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CHARACTERIZATION OF NUTRIENT UPTAKE MECHANISMS OF RESISTANT BACTERIA AND SEARCH FOR INHIBITORS USING BIOINFORMATICS

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ABSTRACT. *Acinetobacter baumannii* and *Klebsiella pneumoniae* are gram-negative pathogens known for their antibiotic resistance, employing mechanisms of cellular communication and nutrient uptake mediated by ABC transporters. The substrate-binding proteins (SBPs) of these transporters play a crucial role in transport across the membrane and the absorption of nutrients, such as polyamines and taurine, which are essential for bacterial survival. This study aimed to characterize and predict the structures of SBPs that transport taurine and polyamines, as well as evaluate potential interactions with ligands and inhibitors. The FASTA sequences of PotD and TauA from *A. baumannii*, as well as PotD, PotF, and TauA from *K. pneumoniae*, were obtained from databases and analyzed using specific software to predict structure and interactions. Molecular docking performed on three-dimensional models of the proteins revealed favorable free energy for the binding of the proteins to their respective ligands, corroborating data from the literature; in particular, PotF from *K. pneumoniae*was identified as a dual transporter of putrescine and spermidine. Additional tests showed that vigabatrin and GABA have the potential to interact with the TauA proteins, while cystamine was found to interact with PotD from *A. baumannii*. These results highlight the feasibility of using these molecules as targets to inhibit nutrient uptake in resistant bacteria, paving the way for the development of new antimicrobials. Identifying these interactions may open new avenues for treating infections caused by these pathogens, contributing to more effective therapeutic strategies in combating bacterial resistance.

Keywords: Bioinformatics; Antibiotic Resistance; Nutrient transport; Molecular Docking; Targeted therapy.

RESUMO. *Acinetobacter baumannii* e *Klebsiella pneumoniae* são patógenos gram-negativos conhecidos por sua resistência a antibióticos, utilizando mecanismos de comunicação celular e captação de nutrientes mediados por transportadores do tipo ABC. As proteínas de ligação ao substrato (SBPs) desses transportadores desempenham um papel crucial no transporte através da membrana e na absorção de nutrientes, como poliaminas e taurina, essenciais para a sobrevivência bacteriana. Este estudo teve como objetivo caracterizar e predizer as estruturas das SBPs que transportam taurina e poliaminas, além de avaliar possíveis interações com ligantes e inibidores. As sequências FASTA de PotD e TauA de *A. baumannii*, bem como PotD, PotF e TauA de *K. pneumoniae*, foram obtidas em bancos de dados e analisadas por meio de softwares específicos para predizer estrutura e interações. A ancoragem molecular realizada com os modelos tridimensionais das proteínas revelou energia livre favorável para a ligação das proteínas aos seus respectivos ligantes, corroborando dados da literatura; em particular, PotF de *K. pneumoniae* foi identificada como um transportador duplo de putrescina e espermidina. Testes adicionais mostraram que vigabatrina e GABA têm potencial para interagir

com as proteínas TauA, enquanto a cistamina foi encontrada como interagente com PotD de *A. baumannii*. Esses resultados destacam a viabilidade de usar essas moléculas como alvos para inibir a captação de nutrientes em bactérias resistentes, abrindo caminho para o desenvolvimento de novos antimicrobianos. A identificação dessas interações pode abrir novas possibilidades para o tratamento de infecções causadas por esses patógenos, contribuindo para estratégias terapêuticas mais eficazes no combate à resistência bacteriana.

Palavras-chave: Bioinformática; Resistência a antibióticos; Transporte de nutrientes; Docking molecular; Terapia direcionada.

INTRODUCTION

Bacteria are becoming increasingly resistant to conventional antibiotics, and this has been documented in the scientific literature. It is a real concern that in the coming decades, the efficacy of today's drugs may be compromised by bacterial resistance. This is concerning because we may see an increase in mortality rates (Ribeiro, 2023).

In most cases, gram-negative bacteria such as *Acinetobacter baumannii* and *Klebsiella pneumoniae* exhibit high levels of resistance to antibiotics. *K. pneumoniae* is known to cause infections of the urinary tract, respiratory tract, central nervous system, bloodstream, among other areas. The resistance mechanisms of *K. pneumoniae* include ESBL+ (extended-spectrum β-lactamase) (Stojowska-Swędrzyńska, 2021), with multiple resistance patterns. This microorganism is involved in outbreaks of hospital-acquired infections in intensive care unit patients worldwide (Dienstmann, 2010).

A. baumannii is considered carbapenem-resistant (Bartal, 2022), showing a colonization profile in hospital environments with highly virulent gram-negative cases. The ability to form biofilms allows the microorganism to secure itself by absorbing various nutrients, contributing to antibiotic resistance and extending bacterial survival (Vieira; Picoli, 2015). There are also indispensable nutrients for bacterial survival, such as polyamines (PAs), which are present in many cell types, from microorganisms to plants and animals. They have low molecular weight and are inorganic cations with a high capacity to interact with negatively charged molecules such as deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), regulating cellular growth and proliferation (Igarashi; Kashiwagi, 2000). The uptake of polyamines is mediated by specific protein complexes responsible for the internalization of these molecules. Another nutrient used by bacteria is taurine, a biogenic organic sulfur molecule essential for sulfur assimilation, which is necessary for the biosynthesis of amino acids and cofactors. Taurine absorption can compensate for the sulfur deficiency of multiple bacteria (Nishikawa et al., 2018; Qu et al., 2019; Pereira, 2017; Kertsz, 2000).

