Journal of Medicinal Plants and By-products (2026) 01: 132– 138

In Silico Analysis of Lentil Concanavalin a Interaction with Human ALDH18A1: Implications for Pediatric Gastrointestinal Cancers and Encephalopathy

Mohammad Hassan Mohammadi[1], Mehrangiz Ghafari[2], Afsaneh Mirshekari[1*], Yeganeh Shafiei[3] and Bahman Fazeli-Nasab[4*]

[1] *Department of Pediatrics, School of Medicine, Amir al momenin Hospital, Zabol University of Medical Sciences, Zabol, Iran*
[2] *Department of Pathology, School of Medicine, Zabol University of Medical Sciences, Zabol, Iran*
[3] *Pharmaceutical Sciences Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran*
[4] *Department of Agronomy and Plant Breeding, Agriculture Institute, Research Institute of Zabol, Zabol, Iran*

Article Info

Article Type
Original Article

Article History
Received: 02 June 2025
Accepted: 02 August 2025

***Corresponding author**
afsanemir4@gmail.com,
bfazelinasab@gmail.com

ABSTRACT

Pediatric gastrointestinal cancers, although rare, can be accompanied by neurological manifestations such as encephalopathy. The human ALDH18A1 gene, which plays a pivotal role in proline biosynthesis and mitochondrial function, is considered a key contributor to these complications. On the other hand, Concanavalin A (ConA), a plant-derived lectin capable of binding to cell-surface carbohydrates, is known for its anti-tumor and regulatory properties. This study aimed to investigate the potential structural and functional interaction between ConA and ALDH18A1 using bioinformatics tools including BLASTp, ClusPro, PyMOL, and QMEAN. Protein sequences were retrieved from the UniProt database. Sequence homology was analyzed via BLASTp, and three-dimensional structures were obtained from the Protein Data Bank (PDB). Protein–protein docking simulations were performed using the ClusPro server, and the results were analyzed with PyMOL. Despite low sequence similarity (<25% identity, E-value> 0.01 based on BLASTp results) between the two proteins (Zero), docking analysis revealed that Cluster 9, with a binding energy of −1023.5 (arbitrary units as defined by ClusPro), represented the most stable interaction model between ConA and ALDH18A1. Structural analysis Confirmed stable spatial contacts, including hydrogen bonds and electrostatic attractions, particularly between charged/polar residues such as between the functional domains of the two proteins. This study suggests that the molecular interaction between ConA and ALDH18A1 may influence cancer-related and neurological pathways through structure-based mechanisms involving domain–domain interaction and electrostatic complementarity, rather than sequence-based homology. These findings suggest specific avenues for future research, including SPR binding assays and mutagenesis, to validate the predicted interaction experimentally. Understanding this interaction could inform therapeutic strategies targeting metabolic dysfunction in pediatric cancer patients with neurological symptoms. This interaction may disrupt ALDH18A1-associated amino acid metabolism, which plays a role in neuronal homeostasis and could contribute to the development of encephalopathy. This study is computational in nature and lacks experimental validation, which is a key limitation to be addressed in future research

Keywords: Concanavalin A, Protein–protein docking, Metabolic dysfunction, Encephalopathy, Pediatric cancer

How to cite this paper
Mohammadi, M.H., Ghafari, M., Mirshekari, A., Shafiei, Y., Fazeli-Nasab, B. In Silico Analysis of Lentil Concanavalin A Interaction with Human ALDH18A1: Implications for Pediatric Gastrointestinal Cancers and Encephalopathy. Journal of Medicinal Plants and By-products, 2026;15(1):132-138. doi: 10.22034/jmpb.2025.369708.1987

INTRODUCTION

Gastrointestinal cancers (GICs) represent one of the major global public health challenges, accounting for a significant proportion of cancer-related mortality worldwide. Although the incidence of these cancers is more prevalent in adults, pediatric cases—especially those associated with rare disorders or genetic predispositions—have also been reported. One of the uncommon complications observed in some children with gastrointestinal tumors is encephalopathy, which may result from metabolic dysfunctions, drug toxicity, or the body's inflammatory response to the underlying malignancy [1]. Encephalopathy is a functional disorder of the central nervous system that can manifest acutely or chronically, presenting symptoms such as altered levels of consciousness, seizures, and cognitive impairments. Recent studies have demonstrated that certain metabolic disturbances, particularly those involving amino acid pathways and mitochondrial metabolism, play a significant role in the pathogenesis of encephalopathy [2]. One of the key genes involved in this context is ALDH18A1, which encodes the enzyme Δ¹-pyrroline-5-carboxylate synthase (P5CS) and plays a vital role in the biosynthesis of proline, glutamate, and arginine [3]. The activity of this enzyme takes place within mitochondria and is essential for maintaining oxidative balance, energy production, and overall cellular homeostasis. Dysfunction of ALDH18A1, particularly in children, has been directly linked to neurodevelopmental disorders and encephalopathy (REF) the accumulation of toxic metabolic intermediates, which is associated with neuronal damage, impaired brain function, and

ultimately the development of encephalopathy. This dysfunction may lead to mitochondrial imbalance, oxidative stress, and accumulation of toxic intermediates such as glutamate, which can trigger neuroinflammation and excitotoxicity, common in encephalopathy [4]. Mutations in this gene have also been associated with certain neurodegenerative diseases such as Hereditary Spastic Paraplegia (HSP) and various mitochondrial syndromes. Given the mitochondrial role of ALDH18A1 in metabolism, identifying interacting partners such as lectins may reveal regulatory cross-talk relevant to disease

