

MOLECULAR DOCKING

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Types of Docking

Binding site Based

- Binding Docking
 - When no information is available about binding site
 - Use whole protein structure surface to bind
 - Slow
 - Can be used to find potential binding site
 - may introduce errors in results
- Targeted Docking (site specific)
 - Is performed in a specific , small region of the protein
 - Require Knowledge about binding site
 - Faster
 - Less errors

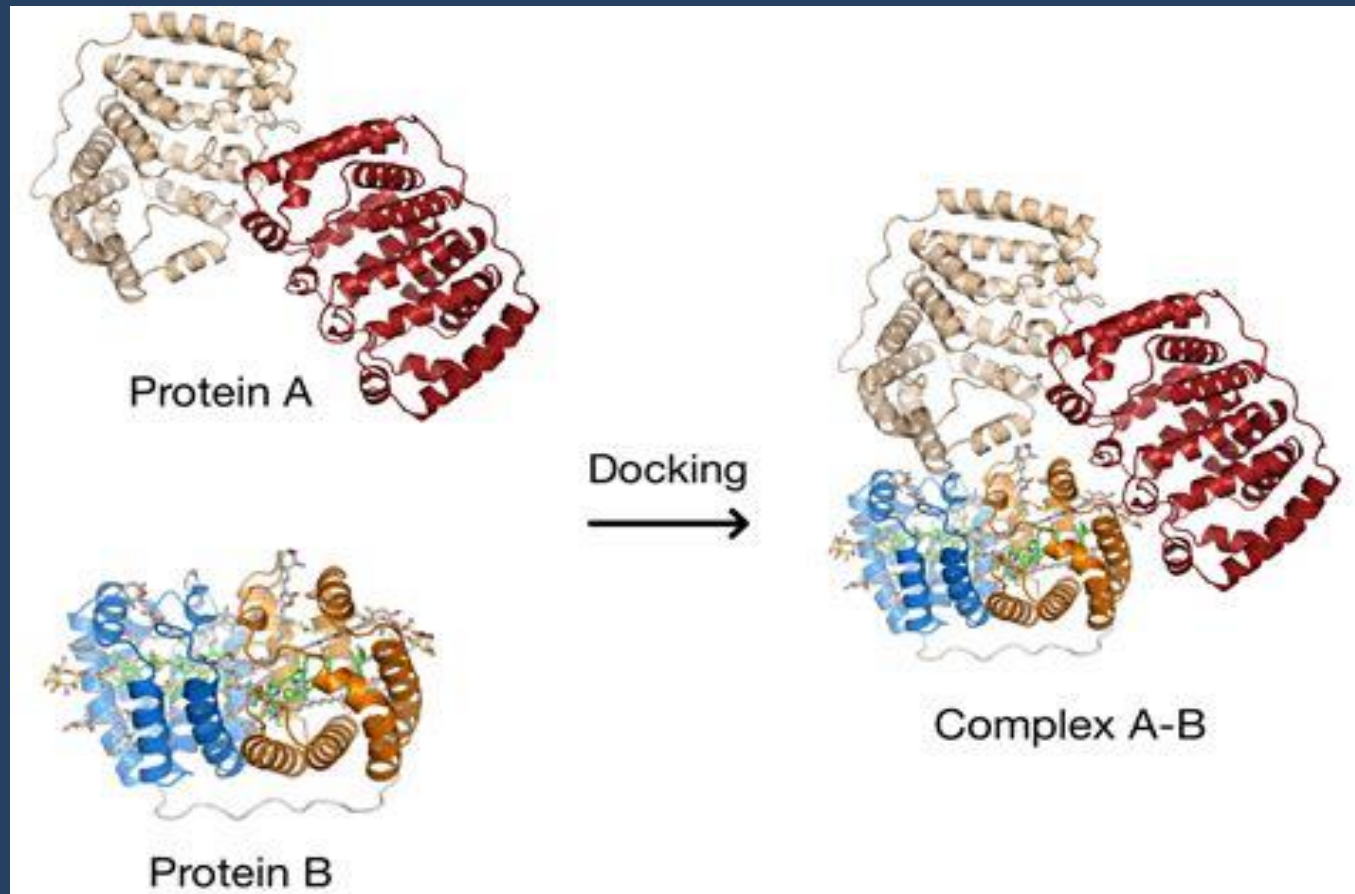
Types of Docking Molecular Based

- Protein – Protein Docking
- Protein – Peptide
- Protein – Ligand
- Protein – DNA
- DNA – Ligand