The utilization of these nutrients by microorganisms is enabled by the presence of transport proteins across the membrane, such as the ABC transporter family (ATP-binding cassette). These proteins can recognize organic and inorganic solutes of biological interest and transporting them across the membrane through active transport. ABC transporters share a common organizational structure: two nucleotide-binding domains that use ATP for energy (ATPases) and two transmembrane domains, or permeases, that form pores in the membranes. Involved in nutrient absorption, substrate-binding proteins (SBPs), or periplasmic proteins, are a class of proteins with a substrate-binding domain that transports essential nutrients (Pereira, 2017; Araújo et al., 2013; Kertsz, 2000; Berntsson et al., 2010). Deletion of these proteins in *Xanthomonas citri* revealed impairment in biofilm production, cell growth and changes in symptoms caused by bacterial infection (Sampaio et al, 2017).

Bioinformatics plays a crucial role in analyzing, processing, and organizing large volumes of biological information, where manual analysis would be unfeasible. Specific tools

developed for interpreting biological information and solving problems contribute significantly to applying informatics and computer science in the biological context. This approach allows us to gain precise insights into the structure and function of proteins, understand genetic phenomena, design modified macromolecules for clinical or industrial use, and assemble small molecules capable of modulating biological function by inhibition or enhancement (Altman, 1998). This understanding is critical to identifying bacterial resistance mechanisms and contributes to the development of new antibiotics, vital in the search for effective therapeutic solutions to the growing challenge of bacterial resistance (Lybrand, 1995).

METHODS

Search for ABC Transporters in A. baumannii and K. pneumoniae

The nucleotide sequences encoding the polyamine and taurine ABC transporter proteins of *Acinetobacter baumannii* and *Klebsiella pneumoniae*, as well as their amino acid sequences in FASTA format, were retrieved from the KEGG database v.107.0 (Kyoto Encyclopedia of Genes and Genomes), which is an important source of genomic data. Promoter regions were identified using Softberry BPROM (Salamov; Solovyev, 2011).

Protein Identification

Using the amino acid sequences, permease proteins were characterized with the TMHMM online program v.1.0.42 (Krogh et al., 2001), identifying the hydrophobic regions typical of transmembrane proteins (Krogh et al., 2001). ATPase proteins were identified using the SMART Domain v.9.0 - Simple Modular Architecture Research Tool (Letunic et al., 2021), detecting conserved domains such as ATP domains (AAA). SBP proteins were identified using the SignalP 5.0 program (Armenteros et al., 2019) to detect the signal peptide responsible for protein translocation across the plasma membrane to function locally in the periplasm (Goodswen; Kennedy; Ellis, 2012). Sequence alignments were performed using Clustal Omega (Larkin et al., 2007).

Modeling and Molecular Docking

Secondary structure prediction was performed using the Psipred program v.4.0 (McGuffin et al., 2000), and the three-dimensional protein structure modeling was carried out using ColabFold v.1.5.5 (Mirdita et al., 2022), which integrates homology and *de novo* methods to rapidly predict atomic-level 3D protein models. Cavities and potential protein interaction regions were identified using the KVFinder program v.1.2.0 (Guerra et al., 2023) and GraSP (Santana et al., 2020). Conserved amino acid positions in the binding pocket were determined, allowing the identification of amino acids known to interact with ligands, as described in the literature.

Molecular docking was performed using Dockthor v.2.0 (Guedes, 2021), an online tool that estimates interactions between proteins and molecules, as well as available free energy (association between molecules), providing an assessment of binding free energy (Guedes, 2021). The quality metric lDDT (Local Distance Difference Test) was used to validate the models. Potential SBP ligands and inhibitors for docking were identified through literature reviews and the Drugbank database v.5.1.12 (Wishart et al., 2018).

RESULTS AND DISCUSSION

ABC transporters for polyamines and taurine in *Acinetobacter baumannii* and *Klebsiella pneumoniae* were identified through the KEGG database. The genes encoding these transporters, as shown in Table 1, are organized into operons, a pattern commonly observed across various bacterial species. For instance, the polyamine transporter is similarly organized in *Xanthomonas citri* (Cremonesi, 2021) and *Staphylococcus* species (Silva et al., 2023), while the taurine transporter follows the same arrangement in *Escherichia coli* (Van Der Ploeg et al., 1997).

Table 1. Organization of data and information collected by Kegg of *Acinetobacter baumannii* and *Klebsiella pneumonia*e. The category of proteins was divided into transmembrane domain (TMD), nucleotide-binding domain (NBD), substrate-binding protein (SBP) and unspecified.

