JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

DATA ANALYSIS OF HUMAN CRBN-DDB1 IN COMPLEX WITH LENALIDOMIDE IN MULTIPLE MYELOMA USING BIOPYTHON

Taruni Bajaj [1] Uma Kumari[1*]
[1]Trainee at Bioinformatics Project and Research Institute, Noida-201301, India
[1]Senior Bioinformatics Scientist, Bioinformatics Project and Research Institute, Noida -201301, India
***Corresponding Author: Uma Kumari**

Abstract: Multiple myeloma (MM) is categorized as one of the incurable clonal plasma cell malignancy prevalent in haematology with high rate of relapse and drug resistance. DNA damage binding protein 1 (DDB1) is a multidomain protein complex indulged in both DNA repair system and ubiquitination process by one of its cognate substrate receptors such as cereblon (CRBN). Cereblon (CRBN) is a E3 ubiquitin ligase which is complexed with CRL4 and binds to immunomodulatory drug (IMiD) such as lenalidomide to induce proteasomal degradation of neosubstrates via proteolysis-targeting chimeras (PROTACs) for targeted cancer therapy. Lenalidomide is a thalidomide derivative commonly used in the treatment of various haematological cancers including multiple myeloma and 5q myelodysplastic syndromes. In this paper, we used biopython for structural and sequence data analysis of human DDB1-CRBN complex with lenalomide in anti-multiple myeloma therapy. Biopython is an open-source tool written in an object - oriented scripting language of Python in Bioinformatics developed to create high quality, reusable modules and classes to solve complex computational problems. Various in-built functions like SeqUtils and libraries such as PDB, url, Pandas and Numpy were employed to parse and alter the sequence data of protein, extract information regarding amino acid composition, molecular weight, isoelectric point, and hydrophobicity as well as to calculate RMSD value. Matplotlib library and Seaborn library were used to create Ramchandran plot and visualize residual interactions among chains and bound ligand. Other tools such as Py3DMol were employed to provide detailed representation of molecular structure, pockets and binding interface. The results demonstrate the power of Biopython as a tool for protein analysis in cancer research. Future research can be extended on this study by investigating the functional consequences of our results and to identify novel cancer biomarkers and therapeutic targets.

Keyword: BioPython, CRBN-DDB1, Multiple Myeloma, Hydrophobicity Analysis, Network Analysis, BioPDB, Proteomics

Introduction

Multiple myeloma (MM) is categorized as one of the incurable clonal plasma cell malignancy prevalent in haematology with high rate of relapse and drug resistance. Several anti-cancerous drugs/agents including immunomodulatory drugs, proteasome inhibitors, selective inhibitors of nuclear export, cereblon E3 ligase modulatory drugs, CAR-T therapy (chimeric antigen receptor), T cell engagers (bispecific antibodies) and monoclonal antibodies have been utilized for their anti-myelomic activity to induce a significant effect on the outcomes. However, the demand of novel agents is still unmet (Wu J. et al., 2023; Schutt J et al., 2024).

DNA damage binding protein 1 (DDB1) makes up an essential component of multidomain protein complex indulged in both DNA repair system by UV damaged DNA binding protein (UV-DDB) and ubiquitination process by cereblon (CRBN) where it plays a role of specific adaptor for binding with substrate receptors. UV-DDB is heterodimeric in nature composed of two subunits DDB1 and DDB2 which helps in recognizing lesions in DNA caused by UV damage, thereby recruiting the protein to begin repair. DDB1 has various cognate substrate receptors such as cereblon (CRBN), DDB1 and CUL4 associated factors (DCAFs) (Yong D et al., 2024).

Cereblon (CRBN) is a type of conserved protein which acts as an adaptor for substrate recognition by CRL4 (Cullin-RING ligase) E3 ubiquitin ligase complex (Ichikawa S. et al., 2022). Lenalidomide is classified as an immunomodulatory drug (IMiD) which is one of the thalidomide derivatives commonly used in the treatment of various haematological cancers including multiple myeloma and 5q myelodysplastic syndromes. The molecular mechanism involves the action of these IMiDs as molecular glues which interacts with cereblon (CRBN), a E3 ubiquitin ligase CRL4 which in turn, induces proteasomal degradation of neosubstrates via proteolysis-targeting chimeras (PROTACs) for targeted cancer therapy (Wang B et al., 2024). Wherein, the binding alters the specificity of CRL4 for substrate which results in the breakdown of transcription factors like Ikaros (IKZF1) and Aiolos (IKZF3) that regulates the production of immune cells such as CD4+ T cells and other hematopoietic cells (Yong D et al., 2024). Various studies have reported that the interaction of IMiDs with CRBN takes place at the hydrophobic pocket in the C terminal domain of CRBN via one of the two chemical rings of thalidomide derivatives i.e. glutarimide rings whereas other phthalimide ring which differs in its functional groups and specificity is responsible for selective interaction

