phylogenetic, and functional analysis of *Y. enterocolitica* is crucial to study its ecology and identify its closely related species and unique genes, which can

*Table 2.* **Table enlisting 16S rRNA gene of the shortlisted 9 microorganisms, their accession IDs, and gene size**

| No. | Bacteria | Accession ID | Gene size |
|---|---|---|---|
| 1 | *Yersinia enterocolitica* | NR_041832.1 | 1461 bp |
| 2 | *Clostridium botulinum* | NR_029157.1 | 1453 bp |
| 3 | *Clostridium perfringens* | NR_121697.2 | 1513 bp |
| 4 | *Bacillus cereus* | NR_074540.1 | 1512 bp |
| 5 | *Listeria monocytogenes* | NR_044823.1 | 1469 bp |
| 6 | *Escherichia coli* | NR_024570.1 | 1450 bp |
| 7 | *Campylobacter jejuni* | NR_041834.1 | 1341 bp |
| 8 | *Salmonella enterica* | NR_041696.1 | 1491 bp |
| 9 | *Staphylococcus aureus* | NR_118997.2 | 1552 bp |

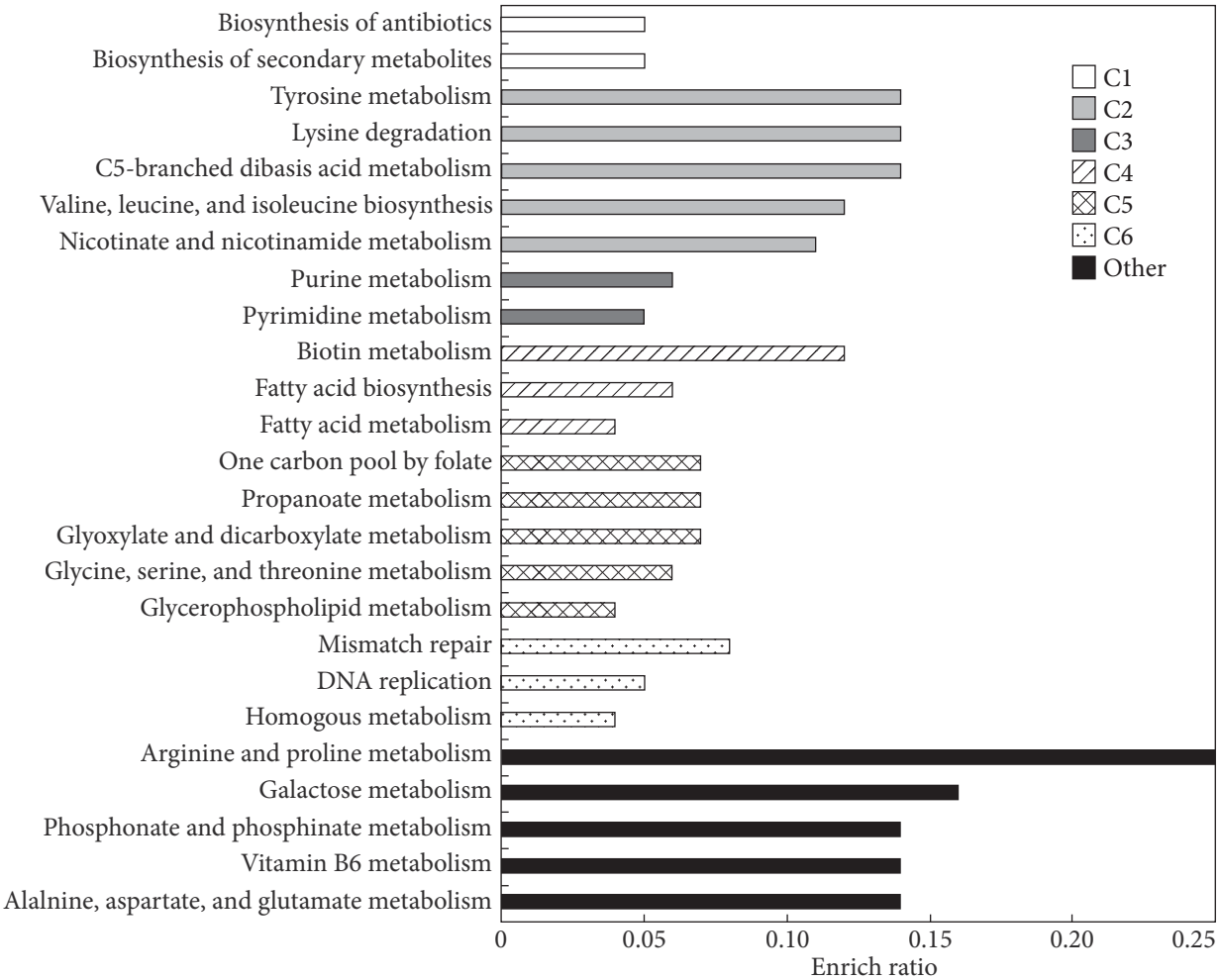


***Fig. 2.*** The figure represents a bar plot. Each row represents an enriched function, and the length of the bar represents the enriched ratio. The Arginine and Proline metabolic pathway was highly enriched with an enrichment ratio > 0.25, and the fatty acid metabolic pathway was slightly enriched, having an enrichment ratio < 0.05. The color of the bar represents different clusters. The top 5 bars with the highest enrichment ratio are displayed for each cluster.

provide insights into novel strategies for controlling pathogenicity and antibiotic resistance.