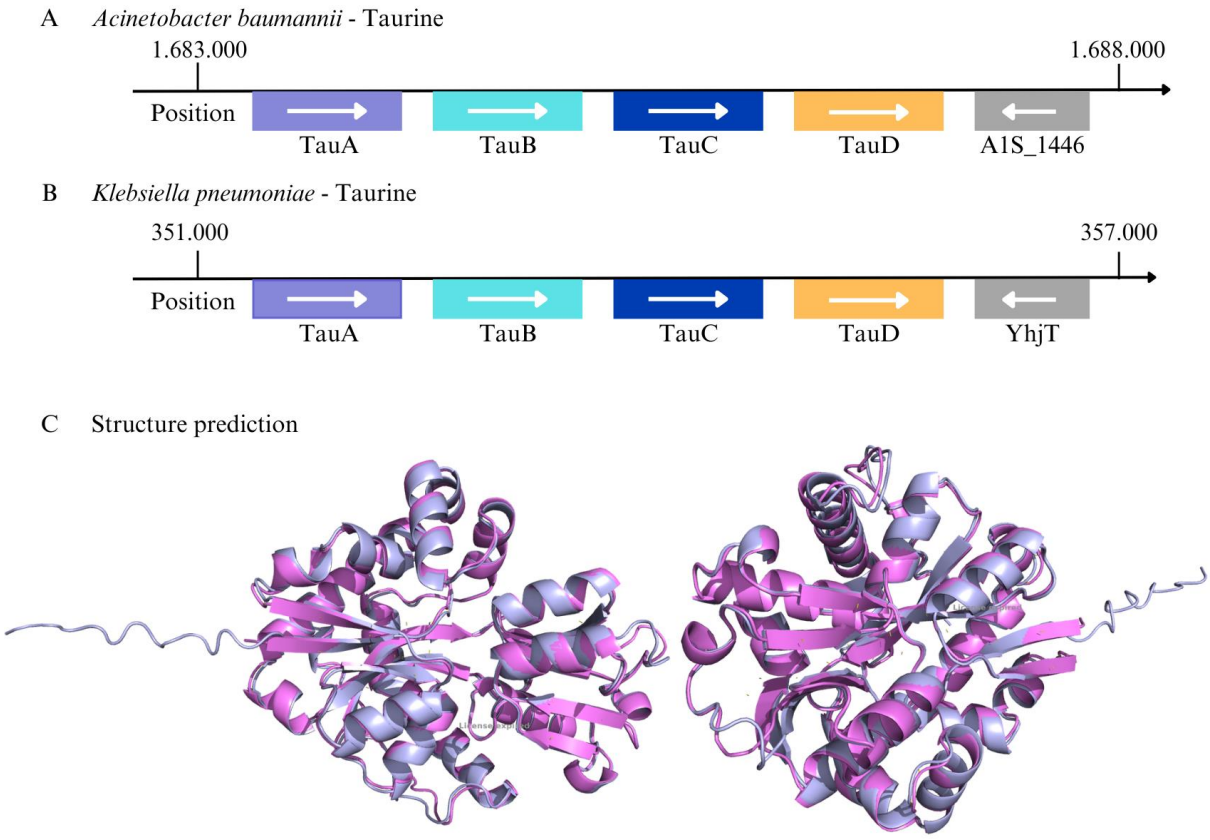
Organism	Nutrient	KEGG Code	Protein	Category
A. baumannii	Polyamine	A1S_1359	PotD	SBP
		A1S_1360	PotA	NBD
		A1S_1361	-	Unspecified
		A1S_1362	PotC	TMD
	Taurine	A1S_1442	TauA	SBP
		A1S_1443	TauB	NBD
		A1S_1444	TauC	TMD
K. pneumoniae	Spermidine	KPN_00311	TauA	SBP
		KPN_00312	TauB	NBD
		KPN_00313	TauC	TMD
		KPN_01129	PotD	SBP
		KPN_01130	PotC	TMD
		KPN_01131	PotB	TMD
		KPN_01132	PotA	NBD
	Putrescine	KPN_00885	PotF	SBP
		KPN_00886	PotG	NBD
		KPN_00887	PotH	TMD
		KPN_00888	PotI	TMD

Genomic analysis revealed that transmembrane domains (TMD) of the taurine transporter is homodimeric and encoded by the *tauC* gene in the operon (Figure 1) while polyamine transporters are heterodimeric, composed of *potB* and *potC* in the spermidine transporter, and *potH* and *potI* in the putrescine transporter (Figure 2). The TMD in ABC transporter are predominantly composed of hydrophilic amino acids, arranged in alpha helices that facilitate interactions with lipid bilayers (Guna, 2018). According to Alam (2023), these helices form transmembrane pores, enabling substrate movement into the cytoplasm. Typically, bacterial TMDs consist of 6 to 10 alpha helices, though complete transporter systems may contain up to 20 segments. In type I bacterial importers, specific TMD regions play a key role in substrate

binding, as demonstrated in crystallographic and mutagenesis studies (Alam, 2023). By examining the amino acid sequences from the FASTA files, proteins such as PotI (*kpn*), PotC (*acb*), PotC (*kpn*), PotB (*kpn*), PotH (*kpn*), TauC (*kpn*), and TauC (*acb*) were identified as possessing transmembrane domains (Figure 3).

Notably, polyamine transporters demonstrate structural diversity among species, potentially affecting their efficiency in nutrient uptake. For instance, the PotC (*acb*) protein showed significant structural differences compared to other transmembrane proteins, with a total of 12 transmembrane alpha helices. This deviation was similarly observed in other organisms, as Dawson and Locher (2006) identified analogous structural differences in ABC transporters. These variations likely reflect adaptations to species-specific nutrient transport needs, providing insights into the broader functionality of ABC transport systems in bacterial pathogens.

Figure 1. Schematic representation of the results generated by the Kegg database, showing the possible genetic organization of *Acinetobacter baumannii* (A) and *Klebsiella pneumoniae* (B), represented by the regions where the genes encoding the ABC transporter proteins for taurine are located. Alignment of predictive results of the three-dimensional structures of the TauA proteins from *A. baumannii* and *K. pneumoniae* (C). The genes encoding the ABC transporter proteins for taurine in *A. baumannii* are organized into an operon that includes the TauA gene (purple), TauB (light blue), and TauC (dark blue). Genes outside the operon are highlighted in gray and are transcribed in the reverse orientation (A). Similarly, the genes encoding the ABC transporter for taurine in *K. pneumoniae* are organized in an operon that includes the TauA gene (purple), TauB (light blue), and TauC (dark blue), with genes outside the operon also highlighted in gray (B). The structural prediction results of the TauA proteins from *A. baumannii* (purple) and *K. pneumoniae* (pink) were visualized after alignment of the two proteins (C).



