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# Functional Analysis of DVL Proteins Based on Signal Pathways and Their Potential as Drug Targets

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***Abstract*—** *The Dishevelled (Dvl) protein is a key regulator in the Wnt signaling pathway and plays an essential role in various biological processes, including cell proliferation, differentiation, and tumor development. In this study, a comprehensive computational analysis of the structural characteristics and potential binding sites of human Dvl proteins was performed. The amino acid sequences of Dvl1, Dvl2, and Dvl3 were obtained from public databases, and their three-dimensional structures were predicted using AlphaFold3. Model quality was evaluated based on pLDDT scores and PAE matrices, demonstrating high reliability in conserved domains.Structural analysis revealed that Dvl proteins share a typical modular architecture consisting of DIX, PDZ, and DEP domains connected by intrinsically disordered regions. Secondary structure analysis indicated that random coils are the dominant structural elements, reflecting high conformational flexibility. Functional domain analysis suggested that the DIX domain is involved in oligomerization and Axin interaction, the PDZ domain mediates ligand recognition, and the DEP domain participates in membrane localization and receptor binding.Furthermore, potential ligand-binding pockets were predicted using PrankWeb, and the highest-scoring pocket was identified as a promising target for small-molecule interaction. These findings provide structural insights into Dvl proteins and offer a theoretical basis for the rational design of targeted degradation molecules and therapeutic strategies for Wnt-related diseases.*

***Keywords*—** *Dishevelled, Wnt signaling pathway, PROTAC, Molecular Dynamics Simulation.*

## I. Introduction

The Wnt signaling pathway is a highly conserved signaling pathway in multicellular organisms that plays an important regulatory role in life processes such as embryonic development, tissue homeostasis maintenance, cell proliferation and differentiation, and self-renewal of stem cells. It was first discovered in fruit flies and its name is based on the fruit fly gene Wingless and mouse oncogene Int-1 [1-6]. With the continuous deepening of research, people have realized the important regulatory role of the Wnt signaling pathway in the occurrence and development of diseases, especially in the occurrence and development of tumors, in normal physiological processes [7].

According to downstream signaling mechanisms, it can be divided into classical Wnt/β - Catenin pathway, non classical Wnt signaling pathway, etc. Among them, classical Wnt signaling pathway is currently the most studied signaling pathway, mainly regulating target gene expression by controlling the stability of β - catenin and nuclear translocation [8]. The non classical Wnt signaling pathways include the Wnt/PCP pathway and the Wnt/Ca $^{2+}$ pathway, which are mainly involved in cell polarity establishment, cell migration, and cytoskeleton formation [9].

In recent years, studies have found that Wnt signaling pathway plays an important role in maintaining the function of tissue stem cells, influencing cell fate decisions and regulating cell microenvironment, and the abnormal activation of wnt signaling pathway is related to a variety of human diseases, such as colorectal cancer, breast cancer, lung cancer, liver cancer, etc. Studying the important regulatory proteins of Wnt signaling pathway and their mechanisms of action will help to understand the molecular mechanism of tumor genesis and development and develop new targeted therapies.

Based on the above research background, this project will take the core protein Dvl of the Wnt signaling pathway as the research object, design and establish targeted degradation molecules for Dvl in combination with PROTAC, further explore its regulatory effect on the Wnt signaling pathway, analyze the potential binding sites of Dvl protein and the mechanism of PROTAC molecule through computer-aided drug design and experimental verification, and attempt to find effective methods for regulating the Wnt signaling pathway.

The development of this study contributes to a deeper understanding of the mechanism of action of Dvl protein in the Wnt signaling pathway, providing new ideas for targeted therapy of tumors related to the Wnt signaling pathway; The targeted degradation scheme of Dvl based on PROTAC can expand the application of targeted protein degradation technology in signal pathway regulation, providing new technical means for the intervention of difficult drug targets. In the long run, this study can not only provide new lead compounds for the development of anti-tumor drugs, but also provide theoretical and experimental basis for the application of targeted protein degradation technology in the biomedical field.

