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Computational Analysis and NGS for Human LDHC Complexed with NAD+ and Ethylamino Acetic Acid (Lung Cancer)

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Abstract: ***This study presents a multidimensional exploration of the structural and functional characteristics of the human Lactate Dehydrogenase C (LDHC) complexed with NAD+ and ethylamino acetic acid (EAA), focusing on its implications in lung cancer. Leveraging data from the Protein Data Bank (PDB) and Molecular Modeling Database (MMDB), a comprehensive analysis was conducted using various computational tools and resources. Structural insights were gained through PDBsum and RasMol, elucidating molecular interactions and identifying potential drug-target sites. Sequence analysis via BLAST and Multiple Sequence Alignment provided further understanding of conserved sequences and structural motifs. Visualization and manipulation of molecular structures were facilitated by PyMOL, enabling the identification of active drug-target sites. Protein-ligand docking studies using the CB-Dock2 server assessed the efficiency of LDHC complexation with NAD+. Structural validation through the SAVES server ensured the reliability of the complex structure. Additionally, biological network analysis using the STRING database revealed associations with gene ontology and structural classification of the protein, offering insights into targeted interventions in the ancestry of the protein. This comprehensive approach provides valuable insights into LDHC's role in cancer biology and offers promising avenues for therapeutic development in lung cancer.***

Keywords: Lactate Dehydrogenase, Lung Cancer, Ethylamino Acetic Acid, Sequence Analysis, Biological Network Analysis, Structural Validation.

I. INTRODUCTION

Lung cancer persists as a challenging global health contest, standing as the starring cause related to cancer mortality worldwide (Luca Bertolaccini *et al*., 2024). Its multifaceted etiology, diverse histological subtypes, and propensity for metastasis underscore the complexity of this disease, necessitating comprehensive investigations into its molecular underpinnings (Jiexi Wen *et al*., 2024). Amidst this clinical urgency, the convergence of computational analysis and Next-Generation Sequencing (NGS) has emerged as a transformative force in cancer research, offering unparalleled insights into the intricacies of tumorigenesis, progression, and therapeutic response (Peilin Jia *et al*., 2012).

Computational analysis, NGS technologies, and the human Lactate Dehydrogenase C (LDHC) enzyme in the background of lung cancer (D. Djureinovic et al., 2014). LDHC, a pivotal enzyme in glycolysis, has garnered significant attention in cancer biology due to its dysregulated expression and functional implications in tumorigenesis (Chaithanya Chelakkot et al., 2023). By scrutinizing the structural dynamics and molecular interactions of LDHC, particularly in complex with Nicotinamide Adenine Dinucleotide (NAD^+) and ethylamino acetic acid (EAA) (Hong Tan et al., 2022), this study seeks to unravel novel visions into the pathogenesis of lung cancer and identify potential therapeutic targets..

Human lactate dehydrogenase (LDH) has attracted interest as a promising candidate for cancer treatment and contraception (Xian-Li Zhao et al., 2018). In efforts to regenerate human lactic acid, certain studies involve fermenting Saccharomyces cerevisiae, to establish a yeast cell-centered LDH assay system To reconstruct human lactic acid some research includes fermentation in Saccharomyces cerevisiae, aiming to develop a yeast cell-based LDH assay system (Maria Karkovska et al., 2016). The yeast strains with PDC null mutations, which lack functional endogenous pyruvate decarboxylase genes, demonstrated an inability to undergo alcoholic fermentation (Jin Ho Choo et al., 2018). When exposed to an inhibitor of the electron transport chain, these PDC null strains exhibited inhibited growth.

It was observed that the introduction of the human LDHA gene effectively reinstated growth in the PDC null yeast, relying on the catalytic activity of LDHA (Michael Sauer et al., 2010). Similarly, Introducing human LDHC also rectified the growth impairment in the PDC null strain, albeit with lower lactate production compared to LDHA (Jorge S. Burns & Gina Manda, 2017). On the contrary, human LDHB did not restore functionality to the yeast PDC null mutant, even though it generated lactate in yeast cells (Timothy L Turner et al., 2019). Notably, The expression of LDHB as a fusion protein with red fluorescent protein (RFP) led to the formation of unique cellular structures known as blebs in yeast. In contrast, LDHA-RFP and LDHC-RFP fusion proteins showed distribution throughout the cytosol. Consequently, LDHB displays distinctive features upon expression in yeast cells (Lulu Ahmed et al., 2015). Due to yeast's suitability for genetic investigations and cell-based high-throughput screening, the creation of PDC/LDH strains offers potential for diverse analyses of human LDH (Jin Ho Choo et al., 2018).

Recent studies exploring the human enzyme LDHC complexed with ethylamino acetic acid (EAA) and NAD^+ have provided valuable insights into the structural dynamics and functional implications of this molecular assembly. Computational modeling and molecular dynamics simulations have offered a glimpse into the three-dimensional architecture of the LDHC-NAD^+-EAA complex, shedding light on the intricate interactions between the enzyme and its cofactors (Archana Pan et al., 2021). These studies have revealed potential allosteric sites on LDHC, where EAA binding induces conformational changes that modulate enzymatic activity. Additionally, the stabilizing effect of NAD^+ on the LDHC complex suggests a regulatory role for this cofactor in glycolytic flux and lactate production (Luigi Ippolito et al., 2018). Such findings underscore the complexity of LDHC regulation and its significance in cellular metabolism. Moreover, investigations into the metabolic rewiring associated with LDHC-NAD^+-EAA complex formation have unveiled new dimensions of cancer metabolism. Dysregulated LDHC activity and lactate production are hallmark features of many cancers, including lung cancer. Characterizing the metabolic phenotype of lung cancer cells in the context of LDHC complex formation may elucidate key metabolic pathways driving tumorigenesis and identify metabolic vulnerabilities exploitable for therapeutic intervention (Luigi Ippolito et al., 2018). Furthermore, the identification of small molecules or inhibitors targeting the LDHC-NAD^+-EAA complex holds promise for developing novel cancer therapeutics (Hong Tan et al., 2022).

At the outset, a comprehensive overview of lung cancer sets the stage for this investigation, highlighting its staggering global burden, epidemiological trends, and clinical challenges. Emphasis is placed on elucidating the diverse etiological factors contributing to lung cancer, including tobacco smoke exposure, environmental pollutants, genetic predispositions, and molecular alterations. Moreover, the heterogeneity of lung cancer, encompassing distinct histological subtypes and molecular profiles, underscores the imperative for personalized therapeutic approaches tailored to individual patients (Steven L. Wood et al., 2015).

Delving deeper into the molecular landscape of lung cancer, attention is drawn to the pivotal role of metabolic reprogramming in tumorigenesis. Glycolysis, a hallmark of cancer metabolism, emerges as a focal point of investigation, with LDHC occupying a central position in regulating lactate production and redox homeostasis (Chaithanya Chelakkot *et al.*, 2023). The dysregulation of LDHC expression and activity in lung cancer cells not only fuels energy production and biomass synthesis but also orchestrates signaling pathways implicated in tumor growth, invasion, and immune evasion (Luigi Ippolito *et al.*, 2018).