The SMART Domain program identified the AAA domain in the proteins PotA (*A. baumannii*), TauB (*A. baumannii*), TauB (*K. pneumoniae*), PotA (*K. pneumoniae*), and PotG (*K. pneumoniae*), a hallmark of the nucleotide-binding domains (NBDs) in ABC transporters.

This finding suggests that these proteins depend on ATP hydrolysis to perform specific cellular functions (Jones, 2013).

SBPs are essential components of ABC transporters, characterized by the presence of an N-terminal signal peptide, which is cleaved upon the protein reaching its destination (Von Heijne, 1990). Using the SignalP program, a signal peptide was identified in the TauA proteins of *K. pneumoniae* and *A. baumannii* between amino acids 1 and 24. For PotD from *A. baumannii* and PotF from *K. pneumoniae*, the signal peptide was located between amino acids 1 and 26, while for PotD from *K. pneumoniae*, it was identified between amino acids 1 and 23. These results confirm that the analyzed proteins are SBPs. Their sequences were further utilized for three-dimensional modeling, reinforcing their classification as secreted proteins.

Figure 2. Schematic representation of the results generated by the KEGG database, illustrating the potential genetic organization of *Acinetobacter baumannii* and *Klebsiella pneumoniae*. The regions where the coding genes of ABC transporter proteins are located are highlighted (A, B, and C). Prediction results of the three-dimensional structures of the PotD and PotF proteins from *A. baumannii* and *K. pneumoniae* are aligned (D). The genes identified as encoding ABC transporters of polyamines in *A. baumannii* are organized into an operon that includes the PotD gene (purple), PotA (light blue), and PotC (dark blue), with genes not part of the operon highlighted in red (A). In *K. pneumoniae*, the genes coding for ABC transporters of polyamines are organized into two operons: one includes the PotD gene (purple), PotC, PotB (dark blue), and PotA (light blue) (B), while the other operon includes the PotF gene (purple), PotG, PotH (light blue), and PotI (dark blue), with genes not part of the operon highlighted in gray (C). The prediction results for the structural proteins PotD from *A. baumannii* (purple), PotD from *K. pneumoniae* (yellow) and PotF from *K. pneumoniae* (orange) demonstrate their similarity following alignment (D).

