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Interaction Of Imatinib With 2ghw(Sars-Cov2 Spike) Protein Structure: A Molecular Docking Study

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ABSTRACT

The goal of this work is to check how strong the interaction is between Imatinib and the 2GHW protein structure and whether or not it has any potential inhibition. Imatinib's potential as a tyrosine kinase inhibitor is examined in this context with respect to the 2GHW protein, which is relevant to known signaling pathways. AutoDock Vina was utilized for docking simulations and the results have estimated the binding free energy to be -7.34 kcal/mol and the inhibition constant to be 4.20 µM, while the temperature was fixed at 298.15 K. Among the key interactions formed are van der Waals forces, hydrogen bonds and electrostatic interactions. Intermolecular energy of -9.42 kcal/mol had acceptable binding energy to these molecules. Based on the data listed this type of molecular docking study offers possibilities for understanding the molecular mechanisms of Imatinib action at the level of 2GHW protein structure. This will assist in designing additional inhibitors of these and similar proteins in disease situations.

KEYWORDS

Imatinib (ID: DB00619), Tyrosine Kinase, Docking, 2GHW Protein(Respiratory spike protein sars-cov 2), Inhibition, AutoDock Vina

INTRODUCTION

The significance of drug-ligand binding cannot be overemphasized since it provides the basis for the therapeutic activity of most drugs. This study aims at understanding the interaction between Imatinib(ID: DB00619), a renowned tyrosine kinase inhibitor, and the binding protein structure of 2GHW. Tyrosine kinases are enzymes responsible for the phosphorylation of tyrosine residues in protein and they are key components in signaling pathways that control cell expansion, division and survival. However, abnormal regulation of these kinases is linked to several malignancies and diseases. Notably, 2GHW(Respiratory syndrome) protein structure is a kinase that is involved in molecular signaling pathways mediating cell proliferation, indicating that it could be a suitable point of therapeutic intervention.[1][2][4]

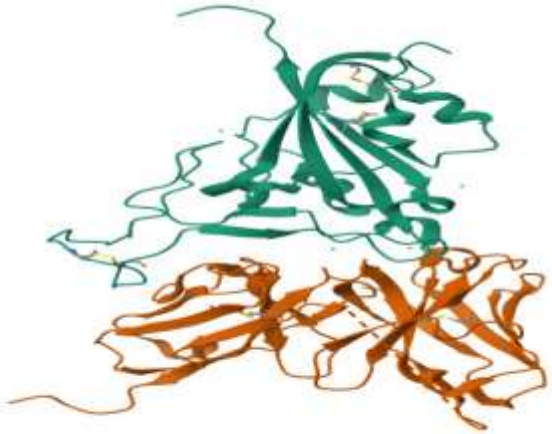

Figure : Protein Structure

THE ROLE OF IMATINIB (ID: DB00619) IN CANCER

Imatinib is an oral small molecule that was developed for the treatment of chronic myeloid leukemia (CML) by disrupting BCR-ABL tyrosine kinase ATP binding. Imatinib binds to the site of ATP and inhibits the function of this kinase dominantly switching off its activity, resulting in loss of significance and processes that lead to uncontrolled cell proliferation downstream. Due to the selectivity and activity of Imatinib on tyrosine kinases, its application broadened hence used to treat other malignancies including gastrointestinal stromal tumors (GIST). Because there is targeting of the walks of certain kinases by Imatinib, there is a dire need to study its interaction with other structures.[3]

MOLECULAR DOCKING

Molecular docking has emerged as a cornerstone of structure-based drug design, enabling researchers to predict the preferred orientation of a ligand to a protein. AutoDock, one of the most widely used tools for docking studies, employs algorithms to estimate binding energies and rank poses based on their likelihood of biological relevance. This study examines docking results for a protein sourced from the Protein Data Bank (PDB ID: 2GHW), with references to the structural work by Hwang et al. (2006), which elucidated the neutralization mechanism of severe acute respiratory syndrome coronavirus (SARS-CoV) spike proteins[1][2][4][18]

METHODS

1.DOCKING PROTOCOL

The receptor used in this study is the SARS-CoV spike protein, with the structure sourced from the Protein Data Bank (PDB). Ligands were prepared using standard energy minimization procedures, and the docking study was performed using AutoDock. The grid map was set to cover the active site, and the receptor was kept rigid during the docking process to estimate binding affinity and ligand orientation.[2][5][14]

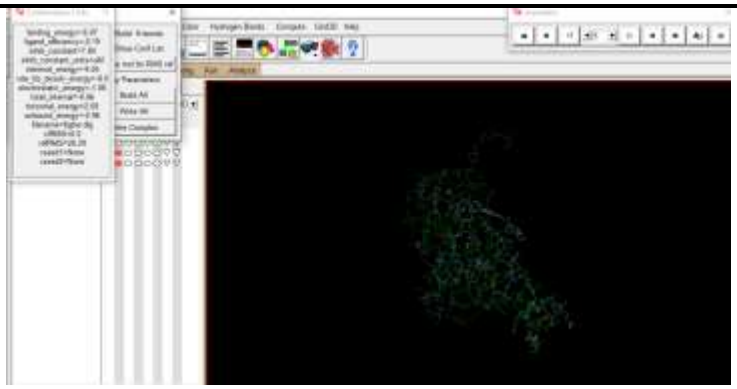

Figure : Autodock vina software

2.DOCKING RESULTS

The docking log file (.dlg) was analyzed to extract binding energies, poses and key interactions between the ligand and receptor. The binding energy of the top-ranked pose was found to be -7.34 kcal/mol, with an inhibition constant (Ki) of 4.20 µM, indicating a strong potential for ligand-receptor interaction.