The narrative then transitions to a discussion on the therapeutic implications of targeting LDHC in lung cancer (Adviti Naik *et al.*, 2024). Preclinical studies have highlighted the efficacy of LDHC inhibition in attenuating tumor growth and metastasis, offering a promising avenue for therapeutic intervention (Banerjee & Mishra, 2019). However, challenges persist in translating these findings into clinical practice, necessitating a deeper understanding of the structural and functional properties of LDHC and its interactions with cofactors such as NAD^+ and EAA (Hong Tan *et al.*, 2022).

In this context, computational analysis emerges as a powerful tool for deciphering the intricate interplay between LDHC, NAD^+, EAA, and lung cancer. Molecular modeling, molecular dynamics simulations, and bioinformatics approaches offer a virtual laboratory for exploring the structural dynamics, ligand binding kinetics, and allosteric regulation of the LDHC complex. Concurrently, NGS technologies empower researchers to unravel the genomic, transcriptomic, and epigenetic landscapes of lung cancer, providing a comprehensive framework for understanding disease heterogeneity and therapeutic vulnerabilities (Lawrence R. *et al.*, 2013).Against this backdrop, the objectives of this thesis crystallize: to elucidate the structural determinants of LDHC-NAD^+-EAA interactions, to delineate the molecular alterations associated with LDHC dysregulation in lung cancer, and to identify candidate therapeutic targets for precision medicine interventions. Methodologically, a multidisciplinary approach encompassing computational modeling, NGS data analysis, and experimental validation forms the cornerstone of this investigation, underscoring the synergy between computational biology and experimental oncology.

Research on the human LDHC enzyme complexed with NAD^+ and EAA, also facilitated by computational techniques such as molecular docking, has yielded significant discoveries with implications for cancer biology and therapy.

By elucidating the structural dynamics, metabolic consequences, and clinical relevance of the LDHC-NAD^+-EAA complex in lung cancer, these studies offer a deeper understanding of cancer metabolism and opportunities for precision medicine interventions (Banerjee & Mishra, 2019). Continued investigation into the LDHC complex, leveraging computational approaches alongside experimental techniques, may unveil further insights into its role in tumorigenesis and facilitate the development of innovative strategies for combating lung cancer and other malignancies.

Overall, this research endeavors to unravel the intricate tapestry of LDHC-mediated metabolic reprogramming in lung cancer through a convergence of computational analysis and NGS technologies. By illuminating the structural underpinnings of LDHC-NAD^+-EAA interactions and unraveling the genomic landscapes of lung cancer, this study aspires to pave the way for the development of targeted therapeutic strategies and personalized interventions in lung cancer management. Through interdisciplinary collaboration and relentless scientific inquiry, we endeavor to advance our understanding of cancer biology and transcend the boundaries of conventional therapeutics toward precision oncology.

II. METHODOLOGY

This study commenced with the meticulous acquisition of the three-dimensional structure of the biological sample (PDB ID 7EPM) from the Protein Data Bank (PDB), leveraging advanced methodologies encompassing X-ray crystallography, NMR spectroscopy, and cryo-electron microscopy.Following data acquisition, a rigorous structural analysis ensued utilizing established tools such as PDBsum and RasMol. These analyses provided detailed insights into the molecular architecture, structural motifs, and intra-molecular interactions governing the biological sample.Sequence analysis was subsequently conducted employing the Basic Local Alignment Search Tool (BLAST) and COBALT, facilitating the elucidation of genetic sequences, identification of homologous regions, and alignment of diverse sequences for comparative analysis.For visualization and manipulation of structural data, PyMOL was employed, enabling the exploration of three-dimensional structures, identification of functional sites, and analysis of molecular dynamics.Protein-ligand docking simulations were conducted utilizing the CB-Dock2 server, employing sophisticated computational algorithms to predict binding affinities and orientations of ligands within the protein structure, thereby elucidating potential drug interactions and molecular mechanisms.The structural integrity of the biological sample was rigorously validated through comprehensive analyses including ERRAT, PROCHECK, and Ramachandran plot analysis using the SAVES server, ensuring the reliability and suitability of the structure for subsequent analyses.Finally, a comprehensive biological network analysis was undertaken leveraging the STRING database, elucidating the functional implications, molecular interactions, and signaling pathways associated with the studied biological complex.In summation, our methodology integrates a suite of computational and experimental techniques to systematically unravel the structural intricacies, decode genetic sequences, and elucidate functional implications, thereby advancing our understanding of neurodegenerative diseases and facilitating targeted therapeutic interventions.

III. RESULTS

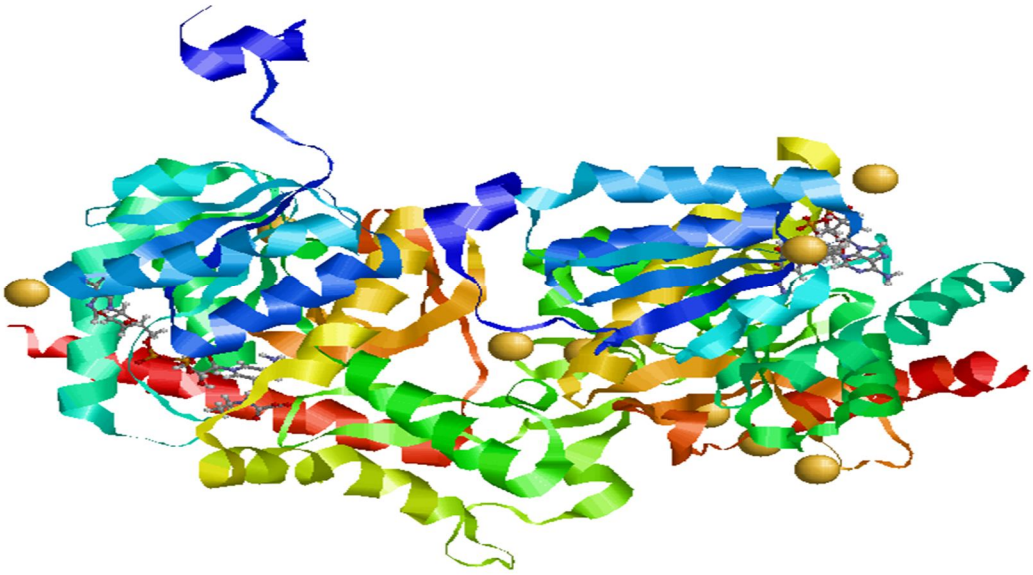

Figure 1: Visualization of the 3-D protein structure by using RasMol.

Visualizing the three-dimensional protein structure using RasMol involves a series of steps to generate graphical representations of the molecular architecture of proteins. Initially, researchers obtain the molecular coordinate data of the protein of interest from a structural database such as the Protein Data Bank (PDB). This data typically consists of the Cartesian coordinates of each atom in the protein molecule. Once the coordinate data is obtained, researchers install RasMol on their computer, as it is a molecular visualization program that allows for interactive manipulation and analysis of biomolecular structures.

