Computational Analysis of the GABA(A) Receptor

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Today, several tens of millions of people suffer from Alzheimer's disease, nicotine addiction and epilepsy. These conditions not only directly cause deterioration of quality of life, but they also often lead to premature death. Because of this, finding treatments for these neurological diseases is a goal of increasing urgency. The cys-loop receptor family of ligand-gated ion channels has been experimentally correlated with these diseases and many others, such as depression, schizophrenia and Parkinson's disease. This project aims to use computational techniques to identify potentially clinically significant compounds that modulate the GABA(A) receptor, one of most prevalent cys-loop receptors in the human body. A homology model of the human GABA(A) receptor was built using a structural template of 3RIF, which is a C. elegans glutamate-gated chloride channel. Amino acid sequences of individual GABAA subunits were obtained using the RCSD Protein Data Bank, which is where the three-dimensional structure of 3RIF was found as well. Individual residues from the GABAA receptor were mapped onto 3RIF using sequence alignment, resulting in an all-atom structural model. Docking drug candidates were screened for receptor modulation of the GABA(A) receptor, and several compounds with clinical potential were identified.