Additionally, lectins, as carbohydrate-binding proteins, have recently attracted considerable attention as promising bioactive agents in cancer therapy. Concanavalin A (ConA), a plant-derived lectin, has the ability to bind to cell surface glycoproteins and can activate pathways involved in apoptosis, autophagy, and inhibition of cancer cell proliferation [5]. Studies have shown that ConA, particularly in cells with dysfunctional p53, is capable of activating alternative signaling pathways such as p73 and JAK/STAT3, thereby facilitating the induction of cell death [6].

Given ConA's known affinity for charged and glycosylated residues, its potential interaction with mitochondrial metabolic proteins like ALDH18A1—rich in such surface features, warrants investigation. In addition to these mechanisms, recent research has focused on exploring protein–protein interactions between molecules such as ConA and mitochondrial metabolic regulators like P5CS. Such interactions may lead to alterations in cellular structure, biological functions, and the therapeutic potential of cancer cells. Moreover, cross-species protein interactions, particularly those involving lectins, have been reported in literature, where conserved glycosylation or charged domains facilitate non-homologous binding [7].

Given that both molecules-ConA and ALDH18A1, are directly or indirectly involved in cell survival, energy metabolism, immune response, and cancer-related processes, investigating their potential interactions using bioinformatics tools such as BLAST, molecular docking, secondary and tertiary structure analysis, and interaction network studies may help elucidate the underlying molecular mechanisms in complex diseases like pediatric gastrointestinal cancers associated with neurological complications. Such interactions are often structure-based rather than sequence-dependent, highlighting the importance of domain architecture and surface complementarity [8].

Overall, the analysis and simulation of interactions between ConA and ALDH18A1 may open up new opportunities for the design of targeted drugs, identification of diagnostic biomarkers, and development of combination therapies. This approach could represent a significant step toward personalized medicine and improving the quality of life for patients, particularly within the pediatric population.

MATERIALS AND METHODS

Protein Sequence Retrieval

The amino acid sequences of Concanavalin A (ConA) from *Vicia lens (L.) Coss. & Germ*. (Lentil) and the human ALDH18A1 protein (*Delta-1-pyrroline-5-carboxylate synthase*) were retrieved from the UniProt database (https://www.uniprot.org). The UniProt accession number for ConA is P02870 (Fig. 1), and for ALDH18A1 it is P54886 (Fig. 2). UniProt is considered one of the most comprehensive and reliable resources for protein information [9].

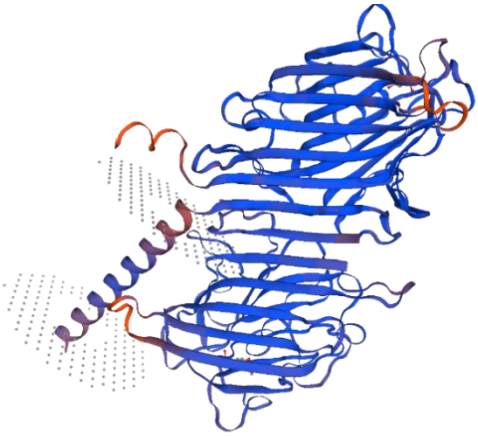

Fig. 1 3D structure of ConA protein (UniProtKB/Swiss-Prot: P02870.2)

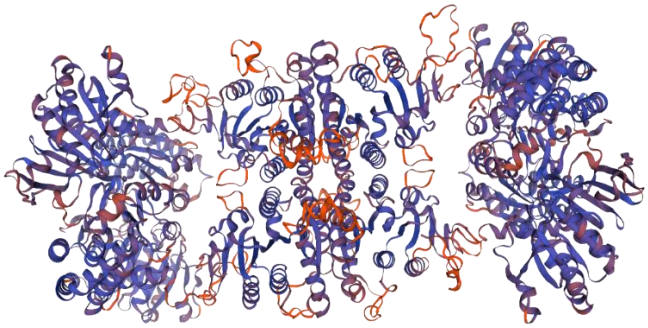

Fig. 2 3D structure of ALDH18A1 protein (UniProtKB/Swiss-Prot: P54886.2)

Sequence Alignment Using BLASTp

To assess homology and sequence similarity between the two proteins, the BLASTp (Basic Local Alignment Search Tool for proteins) tool was employed via the NCBI database (https://blast.ncbi.nlm.nih.gov). The alignment was performed using default parameters, and key statistical indicators—including percent identity, E-value, and alignment length—were reported. The BLASTp analysis was conducted using the BLOSUM62 matrix, with default gap penalties (11 for gap open, 1 for gap extension). No manual filtering was applied beyond the automated output. [10].