In RasMol, the command line calculation of atoms in the protein (7EPM) involves accessing and manipulating the molecular structure directly through text-based commands. Users can input commands such as "select" to specify atoms or residues of interest based on criteria such as atom type, residue type, or spatial coordinates. By using commands like "show" or "hide," users can control the visibility of selected atoms, allowing them to focus on specific regions or features within the protein structure. Additionally, commands like "center" or "zoom" enable users to orient and magnify the view of the protein to facilitate detailed analysis. Through this command line interface, users have fine-grained control over the visualization and analysis of protein structures, enhancing their ability to explore and interpret molecular data efficiently.

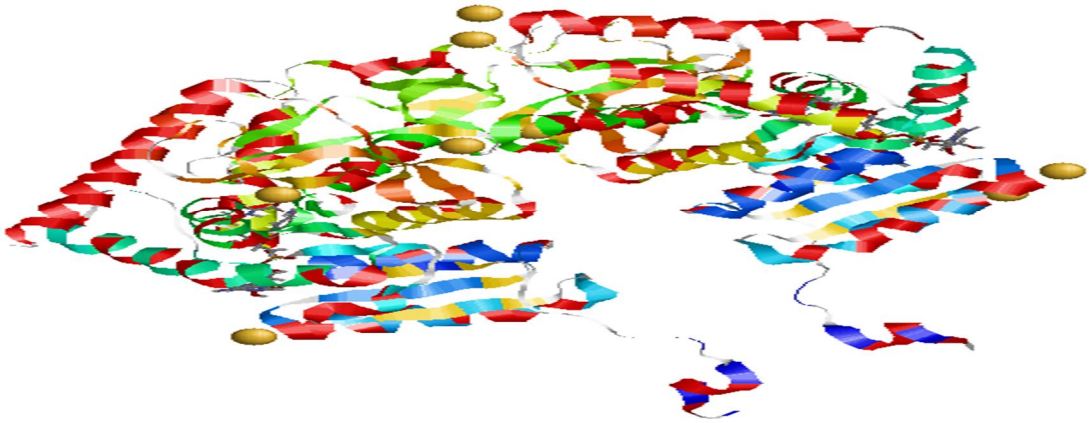

Figure 2: Beta-helix structure is showing in Yellow (7epm).

In the visualization provided, the beta-helix structure is represented by the color yellow, serving as a distinctive visual indicator within the molecular model. The yellow hue highlights regions of the protein exhibiting the characteristic repeating pattern of beta strands arranged in a helical configuration. This structural motif is crucial for understanding the protein's overall architecture and function, as beta helices often play essential roles in stabilizing protein folds, facilitating molecular interactions, and mediating biological processes. By colorizing the beta-helix structure in yellow, it becomes readily discernible amidst the complex three-dimensional landscape of the protein, aiding researchers in their analysis and interpretation of its structural features and functional implications.

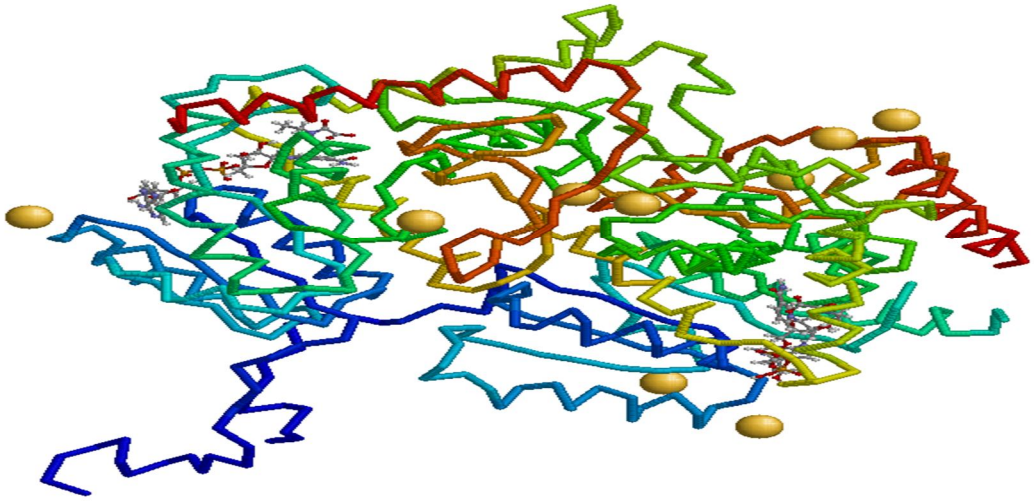

Figure 3: Backbone representing Phosphorus Nucleic Acid in the protein (7epm).

The backbone representing phosphorus nucleic acid in the protein is a crucial element highlighted for its significance in nucleic acid structure and function. The backbone, often depicted in a distinct color or style, serves to delineate the linear arrangement of phosphorus atoms within the nucleic acid chain, forming the backbone of the molecule. This backbone is fundamental in providing structural stability to the nucleic acid strand, while also facilitating interactions with other molecules such as proteins and small ligands. By visually emphasizing the phosphorus backbone, researchers can better understand the spatial arrangement of nucleic acids within the protein structure, enabling insights into molecular interactions, genetic information processing, and regulatory mechanisms essential for cellular function and gene expression.

Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
Chain A, L-lactate dehydrogenase C chain [Homo sapiens]	Homo sapiens	695	695	100%	0.0	100.00%	341	7EPM_A
L-lactate dehydrogenase C chain [Homo sapiens]	Homo sapiens	665	665	97%	0.0	99.40%	332	NP_002292.1
lactate dehydrogenase C [synthetic construct]	synthetic construct	664	664	97%	0.0	99.10%	333	AAX29886.1
lactate dehydrogenase C4 [Homo sapiens]	Homo sapiens	664	664	97%	0.0	99.09%	332	ADG58108.1
lactate dehydrogenase c variant 1 [Homo sapiens]	Homo sapiens	663	663	97%	0.0	99.09%	332	AEW43812.1
lactate dehydrogenase c [Homo sapiens]	Homo sapiens	662	662	97%	0.0	99.09%	332	AEW43811.1
lactate dehydrogenase C [Homo sapiens]	Homo sapiens	662	662	97%	0.0	99.09%	332	AAP37402.1
L-lactate dehydrogenase C chain [Gorilla gorilla gorilla]	Gorilla gorilla gorilla	661	661	97%	0.0	98.79%	332	XP_004050839.1
L-lactate dehydrogenase C chain isoform X1 [Nomascus leucogenys]	Nomascus leucogenys	661	661	97%	0.0	98.49%	350	XP_030685503.1
lactate dehydrogenase (E.C. 1.1.1.27) [Homo sapiens]	Homo sapiens	661	661	97%	0.0	98.79%	332	AAA59507.1

Figure 4: Showing some of the examples from similar or dissimilar species which are the most similar to the 7EPM by using BLAST Description.

