Molecular Docking of Endoglucanase a Protein - Enzyme Interaction

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***Abstract*— Endoglucanase is one of the three enzymes required to synergistically hydrolyze cellulose to sugar monomers which can be fermented into ethanol. Hence efforts to improve the efficiency of this enzyme, using experimental and computational approaches have been continuing vigorously. As an attempt computational molecular docking studies to understand the interactions in the active site regions and to suggest mutations to improve the binding characteristics was carried out in this study. The docking of ligands into active site was carried out using PIPER to evaluate the docking efficiency. The compound was docked against tubulin a cancer target. The active site is confirmed by comparing the docked structure and its was given better result compared to the control 5 fluorouracil a commercial drug.**

***Keywords*— Molecular docking, Enzyme, Protein, Interactions**

I. INTRODUCTION

Molecular docking is also referred to as small molecular docking. Molecular docking is a study of how two or more molecular structures, for instance, drug and catalyst or macromolecule receptor, match along to be a perfect fit [1]. Binding orientation of small-molecule drug candidates to their macromolecular targets predicts the affinity and activity of a given small molecule [2]. Protein–protein docking is a simple procedure, which involves docking of two protein molecules without any need of experimental measurement. Flexible and rigid docking is followed in this type of docking [3]. Shape complementarity is the most essential ingredient of the scoring functions for protein–protein docking [4]. The steady rise in the number of protein structures elucidated has boosted the number of protein–protein docking studies, and intensive research is being carried out in the field. Many proteins that remain rigid after forming a complex can also be docked [5]. Protein–ligand docking is the most commonly used docking technique. It predicts the position of a ligand when it is bound to its receptor molecule, in this case, a protein. The ligand might act as an inhibitor or a promoter. Large libraries of ligands are scanned to choose potential drug candidates [6]. As an attempt computational molecular docking studies to understand the interactions in the active site regions and to suggest mutations to improve the binding characteristics was carried out in this study. The docking of ligands into active site was carried out using PIPER to evaluate the docking efficiency. The compound was docked against tubulin a cancer target [7] . The active site is confirmed by comparing the docked structure and its was given better result compared to the control 5 fluorouracil a commercial drug.

II. MATERIALS AND METHODS

A. STRUTURE RETRIEVAL

Target

Target-based drug discovery begins with the identification of the function of a potential therapeutic drug target and understanding its role in the disease process. The crystal structure of TUBULIN an cancer target with resolution 3.58 Å was used as a target structure in current study. It was obtained from RCSB Protein Data Bank (http://www.rcsb.org/pdb/home/home.do) with the PDB ID: 1SAO