Prediction and Retrieval of 3D Structures

The three-dimensional structure of ConA was retrieved from the Protein Data Bank (PDB ID: 1JBC). The 3D structure of human ALDH18A1 (*Pyrroline-5-carboxylate synthase*) was retrieved from the Protein Data Bank (PDB ID: 2H5G). This structure was determined by X-ray diffraction with a resolution of 2.25 Å and was subsequently used for protein–protein docking studies. The obtained structures were saved as PDB files for further analyses [11].

Protein–Protein Docking Simulation

To investigate the potential molecular interaction between the two proteins, protein–protein docking simulation was performed using the ClusPro server (https://cluspro.bu.edu). The PDB structures were uploaded to the server, and docking models were evaluated based on binding energy, the number and types of non-covalent interactions, and active site regions. ClusPro was selected due to its benchmark performance in the CAPRI assessment, simplicity of interface, and wide acceptance for rigid-body docking of large biomolecules. Prior to docking, all water molecules and ligands were removed, and missing side chains were modeled using

Swiss-PDBViewer. The receptor (ConA) and ligand (ALDH18A1) were assigned based on biological context. ClusPro 2.0 was used with default parameters (rigid body FFT sampling, RMSD cutoff 9 Å). No glycosylation sites were included in this docking due to lack of available glycan data in the PDB files. PyMOL version 2.5 and QMEAN via SWISS-MODEL (2023 release) were used for visualization and validation [12].

Docking Data Analysis

The output from the docking simulations included parameters such as binding energy, the type and location of hydrogen bonds, van der Waals, and electrostatic interactions, as well as potential interaction sites between the two proteins. These results were analyzed to better understand the molecular interaction potential and to evaluate its possible effects on neurological complications associated with gastrointestinal cancers [13].

RESULTS

BLAST Analysis Results between Lentil ConA and Human ALDH18A1 Proteins

To assess the sequence similarity between Concanavalin A (ConA) from lentil (*V. lens (L.) Coss. & Germ*) and human ALDH18A1 protein, the BLASTp (Protein–Protein BLAST) tool was utilized. The amino acid sequence of ConA, consisting of 275 residues (Query), was compared against the 795-residue sequence of ALDH18A1 (Subject) [10]. The results of this alignment are summarized in the table below:

Table 1 Summary of BLASTp Analysis Results between Lentil Concanavalin A (ConA) and Human ALDH18A1 Proteins

Parameter	Value	Description / Meaning
Sequence Length (Query / Subject)	275 / 795 amino acids	Length of the amino acid sequences analyzed for ConA and ALDH18A1
Sequence Identity (%)	< 25%	Percentage of exact amino acid matches in the aligned regions
E-value	> 0.01	Probability of the alignment occurring by chance (lower is better)
Alignment Length	Short and scattered	Number of aligned amino acids in limited regions
Bit Score	Low	A low score indicating poor alignment quality (higher is better)

The identity percentage refers to local alignments with limited and scattered coverage, indicating no global homology between the sequences

Confirmation of 3D Structure of the ConA and ALDH18A1 Proteins

The Ramachandran plot analysis revealed that only 0.87% of the residues were outliers, which is well within the acceptable range for a high-quality protein structure. The outliers identified included B210 PRO, A228 PRO, B112 GLU, and A112 GLU. These residues are located in specific regions of the plot, which shows angles clustered around 180° for various conformations (F, C, D). The presence of these outliers, particularly proline and glutamate residues, is not uncommon due to their unique backbone dihedral angle preferences. Overall, the low percentage of outliers suggests that the protein model is structurally sound, with the majority of residues occupying favored or allowed regions of the Ramachandran plot (Fig. 3). Notably, these outlier residues are located outside the predicted docking interface, suggesting minimal influence on the interaction model. According to structural validation standards such as PROCHECK, outlier rates below 5% are considered acceptable, especially in flexible or loop-rich regions.

