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

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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. In order to be a potential drug candidate, the inhibitor had to be a small molecule that could be easily administered. 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. 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 a competitive ELISA assay and exhibited an 80% success rate as an inhibitor of the given interaction. 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.

**Awards Won:**