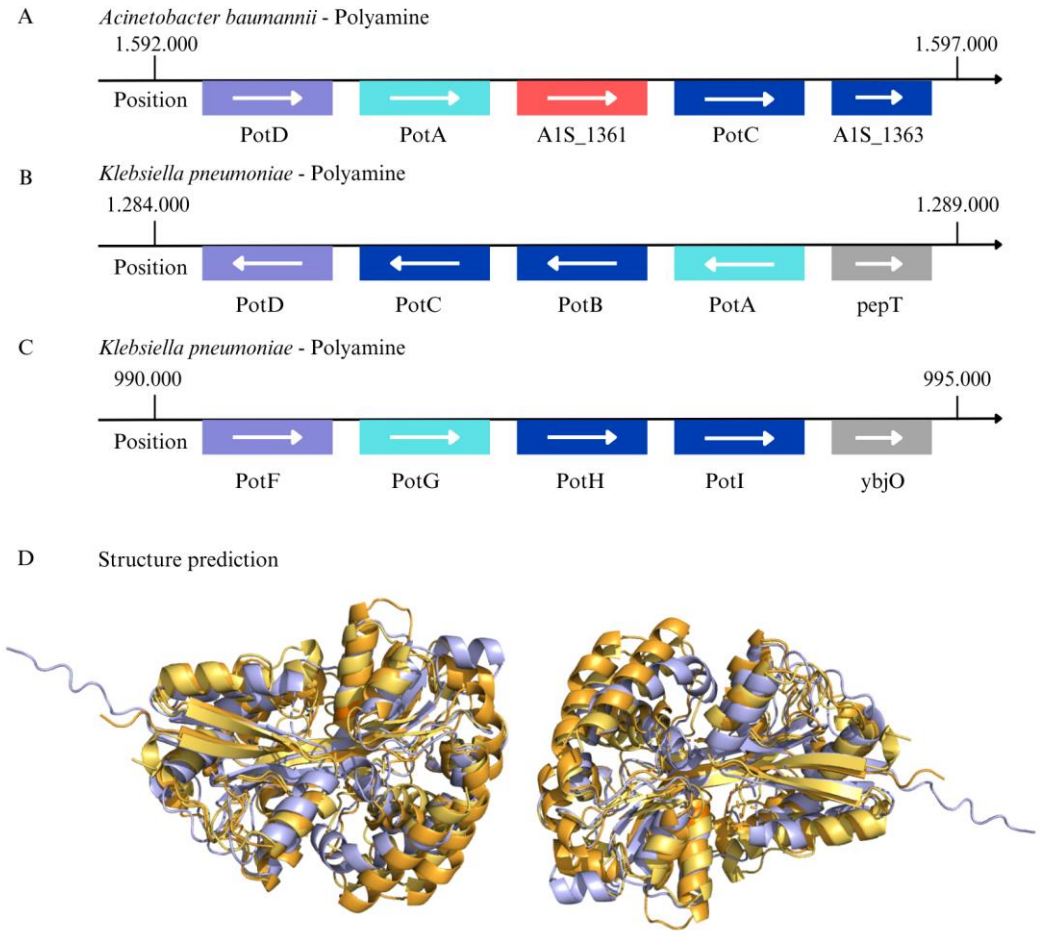
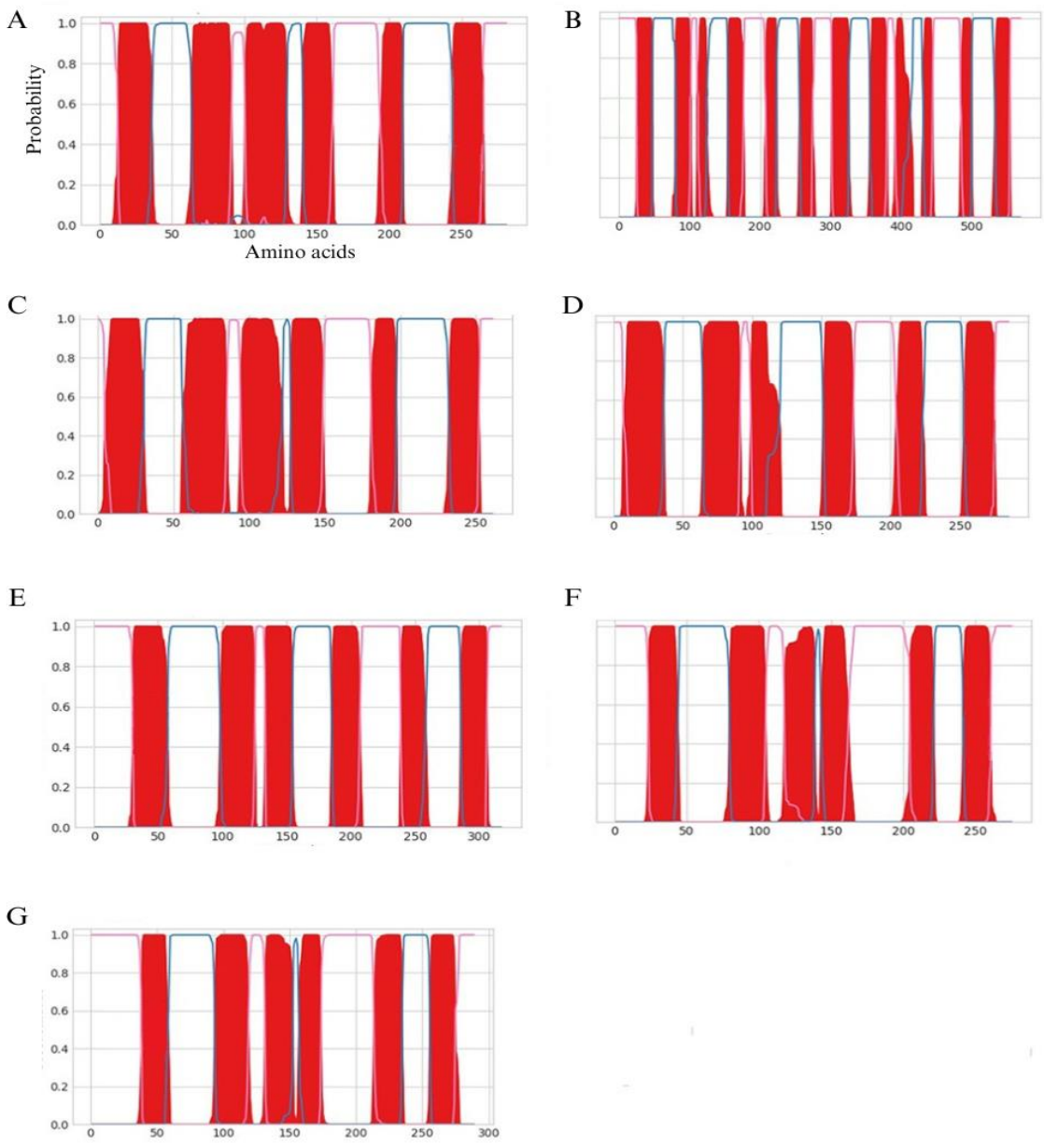


Figure 3. The TMHMM analysis highlights the predicted transmembrane regions in the protein sequences. The *x*-axis represents the position of amino acids within the sequence, while the *y*-axis indicates the probability of the prediction. The analyzed proteins include (A) PotI (*K. pneumoniae*), (B) PotC (*A. baumannii*), (C) PotC (*K. pneumoniae*), (D) PotB (*K. pneumoniae*), (E) PotH (*K. pneumoniae*), (F) TauC (*K. pneumoniae*), and (G) TauC (*A. baumannii*). Transmembrane regions are shown in red, cytoplasmic regions in pink, and extracellular regions in blue. These transmembrane regions classify the proteins as TMDs. Most of the analyzed proteins contain 6 to 10 transmembrane alpha helices, except PotC (*A. baumannii*), which possesses 12 transmembrane alpha helices.



The three-dimensional model of the SBP proteins is presented alongside a cavity analysis of potential interactions within the binding pocket (Figure 4). Additionally, the lDDT (Local Distance Difference Test) was utilized to evaluate the generated quality metric factor. This robust tool exhibits a high correlation with model evaluation, and the automated method provides visualization of the protein model, with colors indicating the model's reliability (Mariani et al., 2013). To establish the relationship between the amino acid sequences of proteins found in other organisms, the models were compared with protein structures previously

solved by X-ray crystallography. The structures compared include PotD (PDB ID: 1POT), PotF (PDB ID: 6YE8), and TauA (PDB ID: 6ST0) from *Escherichia coli* (*eco*), as shown in Table 2.

Table 2. Description of SBPs described in the scientific literature as polymine and taurine transporters by PDB (Protein Data Bank). The alignment results with TauA, PotD and PotF are shown by the perception of query coverage and identity.