Using BLAST (Basic Local Alignment Search Tool) description, similar or dissimilar species to the protein structure 7EPM can be identified based on sequence homology. BLAST analysis compares the amino acid sequence of the query protein (7EPM) to sequences in a vast database, revealing evolutionary relationships and functional similarities. Species with highly similar sequences to 7EPM are likely to share biological functions and structural characteristics, indicating a conserved role across evolutionarily related organisms. Conversely, species with dissimilar sequences may offer insights into divergent functions or specialized adaptations. By analyzing BLAST results, researchers can gain valuable information about the evolutionary conservation and functional diversity of proteins, guiding further investigations into their roles in different biological contexts.

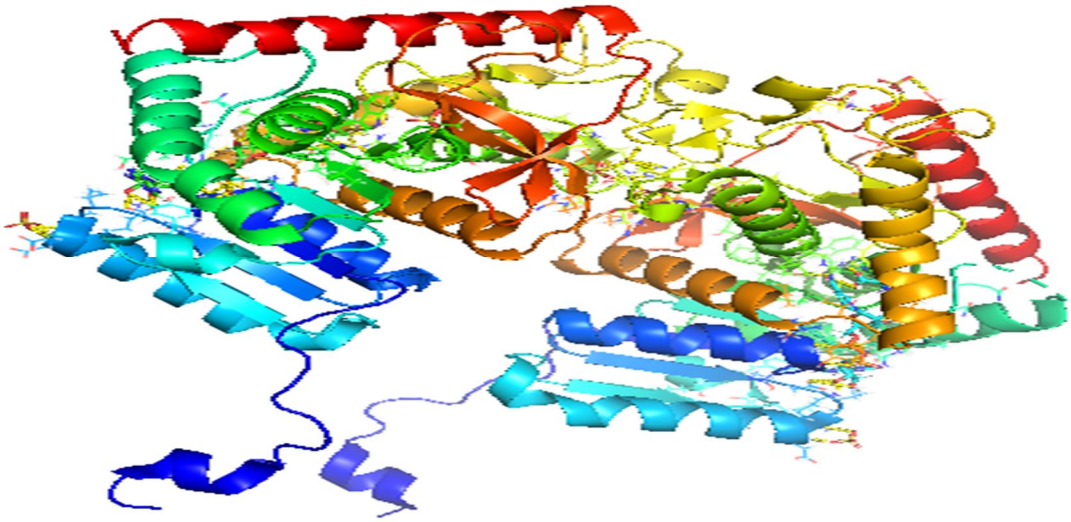

Figure 5: Showing the N-terminal and C-terminal of the protein (7epm).

In the context of protein structure, the N-terminal and C-terminal regions denote the beginning and end of the polypeptide chain, respectively. The N-terminal, or amino-terminal, region comprises the first amino acid residue of the protein sequence, while the C-terminal, or carboxy-terminal, region consists of the final amino acid residue. These termini play crucial roles in determining the protein's structure, function, and interactions.

The N-terminal often contains signal peptides or targeting sequences involved in protein localization and post-translational modifications, while the C-terminal may harbor motifs responsible for protein-protein interactions or enzymatic activity. Visualizing the N-terminal and C-terminal regions of a protein provides insights into its overall orientation and structural organization, aiding in the interpretation of its biological function and regulatory mechanisms.

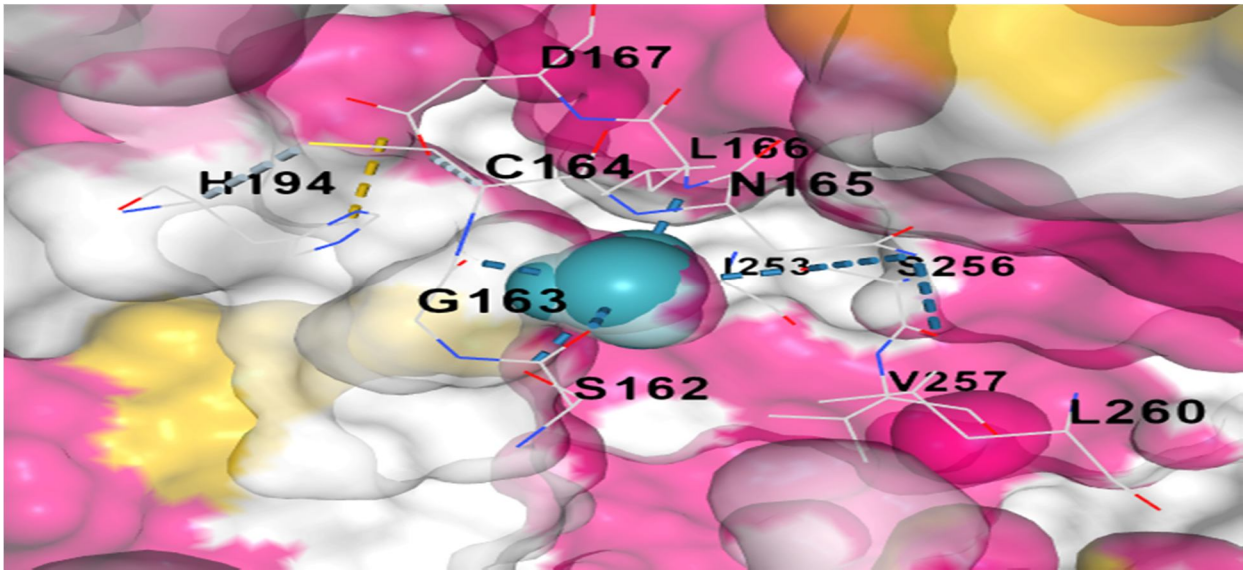

Figure 6: Azane (dichloroplatinum) docking result.

Table 3.1: showing the binding score of effective drugs.

S.No.	Drug name (CurPocket ID)	Vina Score	Cavity Volume (A^3)	Centre			Docking Size		
				x	y	z	x	y	z
1.	Azane (dichloroplatinum) (C2)	-1.2	2979	-81	42	-2	26	31	19

Docking results provide crucial insights into the interaction between small molecules and target proteins, aiding in drug discovery and development. For Docetaxel, Methotrexate, and Azane (dichloroplatinum), the docking results elucidate the binding affinity and orientation of these compounds within their respective target proteins. In the case of Docetaxel, a chemotherapy agent used to treat various cancers, the docking result reveals its interaction with the target protein, potentially inhibiting its function and impeding tumor growth. Similarly, the docking result for Methotrexate, a medication used to treat cancer and autoimmune diseases, sheds light on its binding mode and potential therapeutic efficacy. For Azane (dichloroplatinum), which is likely referring to cisplatin, a chemotherapy drug, the docking result elucidates its interaction with target proteins, offering insights into its mechanism of action and potential as an anticancer agent. Overall, docking results play a crucial role in rational drug design and optimization, providing valuable information for the development of novel therapeutic interventions.