Types of Docking

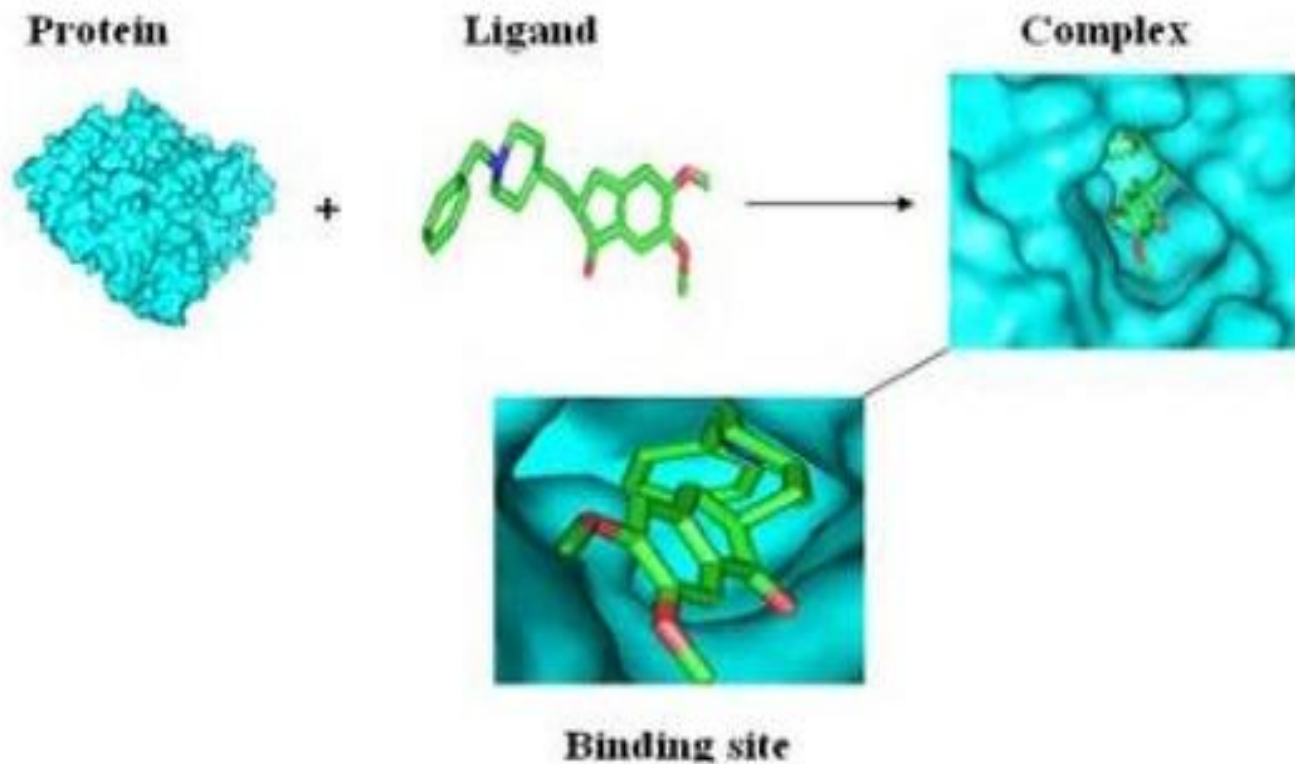
Molecular Based

- Protein – Protein Docking



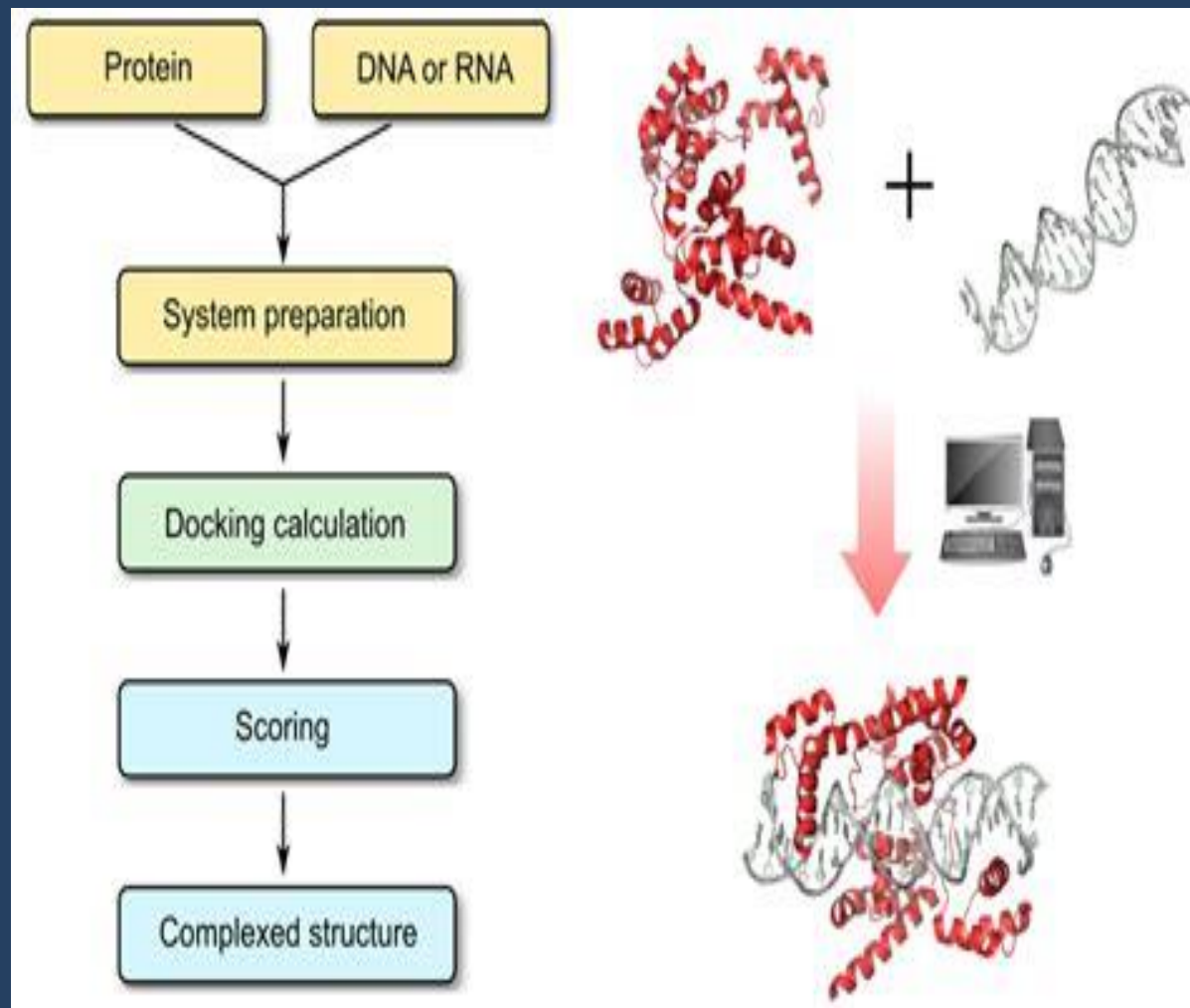
Types of Docking Molecular Based

- Protein – Ligand



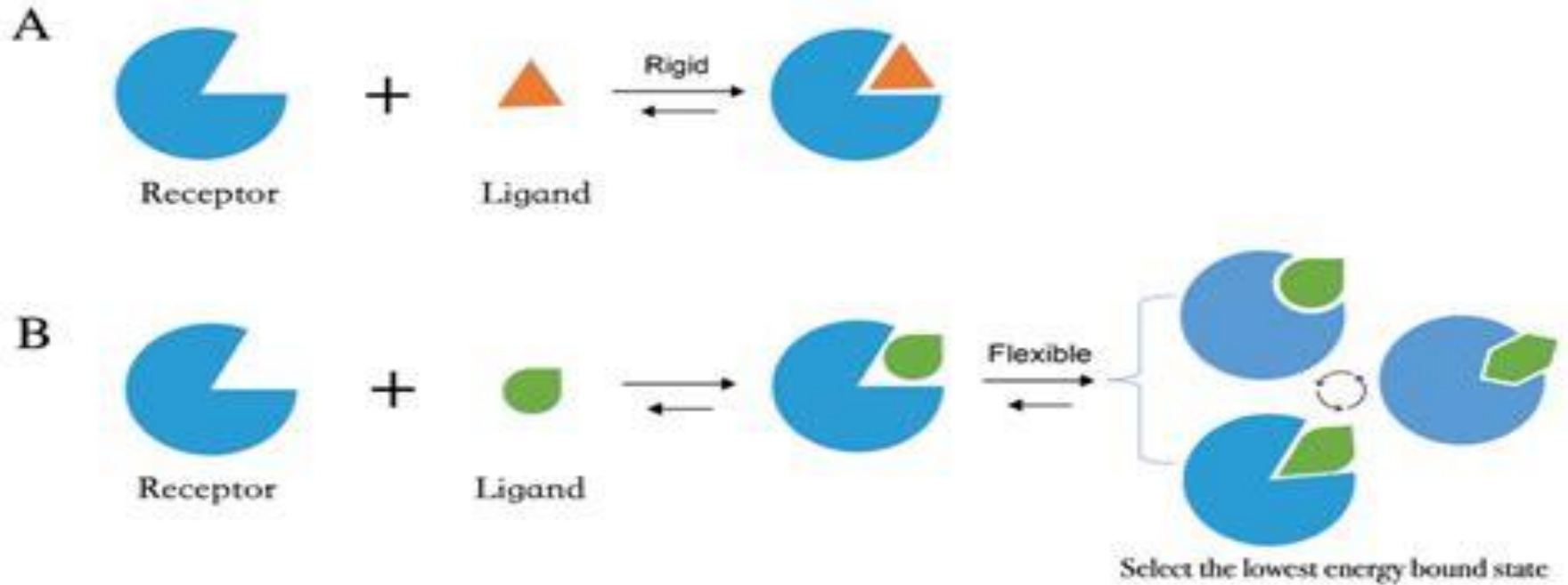
Types of Docking Molecular Based

- Protein – DNA



Types of Docking Flexibility Based

- Rigid Receptor – Ligand Docking