## II. Methods

### *2.1 Dvl protein sequence acquisition*

In order to obtain human derived Dvl proteins for subsequent structural prediction and molecular simulation results, screening was conducted through public protein databases. Firstly, in the UniProt database （ https://www.UnipRot.org ） Use the keyword 'Dishevelled' and limit the species to Homosepiens, enter the Dvl protein family entry. Using manually annotated information from the database



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to obtain three subtypes of human Dvl protein: Dvl1, Dvl2, and Dvl3.

Select Dvl2, which has a comprehensive research foundation and is the most clear in the Wnt/β - Catenin signaling pathway, as the main research sample. Download the standard sequence of human Dvl2 protein (UniProtID: O14641) from the UniProt database, and download its complete amino acid sequence (FASTA) for computational analysis.

In order to obtain sequences with certain accuracy and stability, further analysis was conducted in the NCBI database （https://www.ncbi.nlm.nih.gov） The Dvl2 protein sequence was obtained through BLAST alignment, and it was found to be completely similar to the sequence obtained from the UniProt database without truncation or annotation bias, providing the sequence for subsequent structural prediction and simulation analysis.

### *2.2 AlphaFold3 Structure Prediction*

Open the browser, access the AlphaFold Server web page, log in to your account, click on the task creation box "Addendity", select "protein" according to the molecular type, enter the amino acid sequence of the target protein. This article only calculates the monomer structure prediction of the protein, so only one protein chain sequence is calculated.

After inputting, click "Continue and preview job" to enter the task preview, check the sequence and parameter information, ensure there are no errors, and then click "Confirm and submit job" to submit the prediction task. The server automatically completes the calculation steps such as sequence feature extraction, homologous information fusion, and structural modeling.

After the prediction is completed, click download on the results page to download the prediction result file. The prediction result file is usually. cif, which includes the three-dimensional structure coordinates of the protein and related confidence levels. The model evaluation metrics provided in the result file are PTM（predicted Template Modeling score）、ipTM （interface predicted Template Modeling score）。Among them, the value of pTM is used to evaluate the predictive quality of the overall structure, which is generally considered to have good overall folding. The value of IPTM is used to evaluate the quality of interfacial prediction between molecules. IpTM>0.8 is the credibility of interfacial prediction, 0.6-0.8 is the moderate credibility, and less than 0.6 is unreliable.

Finally, import the downloaded. cif structure file into PyMOL molecular visualization software for structural observation and organization.

### *2.3 Analysis of protein structural characteristics*

Use DSSP online tool to analyze protein structures.

Open the browser and enter the DSSP web page. Click on the "Output" option in the input menu, select "classic DSSP" as the output type, click on the "Input" option, select "PDBFile" as the input type, upload the processed protein structure.pdb file below, complete the parameter settings, open the task information, confirm that the input file and calculation parameters are correct, and click "submit" to complete the calculation task.

The server automatically completes the analysis task of protein secondary structure. After the calculation is completed, it returns to the result page and clicks "Download" to download the results. The analysis results are usually in. dssp format and record the secondary structure type information corresponding to each amino acid residue.

Finally, organize and analyze the DSSP result files, extract the secondary structure distribution of the protein as a whole and local regions, and focus on the proportion and spatial distribution characteristics of alpha helical structures.

### *2.4 Potential binding site analysis of proteins*

Use PrankWeb online server for analysis. This platform is based on the P2Rank algorithm and can identify protein surface structural features through machine learning methods to predict possible ligand binding pockets.

Firstly, open the browser and access the PrankWeb server. Select the "Upload your own structure" option in the user interface and upload the protein 3D structure file (. pdb format) that has been predicted and processed to the server.

Subsequently, after confirming that the input file is correct, click "Predict" to submit the calculation task. The server will automatically scan the protein surface and identify potential binding sites based on geometric features, residue distribution, and physicochemical properties.

After the calculation is completed, enter the result page, and the system will return the combined pockets of multiple predictions, sorted according to the prediction score. Each binding site is accompanied by a corresponding probability score and information on the key residues that make up the pocket, while providing three-dimensional structural visualization results.