Figure 7: Sequence analysis of the protein (7EPM) by using InterPro Scan.

Sequence analysis of proteins using InterPro Scan involves the identification of functional domains, motifs, and other important features within the protein sequence. This process utilizes a comprehensive database of protein families, domains, and functional sites to annotate the input sequence. By scanning the protein sequence against this database, InterPro Scan identifies conserved domains, repeats, and other characteristic motifs, providing valuable insights into the protein's structure, function, and evolutionary relationships. Additionally, InterPro Scan may predict potential post-translational modification sites, signal peptides, and transmembrane regions, further enhancing our understanding of the protein's biology. Overall, InterPro Scan is a powerful tool for elucidating the molecular characteristics of proteins and uncovering clues about their roles in cellular processes.

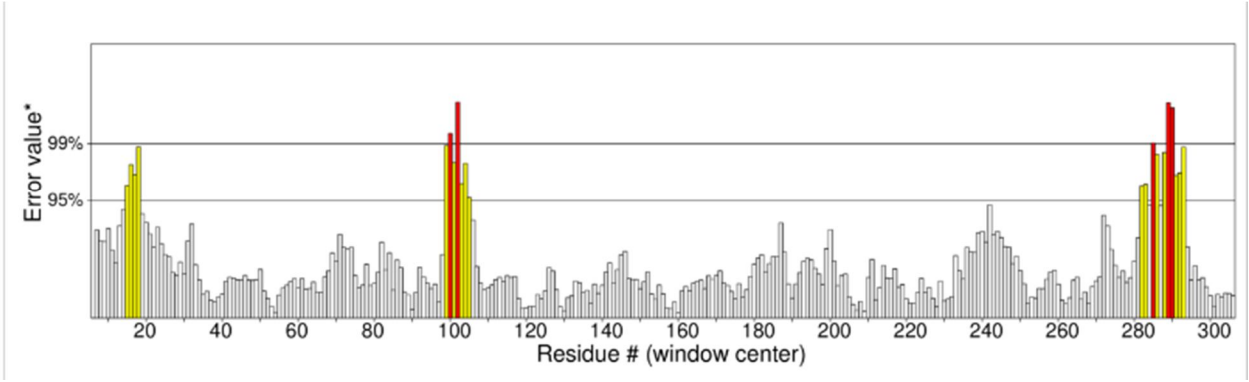

Figure 8: ERRAT protein quality estimation with Overall Quality Factor 95.29. In which red colour represents the disallowed regions of the protein.

The ERRAT protein quality estimation assigns an Overall Quality Factor to assess the reliability of a protein structure. In this case, the Overall Quality Factor of 95.29 indicates a high-quality protein structure. However, regions of the protein structure may be flagged as disallowed, typically represented in red. These disallowed regions suggest potential structural irregularities or distortions that could impact the overall reliability of the protein model. Therefore, while the Overall Quality Factor is high, it's important to address and further investigate these disallowed regions to ensure the accuracy and integrity of the protein structure.

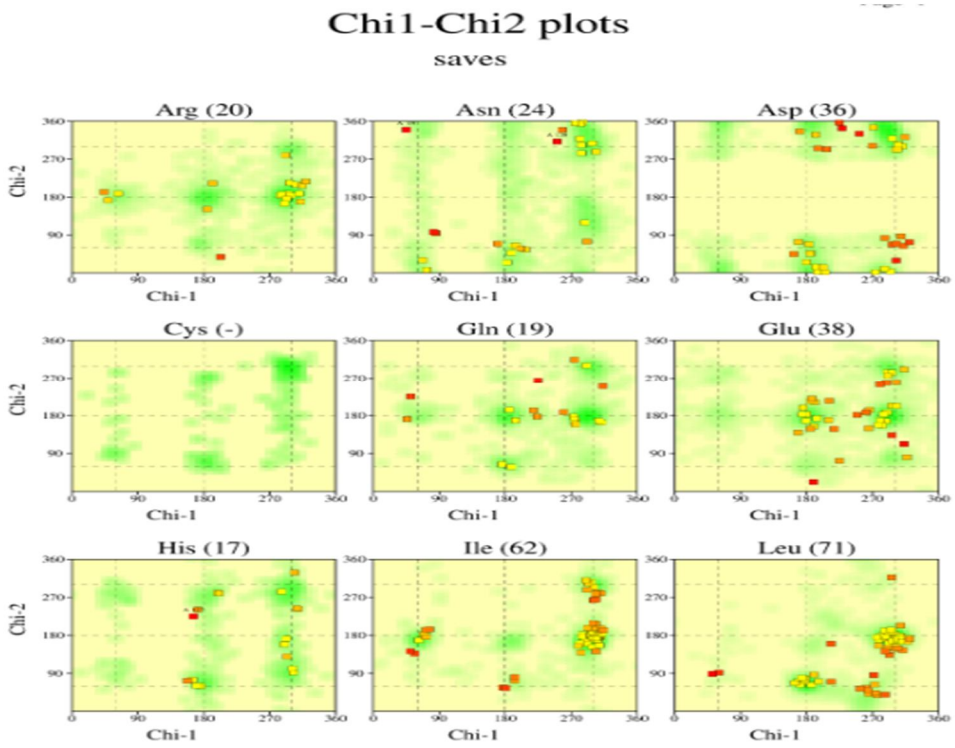

Figure 9: Chi1-Chi2 plots showing no. of residuesand favourable confirmations obtained from an analysis of 163 structures at resolution 2.0A.

The Chi1-Chi2 plots provide valuable insights into the conformational space of amino acid side chains within a protein structure. In this analysis of 163 structures at a resolution of 2.0 Å, the plots reveal the distribution of residues and favorable conformations across different regions of the protein. By examining the Chi1 and Chi2 dihedral angles of each residue, the plots illustrate the preferred rotameric states adopted by amino acid side chains. A comprehensive analysis of these plots can uncover patterns of side-chain conformational preferences and identify potential structural motifs or interactions within the protein.