- Rigid Receptor – Flexible ligand Docking
- Flexible Receptor - Ligand Docking



Specialized Types of Docking

- Induced fit docking (Allowing backbone flexibility)
- Hydrated Docking (solved binding site)
- Metal ion docking (metal ion require special force fields)

What happens in docking

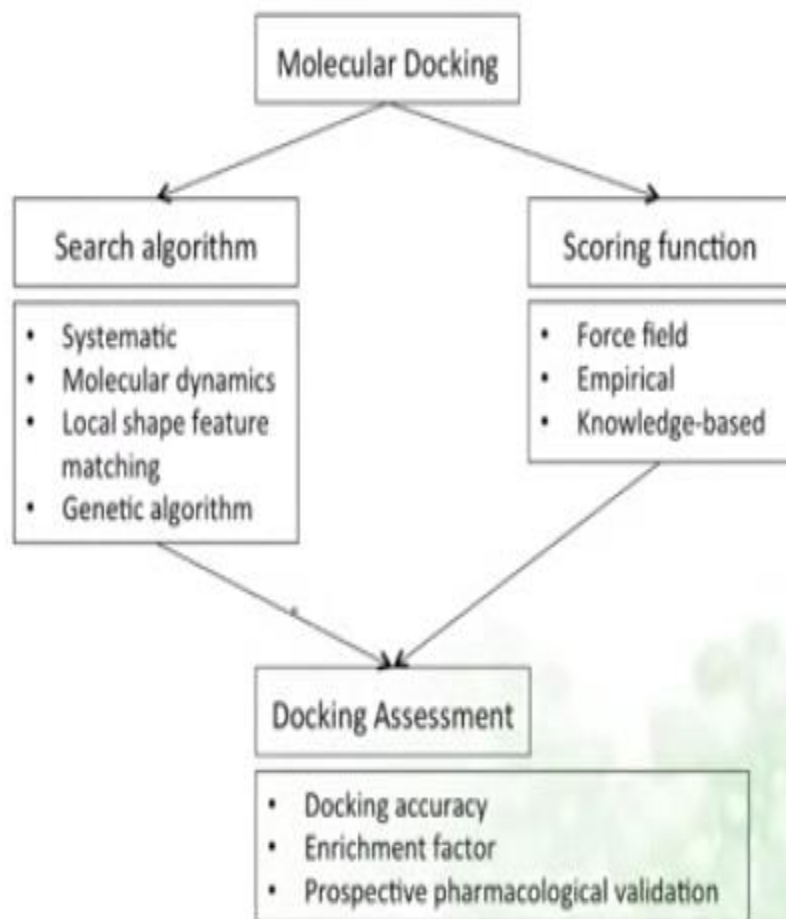
- Protein & ligand structures are **prepared** for docking
- Ligand is **matched** for fit at all possible locations on protein surface in all possible conformations by algorithm
- Each time ligand is moved or rotated, certain **score** is given to the whole complex based on various scoring schemes
- Based on the scores, ligand poses are ranked & **affinity** is calculated for each ligand