Organism	PDB Code	Aligned to	Query Cover	Percentual Ident
eco	6ST0	TauA (*acb*)	94%	55,89%
eco	6ST0	TauA (*kpn*)	99%	88,89%
eco	6YE8	PotD (*acb*)	41%	25%
eco	1POT	PotD (*kpn*)	93%	91,69%
eco	1POT	PotF (*kpn*)	92%	91,86%

The interactions between SBPs and their respective ligands (polyamines and taurine) were evaluated to support their proposed roles in the transport of these nutrients. Additionally, potential interactions of the proteins with molecules such as cystamine and acetyl-spermine were observed. Cystamine is a molecule that likely binds to putrescine (Hoet, 1993). Studies involving conjugated acetyl-spermine suggest that this molecule may inhibit polyamines (Burns, 2001). GABA is known to be a substrate for TauT (the taurine transporter). A study by Rasmussen et al. (2016) analyzed the ability of GABA mimetics to interact with TauT, correlating absorption rates with molecular data. It was shown that GABA mimetics, such as vigabatrin (an antiepileptic drug), inhibit taurine uptake in hyperosmotic mouse SKPT renal cells. There is limited information regarding GABA metabolites in relation to ABC transporters in bacteria. Therefore, the relationship between GABA, vigabatrin, and TauA proteins of *K. pneumoniae* and *A. baumannii* was evaluated. Results indicated potential interactions for both molecules based on the free energy results from molecular docking.

The analysis results suggested that the proteins are the most potentially specific transporters, as described. Furthermore, the analysis was conducted with other molecules on the proteins to provide functional suggestions that may impede nutrient transport (Figure 5). The PotD and TauA proteins from *A. baumannii* exhibited free energies of -40.278 kcal/mol and -42.029 kcal/mol, respectively, when interacting with spermidine and taurine. For *K. pneumoniae* transporters, the calculated free energies were as follows: PotD (-14.582 kcal/mol), PotF (-25.551 kcal/mol with putrescine and -30.474 kcal/mol with spermidine), and TauA (-39.957 kcal/mol) interacting with spermidine, putrescine, and taurine, respectively. The interactions between SBPs and other molecules displayed significant free energy values and conserved amino acids that interact in the sequences (Table 3). When compared to described and solved proteins in the scientific literature, this indicates a high probability of transporting these respective nutrients.

Molecular docking has shown that other potential amino acids can realize interactions in transport. In TauA from *K. pneumoniae*, amino acids S^{78}, S^{83} e N^{248} were shown to interact with GABA molecules. In the *A. baumanii* TauA protein analyzed with vigabatrin, an interaction with V^{23} was seen. In this docking analysis, additional potential amino acids were identified that interact during transport (Table 3). In the PotD protein from *A. baumannii*, the amino acids A^{17}, D^{44}, S^{45} and E^{237} were shown to interact with cystamine. were found to interact with cystamine. Similarly, in the PotD protein from *K. pneumoniae*, the amino acids involved in the interaction with cystamine were D^{88}, Q^{90} and T^{272}.

Figure 4. Three-dimensional structure of the SBP protein. The amino acids that interact most with ligands are highlighted in the box on the right. The binding pocket of each protein, as visualized by the KVFinder program, is shown in gray. (A) PotD protein from *A. baumannii*; (B) PotF protein from *K. pneumoniae*; (C) PotD protein from *K. pneumoniae*; (D) TauA protein from *A. baumannii*; (E) TauA protein from *K. pneumoniae*. The model proteins are displayed with the corresponding amino acids that are most like the solved model. The binding pocket is indicated in the box on the right.