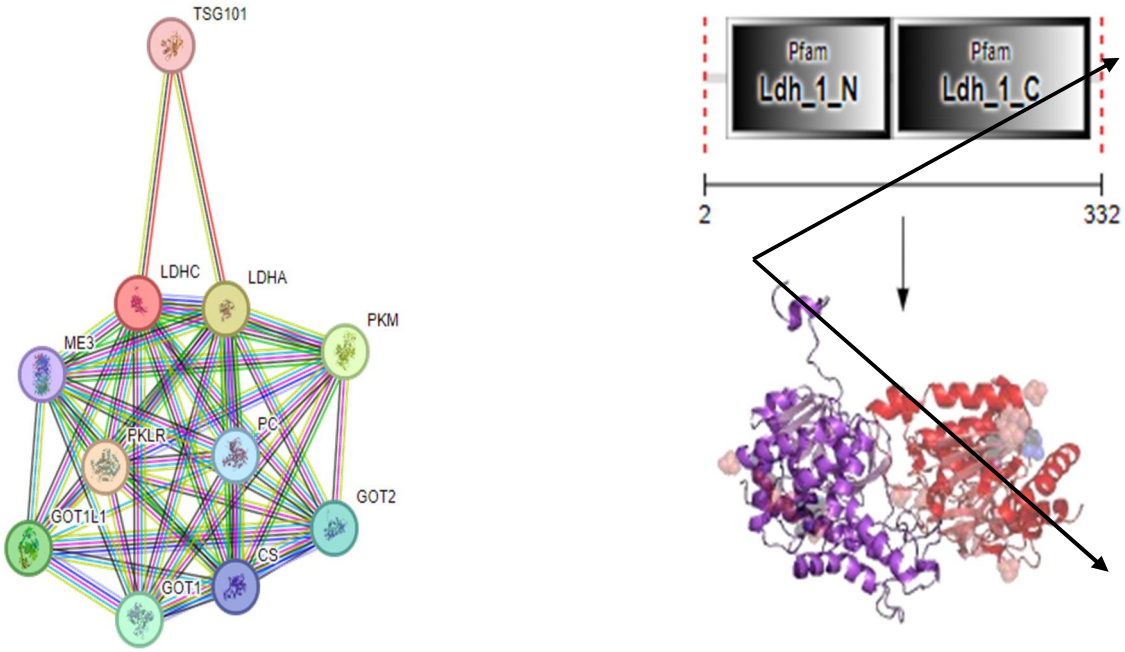

Figure 10: String network visualization of protein interaction with LDHC and showing the 99.4% similarity of 7EPM PDB structure.

The STRING network visualization of protein interactions involving LDHC provides a comprehensive depiction of the molecular interactions and functional associations of LDHC with other proteins. By integrating experimental data, computational predictions, and existing knowledge from curated databases, the STRING network reveals the intricate web of protein-protein interactions involving LDHC. Furthermore, the visualization highlights the remarkable 99.4% similarity of the 7EPM PDB structure with other related proteins, underscoring the conservation of structural features and functional domains across evolutionary distant species. This high degree of similarity suggests functional conservation and implies potential roles for LDHC in fundamental cellular processes across diverse organisms.

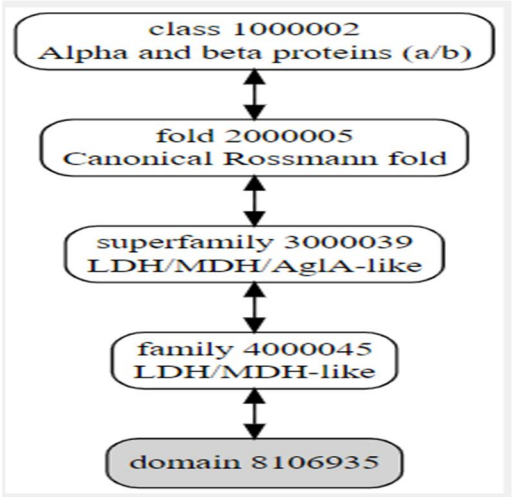

Figure 11: Showing the ancestry of the protein in SCOP.

The ancestry of the protein in the Structural Classification of Proteins (SCOP) database provides insights into its evolutionary relationships and structural homologies with other proteins. SCOP categorizes protein structures into hierarchical levels based on their structural and evolutionary relationships, allowing for the classification of proteins into superfamilies, families, and domains. By examining the SCOP ancestry of the protein, one can identify its evolutionary origins and discern common structural motifs shared with other proteins. This information facilitates the understanding of the protein's functional properties, evolutionary history, and potential roles in cellular processes. Furthermore, exploring the SCOP ancestry can provide clues about the protein's evolutionary trajectory and diversification across different organisms.

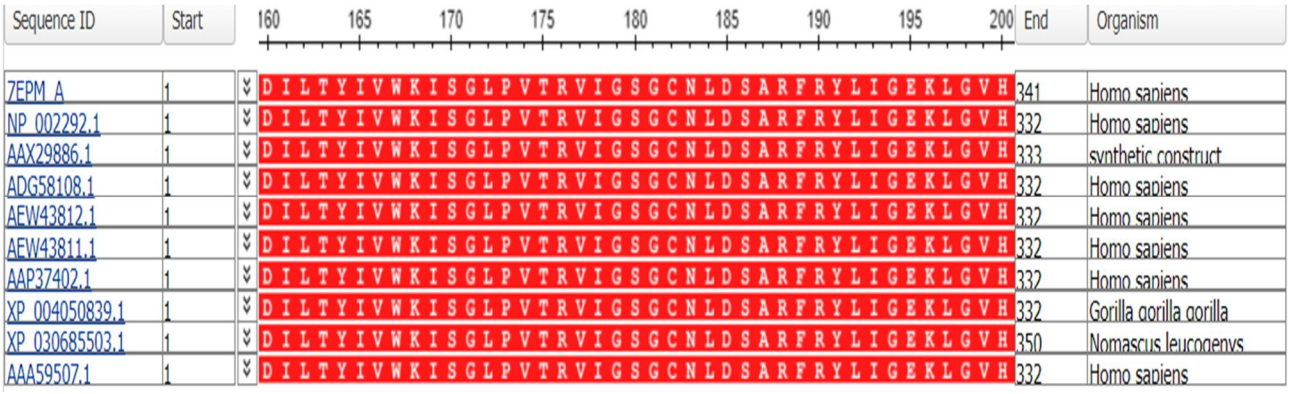

Figure 12: Red indicates highly conserved positions in CABALT using Multiple sequence alignment.

In the context of multiple sequence alignment (MSA) conducted using COBALT, the color red typically signifies highly conserved positions across the aligned sequences. These conserved positions indicate residues that have remained unchanged or have undergone minimal variation throughout evolution, suggesting their critical functional or structural importance. When analyzing the MSA results, regions highlighted in red denote amino acid residues that are highly conserved across the protein sequences being compared. These conserved residues are often associated with key functional domains, active sites, or structural elements crucial for the protein's stability and activity. Identifying highly conserved positions through COBALT MSA aids in pinpointing residues essential for protein function and can guide further experimental investigations into their roles in biological processes.

