

Siemens Competition

Math : Science : Technology

Regional Finalist

Name: Vincent Tang

High School: Los Alamos High School

Mentor: Professor Jing Chen

Project Title: *Characterization and Identification of HMGCL as a Therapeutic Target in BRAF V600E Positive Melanoma (Microbiology)*

The BRAF V600E mutation is present in more than 60% of all diagnosed melanoma cases, and represents an attractive target for therapeutic treatment, especially for metastatic melanoma, which has a particularly poor prognosis due largely to the development of drug resistance. Previous research has identified HMGCL as a critical component to the binding between BRAF V600E and MEK1 within the MEK-ERK signalling cascade, thus establishing it as a novel therapeutic target in cancers containing the mutation. Here we developed a comprehensive procedure for the large scale drug screening of potential HMGCL inhibitors. It consists of three components: HMGCL synthesis, purification, and a drug screening assay. Over the summer of 2014, we have successfully carried out the screening of a 2000-drug library with this procedure, illustrating that HMGCL purification and drug screening can be done in an effective and efficient manner, and that our approach can be readily extended to test larger drug libraries. Our screening has also yielded two positives, lactulose and pararosanine pamoate, both known drugs of unrelated clinical applications. This opens the door to further research into their molecular structures and the mechanisms of their interactions with HMGCL, potentially allowing for tailored drug design to increase effectiveness.