with neosubstrates (Yamanaka S. et al., 2023). The selection of proteins for degradation by E3 ubiquitin ligase complex is done by recognizing the degrons present at C terminal that enhance the process of ubiquitination and degradation (Ichikawa S. et al., 2022).
In this paper, we used biopython for data analysis of human DDB1-CRBN complex with lenalomide in anti-multiple myeloma therapy. Biopython is an open-source tool written in 1999 in an object - oriented scripting language of Python in Bioinformatics and published by Brad Chapman and Jeff Chang in 2000. The goal behind this Biopython project was to make computations in Python easier by providing accessible libraries to people (Brad Chapman and Jeffrey Chang, 2000). Among various projects organised by Open Bioinformatics Foundation (OBF), Biopython is one of them, which was developed to create high quality, reusable modules, and classes to solve complex computational problems. OBF organised Biopython website supports other related projects also such as BioPer, BioSQL, BioRuby and more. Some of the features like accessibility to online Bioinformatic databases (ExPASy), potential to parse various file formats (FASTA, Clustalw, BLAST, PubMed, GenBank, SCOP, KEGG and SWISSProt), crosslinking with various programs like clustalw alignment, Blast from NCBI, command line tools, dealing with sequences, and other sequence features etc are provided by Biopython. Other modules include Bio.Motif and Bio.Phylo that are used to analyse sequence motifs and visualization of evolutionary relationships (phylogenetic trees), respectively (Kukreja V., and Kumari, U., 2023). Several research laboratories have collaborated to carry out Biopython studies which has separate scripts and modules to perform sequence alignment, protein structure, phylogenetics, sequence motifs, and machine learning (Uma Kumari and Shruti Gupta, 2023).

Materials and methodology

The protein structure of DDB1-CRBN in complex with lenalidomide was retrieved from Protein Data Bank (PDB) with accession code **9FJX**. In this paper, computational tool like Biopython was utilized to study the structure and sequence analysis of protein. Alphafold Server is a web-based server which provides information regarding various proteins, DNA, RNA, ions, ligands and other biomolecules that are present within a structure and thus, used in structural modelling. The server was used to predict the structural model of our proteomic sample. In Biopython, sequence alignment was done and phylogenetic tree was made to determine evolutionary relationships by performing BLAST and multiple sequence alignment tool (Clustal Omega) respectively. BIT score was determined and network analysis was done to demonstrate the interaction with other similar proteins. Various in-built functions like SeqUtils and libraries such as PDB, url, Pandas and Numpy were employed to parse and alter the sequence data of protein, extract information regarding amino acid composition, molecular weight, isoelectric point, and hydropathy as well as to calculate RMSD value. Matplotlib library and Seaborn library were used to create Ramchandran plot and visualize residual interactions among chains and bound ligand. Other tools such as Py3DMol helped in providing detailed representation of molecular structure, pockets and binding interface (Adya A P and Uma Kumari, 2025, Uma Kumari, Gurpreet Kaur *et al*,2024). The study provides valuable insights and detailed information about the proteomic sample which might be useful for further investigation.

Result and discussion

Structural analysis and visualization

A. ALPHA FOLD SERVER FOR PROTEIN MODELING

Alphafold Server was used to model the chains of proteomic sample. In pLDDT (predicted local distance difference test) plot, the x-axis (Scored Residue) and y-axis (Aligned Residue) represent residue positions in the protein sequence. The protein analysis represents that the local residue-residue distances are well predicted in both chain A as well as chain B. The strong diagonal line suggests a well-folded structure, where residues align with high confidence. The color gradient indicates the expected position error in Ångströms.

CHAIN A

In chain A, more lighter regions have lower pLDDT score which signifies higher uncertainty in predicted distances. The presence of block-like structures within the plot suggests distinct structural domains with well-defined intra-domain interactions but uncertain inter-domain relationships, indicating that the model is less confident in its prediction for this chain (i.e. **lower confidence** and **higher prediction error**). This suggests that **chain A has a more flexible or disordered structure**.

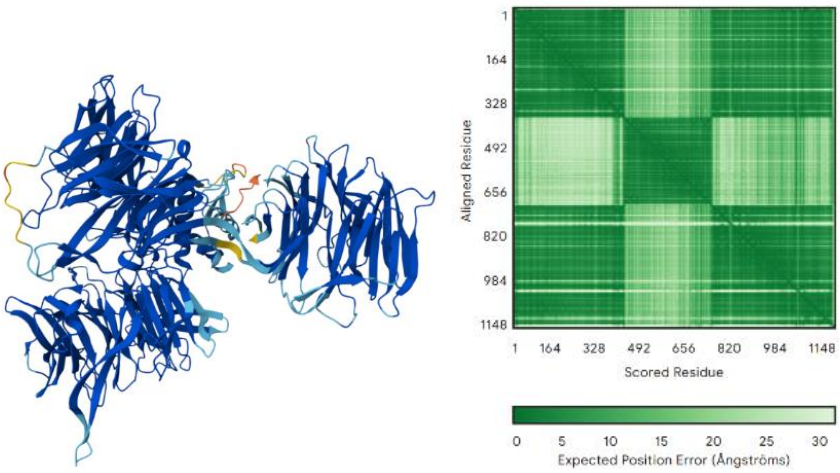

Figure 1: Molecular structure and pLDDT plot of chain A in Alphafold Server

CHAIN B

In chain B, more darker regions have higher pLDDT score which indicates that the model is more confident in its prediction (i.e. **higher confidence** and **lower prediction error**). This suggests that **chain B has a more stable or well-defined structure**.