This study identified eight microorganisms having similar ecological and pathogenic characteristics to those of *Y. enterocolitica,* and pangenomic analysis revealed unique genes specific to *Y. enterocolitica,* such as glmU, ilvB, asnB, gabD, putA, glmS, ushA, cpdB, deoB, and cyaB.

Furthermore, an enrichment analysis of the uniquely identified genes was performed to reveal biological pathways and functions associated with these genes.

It was observed that the galU, glmU, glmS, gcvT, acs, tal, putA, speF, and ilvB genes were found to be significantly enriched in the biosynthesis of antibiotics pathway and were linked with the synthesis of siderophores, activation of osmoregulated periplasmic glucans (OPGs), and resistivity against antibiotics. The pathway mentioned above has been reported to contribute to *Yersinia's* virulence significantly such as OPGs regulating *Yersinia* to form large cell aggregates known as biofilms that are involved in many physiological changes protecting bacteria

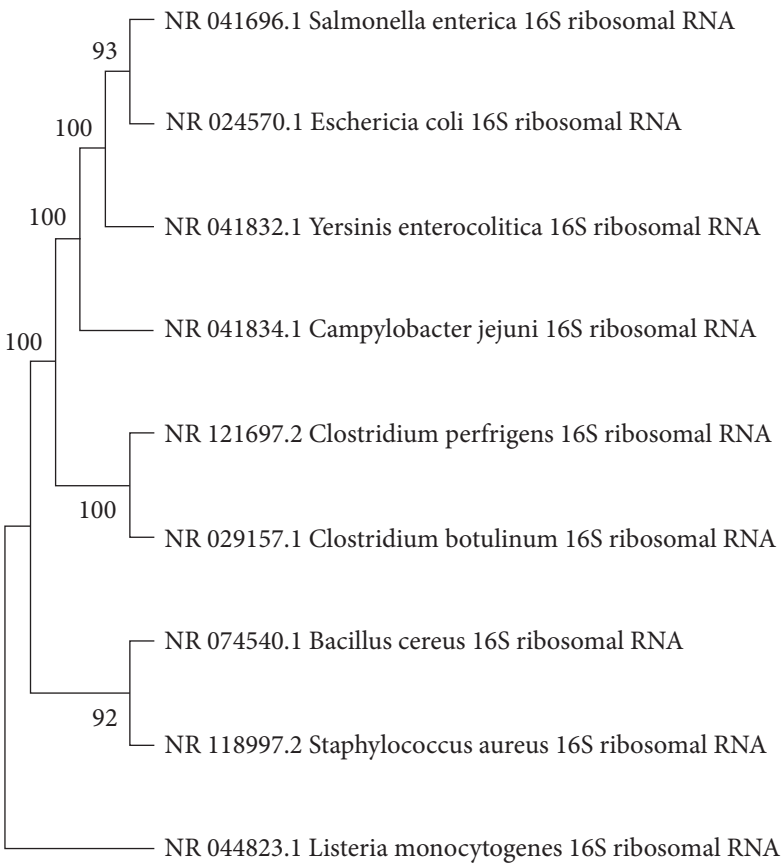


***Fig. 3.*** Figure illustrating a phylogenetic tree of the shortlisted microorganisms where the branches are labeled with microorganism name, 16S rRNA gene, and associated accession ID

against various environmental stresses. Moreover, bacteria that grow in a biofilm are generally more resistant to antibiotics. Hence, OPGs that promote biofilm formation also increase the tolerance of *Y. enterocolitica* to antibiotics [35].