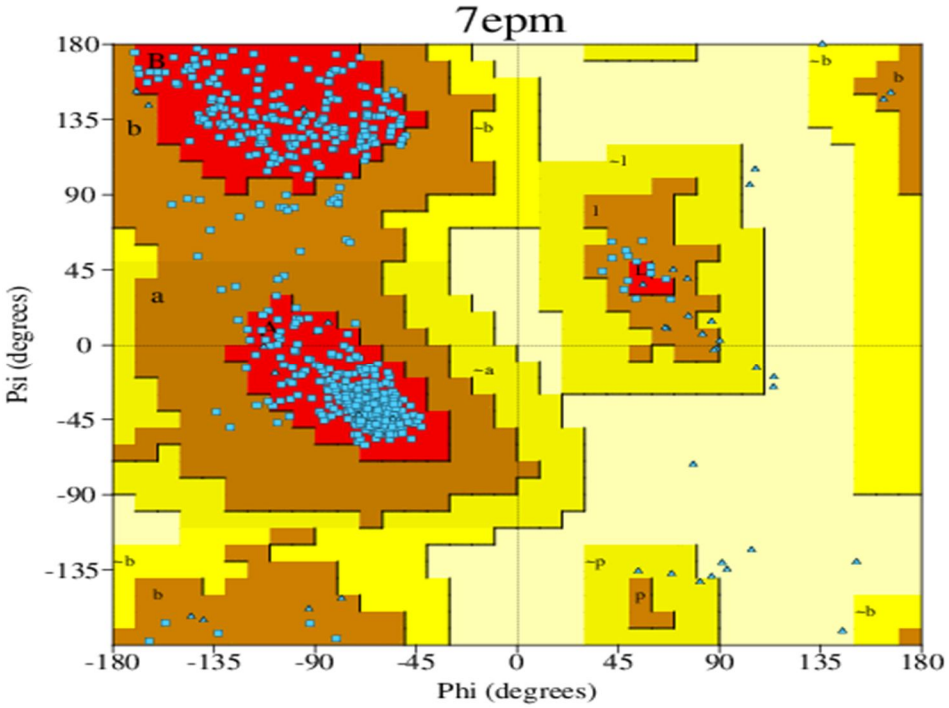

Figure 13: Ramachandran plot of protein 7EPM showing the most favorable regions [A,B,L] in PROCHECK statistics.

The Ramachandran plot of protein 7EPM, as depicted in the PROCHECK statistics, highlights the distribution of phi (ϕ) and psi (ψ) torsion angles for each amino acid residue within the protein structure. In this plot, the most favorable regions, denoted as A, B, and L, represent areas where the backbone dihedral angles conform to energetically favorable configurations conducive to stable protein structures. Region A signifies residues with phi-psi combinations that are highly favored, corresponding to well-defined secondary structure elements such as alpha helices and beta strands. Region B encompasses residues with slightly less favorable phi-psi angles but still within acceptable limits, contributing to the stability of the protein structure. Additionally, Region L includes residues with phi-psi angles that are less favored but still permissible, indicating some flexibility or deviation from ideal conformations. Overall, the presence of residues within these favorable regions on the Ramachandran plot underscores the structural integrity and reliability of the protein 7EPM, affirming its suitability for subsequent analyses and interpretations.

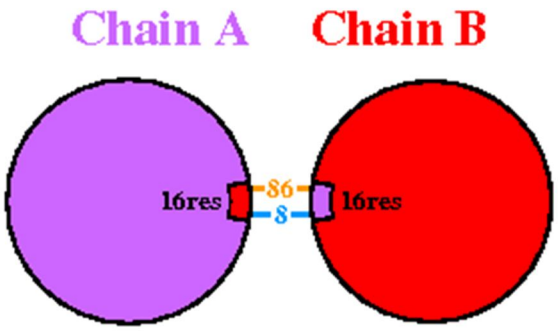

Figure 14: Schematic diagram representation of protein-protein interface of both A and B chains.

The schematic diagram represents the protein-protein interface of both A and B chains, with different types of interactions depicted using distinct colors. In this visualization, the red color highlights the presence of salt bridges, which are crucial electrostatic interactions between positively and negatively charged amino acid residues at the interface. Blue color denotes hydrogen bonds, illustrating the formation of stabilizing interactions between hydrogen atoms and electronegative atoms such as oxygen or nitrogen. Additionally, the orange color represents non-bonded contacts, signifying proximity between atoms from different chains without direct chemical bonding.

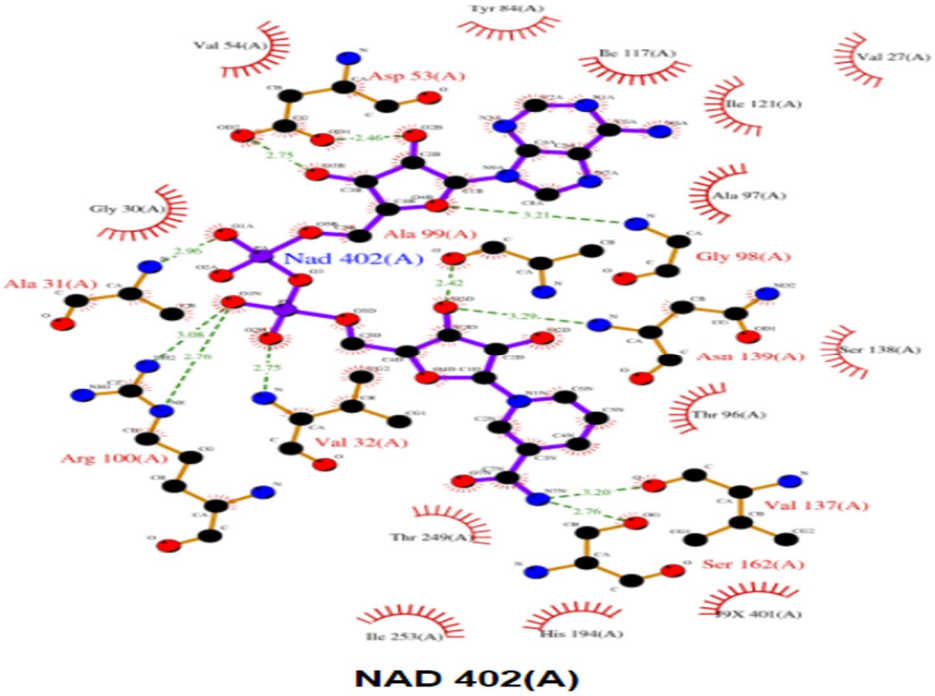

Figure 15: Ligplot interactions with ligand NAD in protein with 7EPM code.

The Ligplot interactions visualization depicts the interactions between the ligand NAD and the protein encoded by the 7EPM code. In this representation, various types of interactions between the ligand and the protein residues are illustrated. Hydrogen bonds, represented by dashed lines, indicate specific interactions between hydrogen atoms of the ligand and electronegative atoms of the protein residues. Additionally, hydrophobic interactions are depicted by arcs, illustrating non-polar interactions between the ligand and hydrophobic residues of the protein. Furthermore, water-mediated interactions are also shown, indicating instances where water molecules facilitate interactions between the ligand and the protein residues. This visualization provides a detailed overview of the molecular interactions driving the binding of NAD to the protein, offering insights into the structural basis of their interaction and potential implications for biological function.