Mechanics

Scoring function

- Different criteria are used by different algorithms available for docking
 - Shape complementarity
 - Chemical
 - Knowledge based
 - Forced fields
 - Empirical

Summary



Protein preparation

- Check integrity
- Look missing residues
- Look binding sites
- Understand the protein structure
- Remove any non a.a
- Add hydrogen bond & charges

Ligand preparation

- Preparing small molecules for docking
 - Add hydrogen bond
 - Select rotatable bond
 - Check structure
 - Generate conformers

Example

To evaluate ligand–protein interactions

Example 1

Ligand prepared

- a lead compound



Fig. 2. Optimized structures of the compounds.

Protein prepared

- DdLA isoform of d-alanine–d-alanine ligase from *P. aeruginosa*

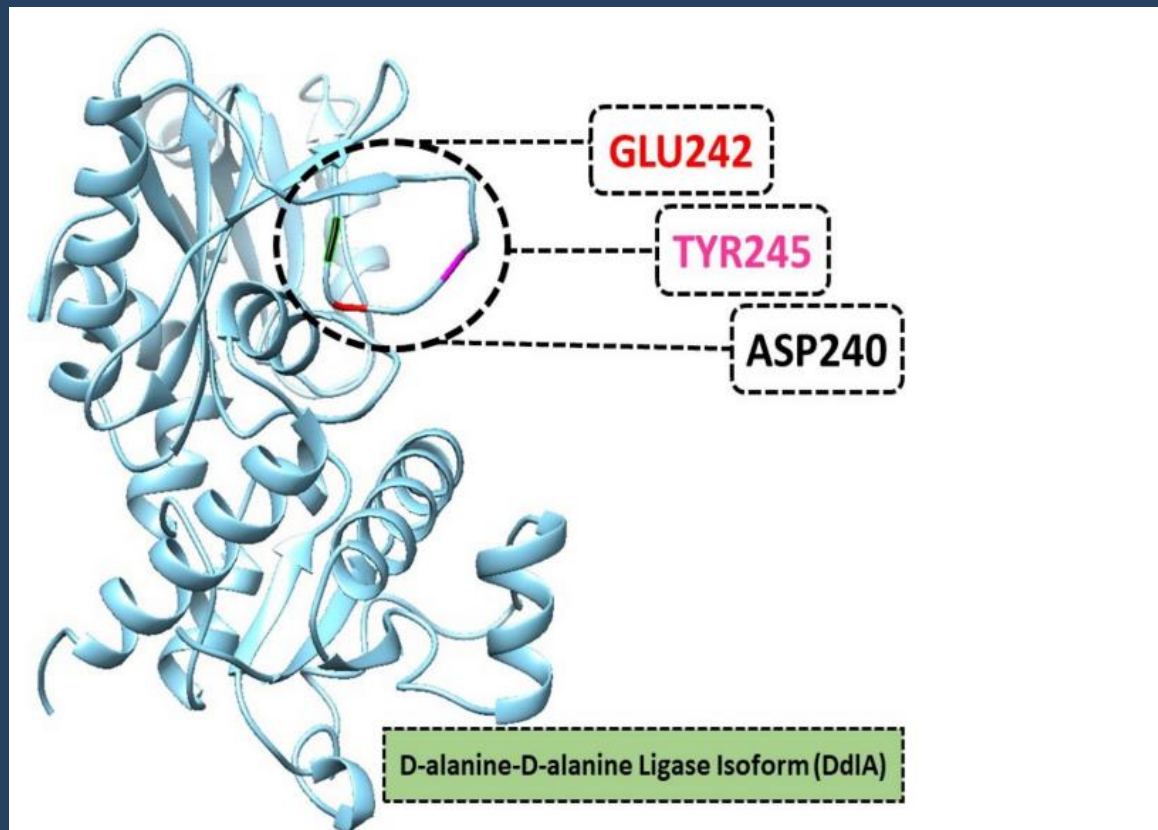


Fig. 3. Three-dimensional structure of the D-alanine-D-alanine ligase (DdLA) enzyme, highlighting key active site residues: GLU242, TYR245, and ASP240.