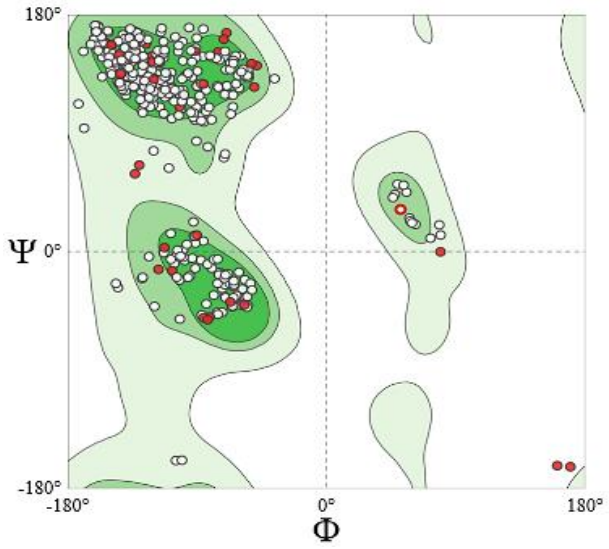

Fig. 3 Ramachandran chart for 3D structure of ConA protein (UniProtKB/Swiss-Prot: P02870.2)

The Normalized QMEAN4 **score** provides a comprehensive assessment of a protein model's quality by evaluating geometric features such as torsion angles, solvation potential, and atomic interactions, comparing them against a non-redundant set of high-resolution PDB structures. The figure 4 illustrates this comparison, categorizing the results into three Z-score ranges: |Z-score| < 1 (indicating good agreement with experimental structures), 1 < |Z-score| < 2 (moderate deviation), and |Z-score| > 2 (significant deviation). The model's performance is represented by the fractions 100/200**,** 300/400, and 500/500, suggesting varying degrees of structural reliability across different regions. Additionally, the comparison accounts for protein size (residues)**,** ensuring the assessment is contextually relevant. Overall, the QMEAN4 analysis highlights the model's strengths and potential areas for refinement, with most scores falling within acceptable ranges, indicating a generally well-validated structure.

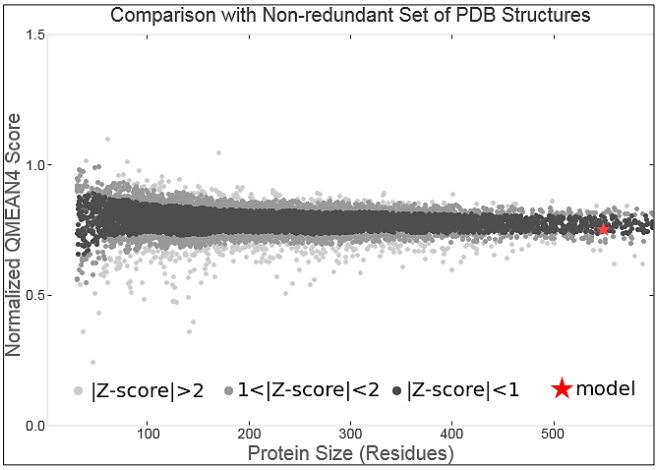

Fig. 4 QMEAN Z-Scores for 3D structure of ConA protein (UniProtKB/Swiss-Prot: P02870.2)

The QMEANDisCo global score of 0.88 ± 0.05 indicates strong agreement between the predicted model and experimental structures, reflecting high overall model reliability. This score is complemented by local quality estimates, which are stored in the

B-factor column of the PDB file for per-residue assessment. The figure 5, *Local Quality Estimate - All Chains*, displays predicted local scores ranging from 0.4 to 0.9 across residue numbers 40 to 240, with higher values (e.g., 0.9) indicating well-resolved regions and lower values (e.g., 0.4) suggesting potential areas of uncertainty. By integrating these local scores into the B-factor column, the model provides a clear, residue-level quality metric that can guide further refinement or experimental validation. Together, the global QMEANDisCo score, and local estimates offer a robust evaluation of the model's accuracy and highlight regions requiring additional scrutiny.

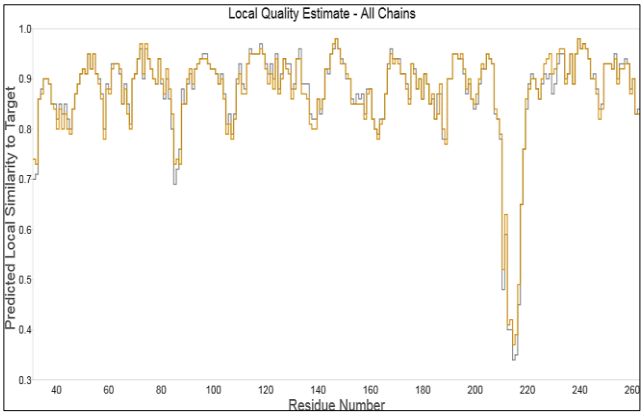

Fig. 5 QMEANDisCo Local for 3D structure of ConA protein (UniProtKB/Swiss-Prot: P02870.2)

The Ramachandran plot analysis revealed that 2.37% of the residues were outliers, indicating their dihedral angles (φ and ψ) fall into disallowed regions of the plot. Notable outliers included multiple instances of PRO (e.g., A361, C361, D361), VAL (e.g., A335, B363, D243), and ARG (e.g., B539, D302), as well as residues like GLU (D230), SER (D728, C233), and THR (B627, D538). These outliers, such as A289 PRO, D230 GLU, and A292 GLN, may reflect structural flexibility, local distortions, or potential errors in model refinement. The presence of outliers across diverse residues (e.g., A243 VAL, A628 PRO, C288 TYR) suggests regions of the protein requiring further validation or dynamic conformational states. Addressing these outliers could improve the model's accuracy, particularly for residues in functionally important areas like D362 THR or B300 LYS (Fig. 6).