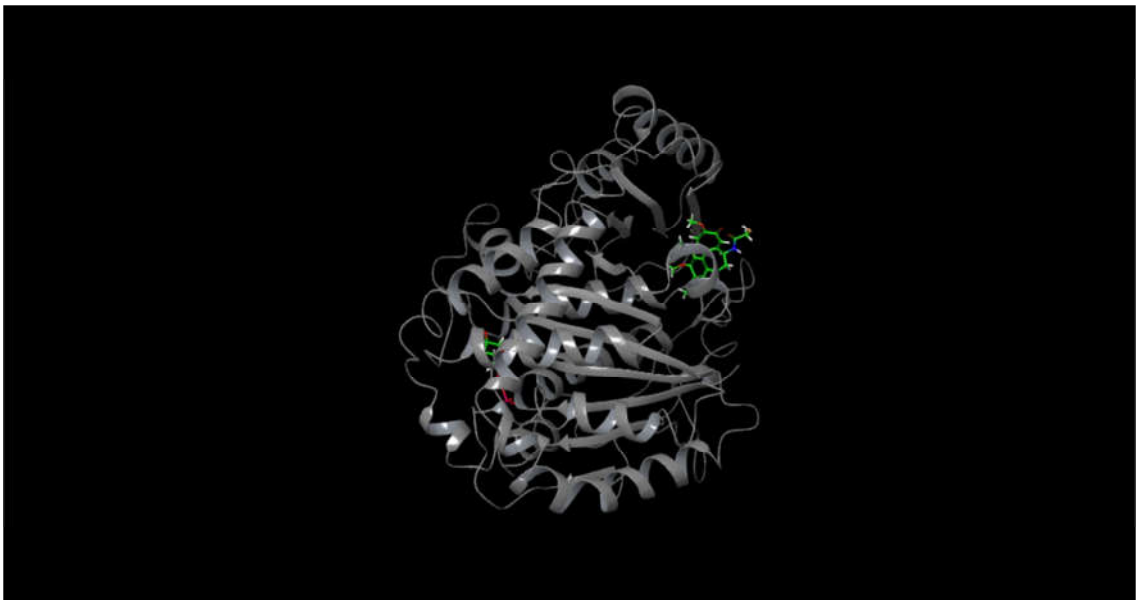

Figure-1 Target Tubulin

Ligands

The enzyme endoglucanase was selectd as drugs there structure where downloaded from RCSB Protein Data Bank with the PDB ID 2ENG

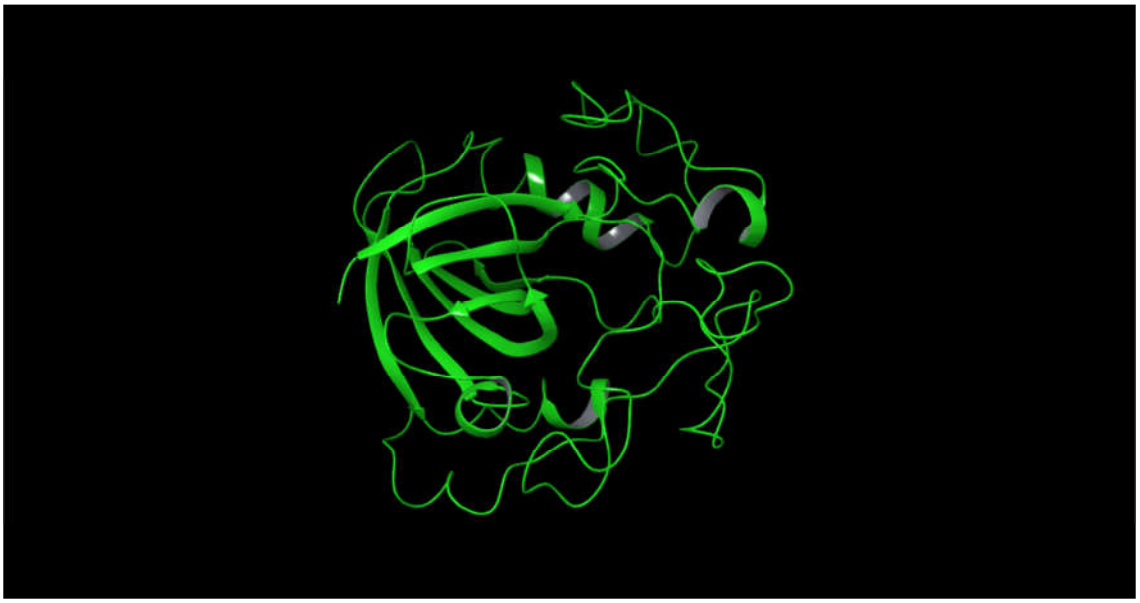

Fig. 2. 2ENG (ENDOGLUCANASE)

Preparation Of Protein And Enzyme Structure

The Protein Preparation Wizard (PrepWizard) in Maestro was used to prepare the proteins in this study. The missing hydrogen atoms and side chains where built by prime, bond orders to HET groups are generated , Removed co-crystallized water molecules with less than 3 H- bonds to water molecules, the HET states where generated by Epick and the lowest energy state is choosed, Optimized the protein's hydrogen bond network by means of a systematic, cluster-based approach. Performed a restrained minimization that allows hydrogen atoms

to be freely minimized, while allowing for sufficient heavy-atom movement to relax strained bonds, angles, and clashes and the final minimized structure with force field is used for further studies

Protein-Enyme Docking

PIPER is an FFT-based protein docking program with pairwise potentials tool is chosen for docking purpose . In the receptor tab the minimized target tublin is chosen and in the ligand tab the enzymes are chosen and the docking was run for individual enzymes separately and the maximum number for confirmation generation was set to thirty. Standard mode docking was chosen.