Result of protein ligand interaction

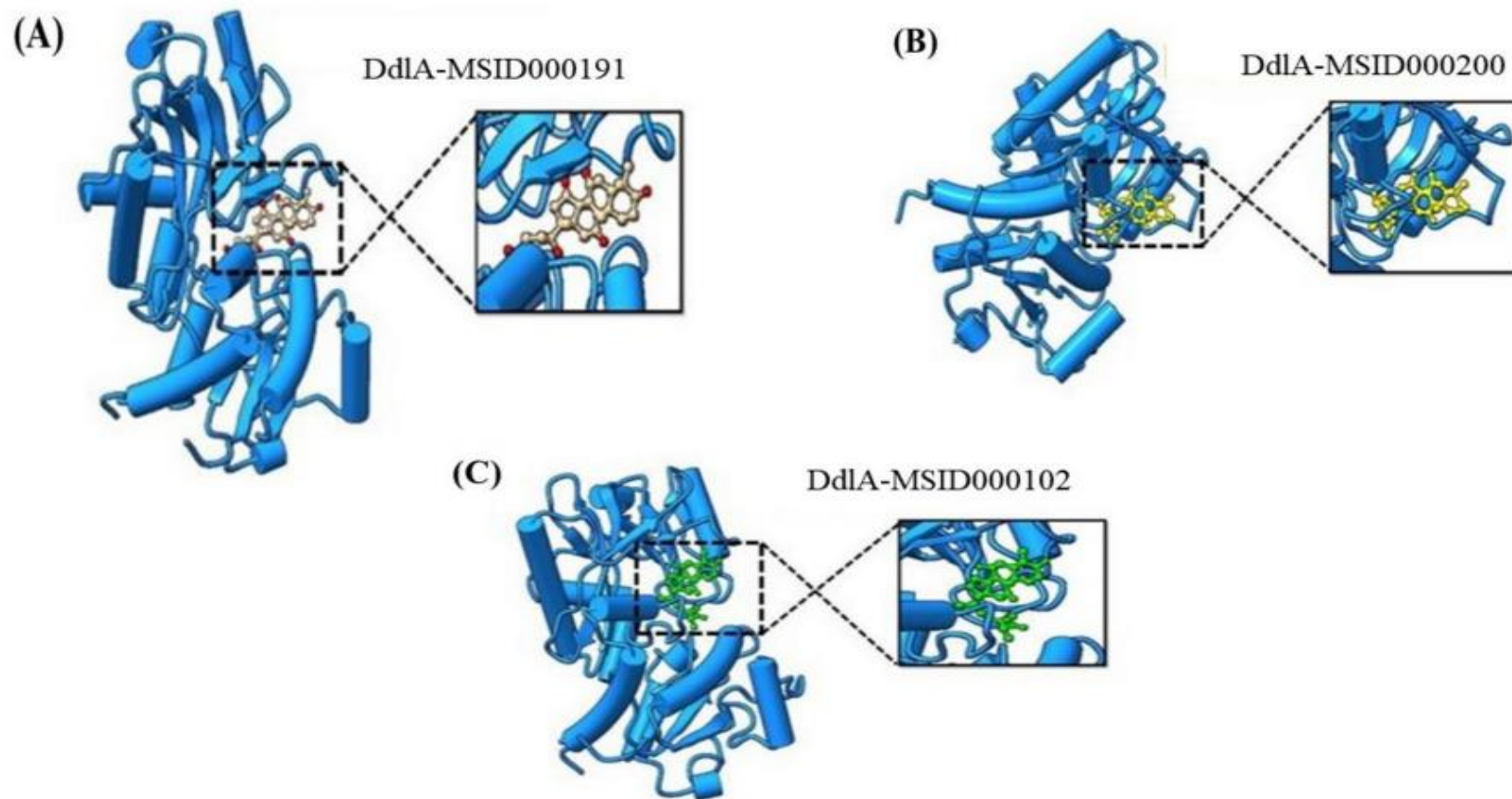


Fig. 4. Three-dimensional (3D) binding positions and docking interactions of the target D-alanine-D-alanine ligase (PDB ID: 8EVV) with ligands: (A) MSID000191, (B) MSID000200, (C) MSID000102.