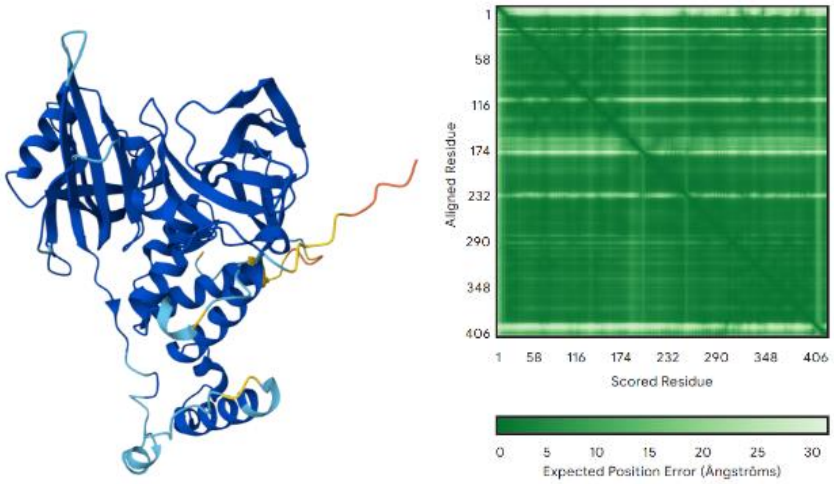

Figure 2: Molecular structure and pLDDT plot of chain B in Alphafold Server

B. RAMACHANDRAN PLOT and DSSP (DICTIONARY OF SECONDARY STRUCTURE OF PROTEIN)

To analyse the secondary structure of protein, DSSP module was used from Biopython to assign secondary structure elements to each residue and PDBparser module was utilized to parse Protein Data Bank (PDB) file and extract necessary information.

Ramachandran plot provides a visual graphical representation of the backbone conformation of proteins using dihedral angles phi and psi of amino acid residues. Biopython scripts like PDBparser and matplotlib were employed to generate Ramchandran plot and visualize the favoured and disallowed regions in the backbone conformation of protein structure. DSSP module was thereby used to assign various types of secondary structure to its residues through DSSP analysis.

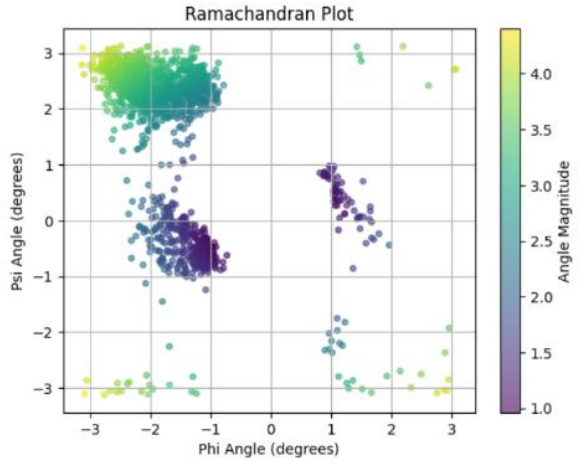

Figure 3: Ramachandran plot

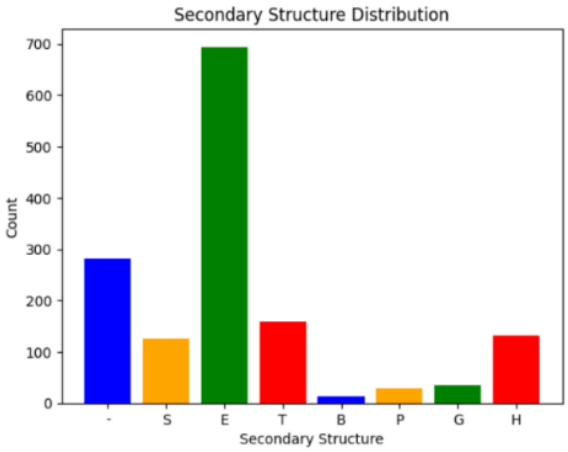

Figure 4: DSSP analysis

The presence of clusters in Ramchandran plot suggests that the protein has a mixed secondary structure composition, consisting of both alpha helices and beta sheets. On the other hand, DSSP output signifies the presence of residues with various states of secondary structures such as, alpha helix (H), beta sheets (B), bend (S), turn (T), extended beta sheets (E), kappa helix (poly-proline II helix) (P) and 3_10-helix (G) and many unknown non-special secondary structures.

This helps researchers gain a deeper understanding of the proteomic structure and its function and identify potential areas for further investigation.

C. GRAPHICAL REPRESENTATION OF CONTACT DISTANCES BETWEEN INTERACTING CHAIN A AND CHAIN B BY BIT SCORE

i. Protein-protein contact map between chain A and chain B residues

In Biopython, Pandas, NumPy and Matplotlib libraries were used to generate the scatter plot. The plot reveals a complex pattern of interaction between residues in chain A and chain B through distance between them. Wherein, the distribution of distances between residues, provides an insight into protein-protein interface.

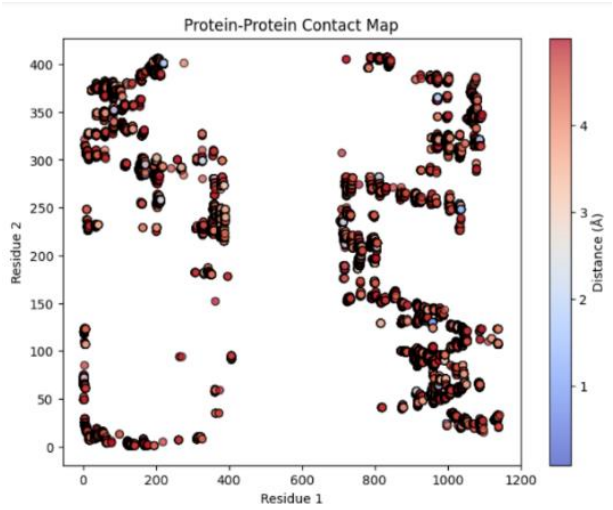

Figure 5: Scatter plot for chain A-chain B residue contact using Biopython

ii. Histogram plot of contact distances

The plot shows the distribution of distances between residues in both chains with the peak distance at around 5Å, which indicates that the most contacts occur within this distance range. The plot signifies that the chain A-chain B complex has a range of interaction types, from close-packed to more distant.