Finally, download the predicted result file and analyze the potential binding sites ranked high using a visual interface.

## III. Results and Discussion

### *3.1 AlphaFold3 Structure Prediction*

In recent years, breakthrough progress has been made in protein structure prediction methods based on deep learning, and AlphaFold developed by the DeepMind team has shown excellent performance in protein structure prediction. AlphaFold3 has optimized the structure prediction algorithm based on previous versions, and further achieved good results in predicting protein complex structures and molecular interactions. Therefore, using AlphaFold3 to predict the three-dimensional structure of Dvl2 protein and obtain a reliable structural model provides structural support for subsequent molecular docking and molecular dynamics simulation studies.

### *3.2 Protein Structure Prediction*

When using AlphaFold to predict full-length sequences of human sources Dvl1, Dvl2, and Dvl3, the model is shown in Figure 22. The results showed that all three DVL proteins have typical modular structures, consisting of relatively independent conserved folding domains and longer disordered connecting regions. Overall, the three can be divided into N-terminal DIX



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domain, central PDZ domain, and C-terminal DEP domain, and there are longer intrinsic disordered regions (IDRs) between them.

In terms of sequence length, as shown in Figure 21, the model lengths are hDvl1:695AA, hDvl2:730AA, and hDvl3:715AA, respectively. From the low error diagonal block regions and structural annotations of the PAE matrix, it can be roughly estimated that the DIX domain of hDvl1 is about 1-139AA, the PDZ domain is about 278-417AA, and the DEP domain is about 430-556AA; the DIX domain of hDvl2 is about 1-146AA, the PDZ domain is about 292-438AA, and the DEP domain is about 450-584AA; the DIX domain of hDvl3 is about 1-143AA, the PDZ domain is about 286-429AA, and the DEP domain is about 440-572AA.

Overall, the structural domain composition and spatial topology of the three Dvl proteins are similar, all belonging to typical DIX-PDZ-DEP domains. The overall topology of the three proteins is relatively similar, but the relative arrangement of domains between different homologous proteins still varies. The DIX, PDZ, and DEP domains in hDvl1 are relatively compact, while the spatial distance between each domain in HDvl2 and HDvl3 is farther, making it more prone to domain separation. This means that there may be some differences in the full-length conformational dynamics between different Dvl homologous proteins, which

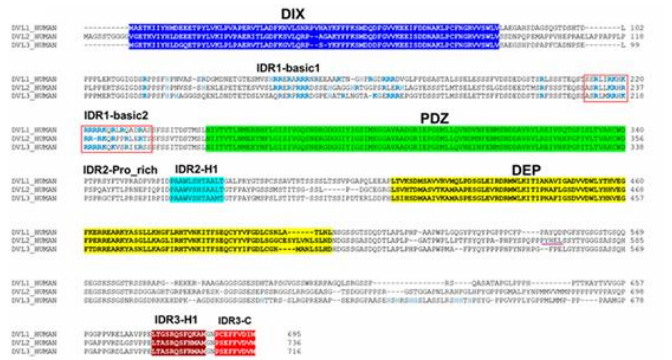


Figure 1. Human Dvl proteins have three paralogs, Dvl 1/2/3

### 3.3 Quality evaluation

Firstly, from the color of the three-dimensional structural diagram, the three conservative domains of DIX, PDZ, and DEP are mostly dark blue or light blue, corresponding to pLDDT>90 or 70<pLDDT<90 in the legend, indicating that the prediction of local structures in the predicted domains is more reliable; The long chain like regions linking various structural domains are mostly yellow or orange, corresponding to pLDDT<70 in the legend, without stable secondary structures and high flexibility, which is similar to the characteristic of Dvl protein as a multi domain signal transduction protein.

