In silico Screening and Analysis of Inhibitory, Anti-prion Ligands for Prevention of Pathogenic Prion Conversion

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Prions, also known as pathogenic neuronal agents, are groups of proteins found clustered in the brain and are responsible for regulatory processes including neuritogenesis, neuronal homeostasis, and cell signaling. When prions undergo conformational changes by the aggregation of beta-sheets in their complexes, prions are converted to their pathogenic counterparts (PrPSc) and toxically contribute to overall neurodegeneration. A pharmacokinetic approach that is often used in drug discovery is the use of molecular docking tools and applications. Molecular docking tools utilize the concept of investigating the chemical interactions between a receptor and its corresponding ligand and are taken as the first step into investigating the potential of investigative drugs. By a combination of in silico approaches, including the prediction of binding sites of prion protein fragments, docking of medications to predicted binding sites, and visualization of newly formed complexes, the interactions between suggested medications and the target protein are analyzed. Based on the developed approach, the binding affinities suggested that the medications explored displayed anti-prion potential as all fell within a range of conformational stability, which is roughly equivalent to < -5.0 kcal/mol. While the data collected could be further investigated using other computational methods, the prediction-based and mostly hypothetical values can be useful when analyzing prior to in vitro testing, which can be costly and require abundant funding.