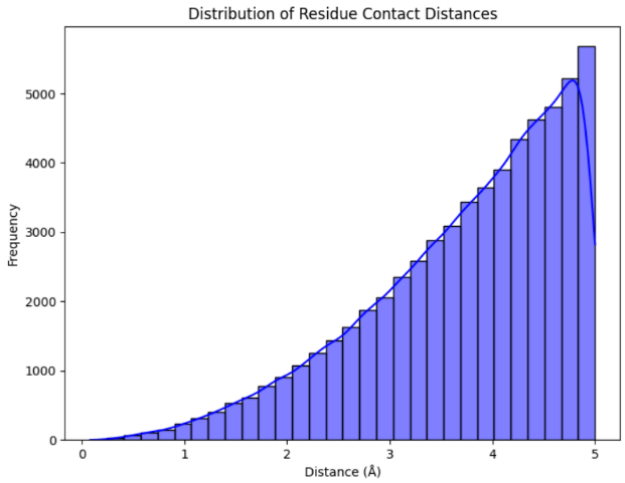

Figure 6: Histogram plot showing residual contact distances using Biopython

iii. Violin plot of contact distances

The plot provides a more detailed view of distance distribution between the residues. It reveals that the median distance is at 4Å, indicating that most interactions occur at this distance. A range of distances with some contacts occuring at much shorter or longer distance suggests that the complex has a degree of flexibility or dynamic behavior.

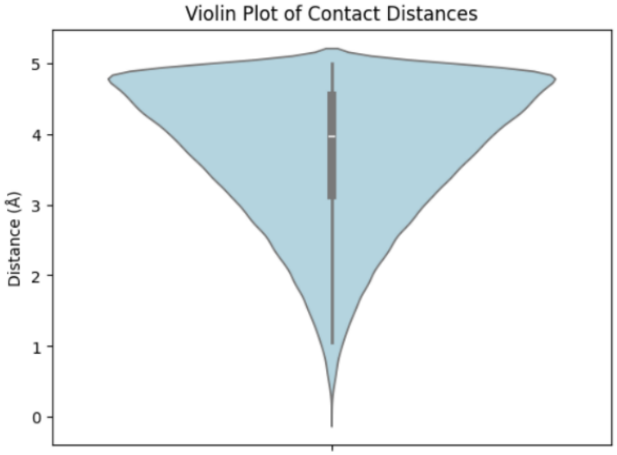

Figure 7: Violin plot for residual contact distances using Biopython

iv. 3D Scatter plot of chain A and chain B residues

The plot shows the residual arrangement in 3D space which provides an insight into the overall structure of complex. The chain A and chain B interface shows the arrangement and interaction of residues from each chain within a space.

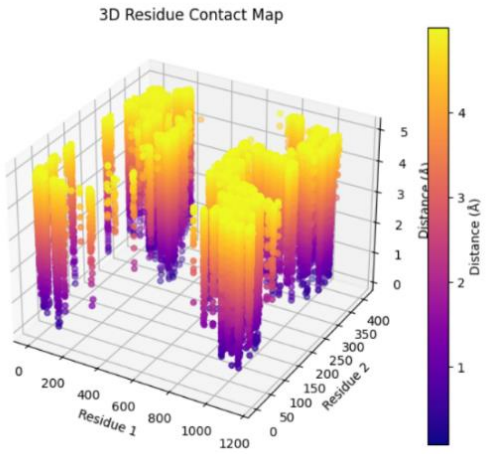

Figure 8: 3D representation of residual interaction between chain A and chain B

v. 3 D scatter plot of alpha carbons in chain A and chain B residues

Structural domains and clustering patterns within the protein complex were visualized using 3D scatter plot of alpha carbons. The closely packed alpha carbons of chain A and chain B indicates that the two chains are interacting closely. The graph represents the spatial arrangement of residues in chain A and chain B which provides valuable insights for the qualitative assessment of their interaction. Furthermore, the specified directional orientation of both chains may indicate that the chains have specific functional relationship.

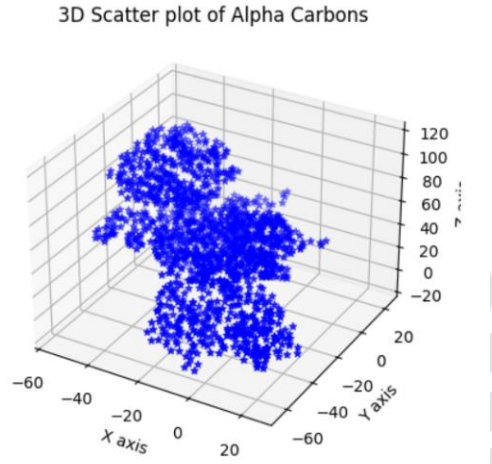

Figure 9: 3D scatter plot of distances between alpha carbons in chain A and chain B residues

vi. Residual distance between chain A and chain B

The plot displays the pairwise distance between residues in chain A and chain B, with a gradient ranging from 0 to 140Å. The dark blue regions indicate the residues that are in close proximity (distances close to 0Å), highlighting strong interactions between residues, whereas the yellow regions indicate the residues that are far apart (distances around 140Å) suggesting weaker interactions or lack of direct contact between residues.