Secondly, the prediction errors of different structural regions can be observed from the PAE (Predicted Aligned Error) matrix in the lower row of Figure 2. The dark green region in the PAE matrix is the area where the prediction error between residues is relatively small. There are multiple low error diagonal blocks present in the PAE maps of the three types of Dvl proteins, representing the DIX, PDZ, and DEP domains respectively, making spatial conformation prediction more reliable.

Taking hDvl2 as an example, its PAE matrix forms three distinct low error diagonal blocks in the 1-146 AA, 292-438 AA, and approximately 450-584 AA regions, corresponding to the DIX, PDZ, and DEP domains. Similar patterns also appear in hDvl1 and hDvl3, further indicating that the three homologous proteins have high conservation in domain folding.

Taking hDvl2 as an example, there are three low error diagonal blocks in the PAE matrix, namely 1-146 AA, 292-438 AA, and approximately 450-584 AA, corresponding to the DIX, PDZ, and DEP domains. This type of approach appears simultaneously in hDvl1 and hDvl3. This indicates that the folding of the three homologous protein domains has high conservation.

However, the non diagonal regions of the PAE matrix, especially the areas of PDZ-DEP and PDZ-IDR3_C in the red dashed box in the figure2, become lighter in color, and the relative spatial positioning prediction values between different structural domains have larger errors. Although AlphaFold can accurately predict the internal structure of structural domains, there is still some uncertainty in the relative orientation between domains, similar to the IDRs commonly found in Dvl proteins, indicating that this type of signaling protein may have significant conformational plasticity.

### 3.4 Secondary Structure Composition

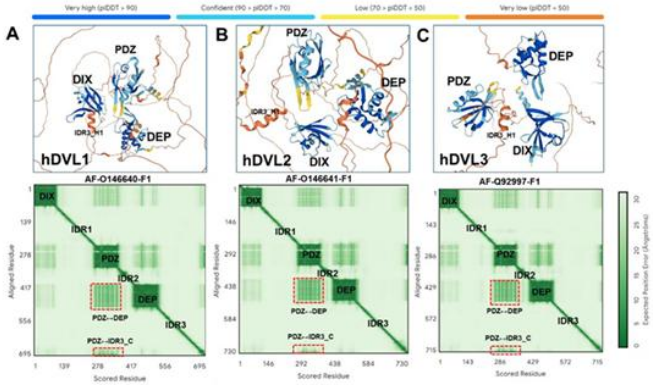


Figure 2. AF3-predicted Dvl proteins (A) human Dvl1 (B) Dvl2 and (C) Dvl3

In order to investigate the structural characteristics of the Dvl protein, the three-dimensional structural models of Dvl1, Dvl2, and Dvl3 proteins predicted by AlphaFold were used to perform statistical analysis of the secondary structure composition using DSSP. The statistical results are shown in Figure 2. Overall, the secondary structure composition of the three Dvl homologous proteins is similar, mainly consisting of random coil structures, followed by alpha helix, beta sheet, and turn structures.

The proportions of α - helix, β - fold, angle, and random coil structures in the Dvl1 protein were 14.1%, 12.9%, 14.4%, and 58.6%, respectively; The proportions of α - helix, β - fold, corner, and random coil structures in the Dvl2 protein were 11.8%, 12.5%, 18.5%, and 57.2%, respectively; The proportions of α - helix, β - fold, twist, and random curl structures in the Dvl3 protein are 12.8%, 12.8%, 15.2%, and

59.1%, respectively. It can be seen that the proportion of randomly coiled structures in all three proteins exceeds half, making it the most predominant type of secondary structure, indicating that the overall structural flexibility of Dvl protein is relatively good.

In addition, the proportion of α - helix and β - fold structures in the three Dvl proteins is not high, both about 12% -14%, indicating that the conserved domain regions of the three Dvl proteins have similar stable folds; The proportion of T in the corner structure of Dvl2 protein is slightly higher than that of Dvl1 and Dvl3, indicating that there may be stronger conformational flexibility in the domain connection region.