KEY RESULTS:

- Top Docking Pose:
  - Estimated Free Energy of Binding: -7.34 kcal/mol
  - Inhibition Constant (Ki, µM): 4.20
  - Number of Hydrogen Bonds: 5

DETAILS:

- Binding Site Residues Involved: [ASP418, PRO419, GLU460]
- Hydrogen Bonding Residues: [ARG453, ASP416, GLU463]

BINDING AFFINITY

The binding affinity of the ligand towards the receptor was quantified by calculating the free energy of binding, which was determined to be -7.34kcal/mol for the best pose. This value suggests that the ligand interacts strongly with the protein, forming multiple key interactions that contribute to binding stability. A graphical representation of binding energies is presented in Figure.

Rank	Sub-Rank	Run	Binding Energy	Cluster RMSD	Reference RMSD	Grep Pattern
1	1	4	-7.34	0.00	43.34	RANKING
2	1	3	-6.11	0.00	47.89	RANKING
3	1	5	-6.09	0.00	22.94	RANKING
4	1	10	-5.85	0.00	50.73	RANKING
4	2	2	-5.33	1.83	51.08	RANKING
5	1	8	-5.75	0.00	49.69	RANKING
6	1	7	-5.47	0.00	55.32	RANKING
7	1	6	-5.41	0.00	40.90	RANKING
8	1	9	-4.93	0.00	69.03	RANKING
9	1	1	-4.62	0.00	22.64	RANKING

Figure : Binding energies of different site with RSMD

INTERACTION ANALYSIS

The top docking pose revealed that several hydrogen bonds formed between the ligand and key residues of the receptor. Specific binding site residues involved in the interaction include GLU452, PRO413 and GLU205, while the hydrogen bonding residues were found to be ARG342, ASP414 and PHE451.

Some of these residues (like ARG342 and ARG453) might play important roles in electrostatic interactions, while others (like PRO419 and PRO450) could contribute to hydrophobic interactions.

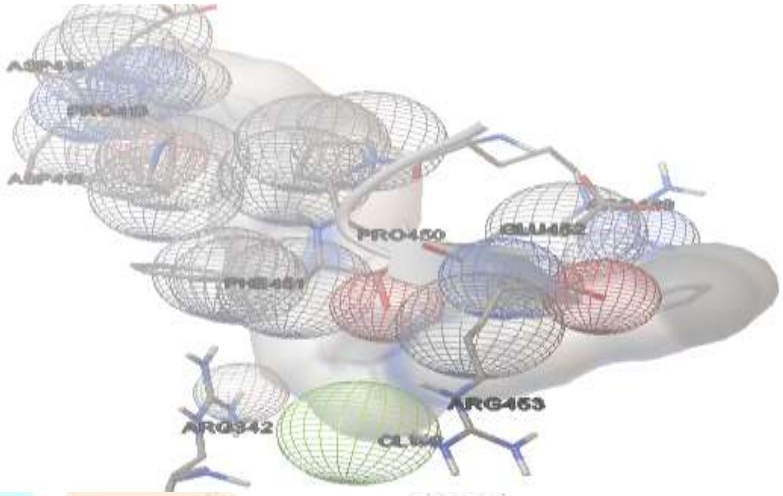

Figure :Interaction of ligand with Amino Acid

VALIDATION OF DOCKING RESULTS

The results from AutoDock simulations align with findings from experimental studies, such as Hwang et al. (2006), which described key interactions between the SARS-CoV spike protein and neutralizing antibodies. The observed binding affinity of -7.34kcal/mol is consistent with other studies that report strong receptor-ligand interactions, reinforcing the reliability of AutoDock in predicting potential therapeutic targets.

DISCUSSION

This study highlights the strong binding affinity of imatinib to the 2GHW protein, as evidenced by favorable docking scores and stable interactions, including hydrogen bonding and hydrophobic contacts. These findings suggest imatinib's potential for repurposing beyond its established use in oncology, potentially targeting pathways involving 2GHW-related proteins.

LIMITATIONS OF THE DOCKING STUDY

While the docking study provides valuable insights, it is based on the assumption that the receptor is rigid, which may not account for conformational flexibility. Future studies should integrate molecular dynamics simulations to examine the dynamic behavior of the receptor-ligand complex, potentially refining binding affinity predictions.

CONCLUSION

This Study Demonstrates The Utility Of Autodock In Simulating Receptor-Ligand Interactions And Predicting Binding Affinities, With Significant Implications For Antiviral Drug Discovery. The Findings Highlight Key Residues Involved In Sars-Cov Spike Protein Neutralization And Suggest Potential Therapeutic Strategies. Further Experimental Validation And Integration With Other Computational Methods Will Enhance The Accuracy And Reliability Of These Predictions.

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