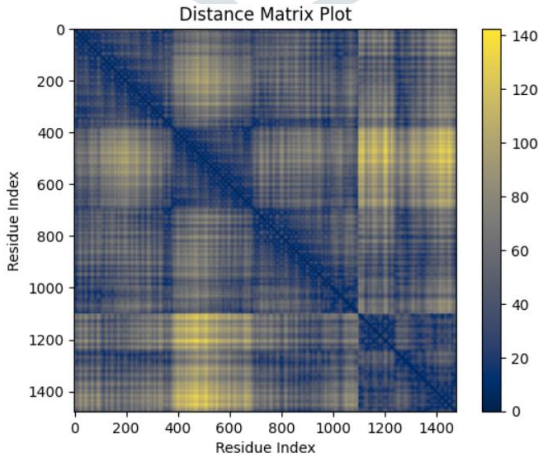

Figure 10: Distance matrix plot between residues using Biopython

vii. Contact map for protein 9FJX

The contact map for protein represents internal interactions within the protein sample 9FJX, indicating potential interaction among the residues. The graph reveals both inter-chain and intra-chain contacts providing insights into the interface between two chains. The high number of inter-chain contacts may indicate strong interaction between two chains.

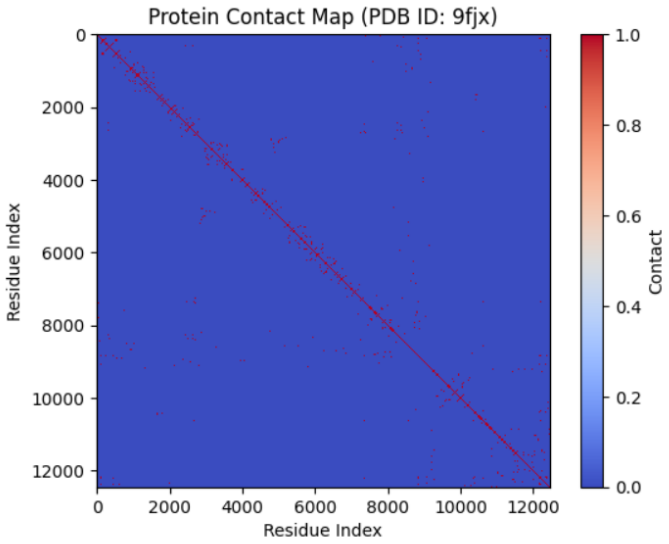

Figure 11: Protein contact map for proteomic sample 9FJX

D. VISUALIZATION OF PROTEIN USING PY3DMOL

Biopython library such as Py3Dmol was used to visualize the 3D structure of protein 9FJX, retrieved from PDB database. The visualization offers insights into the protein's structural features such as alpha-helices, beta sheets and loops. This helps in identifying potential binding sites, such as cavities or surface pockets as well as in providing information regarding molecular interactions, such as hydrogen bonding or hydrophobic interactions.

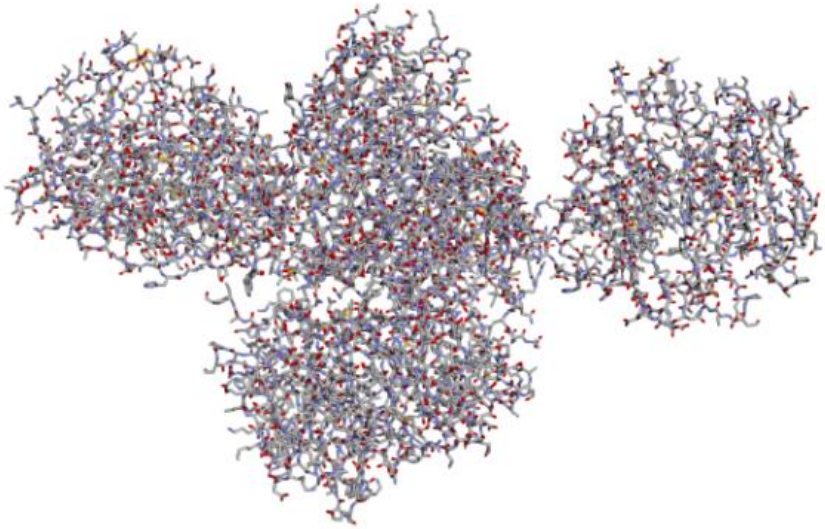

Figure 12: Visualization of protein 9FJX using Py3Dmol in Biopython

E. MOLECULAR PROPERTIES AND HYDROPHOBICITY ANALYSIS

The molecular weight was calculated for chain A and chain B and observed to be 128006.56770000057 Da and 46688.35320000003 Da, respectively. Their isoelectric point (pI) indicates acidic nature of protein at 5.163674736022948 and 6.8498033523559565 under normal physiological conditions.