Overall, Dvl1, Dvl2, and Dvl3 proteins exhibit highly conserved features in their secondary structure composition, consisting of relatively stable regular secondary structures (alpha helices and beta folds) and a large number of flexible random coiled structures. This structural pattern of "stable domain+flexible junction" is a typical feature of many signal transduction proteins, which facilitates conformational changes in proteins in different signal complexes and their participation in various protein-protein interactions.

*3.5 Key structural domain analysis*

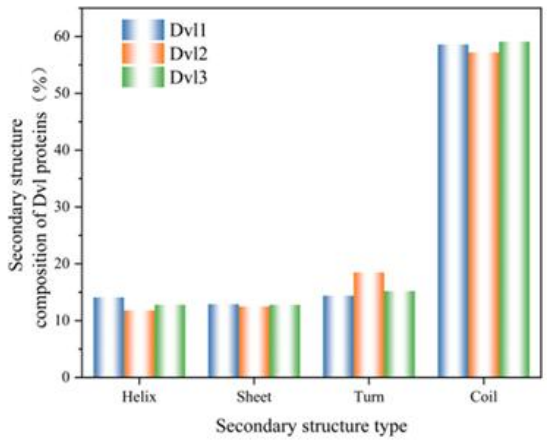


Figure 3. Secondary structure composition of three Dvl subtype proteins

Dvl (Disheveled) protein is a typical multi domain signal transduction protein, which contains three highly conserved functional domains: DIX (Disheveled and Axin) domain, PDZ domain, and DEP (Disheveled, Egl-10, and Pleckstrin) domain. These domains are involved in the regulation of the Wnt signaling pathway at different levels and jointly mediate the formation of signal complexes through various protein-protein interactions. According to the UniProt database annotations and AlphaFold predicted structural results, the overall domain distribution of the Dvl protein is shown in Figure 4 (A), where the N-terminus is the DIX domain, the middle is the PDZ domain, and the C-terminus is the DEP domain, connected by multiple disordered regions (IDR).

Dvl protein is a multi domain signal transduction protein that contains three conserved domains: DIX domain, PDZ domain, and DEP domain. It is used to control the Wnt signaling pathway and interact with other proteins to form signal complexes. According to the UniProt database annotations and AlphaFold predicted structural analysis, the overall structural domain of the Dvl protein is shown in Figure 4 (A), with the N-terminus being the DIX domain, the middle being the PDZ domain, and the C-terminus being the DEP domain connected by disordered regions (IDR).

The DIX domain is located at the N-terminus of the Dvl protein and is approximately 80 amino acid residues long, as shown in Figure 4 (B). Structural analysis shows that the domain contains five β - folds and one α - helix, belonging to a folded structure. Another structural characteristic of the DIX domain is that it can form oligomers through head tail interactions, enhance local protein concentration, and participate in signal complex assembly. Therefore, this aggregation property can promote the initiation of Wnt signaling. It can be observed that the DIX domain of Dvl can not only form homodimers, but also undergo heterologous interactions with the DIX domain of Axin protein. The DIX homodimer interaction strength of Dvl1 is higher than that of Dvl2 and Dvl3, and the heterologous interaction between Dvl Axin is stronger than that of Dvl2 or Dvl3. The DIX domain interaction between Dvl Axin is one of the molecular mechanisms that activate the Wnt/β - Catenin signaling pathway.

The PDZ domain is located in the central region of the Dvl protein and is a protein-protein interaction part, as shown in Figure 4 (C). Structural studies have shown that PDZ domains typically consist of six beta chains and two alpha helices. The PDZ domain is a conserved ligand binding pocket that can recognize various C-terminal peptide motifs and small molecule ligands. The PDZ domain can recognize multiple types of PDZ binding motifs, such as class I motifs (S/T) - X - Φ (where Φ is a hydrophobic residue), class II motifs Φ - X - Φ, and class III motifs D/E-X - Φ. In addition, the short peptide sequence (IDR3_C) in the C-terminal region of the Dvl protein can bind to the PDZ binding motif, indicating that the binding pocket of the PDZ domain has great structural plasticity and can accommodate various types of ligands, thereby participating in the regulation between classical and non classical Wnt signaling.