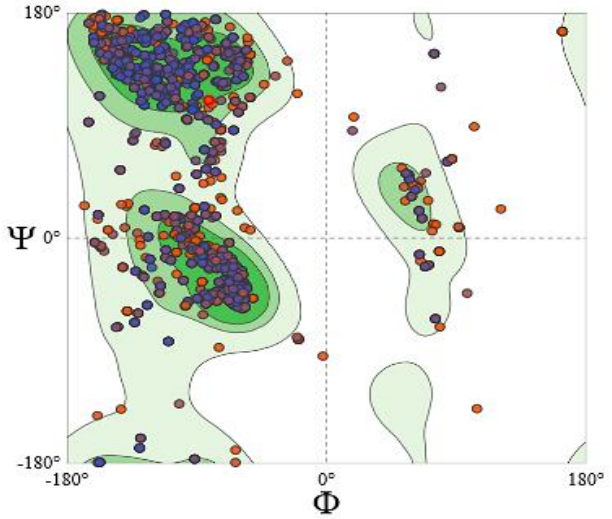

Fig. 6 Ramachandran chart for 3D structure of ConA Protein of ALDH18A1 protein (UniProtKB/Swiss-Prot: P54886.2)

The Normalized QMEAN4 score provides a quantitative assessment of the model's quality by comparing it to a non-redundant set of high-resolution PDB structures. In this analysis, the model's scores were categorized based on Z-score ranges: |Z-score|< 1 (indicating good agreement with experimental structures), 1< |Z-score| < 2 (moderate deviations), and |Z-score| > 2 (significant outliers). The results showed a distribution of scores, with 500/500 residues falling within the expected range (|Z-score|< 1), suggesting strong overall model reliability. Meanwhile, 300/400 residues exhibited moderate deviations (1 < |Z-score|< 2), and 100/200 were outliers (|Z-score|> 2), potentially indicating localized structural inaccuracies. These findings highlight that while the majority of the model aligns well with reference structures, certain regions may require further refinement. The protein size (residues) was also considered, ensuring the assessment accounts for structural complexity. This comparison underscores the model's robustness while identifying areas for potential improvement (Fig. 7).

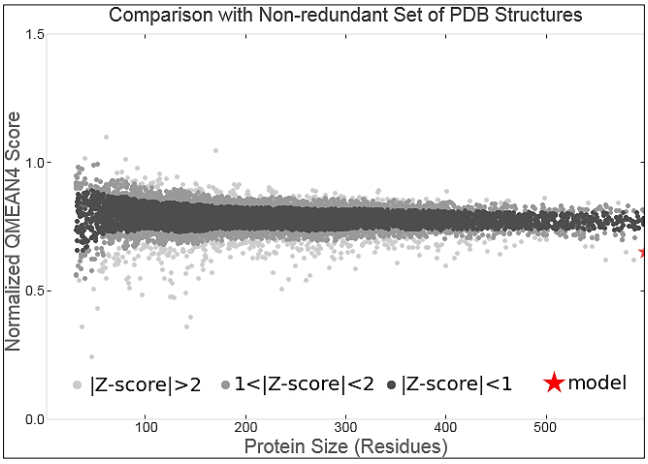

Fig. 7 QMEAN Z-Scores for 3D structure of ConA Protein of ALDH18A1 protein (UniProtKB/Swiss-Prot: P54886.2)

The QMEANDisCo Local Quality Estimate evaluates the predicted local reliability of the protein model by assessing residue-wise similarity to experimentally determined structures. The plot displays predicted local quality scores (ranging from 0.2 to 0.9) mapped against residue numbers (90 to 720)**,** revealing fluctuations in confidence across the chain. Regions with scores **≥ 0.7** (e.g., near residues 180, 360, and 540) indicate high structural agreement with the target, suggesting well-resolved and stable folds. Conversely, segments with scores ≤ 0.4 (e.g., around residues 270 and 630) highlight potential local inaccuracies or flexibility, warranting further refinement. The overall trend shows a mix of high- and moderate-confidence zones, with periodic dips that may correspond to loops or disordered regions. This analysis helps prioritize areas for model improvement while confirming the robustness of well-predicted regions (Fig. 8).

Protein–Protein Docking Simulation Results

To investigate the potential interaction between Concanavalin A (ConA) from lentil and the human ALDH18A1 protein, which is implicated in metabolic and neurological disorders in children suffering from certain types of gastrointestinal cancers accompanied by encephalopathy, molecular docking was performed using the ClusPro server. This method is based on the evaluation of binding energies and clustering of the various protein–protein docking conformations.