The hydrophobicity analysis was done and grand average of hydropathy values (GRAVY) were measured for each chain of protein. The lower grand average of hydropathy values of -0.1227 and -0.3108 confirms the overall **hydrophilic nature of protein**.

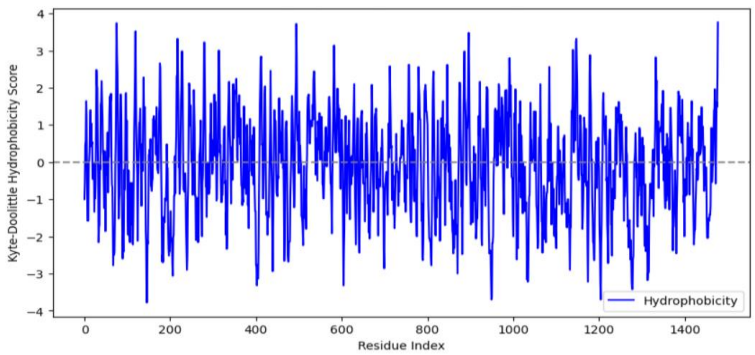

Figure 13: Hydrophobicity distribution of protein 9FJX

Sequence analysis

A. NETWORK GRAPH

BLASTp (Basic local alignment search tool for proteins) was performed and xml files were parsed to identify the proteins with highest BIT score (top hits) for each chain of protein 9FJX which shows sequence similarity relationships between different sequences, allowing for identification of closely related sequences.

Proteins with top 10 blast hits were used to create a network graph, wherein each node in the graph represents the homologous sequence of protein and edges connecting the nodes represent similarity relationship between sequences, as determined by BLAST algorithm. The edges were weighted with percentage identity values, indicating the degree of similarity between sequences.

CHAIN A

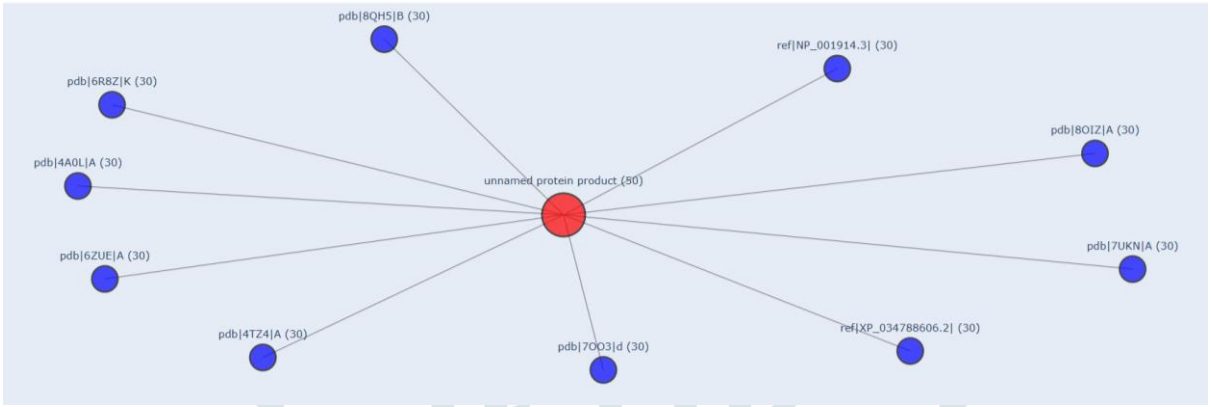

Figure 14: Network analysis of BLAST hits for chain A (unnamed protein product) of protein 9FJX

Proteins with PDB IDs 6R8Z, 4TZ4, 7OO3, 6ZUE, 4A0L, 8QH5, 8OIZ, 7UKN, and reference codes XP_034788606.2 and NP_001914.3 shows significant sequence similarity with Chain A namely, unnamed protein product.

CHAIN B

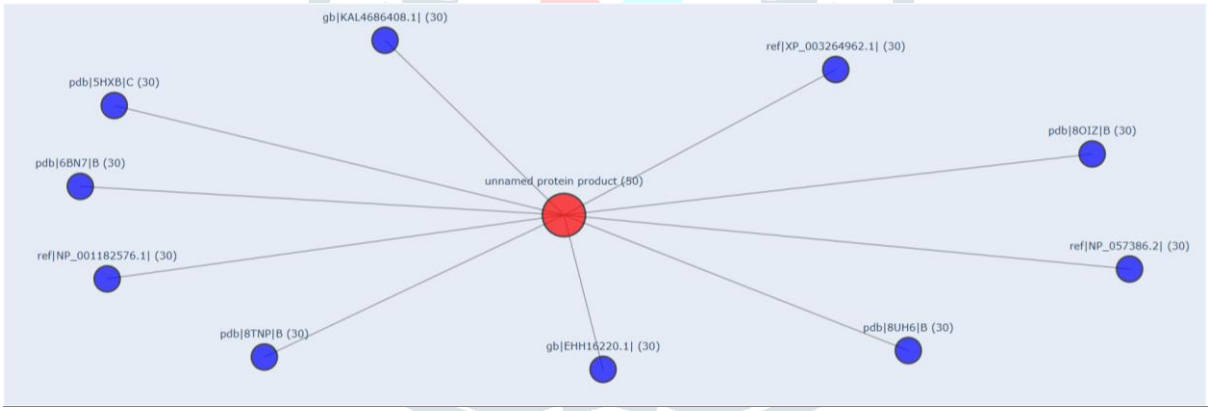

Figure 15: Network analysis of BLAST hits for chain B (unnamed protein product) of protein 9FJX

Proteins with PDB IDs 5HXB, 6BN7, 8TNP, 8UH6, 8OIZ, and reference codes KAL4686408.1, XP_003264962.1, NP_057386.2, EHH16220.1 and NP_0011182576.1 shows significant sequence similarity with Chain B namely, unnamed protein product.