The DEP domain is located at the C-terminus of the Dvl protein and is a structural module involved in membrane localization and assembly, as shown in Figure 4 (D). Structural studies have shown that the DEP domain consists of three alpha helices, a beta hairpin composed of two beta chains, and some short beta chains. It contains an important "DEP finger" structure with positively charged amino acid residues that can interact electrostatically with the negatively charged lipid molecule PIP2 inside the plasma membrane, allowing the Dvl protein to be localized on the membrane; The DEP domain can also interact with the cytoplasmic domain of FZD receptors and participate in the formation of Wnt signaling complexes. Structural studies have shown that in the FZD Dvl complex, the DEP-FI region of the DEP domain is inserted into the cytoplasmic cavity of the FZD receptor and interacts with its hydrophobic interface to stabilize the receptor signal protein complex. In addition to participating in receptor binding, the



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DEP domain may form dimers through domain exchange, thereby promoting the assembly of DIX domain oligomers and participating in the formation and directional regulation of Wnt signaling.

### *3.6 Study on drug release performance of hydrogels*

To identify potential small molecule binding sites on the surface of Dvl protein, based on the three-dimensional structure model predicted by AlphaFold, the PrankWeb server (P2Rank) was utilized to predict potential binding pockets on the protein surface. By observing the geometric structural features and residue environment of the protein surface, structural grooves that may bind to ligands were identified.

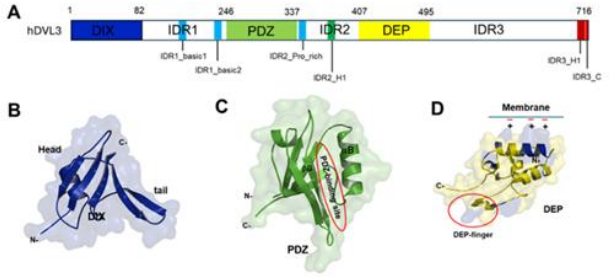


Figure 4 (A) Structure diagram of hDvl3 protein. (B–D) AlphaFold-predicted structure of the highly conserved domains: DIX, PDZ, and DEP domain

The prediction results revealed the identification of three potential pockets on the surface of Dvl protein (Table 1). Among them, Pocket 1 had the highest comprehensive score (score=5.76) with a prediction probability of 0.297. This pocket was composed of residues Ala318, Ala319, Ala324, Ala326, Ala350, Ala444, and residues 490–502. These residues all exhibited relatively distinct surface groove structures, endowed with potential binding capabilities for small molecules.

In comparison, Pocket2 has a relatively lower score and probability (Score = 3.05, Probability = 0.103), while Pocket3 has a prediction probability of only 0.01, indicating a lower likelihood of being a true ligand binding site. Therefore, this study primarily focuses on Pocket1 region as a potential functional binding site.

TABLE 1. Dvl binding pocket prediction score

| Name | Rank | Score | Probability | Sas Points | Surface Atoms |
|---|---|---|---|---|---|
| Pocket1 | 1 | 5.76 | 0.297 | 54 | 28 |
| Pocket2 | 2 | 3.05 | 0.103 | 54 | 27 |
| Pocket3 | 3 | 1.15 | 0.01 | 11 | 15 |

## IV. CONCLUSIONS

This chapter systematically conducted computational analysis on the structural characteristics and potential binding interfaces of Dvl protein. Firstly, human Dvl protein sequences were obtained from UniProt and NCBI databases, and Dvl2, which has been extensively studied, was selected as the main research object. Subsequently, AlphaFold3 was used to predict the three-dimensional structures of Dvl1, Dvl2, and Dvl3 proteins, and the model quality was evaluated through pLDDT scoring and PAE matrix. The results indicate that the overall structure of the Dvl protein consists of three highly conserved domains (DIX, PDZ, and DEP) and multiple intrinsic disordered regions. Among them, the domain region has high predictive reliability, while the connecting region exhibits significant structural flexibility.

