Binding pocket identification and determination of overlapping with different software tools for V8 Protease (1QY6) from Staphylococcus aureus

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ABSTRACT

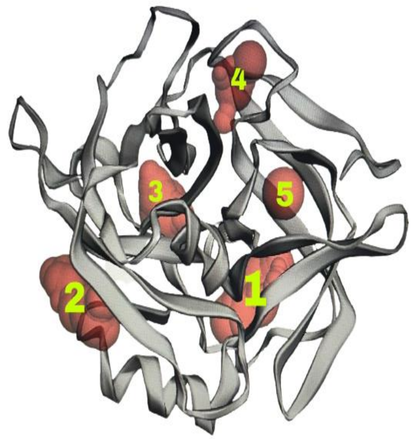
This study aimed to identify the best binding pocket of V8 Protease (1QY6) from Staphylococcus aureus and determine the percentage of overlapping using different software tools. The binding pockets were identified based on geometry, hydrophobicity, electrostatic force of attractions, amino acid residues, and chemical fragment interactions. The software tools used were Deepsite, FTSite, and CASTp. The top three binding pockets identified by Deepsite and the top five by CASTp were compared to determine the overlap. The results showed that pocket 3 had the highest percentage of overlapping amino acids between Deepsite and CASTp, with an overlap of 56% and 23%, respectively. The total overlap between the tools was 19%. The study concludes that Deepsite has superior specificity and efficiency for determining the binding pocket and that pocket 3 may function as the best binding pocket for the protease protein. These findings can contribute to the functional elucidation of proteins involved in cellular processes and aid in drug development.

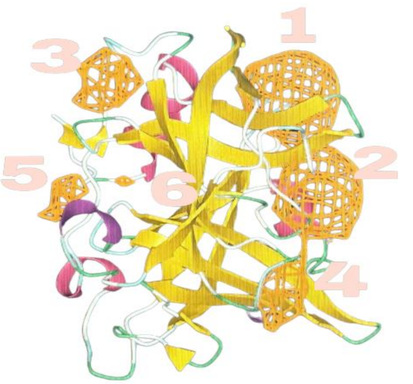
OBJECTIVE

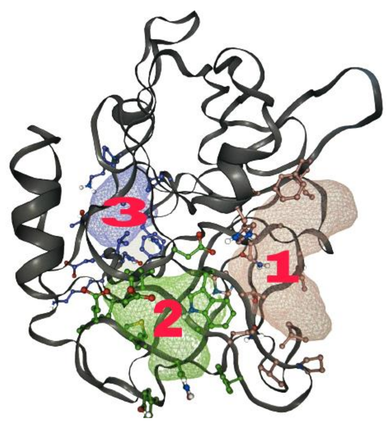
To determine the percentage overlapping and identify the best binding pocket of V8 Protease (1QY6) from Staphylococcus aureus.

INTRODUCTION

The function of proteins in various intra- and inter-cellular activities is essential, and protein-ligand interactions play a vital role in biochemical functionality across all kingdoms of life. The specific characteristics required for a protein pocket to bind a ligand include volume, shape, and physicochemical parameters such as geometry, hydrophobicity, electrostatic force of attraction, and amino acid residues. Software tools such as Deepsite, FTSite, CASTp, and F pocket can help determine these characteristics of the protein, and Deepsite, which uses a deep learning model, has shown superior specificity and efficiency for determining the binding pocket. FT Site uses the geometry of the protein with amino acid residues present on the surface, while CASTp uses the volume, shape, and surface area of the pocket to determine binding pockets. Understanding these binding pockets can aid in the design of drug molecules to interact with specific protein pockets, enabling better treatment of diseases.





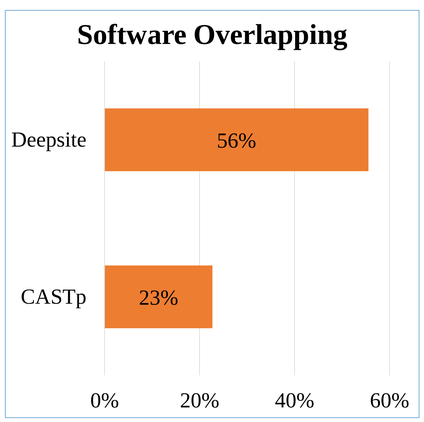


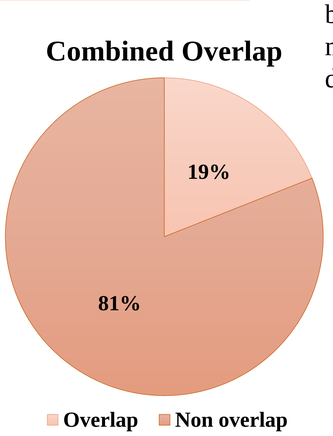
METHOD

The study involved retrieving the protease protein's PDB file from the Protein Data Bank and using software programs such as Deepsite, CASTp, and FTsite to identify its binding pockets. The amino acid residues that fit into each of the identified pockets were downloaded, and their unique sequence identifiers were noted. The software tools used different algorithms to identify the pockets, with Deep site using a 3D convoluted neural network, CASTp using volume and surface area, and FTsite using both the shape of the protein and conventional methods. The overlap of the binding pockets identified by the software tools was determined by entering the amino acid values into Excel.

The result of overlapping

CASTp & Deepsite		CASTp PocID	DeepsitePocID
SeqID	AA		
118	SER	1	3
179	GLU	1	3
181	ILE	1	3
20	ALA	3	3
21	PRO	3	3
116	THR	3	3
178	ASN	3	3
180	VAL	3	3
168	ASN	5	2
169	SER	5	1
184	HIS	5	2
185	TRP	5	1
186	GLY	5	2





RESULT

Based on the procedure, we calculated the results in Excel and discovered that the best binding pocket for the protease protein (1QY6) is pocket 3. We also discovered that 5 amino acids were matched out of 9 amino acids in pocket-3 of the deepsite pocket tool with the CASTp software tool, giving us an overlap of 56%, and 5 amino acids were matched out of 22 amino acids in CASTp, giving us an overlap of 23%. We did find that not a lot of amino acids from the FT site matched with Deepsite and CASTp, though. Between the Deepsite and CASTp, there is an overall cumulative overlapping of 19%.

CONCLUSION

The comparison of three different software tools (Deepsite, FTsite, and CASTp) for identifying the binding pocket of the protease protein (1QY6) resulted in different results with no agreement among the binding pockets established by each tool. However, binding pocket 3 showed the most overlap between Deepsite and CASTp, indicating that Deepsite may have superior specificity and efficiency for determining binding pockets compared to other tools. The total overlap between the software tools was 19%, demonstrating the importance of using multiple tools to identify potential binding pockets. Based on the findings, binding pocket 3 of the protease protein (1QY6) may function as the best binding pocket for drug design studies targeting this protein.

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