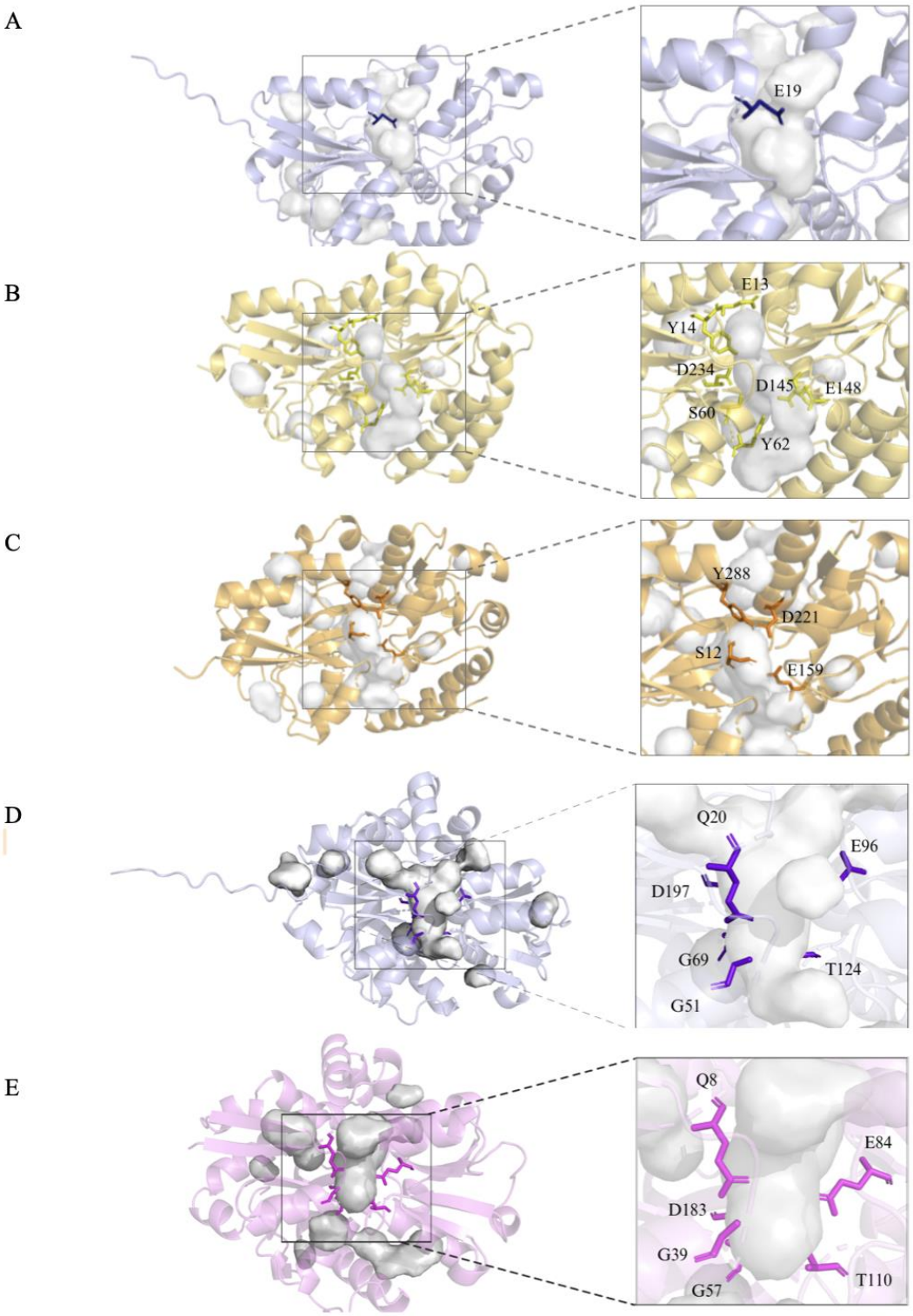


Figure 5. Interaction between pocket amino acids and possible ligands: spermidine (SPD), cystamine (CYS) and putrescine (PUT), taurine (TAU), vigabatrin (VIG) and GABA. Free energy values (kcal/mol) below each interaction. (A) Proteina PotD from *A. baumannii*; (B) PotF from *K. pneumoniae*; (C) PotD from *K. pneumoniae*; (D) TauA from *A. baumannii*; (E) TauA from *K. pneumoniae*.