This chapter mainly conducts computational analysis on the structural characteristics and possible binding interfaces of Dvl protein. Firstly, human Dvl protein sequences were obtained from UniProt and NCBI. AlphaFold3 was used to predict the three-dimensional structures of Dvl1, Dvl2, and Dvl3 proteins, respectively. The pLDDT score and PAE matrix were used to evaluate the quality of the model. The results showed that the overall structure of Dvl protein consisted of three highly conserved domains (DIX, PDZ, and DEP) and multiple disordered regions. The domain regions had high reliability, and the connecting regions had good structural flexibility.

Further analysis of the protein's secondary structure composition using the DSSP program revealed that the Dvl protein exhibits random curling, with a low ratio of alpha helices and beta folds, making it a typical "stable domain flexible junction" structure. Structural domain analysis shows that the DIX domain is mainly involved in protein oligomerization and Axin binding, the PDZ domain is a protein interaction module that can recognize multiple ligand sequences, and the DEP domain is mainly involved in membrane localization and Frizzled receptor binding.

On this basis, this study further utilized PrankWeb to predict the potential binding pocket of Dvl protein, identifying multiple possible small molecule binding regions, among which Pocket1 had the highest prediction score. In addition, analysis of the intrinsic disordered regions (IDR1, IDR2, and IDR3) of the Dvl protein revealed that these regions exhibit significant structural flexibility and may be involved in protein interactions. The basic2 fragment in the IDR1 region may form a short alpha helix structure and have potential membrane binding ability.

On this basis, this chapter predicted the potential binding pockets of Dvl protein and obtained multiple possible small molecule binding pockets, with Pocket1 receiving the highest prediction score. At the same time, it was found that the disordered regions inside the Dvl protein (IDR1, IDR2, and IDR3) have structural flexibility and may participate in protein interactions. The Basic2 fragment in the IDR1 region may be a short alpha helix and may have membrane binding function.

Based on the above results, it can be concluded that the Dvl protein is a typical multi domain signal protein structure, and its disordered regions may play a role in the interactions between proteins and the assembly of signal complexes. Therefore, it can serve as a structural basis for targeted molecule design, facilitating the subsequent design of functional molecules that regulate the Wnt signaling pathway.

## REFERENCES

1. Qin, K., et al., *Canonical and noncanonical Wnt signaling: Multilayered mediators, signaling mechanisms and major signaling crosstalk.* Genes & Diseases, 2024. 11(1): p. 103-134.
2. Hayat, R., M. Manzoor, and A. Hussain, *Wnt signaling pathway: A comprehensive review.* Cell Biol Int, 2022. 46(6): p. 863-877.
3. Wharton, K.A., Jr., *Runnin' with the Dvl: proteins that associate with*

*Dsh/Dvl and their significance to Wnt signal transduction*. Dev Biol, 2003. 253(1): p. 1-17.
4. Liu, J., et al., *Wnt/β-catenin signalling: function, biological mechanisms, and therapeutic opportunities.* Signal Transduction and Targeted Therapy 2021 7:1, 2022-01-03. 7(1).
5. Park, W.J. and M.J. Kim, *A New Wave of Targeting 'Undruggable' Wnt Signaling for Cancer Therapy: Challenges and Opportunities.* Cells, 2023. 12(8).
6. Pećina-Šlaus, N., et al., *Wnt Signaling Inhibitors and Their Promising Role in Tumor Treatment.* Int J Mol Sci, 2023. 24(7).
7. Wu, X., et al., *Wnt/β-catenin mediated signaling pathways in cancer: recent advances, and applications in cancer therapy.* Molecular Cancer, 2025. 24(1): p. 171.
8. Calvisi, D.F., et al., *Activation of the canonical Wnt/β-catenin pathway confers growth advantages in c-Myc/E2F1 transgenic mouse model of liver cancer.* Journal of hepatology, 2005. 42(6): p. 842-849.
9. Hu, D.J.-K., et al., *Non-canonical Wnt signaling promotes directed migration of intestinal stem cells to sites of injury.* Nature Communications, 2021. 12(1): p. 7150.

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