The frequent application of antibiotics in veterinary medicines as growth enhancers in animals such as pigs increases the significance of antimicrobial-resistant *Y. enterocolitica* strains resistant to ampicillin, novobiocin, cefamandole, and bacitracin. Thus, animals are carriers of this zoonotic pathogen and therefore, a surveillance system that can properly monitor *Y. enterocolitica* in slaughterhouses is required [36].

Similarly, asnB, gabD, putA, and glmS genes were found to be involved in the glutamate metabolism pathway, which may balance the flow of nitrogen that is regulated by the FIhD/FIhC complex and is temperature-dependent. Furthermore, it helps in the regulation of motility that helps in the pathogenicity of *Y. enterocolitica* [37].

Additionally, the genes ushA, cpdB, deoB, and cyaB were involved in the synthesis of purine and pyrimidine pathway where the flagellar master component FIhD/FIhC complex acts as a precursor for synthesizing purines and pyrimidines and causes changes in the phenotype of *Y. enterocolitica* such as the temperature at which it grows, synthesis of flagella, and production and secretion of virulence factors responsible for pathogenicity [38, 39]. According to previous studies, *Y. enterocolitica* causes severe difficulties during blood transfusion when preserving red blood cells below 4 °C, thus acting as a pathogen in frozen food [40, 41]. Therefore, this pathway serves as an important ecological factor of *Y. enterocolitica*.

Moreover, ushA produces byproducts uridine monophosphate and glucose-1-phosphate by the degradation of uridine diphosphate glucose, which is then utilized by the cell, deoB is involved in the transfer of phosphate group between C1 and C5 carbon atoms of pentose whereas cpdB breaks ribonucleic acid (RNA) by transforming 2',3'-cyclic nucleotide into a 3' nucleotide and then converts it to its correlating nucleoside and phosphate forms [42]. Collectively, these genes are involved in the synthesis of purine and pyrimidine, which are further associated with the ecology and pathogenicity of bacteria as described above.

Additionally, phylogenetic analysis was performed to identify the evolutionarily related species of *Y. enterocolitica*. A phylogenetic tree analysis is used as a method for the classification of organisms where 16S rRNA is most frequently used [43]. In our phylogenetic analysis of 16S rRNA, *E. coli*, *C. jejuni,* and *S. enterica* were found to be closely related to *Y. enterocolitica,* thereby showing similar ecological properties and pathogenic characteristics; as mentioned previously, these bacteria cause gastrointestinal diseases, spread in the environment through soil, manure, and slaughterhouses, and are resistant to antibiotics [44]. Moreover, soil serves as a breeding ground for the genetic interactions among bacteria and exchange of genetic material takes place there, as antibiotic resistance genes are present in mobile genetic elements (MGEs) like plasmids and transposons, therefore they are able to move between bacteria of different phylogenetic descendants, and these bacteria are also observed in the intestinal tracts of hosts, thereby causing gastrointestinal diseases similar to *Y. enterocolitica* [45].

Hence, it was revealed through these results that *Y. enterocolitica* is similar to *E. coli*, *C. jejuni,* and *S. enterica* in terms of ecology, soilborne pathogenicity, and antimicrobial resistance which is linked directly or indirectly with the synthesis of purine and pyrimidine and play a role in the production of biofilm and intestinal colonization, thus causing foodborne gastroenteritis and acting as a precursor of metabolic pathways [46], respectively.

Therefore, in a perspective, the ushA, cpdB, and deoB genes involved in synthesizing purines and pyrimidines should be deleted, and thus the modified intestinal pathogen *Y. enterocolitca* should be considered for manufacturing live attenuated vaccines that can be proved to control pathogenicity and antimicrobial resistance as these genes are linked to the ecological changes responsible for developing the pathogenicity of *Y. enterocolitic*a and similar microorganisms.

