CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Rohan Arora

Project Number

S0502

Project Title

Using Virtual Screening Methods to Identify a Novel and Noninvasive Method of Heart Disease Treatment and Prevention

Abstract

Objectives/Goals

Heart Disease is the top killer in the United States, causing 600,000 deaths annually. Current methods of prevention for this disease cause discomfort to 30% of the population and may be invasive. This project sought a novel method to reduce the risk of heart disease by inhibiting a key interaction between LDLR (Low Density Lipoprotein Receptor) and PCKS9 (Proprotein convertase subtilisin/kexin type 9), the molecule that causes this receptor to malfunction.

Methods/Materials

In order to be a potential drug candidate, the inhibitor had to be a small molecule that could be easily administered without the use of invasive techniques (i.e injections). Inhibition criteria was established based on control interactions at key residues and a simulation program (Autodock Vina) was used to complete a series of virtual screenings which simulated various molecules bonding to the PCSK9 molecule as potential allosteric or competitive inhibitors. Then a practical verification of the simulation results was conducted by performing a competitive ELISA assay in laboratory environment.

Results

The identified molecule which met all requirements and had the lowest affinity of binding (-8.0 kcal/mol) held the ZINC ID of ZINC00990239. Its interaction with key competitive residues CSY378, ILE369, and PHE379 was observed using AutoDock Tools (binding analysis software). However, this molecule was not available for the verification step so another top molecule, ZINC04214344 (affinity: -7.6 kcal/mol, competitive inhibitor at residues ILE 369 and PHE379), was used. This molecule was shown to have practical, de facto applications through the assay and exhibited an 80% success rate as an inhibitor of the given interaction.

Conclusions/Discussion

The results show that it is very possible for the identified molecule to inhibit the interaction between LDLR and PCSK9 effectively. If shown to be successful in human trials the identified small molecule has the potential to provide a better prevention mechanism for the most deadly disease in the nation, saving thousands of lives annually.

Summary Statement

My project involved the use of virtual simulations and laboratory assays to identify and demonstrate a novel way to treat heart disease that is more cost-effective, comforting, and inclusive than current methods.

Help Received

Qualified Scientist made sure safety requirements were met