This analysis can help identify functional partners or proteins that share similar functions, analyse evolutionary relationships and inform protein engineering efforts by identifying potential sites for modifications.

B. RMSD CALCULATIONS

To quantify the structural similarity between chain A and chain B, root mean square deviation (RMSD) was calculated using Biopython's PDB module. PDBParser was used to parse protein structures and RMSD values were calculated using a custom function calculate_contacts, which was modified to compute the RMSD between chain A and chain B. The distance cutoff of less than 5Å was considered.

	Model 1	Chain 1	Residue 1	Model 2	Chain 2	Residue 2	Distance
0	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	4.175035
1	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	4.320420
2	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	4.296849
3	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	3.330787
4	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	(((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (...	((<Atom N>, <Atom CA>, <Atom C>, <Atom O>), (<...	(<Atom N>, <Atom CA>, <Atom C>, <Atom O>, <Ato...	4.729961

Figure 16: RMSD calculation using Bio.PDB in Biopython

The **RMSD values** ranging from **3.330787Å to 4.729961Å**, indicates a **moderate level of structural similarity** between the two chains. This also suggests that the two chains have some structural deviations, with an **average distance of 4.2Å** between the aligned atoms. This provides valuable insights into the identification of regions with significant structural differences between the two chains.

C. AMINO ACID COMPOSITION IN CHAIN A AND CHAIN B

The frequency of amino acids in both chain A and chain B of protein were analysed and histogram plot was created using SeqUtils and Matplotlib library. The plot displays the percentage composition of each amino acid in both chains.

CHAIN A **CHAIN B**

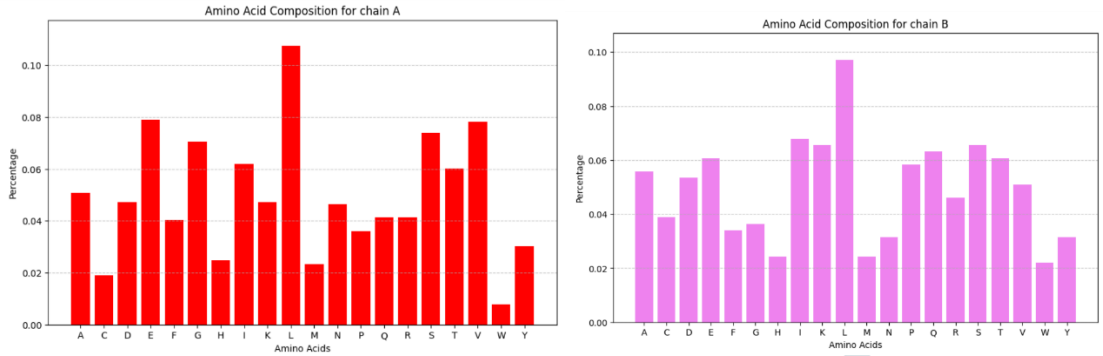

Figure 17: Amino acid composition of chain A and chain B in proteomic sample 9FJX

The histogram plot reveals that the most abundant amino acids in chain A are Leu (0.11%), Val (0.08%) and Glu (0.08%). Whereas, chain B consists of Leu (0.10%), Ile (0.07%) and Lys (0.07%) in abundance, which represents that both chains have a similar overall amino acid composition, with a mix of polar and non-polar residues. Both chains consist of prominent hydrophobic and hydrophilic residual compositions which is essential for maintaining the protein's structure, function and evolution. The presence of non-polar residues in both chains suggests a hydrophobic core which may contribute to the stability of protein. Furthermore, the differences in residual composition in both chains may influence their functional properties such as substrate binding or other chemical activity.

D. PHYLOGENETIC ANALYSIS

To investigate the evolutionary relationships between the protein sequences, the proteomic sequences were retrieved from BLAST search and multiple sequence alignment was done using Clustal Omega for both chain A and chain B. The aligned sequences were used to construct a phylogenetic tree using Biopython's phylo module.
The phylogenetic tree reveals the clustering patterns among protein sequences which may indicate functional conservation among protein sequences, suggesting shared biological functions and the branch lengths represent genetic distance between the sequences, with longer branches indicating greater divergence.

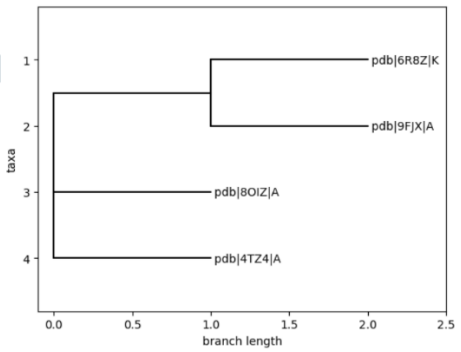

Figure 18 (a): Phylogenetic analysis of chain A of protein sample 9FJX using Biopython

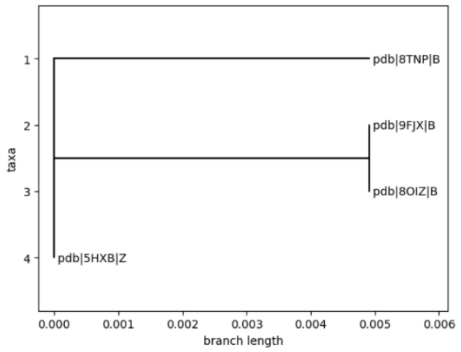

Figure 18 (b): Phylogenetic analysis of chain B of protein sample 9FJX using Biopython

The observations include chain A of 9FJX shows very close sequence similarity in its structure with 6R8Z, whereas chain B of 9FJX shows sequence similarity with 8OIZ and 8TNP. The results offer insights into their evolutionary history, functional conservation, and sequence divergence.