PROTIEN- ENZYME INTERACTION ANALYSIS

Scrodinger has a module to analysis the result produced from the PIPER module. The lower energy docked protein was chosen from the workspace and the target protein chain was chosen to Group 1 window and the enzyme was chosen to the Group 2 window and then determination protein interaction was executed which gives the interaction between the protien- enzyme complex.

III. Results and Discussion

Residue	This column lists residues in either group that have contact-type interactions with residues in the other group.
Closest	This column lists residues from the other group that are within a specified distance of the residue listed in the Residue column. The default distance is 4.0 Å.
Specific Interactions	Text list of specific interactions between the residue listed in the Residue column and residues in the other group. The list covers hydrogen bonds, salt bridges, pi-pi interactions, disulfides, and van der Waals clashes.
# HB	Number of hydrogen bonds between the residue listed in the Residue column and residues in the other group.
# Salt Bridges	Number of salt bridges between the residue listed in the Residue column and residues in the other group. The criteria for detecting salt bridges can be changed in the Advanced Settings dialog box, prior to the analysis.
# Pi Stacking	Number of pi-pi stacking interactions between the residue listed in the Residue column and residues in the other group.
# Disulfides	Number of disulfide bonds between the residue listed in the Residue column and residues in the other group.
# vdW Clash	Number of van der Waals clashes between the residue listed in the Residue column and residues in the other group. A clash is defined as an overlap of the van der Waals radii of two atoms by more than a specified cutoff.
vdW Complementarity	Van der Waals shape complementarity between the residue listed in the Residue column and residues in the other group, as defined by Lawrence, M.C. and Colman, P. M., J. Mol. Biol.1993, 234, 946–950.
Buried SASA	Fraction of the solvent-accessible surface area of the residue listed in the Residue column that is buried by the interaction with residues in the other group

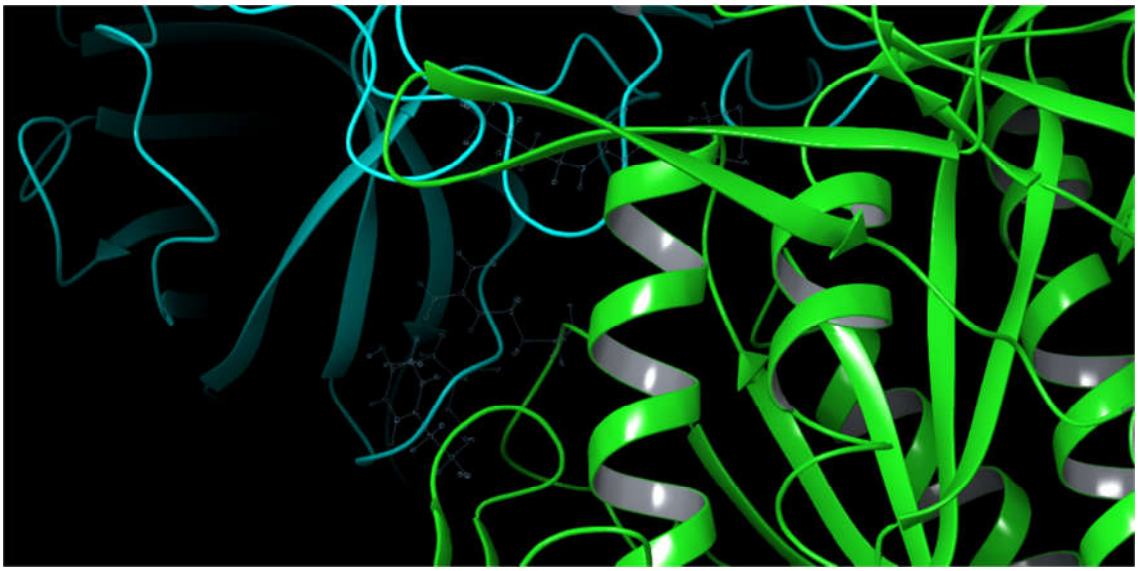

Fig. 2 Docked protein-enzyme complex of Uridine phosphorylase and endoglucanase (Hydrogen bond formation)