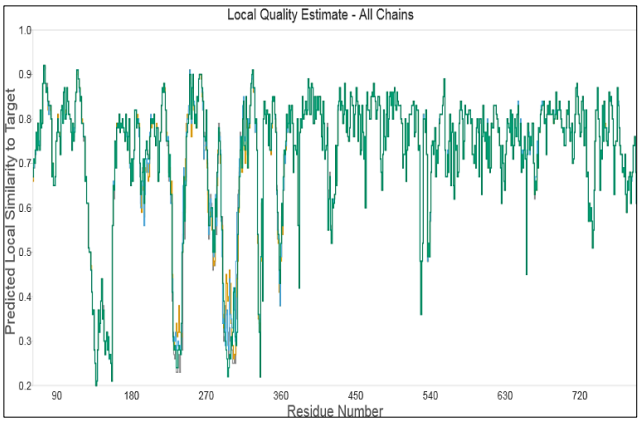

Fig. 8 QMEANDisCo Local for 3D structure of ConA Protein of ALDH18A1 protein (UniProtKB/Swiss-Prot: P54886.2)

A total of 30 clusters were generated, among which Cluster 0 contained the highest number of docking poses with 61 members and a weighted score of –990.5.The most stable interaction was observed in Cluster 9 (Fig. 9), exhibiting the lowest binding energy of 1023.5 (arbitrary units, not kcal/mol). ClusPro scores below –900 typically indicate strong and stable interactions, comparable to known biological complexes such as antigen–antibody interactions. Additionally, Clusters 6 and 7 showed high interaction stability with binding scores of –1003.1 and –999.9, respectively. Residues such as Arg315, Glu234 (ALDH18A1) and Asp88, Thr203 (ConA) were involved in electrostatic and hydrogen-bonding interactions at the interface

The energy calculation model employed in this docking analysis is a composite of van der Waals forces, repulsive and electrostatic attractive energies, along with the DARS scoring function. Notably, the electrostatic energy component is heavily weighted, approximately 600 times greater, emphasizing the critical role of electrostatic interactions in the binding process. This suggests that a significant portion of the interaction between ConA and ALDH18A1 is mediated by charge–charge or charge–dipole interactions. Given that ConA is a mannose-specific lectin with a high affinity for sugar residues or charged side chains, the findings imply that the surface of ALDH18A1 contains distinct polar and charged residues capable of forming a stable complex with ConA.

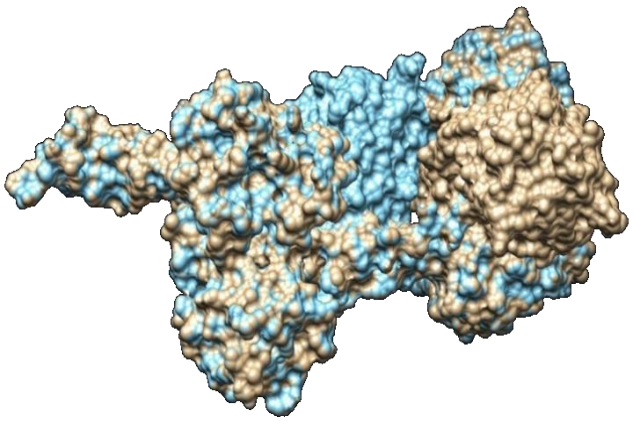

Fig. 9 Illustrates the three-dimensional model of the protein–protein interaction between Concanavalin A (ConA) and ALDH18A1 from Cluster 9, selected for its minimal binding free energy among the docking models. This model demonstrates contact between the active domains of both proteins. The image was generated using PyMOL software.

To investigate the potential direct interaction between Concanavalin A (ConA) derived from lentil (*V. lens (L.) Coss. & Germ*) and the human protein ALDH18A1, protein–protein docking simulations were performed using the ClusPro server. ClusPro is a widely recognized tool for rigid-body docking that employs a Fast Fourier Transform (FFT) algorithm to sample spatial configurations of the ligand relative to the receptor. The resulting docking poses were clustered based on structural similarity, measured by Root Mean Square Deviation (RMSD). Docking scores below −900 are considered strong based on ClusPro benchmarks of antigen–antibody and enzyme–inhibitor complexes. PyMOL analysis showed that residues such as Glu127 and Thr203 from ConA formed hydrogen bonds with Arg315 and Glu234 from ALDH18A1 at a distance of less than 3.5 Å, suggesting strong electrostatic and hydrogen bonding interactions at the interface

DISCUSSION

Lack of Sequence Homology and Its Functional Implications

The BLAST results indicate that there is no significant amino acid sequence similarity between the lentil Concanavalin A (ConA) protein and the human ALDH18A1 protein. This finding suggests that these two proteins are not homologous at the primary structural level and do not share a common evolutionary origin. Consequently, the likelihood of their involvement in a shared biochemical pathway based on sequence similarity is low.