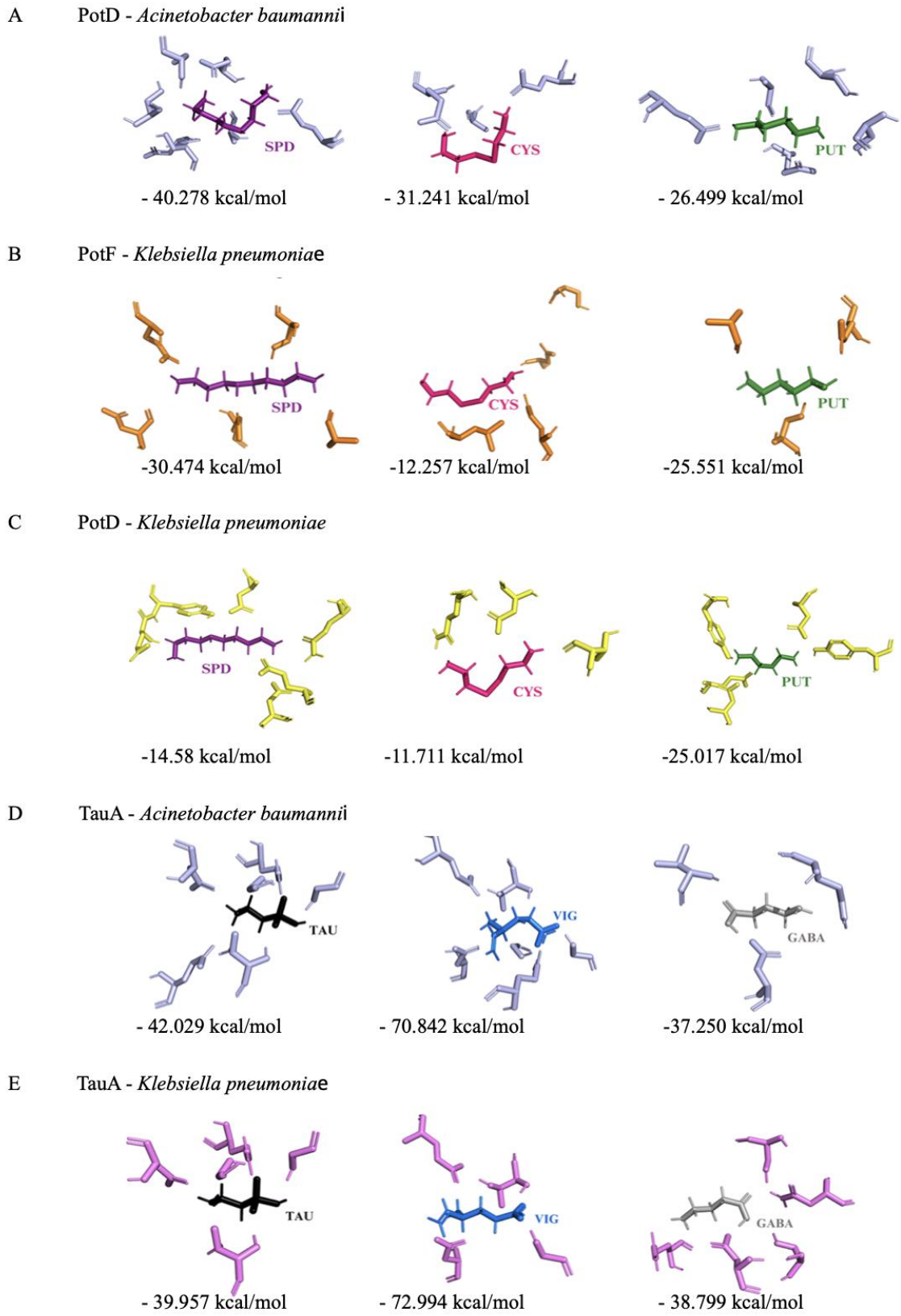


Table 3. Relation of identified amino acid docking sites that may interact with taurine, GABA and vigabatrin in TauA, PotD and PotF from *A. baumannii* (*acb*) and *K. pneumoniae* (*kpn*). Correlated with amino acids of *E. coli* roteins (*eco*) involved in taurine and polyamines transport described in the scientific literature.

Protein	Organism	Molecule	Interacting amino acids							
TauA	*eco*	Taurine	Q^{30}	G^{61}	G^{79}	E^{106}	T^{132}	D^{205}	-	-
	acb	Taurine	Q^{20}	G^{51}	G^{69}	E^{96}	T^{124}	D^{197}	-	-
		GABA	Q^{20}	-	-	-	-	D^{197}	-	-
		Vigabatrin	Q^{20}	G^{51}	G^{69}	E^{96}	T^{124}	D^{197}	-	-
	kpn	Taurine	Q^{8}	G^{39}	G^{57}	-	T^{110}	D^{183}	-	-
		GABA	Q^{8}	-	-	-	-	D^{183}	-	-
		Vigabatrin	-	G^{39}	-	E^{84}	T^{110}	D^{183}	-	-
PotD	*eco*	Spermidine	E^{36}	Y^{37}	S^{83}	Y^{85}	D^{168}	E^{171}	D^{257}	Q^{327}
	acb	Spermidine	E^{19}	-	-	-	-	-	-	-
		Putrescine	E^{19}	-	-	-	-	-	-	-
		Cystamine	E^{19}	-	-	-	-	-	-	-
	kpn	Spermidine	E^{13}	Y^{14}	-	-	D^{145}	-	D^{234}	-
		Putrescine	-	Y^{14}	-	-	D^{145}	E^{148}	D^{234}	-
		Cystamine	-	Y^{14}	S^{60}	Y^{62}	D^{145}	E^{148}	D^{234}	-
PotF	*eco*	Putrescine	S38	E^{185}	D^{247}	Y^{314}	-	-	-	-
	kpn	Spermidine	-	E^{159}	-	-	-	-	-	-
		Putrescine	-	E^{159}	-	-	-	-	-	-
		Cystamine	S12	E^{159}	D^{221}	Y^{288}	-	-	-	-

Based on the free energy observed during interactions with spermidine and putrescine, PotD and PotF from *Klebsiella pneumoniae* appear to function as a dual transporter. This phenomenon, previously reported by Cremonesi (2021), may indicate enhanced efficiency in the uptake of polyamines into the cell. In the molecular docking analysis, specific amino acids were characterized for their potential role in transport interactions. In the PotF protein of *K. pneumoniae*, the amino acids D^{37}, E^{40}, S^{61} and L^{322} were identified as interacting with cystamine (Table 3). Overall, no studies in the scientific literature were found that specifically addressed the roles of these prominent amino acids in the transport of taurine (Table 3), spermidine (Table 4), and putrescine (Table 5). The analysis conducted in this study was predictive in nature, and the obtained data can serve as a basis for future research.

CONCLUSION

This study reveals a coherent pattern in the organization of transporter genes, particularly within operonic structures, as evidenced by our KEGG analysis. The identified proteins exhibit characteristics typical of ABC transporters, categorized into permeases, ATPases, and substrate-binding proteins (SBPs). The *potD* and *tauA* gene in *Acinetobacter baumannii* and *Klebsiella pneumoniae* and the *potF* gene in *K. pneumoniae* were identified as encoding the SBPs of their respective transporters, consistent with literature and database findings. The negative free energy values from molecular docking analyses suggest that PotD proteins function as spermidine transporters, the PotF protein is likely involved in putrescine transport. Our findings also suggest that TauA proteins from both *A. baumannii* and *K. pneumoniae* are involved in taurine transport and possibly interact with molecules such as GABA, vigabatrin, and cystamine, highlighting the potential of these proteins as promising therapeutic targets. These interactions suggest opportunities for drug development aimed at modulating transporter activity to address antimicrobial resistance. The application of bioinformatics tools, such as molecular docking, is pivotal in identifying novel inhibitors and antimicrobial agents, particularly as drug-resistant strains continue to pose significant global health challenges. By focusing on transporter proteins, this study contributes to the broader efforts to combat antimicrobial resistance, offering a framework for exploring their role as therapeutic targets to reduce infection rates and improve patient outcomes.

Future research should incorporate experimental validations to strengthen the findings presented here. Biochemical and structural assays, along with in vitro and in vivo studies, are essential to confirm the predicted interactions and elucidate the precise biological roles of these transporter proteins. Such efforts would not only validate the bioinformatics predictions but also provide critical insights into the mechanisms underlying transporter-mediated processes, potentially advancing the development of targeted therapies.

By employing computational techniques, this study enhances the understanding of transporter gene organization and functionality, laying a robust foundation for subsequent investigations. The integration of bioinformatics and experimental approaches holds significant promise for the discovery of innovative inhibitors to combat pathogenic bacteria, addressing an urgent need in the era of escalating antimicrobial resistance.

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