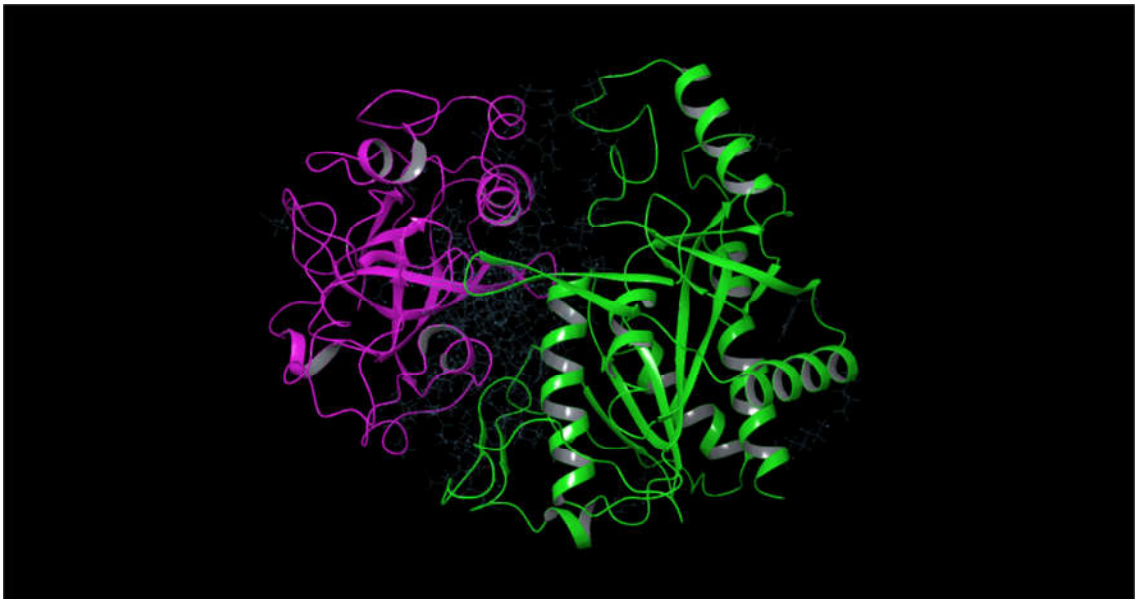

Fig. 4 Docked protein-enzyme complex of Uridine phosphorylase and endoglucanase

Docking was done in PIPER. PIPER performs exhaustive evaluation of an energy function in discretized 6D space of mutual orientations of two proteins. We sample 70,000 rotations which approximately correspond to sampling at every 5 degrees in the space of Euler angles. In the translational space the sampling is defined by the 1.2 Å grid cell size. The energy-like scoring function describing the receptor-ligand interactions is defined on this grid and is efficiently calculated using Fast Fourier transforms. Results are clustered with a 10 Å cube size, and one or several lowest energy translations for the given rotation are retained. Finally, results from different rotations are collected and sorted. The novelty of the PIPER algorithm is that the scoring function includes an energy term of the form Epair = $\Sigma i \Sigma j \varepsilon ij$, where εij is a pairwise interaction potential between atoms i and j. The key to the efficient use of this potential within the FFT framework is the eigenvalue-eigenvector decomposition of the interaction matrix. The complete scoring function is given as the sum of terms representing shape complementarity, electrostatic, and desolation contributions, the latter described by the pairwise potential. We have shown that PIPER increases the number of near-native conformations in the top 1000 or 2000 structures relative to other FFT-based docking programs

From the 30 pose created, Pose 2 was chosen which has the highest piper score -107.810000 and the pose energy of -803.831000 and it has the maximum cluster size of 95. Hydrogen bond is formed between

endoglucanase Asp 114 and B chain of Uridine phosphorylase Tyr 35, Arg 94 with the bond length of 2.4 Ao ,3.8 Ao . And hydrogen bond formed between endoglucanase Arg 146 and B chain of Uridine phosphorylase Met 110 with a bond length of 2.0 Ao . And hydrogen bond formed between endoglucanase Asp 114 and B chain of Uridine phosphorylase Arg 94 with a bond length of 3.3 Ao. And hydrogen bond formed between endoglucanase Asp 114 and B chain of Uridine phosphorylase Tyr 35 with a bond length of 2.4 Ao. And hydrogen bond formed between endoglucanase Asp 133 and B chain of Uridine phosphorylase Met 110 with a bond length of 3.2 Ao . The protein – enzyme reaction was occur between 2ENG and 3NBQ. >2ENG_A, 210 bases.