**Conclusions.** This research emphasizes the importance of comprehensively analyzing *Y. enterocolitica*, a zoonotic food-borne pathogen. The study identified unique genes specific to *Y. enterocolitica* through a pan-genomic analysis associated with various biological pathways and functions. Enrichment analysis revealed the significant involvement of certain genes in the biosynthesis of antibiotics pathways and resistance against antibiotics. The presence of *Y. enterocolitica* in animals and the use of antibiotics in livestock production contribute to the emergence of antimicrobial-resistant strains, necessitating a surveillance system in slaughterhouses. Genes involved in glutamate metabolism, purine, and pyrimidine synthesis play crucial roles in *Y. enterocolitica*'s pathogenicity and adaptation in different environments. Phylogenetic analysis showed its relatedness to species like *E. coli*, *C. jejuni*, and *S. enterica*, sharing ecological properties, pathogenic characteristics, and antibiotic resistance. Genetic material exchange among bacteria contributes to the spread of resistance genes and gastrointestinal diseases. Deleting specific genes involved in purine and pyrimidine synthesis and creating a live attenuated vaccine can be a potential strategy for controlling *Y. enterocolitica*'s pathogenicity and antimicrobial resistance. Understanding relationships with related microor-

ganisms is crucial for future research and effective management approaches.

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## ГЕНОМІКА, ФІЛОГЕНЕТИЧНИЙ ТА ФУНКЦІОНАЛЬНИЙ АНАЛІЗ *YERSINIA ENTEROCOLITICA*, ЗБУДНИКА ЗАХВОРЮВАНЬ ШЛУНКОВО-КИШКОВОГО ТРАКТУ, ПОРІВНЯНО З ІНШИМИ ГРУНТОВИМИ БАКТЕРІЯМИ, ЩО ВИКЛИКАЮТЬ ХВОРОБИ

*Yersinia enterocolitica* — патогенний мікроорганізм, що передається через заражену їжу, викликає захворювання шлунково-кишкового тракту та запалення лімфатичних вузлів. Зростання кількості стійких до лікування штамів *Y. enterocolitica* становить серйозну загрозу для здоров'я населення, що зумовлює необхідність дослідження його екології, споріднених видів та унікальних генів, пов'язаних із вірулентністю та стійкістю до антибіотиків. У цьому дослідженні було ідентифіковано вісім мікроорганізмів, подібних до *Y. enterocolitica*, та проведено пангеномний аналіз, який виявив специфічні гени, притаманні лише *Y. enterocolitica*. При аналізі цих генів виявлено їхню участь у продукції сидерофорів, осморегуляторній активації периплазматичного глюкану та антибіотикорезистентності. Ці шляхи, разом з утворенням біоплівки та підвищенням резистентності до антибіотиків, є життєво важливими для забезпечення вірулентності ієрсиній. Крім того, специфічні гени, пов'язані з метаболізмом глутамату, регуляцією азоту, рухливістю, синтезом пуринів і піримідинів, можуть сприяти патогенності *Y. enterocolitica*, росту та виробленню факторів вірулентності. Філогенетичний аналіз продемонстрував еволюційний зв'язок між *Y. enterocolitica* та подібними видами, такими як *Escherichia coli*, *Campylobacter jejuni* та *Salmonella enterica*, що підтвердило необхідність моніторингу *Y. enterocolitica* на бойнях через наявність тварин-носіїв. Результати дослідження проливають світло на екологічні фактори та генетичні механізми, що зумовлюють патогенність та стійкість *Y. enterocolitica* до антибіотиків. Потенційною стратегією контролю патогенності та стійкості до протимікробних препаратів може стати націлювання на гени, що беруть участь у синтезі пуринів та піримідинів, такі як ushA, cpdB та deoB. Розуміння взаємозв'язків та генетичних взаємодій між *Y. enterocolitica* та спорідненими мікроорганізмами має вирішальне значення для розробки ефективних підходів до епідеміологічного нагляду та лікування в майбутньому.

***Ключові слова:*** *Yersinia enterocolitica, харчовий патоген,* антибіотикорезистентність, пангеномний аналіз, екологія.