CALIFORNIA STATE SCIENCE FAIR
2017 PROJECT SUMMARY

Name(s)
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Project Number
S1529

Project Title
A Novel Approach for Solving Target Mutation-Induced Drug Resistance for HIV-1 Fusion Inhibitors with the Hopfield Neura

Abstract

Objectives/Goals
The formation of a hairpin core structure by the HIV-1 virus transmembrane glycoprotein gp41 is the critical event that triggers viral fusion to the host cell. Fusion inhibitors such as T20 can prevent the formation of a hairpin core by binding with the gp41 N-terminal Heptad Repeat (NHR). However, mutations on the NHR can reduce the binding potency of many inhibitors and can cause HIV-1 drug resistance. This project proposes a novel approach to investigate the binding potencies between the gp41 NHR and various inhibitors, as well as potency loss due to NHR mutations.

Methods/Materials
HIV-1 inhibitors prevent the interaction between the gp41 NHR and CHR that forms the gp41 hairpin core, an essential structure that must be formed in order for a virus to enter a cell. However, mutations on the NHR can affect the potency of inhibitor binding due to changes in molecular interactions. In this project, a hidden Hopfield neural network was identified which can accurately describe the interactions between certain amino acids on the NHR and CHR. The energy model provided by the Hopfield neural network was then applied to study the stability of the hairpin core.
The Hopfield energy model was trained using hydrophobicity scale values from the experimental work from Wimley and White. The energy states (and thus the stability of the structure) of a non-mutated complex and mutated complex were then compared.

Results
Using the Hopfield energy model, the loss of stability of the NHR-inhibitor complex for different mutations and inhibitors was calculated. Results showed that depending on the location of the NHR mutation, some fusion inhibitors will lose their potency while others will still be effective against HIV-1 entry. Results were validated from experimental data.

Conclusions/Discussion
The Hopfield neural network was able to assess the energy stability of the NHR-inhibitor complex. This approach provides a fast way to accurately identify which inhibitor will still be effective against HIV-1 entry based on the mutation. This approach can test for the effectiveness of a new drug before the drug is actually created.

Summary Statement
A hidden Hopfield neural network was identified based on the interactions within the hairpin core, and was applied to study the loss of stability once a mutation occurs.

Help Received
Professor Stephen H. White from the Dept. of Physiology and Biophysics at the University of California, Irvine, and my math teacher Mr. Charles Y. Beilin mentored me on research and answered any questions I had.