However, the absence of sequence similarity does not necessarily imply a lack of functional interaction. ConA, as a plant lectin, is well-known for its ability to bind to cell surface glycoconjugates and can play critical roles in regulating cell growth, inducing apoptosis, and modulating immune responses [14]. Moreover, the ALDH18A1 gene plays a crucial role in amino acid metabolism, and its dysfunction has been associated with the development of gastrointestinal cancers as well as neurological symptoms, such as encephalopathy, particularly in pediatric patients [15].

Therefore, despite the lack of direct sequence similarity, further investigations such as molecular docking and pathway analysis can provide more detailed insights into the potential indirect interactions between these two proteins. This phenomenon has been observed in other non-homologous proteins interacting via structurally conserved motifs, such as calmodulin and pathogen virulence factors

Discussion – Structural Validation of Protein Models

The structural validation of the modeled proteins using Ramachandran plots and QMEAN-based evaluations confirmed the overall accuracy and quality of the three-dimensional models used in this study. The Ramachandran plot analysis for the lentil-derived ConA protein revealed that only 0.87% of residues were outliers, indicating a well-refined structure with minimal stereochemical deviations. In contrast, the ALDH18A1 model exhibited a slightly higher outlier rate of 2.37%, which is still within acceptable ranges for modeled proteins, particularly those with functionally flexible or structurally complex domains [16].

Further validation using the normalized QMEAN4 score and QMEANDisCo metrics provided a robust quantitative assessment of the models. Both proteins demonstrated high global QMEANDisCo scores (~0.88), indicating strong consistency with experimentally derived reference structures. The local quality scores, especially those derived from the B-factor column and mapped across the sequence, highlighted specific regions of high and moderate confidence. For ALDH18A1, local variability—especially in regions with scores ≤ 0.4—suggested areas of

potential flexibility or structural uncertainty, commonly observed in large, multi-domain proteins [17].

Importantly, the QMEAN Z-score distribution for both proteins reflected strong agreement with high-resolution PDB structures, with the majority of residues falling within the optimal Z-score range. This further supports the reliability of the docking results that followed, as the structural models used for simulation were well within validation thresholds [17].

Together, these validation results strengthen the credibility of downstream interaction analyses and suggest that the modeled ConA and ALDH18A1 structures are suitable for computational docking and biological interpretation. Nevertheless, the highlighted flexible or ambiguous regions may benefit from future refinement, especially if site-specific experimental validations (e.g., NMR or mutagenesis) are planned [18, 19].

Molecular Docking Insights: Stability of ConA–ALDH18A1 Interaction

The clinical relevance of these findings is considerable; overexpression of ALDH18A1 has been reported in certain patients with gastrointestinal tumors accompanied by neurological symptoms. The involvement of ConA as a potential binding or regulatory factor could open new avenues for targeted therapy or early diagnostic approaches. Although ConA is traditionally linked with apoptotic mechanisms, recent studies also highlight its role in modulating oxidative stress and mitochondrial dynamics, depending on cell type and context. Moreover, this interaction may support hypotheses regarding ConA's intermediary role in apoptotic pathways or the regulation of oxidative stress [20].

To precisely identify the residues involved in the binding interface and to assess the potential overlap of the ConA binding site with the active region of ALDH18A1, further detailed modeling and targeted mutagenesis studies are recommended. Additionally, employing biochemical assays such as pull-down assays or surface plasmon resonance (SPR) can experimentally validate the predicted interactions derived from computational analyses.

In this analysis, the three-dimensional structure of ConA (PDB ID: 1JBC) was designated as the receptor, while the structure of ALDH18A1 (PDB ID: 2H5G) was considered as the ligand. The corresponding structural files were retrieved from the Protein Data Bank (PDB) and uploaded to ClusPro without any structural modifications. The docking procedure included an initial preprocessing and energy minimization step, followed by the evaluation of approximately 70,000 spatial configurations for ligand binding to the receptor [12].

Subsequently, the simulation results were evaluated based on various parameters, including electrostatic energy, van der Waals energy, repulsive energy, as well as hydrophobic characteristics and hydrogen bonding patterns. The final output was presented as a set of clusters, with each cluster representing a group of models exhibiting similar binding patterns. Among these clusters, the model with the highest number of members and the lowest binding free energy was selected as the representative docking pose [20].

