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Molecular Docking Study of ITPA protein substrate complex

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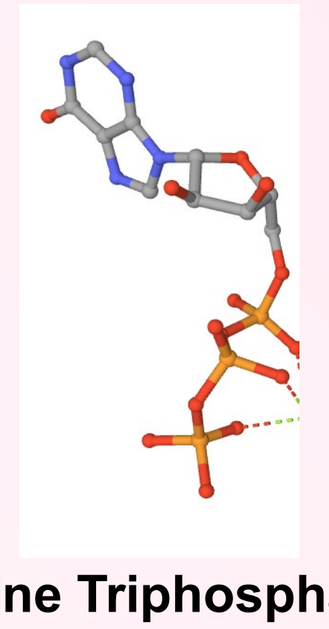
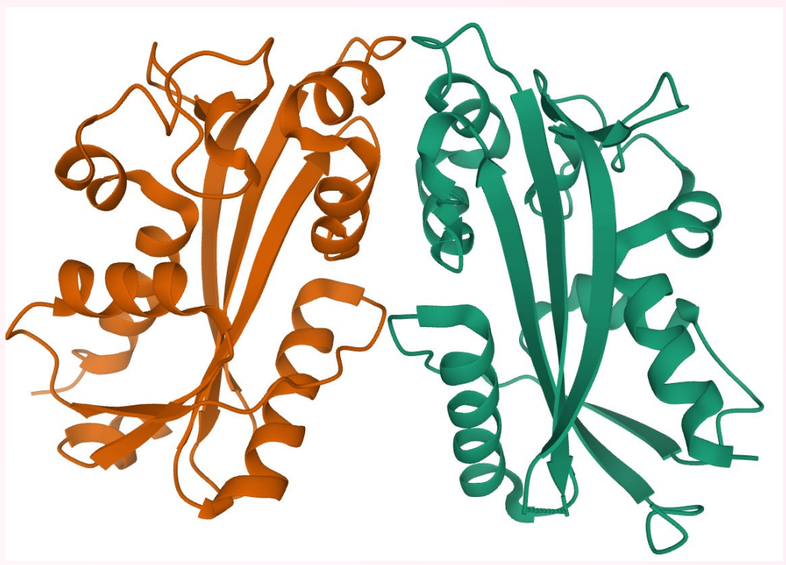
Abstract

Inosine Triphosphatase (ITPA) is an enzymatic molecule that works to prevent the amassed of an intermediate in the formation of purine nucleotides, Inosine Triphosphate (ITP). DNA consists of purine nucleotides, and its metabolic pathway includes the formation of this intermediate. Overpopulation of ITP causes mutations of DNA leading to cancers, increased Inosine levels in DNA and other immunodeficiencies. In order to regulate the ITP concentration, ITPA binds ITP creating a substrate/enzyme complex. In this study, we used computational docking to explore bound conformation and energy of the binding of ITP to ITPA protein. We will use the docking results to reveal how ITPA and ITP bind together. The root-mean-square-deviation, rmsd, will be computed to analyze the similarity of the docked structures. The binding free energies using the intermolecular energy and the torsion entropy penalty will be also calculated. The significance of this research study is to understand the mechanism of ITPA binding. This is important because it could help in the potential prevention of life-threatening diseases.



Inosine Triphosphate (ITP)

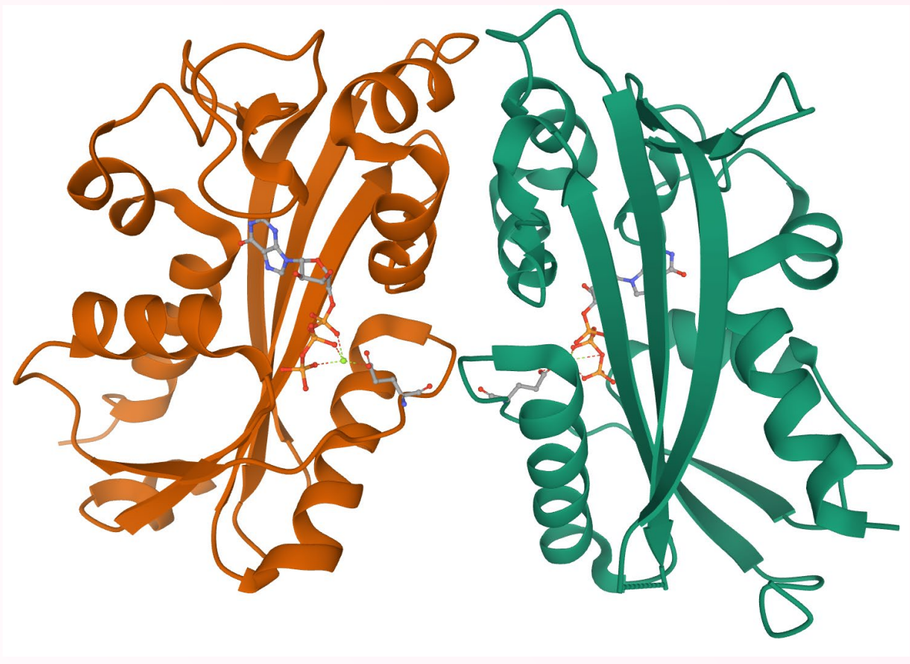


Inosine Triphosphatase (ITPA)

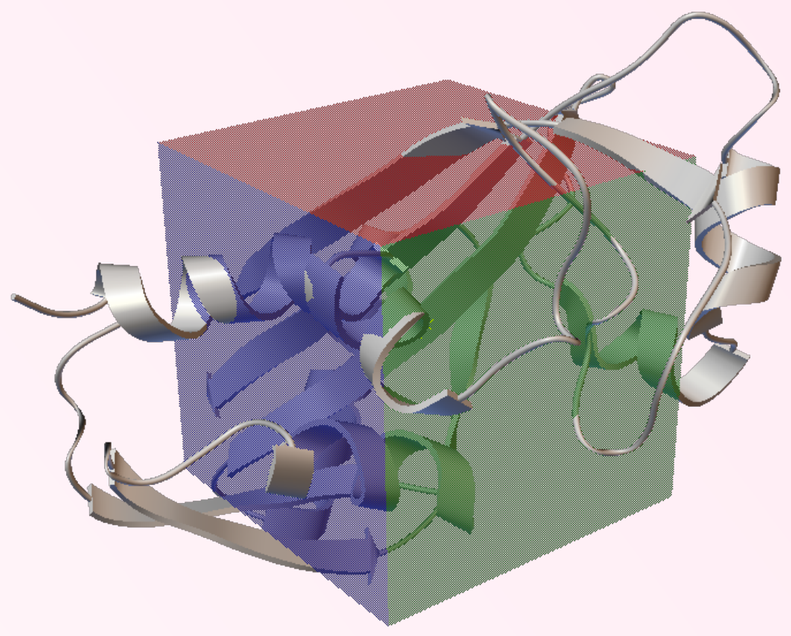
Methodology

Docking gives us the thermodynamic work, or free energy required to bind the receptor and ligand should first be estimated as well as the areas on both ligand and receptor, ITPA and ITP, where the binding would occur. Things taken into consideration when this process occurs are the molecular dispersion/repulsion properties, electrostatics and torsional entropy. With Inosine Triphosphate being our known target molecule, we now look at how the ligand, ITP, binds to it in order to produce the most optimal configuration. Upon each competent arrangement, the free energy scoring method is necessary to rank which arrangements are most likely to occur and be successful in a protein-ligand circumstance. The scoring sheets and free energies are to be recorded for each competent arrangement.

Results



ITP-ITPA Complex



Docking Grid Box