Conclusion

Biopython serves as investigating graphical analysis work on proteomic sample CRBN-DDB1 in complex with lenalidomide (PDB ID: 9FJX) in multiple myeloma to get the deeper understanding of disease mechanism. In Biopython data analysis, we can conclude some insights into its protein structure, binding interactions, and functional implications. By utilizing the extensive toolkit of Biopython, we were able to determine major structural and sequence characteristics of CRBN-DDB1. The results shed new light on the molecular mechanisms of multiple myeloma and demonstrate the power of Biopython as a tool for protein analysis in cancer research. Future research can be extended on this study by investigating the functional consequences of our results. Moreover, the Biopython workflows developed can be reused for other proteins and cancers to identify novel cancer biomarkers and therapeutic targets.

References

1. Wu J, Wang X, Zhang M, Mathews P, Kang Y. RXR Agonists Enhance Lenalidomide Anti-Myeloma Activity and T Cell Functions while Retaining Glucose-Lowering Effect. Cells. 2023 Aug 3;12(15):1993. doi: 10.3390/cells12151993. PMID: 37566072; PMCID: PMC10417536.
2. Yong D, Ahmad S, Mabanglo MF, Halabelian L, Schapira M, Ackloo S, Perveen S, Ghiabi P, Vedadi M. Development of Peptide Displacement Assays to Screen for Antagonists of DDB1 Interactions. Biochemistry. 2024 May 21;63(10):1297-1306. doi: 10.1021/acs.biochem.4c00044. Epub 2024 May 10. PMID: 38729622; PMCID: PMC11112733.
3. Yamanaka S, Furihata H, Yanagihara Y, Taya A, Nagasaka T, Usui M, Nagaoka K, Shoya Y, Nishino K, Yoshida S, Kosako H, Tanokura M, Miyakawa T, Imai Y, Shibata N, Sawasaki T. Lenalidomide derivatives and proteolysis-targeting chimeras for controlling neosubstrate degradation. Nat Commun. 2023 Aug 18;14(1):4683. doi: 10.1038/s41467-023-40385-9. PMID: 37596276; PMCID: PMC10439208.
4. Ichikawa S, Flaxman HA, Xu W, Vallavoju N, Lloyd HC, Wang B, Shen D, Pratt MR, Woo CM. The E3 ligase adapter cereblon targets the C-terminal cyclic imide degron. Nature. 2022 Oct;610(7933):775-782. doi: 10.1038/s41586-022-05333-5. Epub 2022 Oct 19. PMID: 36261529; PMCID: PMC10316063.
5. Wang B, Li M, Cao D, Sun Q, Yu W, Ma J, Ren H, Xu G, Zhou L. Lys-63-specific deubiquitinase BRCC36 enhances the sensitivity of multiple myeloma cells to lenalidomide by inhibiting lysosomal degradation of cereblon. Cell Mol Life Sci. 2024 Aug 13;81(1):349. doi: 10.1007/s00018-024-05390-1. PMID: 39136771; PMCID: PMC11335271.
6. Schütt J, Brinkert K, Plis A, Schenk T, Brioli A. Unraveling the complexity of drug resistance mechanisms to SINE, T cell-engaging therapies and CELMoDs in multiple myeloma: a comprehensive review. Cancer Drug Resist. 2024 Jun 26;7:26. doi: 10.20517/cdr.2024.39. PMID: 39050883; PMCID: PMC11267153.
7. Brad Chapman and Jeffrey Chang. 2000. Biopython: Python tools for computational biology. SIGBIO Newsl. 20, 2 (Aug. 2000), 15–19. https://doi.org/10.1145/360262.360268
8. Kukreja, V. & Kumari, U. Data Analysis of Brain Cancer with Biopython ,IJIRT,Volume 8,Issue 3,2023
9. Uma Kumari, Adya A P, Shruthi Satheesan, Drug Discovery and Biopython Analysis MBP-MCL1 in Myeloid Cell Leukemia. Journal of Emerging Technologies and Innovative Research (JETIR) (Jan, 2025). Volume 12, Issue 1. Pp f178-f187.
10. Uma Kumari, Shruti Gupta, NGS and Sequence Analysis with Biopython for Prospective Brain Cancer Therapeutic Studies. https://doi.org/10.22214/ijraset.2023.50885
11. Uma Kumari,Gurpreet Kaur *et al*,2024,"Biopython/Network Of Protein Identification And NGS Analysis Of Glioma Cancer ATP Competitive Type III C-MET Inhibitor : 7.367 (Calculated by Google Scholar) : Volume 11, Issue 2 : 27-Jun-2024 :pp 41-51 : http://doi.one/10.1729/Journal.40229