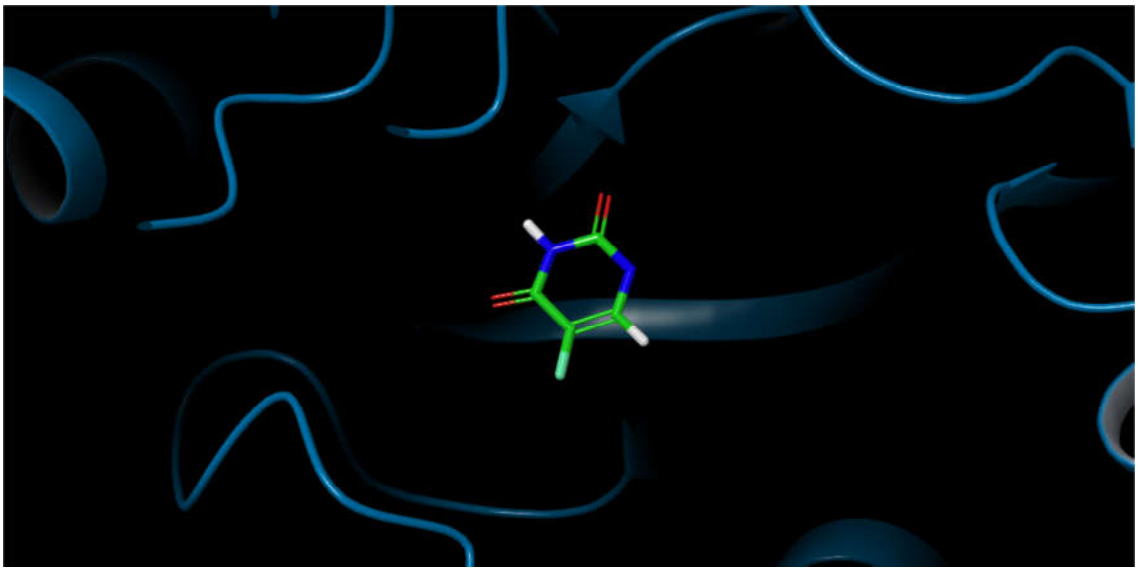

Fig. 5 Uridine phosphorylase with 5-Flurosil

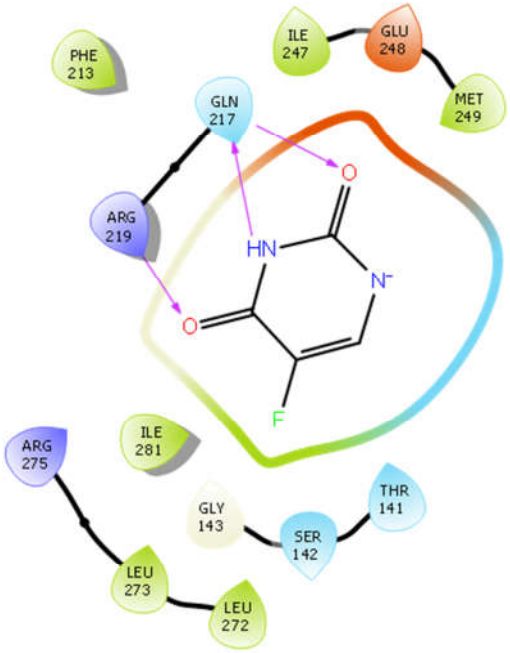

Fig. 6 Interaction between Uridine phosphorylase and 5-Flurocil

The 5-flurosil exhibit three hydrogen bond with the protein molecule Uridine phosphorylase(3BNQ) GLN 217 forms two bond with the Oxygen molecule and amine group with the bond length of 1.97 Ao and 1.95 Ao, Arg 219 forms hydrogen bond with Oxygen atom in 5-flurosil with the bond length of 2.23 Ao

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