Result of protein ligand interaction

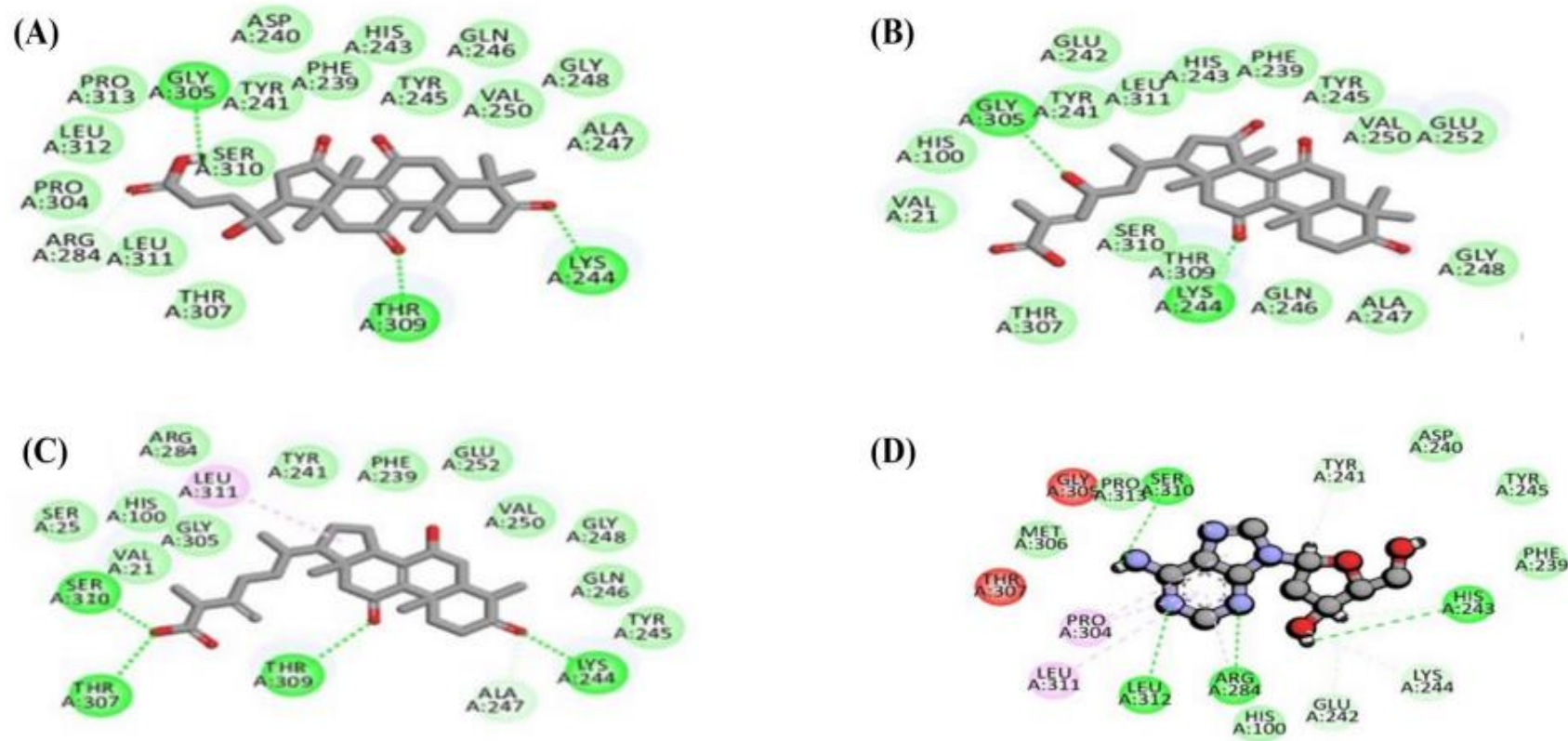
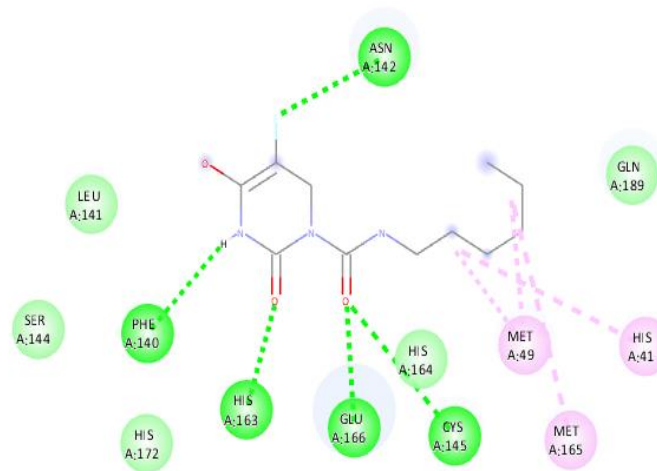


Fig. 6. Two-dimensional (2D) binding positions and docking interactions of the target D-alanine-D-alanine ligase (PDB ID: 8EVV) with ligands: (A) MSID000191, (B) MSID000200, (C) MSID000102 (D) Control.