IV. CONCLUSION

The investigation into the structural and functional intricacies of the human Lactate Dehydrogenase C (LDHC) complex, particularly its interaction with NAD+ and ethylamino acetic acid (EAA), has provided valuable insights into its role in both lung cancer pathogenesis and potential therapeutic interventions. This multidimensional analysis, utilizing data from the Protein Data Bank (PDB), Molecular Modeling Database (MMDB), and various computational tools, has shed light on the complex interplay between LDHC and cellular metabolism, as well as its implications for disease progression and treatment.The exploration into the intricate structural and functional dynamics of human Lactate Dehydrogenase C (LDHC) has been a multifaceted journey, leveraging an array of sophisticated techniques and resources to unravel its significance in the context of lung cancer pathogenesis and therapeutic opportunities. By delving into diverse datasets from repositories like the Protein Data Bank (PDB) and the Molecular Modeling Database (MMDB), in conjunction with employing a suite of computational tools, this multidimensional analysis has yielded profound insights into the complexities of LDHC biology.

At the forefront of this investigation, structural analyses utilizing cutting-edge tools such as PDBsum and RasMol have unveiled the intricate three-dimensional architecture of LDHC. Through meticulous examination, essential molecular interactions and potential binding sites critical to LDHC's function have been illuminated, providing a deeper understanding of its mechanistic underpinnings. Moreover, employing advanced sequence analysis methodologies such as BLAST and Multiple Sequence Alignment has unveiled conserved regions and structural motifs within LDHC, offering invaluable clues regarding its evolutionary significance and functional relevance across species.The endeavor to elucidate LDHC's interaction with crucial cofactors like NAD+ and ethylamino acetic acid (EAA) has been particularly enlightening. Through meticulous protein-ligand docking studies facilitated by the CB-Dock2 server, predictive insights into the efficiency of LDHC complexation with these essential molecules have been garnered. These findings not only enhance our comprehension of LDHC's pivotal role in cellular metabolism but also hold promise for the development of targeted therapeutic strategies tailored toward lung cancer and allied disorders.

A crucial aspect of this investigation lies in the rigorous validation of obtained complex structures, ensuring the robustness and reliability of subsequent analyses and interpretations. Utilizing platforms like the SAVES server, structural integrity and fidelity have been meticulously scrutinized, instilling confidence in the validity of the findings. Furthermore, biological network analyses, employing resources like the STRING database, have unveiled intricate associations between LDHC and gene ontology. These revelations provide invaluable insights into potential pathways for targeted interventions in neurodegenerative diseases and other pathological conditions. This comprehensive investigation stands as a significant milestone in our quest to decipher the molecular intricacies of LDHC and its implications for disease management. By integrating diverse analytical approaches encompassing structural, functional, and computational analyses, this study has provided a holistic perspective on LDHC's multifaceted role in cellular physiology and disease pathology.

Moving forward, the imperative remains to further validate and expand upon the findings presented here. Exploring additional facets of LDHC biology, including its regulatory mechanisms, interaction partners, and drug-ability, holds immense promise for the development of innovative therapeutic interventions. Translational research endeavors aimed at harnessing these insights for the benefit of patients afflicted with lung cancer and related disorders are poised to revolutionize clinical practice and usher in an era of precision medicine.In conclusion, the elucidation of LDHC's structural and functional properties represents a watershed moment in biomedical research. This study underscores the indispensable role of interdisciplinary approaches and underscores the transformative potential of computational tools and resources in unraveling the complexities of biological systems. Through concerted efforts, the insights gleaned from this investigation are poised to catalyze novel therapeutic strategies and pave the way for enhanced patient outcomes in the realm of lung cancer and beyond.

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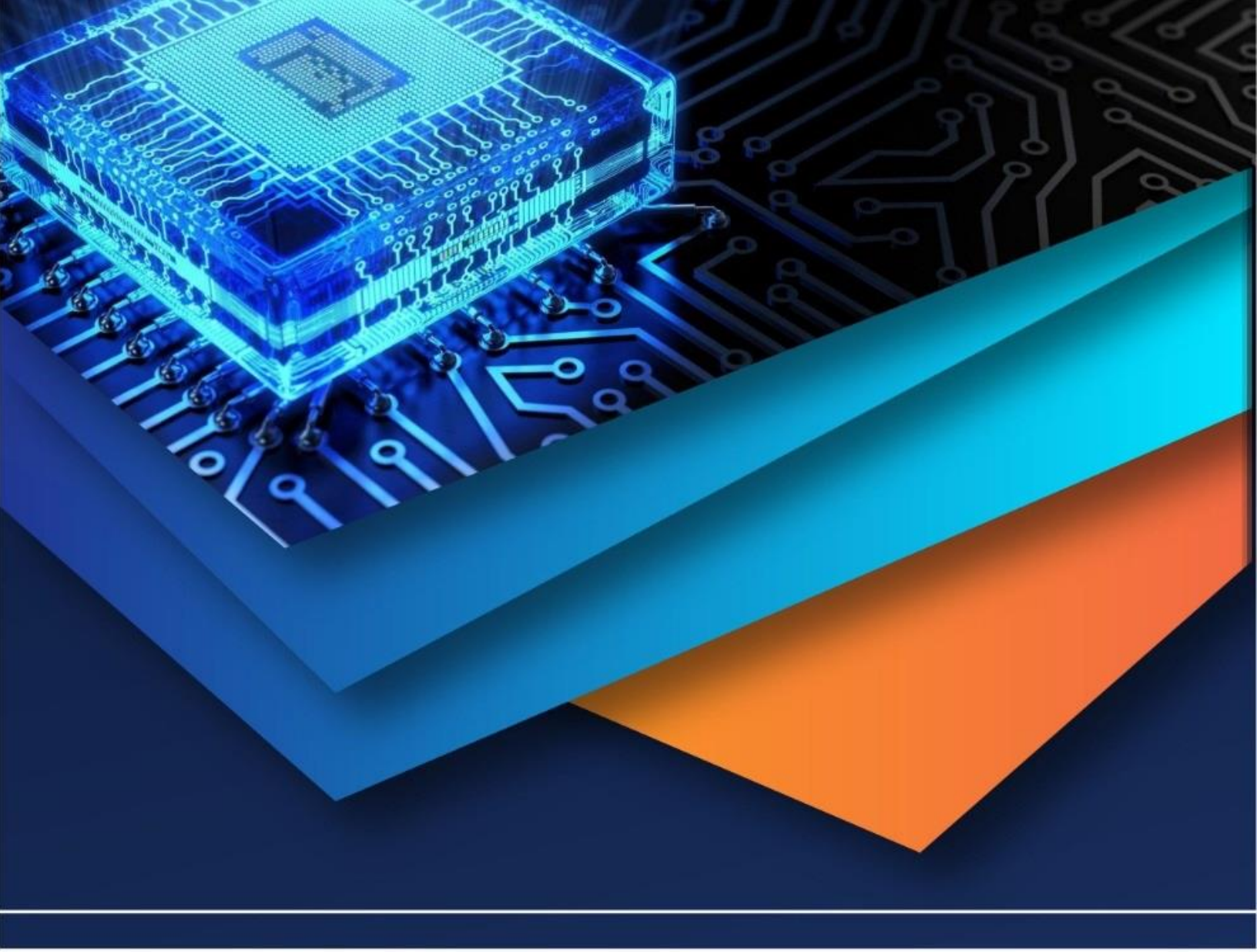

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