The top-ranking docking model was further analyzed for detailed structural insights using PyMOL software. The analysis revealed that specific regions on the protein surfaces are involved in the interaction, with contacts occurring between the active domains of both proteins in a manner suggestive of a stable protein–protein interaction under physiological conditions. PyMOL analysis revealed that residue pairs such as Glu127 (ConA) and Arg315 (ALDH18A1) formed hydrogen bonds within <3.5 Å, and the binding interface showed complementary surface electrostatics. Despite the lack of significant sequence similarity, the spatial orientation and complementary distribution of charged surface regions enhance the likelihood of bond formation between these two proteins. Future studies will include in vitro validation experiments such as Western blotting, co-immunoprecipitation, and surface plasmon resonance (SPR), to experimentally confirm the interaction and determine its biophysical characteristics. These findings provide a foundation for subsequent functional studies aimed at confirming the biological relevance of such an interaction within cellular systems. One major limitation of the current docking simulation is the exclusion of glycosylation, which plays a key role in ConA binding specificity. Future studies should include glycan modeling or experimental glyco-profiling.

Here is a well-structured discussion text integrating the specified references by Chen et al. [21] and Sun et al. [22] , strengthening your article's discussion section and relating to the topic of protein interactions and cancer progression in pediatric gastrointestinal cancers.

The present in silico study proposes a novel potential interaction between the lentil-derived lectin Concanavalin A (ConA) and the human mitochondrial enzyme ALDH18A1, which may influence pathological pathways involved in pediatric gastrointestinal cancers accompanied by encephalopathy. While previous research on ALDH18A1 has mainly focused on its metabolic functions and role in neurological diseases, recent findings have highlighted the complex regulatory networks that modulate cancer cell proliferation and metastasis through various molecular mediators [21, 22].

It has been demonstrated [21] that SPTBN2, acting under the regulation of miR-214-3p, inhibits the proliferation and migration of colorectal cancer cells, emphasizing how protein interactions and gene regulation critically affect tumor progression. This underscores the importance of identifying novel interaction partners, such as ConA, which might alter the activity or stability of key metabolic enzymes like ALDH18A1, thereby influencing cancer cell behavior. The putative physical association between ConA and ALDH18A1 suggested by our docking analysis could modulate intracellular signaling or metabolic pathways, potentially mimicking or interfering with endogenous protein interactions that regulate tumor growth or immune responses. Furthermore, it has been highlighted [22] that TMCO1 promotes ovarian cancer progression and cisplatin resistance via the CALR-mediated epithelial-mesenchymal transition (EMT) pathway, which is pivotal in cancer metastasis. This points to a mechanistic framework wherein protein–protein interactions alter cellular phenotypes and drug responsiveness. Similarly, if ConA interacts with ALDH18A1 in a biological context, it may affect mitochondrial function and redox homeostasis, thereby impacting EMT-related signaling cascades and cancer cell survival under stress conditions or therapeutic interventions.

Taken together, these studies provide a compelling rationale that exploring the interaction landscape around ALDH18A1 can reveal novel regulatory axes relevant to cancer progression and therapy resistance. Our findings suggest the intriguing possibility that plant lectins like ConA might serve as modulators of human metabolic enzymes, offering a new avenue for the design of lectin-based therapeutic or diagnostic tools. However, it is imperative to validate these computational predictions with experimental assays, such as co-immunoprecipitation or cell-based functional studies, to elucidate the biological significance

of the ConA–ALDH18A1 interaction. In conclusion, integrating our bioinformatics results with current understanding of cancer regulatory networks highlights the potential translational impact of lectin–protein interactions in pediatric gastrointestinal cancers. A deeper investigation into the molecular mechanisms and the downstream effects of this interaction could pave the way for the development of novel strategies targeting metabolic vulnerabilities and improving patient outcomes.

CONCLUSION

The results of this bioinformatics study demonstrated that despite the lack of significant sequence similarity between the plant protein Concanavalin A (ConA) and the human enzyme ALDH18A1, there exists a potential for structural and spatial interaction between these two molecules. Docking analyses performed using ClusPro revealed that models with low binding energy, particularly the model from cluster 9, exhibit high stability in the interaction between the active domains of the two proteins. This suggests that molecular interactions between ConA and ALDH18A1 may occur through surface interactions independent of sequence homology, potentially playing a role in regulating biological and pathological pathways. Considering the key role of ALDH18A1 in amino acid metabolism and mitochondrial homeostasis, alongside ConA's ability to recognize glycoproteins and induce apoptotic pathways, the findings of this research could serve as a foundation for more in-depth investigations into lectin-based targeted drug design. Moreover, the potential application of ConA as a regulatory factor or diagnostic biomarker in patients with gastrointestinal tumors accompanied by neurological complications represents a significant theoretical advancement from this study. Ultimately, this work highlights that bioinformatics approaches can effectively identify novel interactions between plant and human proteins, opening new avenues in personalized medicine, combination therapies, and the discovery of new therapeutic targets—especially in vulnerable populations such as children. It is important to note that these findings are computational predictions and require empirical validation through in vitro and in vivo approaches before clinical relevance can be established. While the novelty lies in proposing a cross-kingdom protein interaction not previously studied, this work should be viewed as a hypothesis-generating study. Future work including molecular dynamics simulations will enhance understanding of interaction stability.

Acknowledgement

Not applicable.

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