Example Result of protein ligand interaction



Interactions

- van der Waals
- Conventional Hydrogen Bond

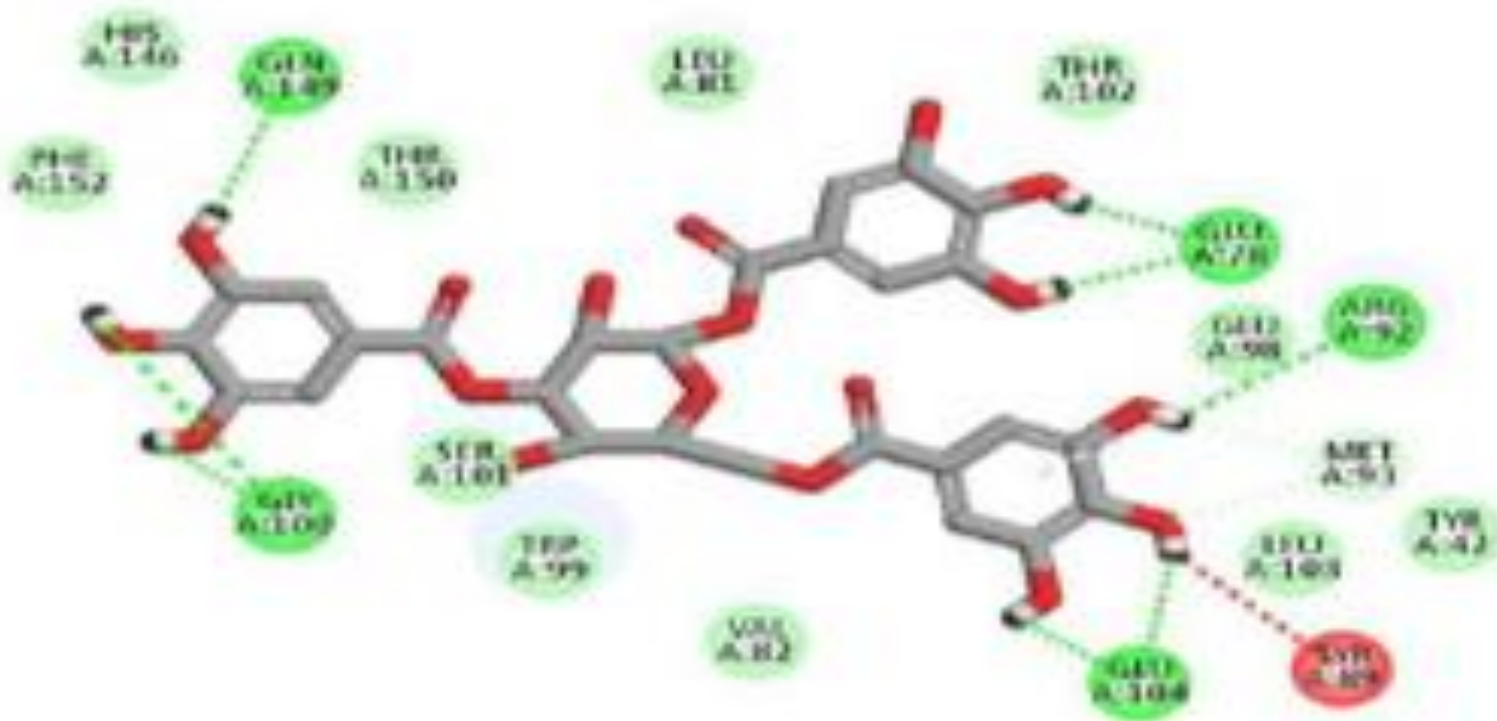
- Alkyl
- Pi-Alkyl

Example 2

- The crystal structure of CCHFV vOTU protease
- Was prepared by
 - correction of bond orders,
 - addition of hydrogen atoms, and
 - energy minimization
- The active site for ligand binding:
 - Lys27, Asp39, Glu51, Asp52, Arg80, Leu81, and Val82.
- Ligand preparation “1,3,6-trigalloyl glucose” as a natural compound

Example 2

A





**Thank you
for listening**