



Colorado Science and Engineering Fair

2025 Team Project Abstract Form

Please print 2 copies of the completed form. Sign both copies, keep 1 for your notebook and submit 1 copy to your Regional Fair Director with your other paperwork.

Title of Project: Disrupting PCSK9 and ANGPTL3 Genes with CRISPR for Hypercholesterolemia Treatment

Team Leader's Name: Jenny Xu

Team Member 1: Jenny Xu

Team Member 2: Amanda Zou

School and City: Fairview High School and Peak to Peak Charter School

Sponsor's Name: Xiaojuan Zhang

Category: Biomedical & Health Sciences

Division: Senior (grades 9 - 12)

Abstract (250 words or less):

Homozygous familial hypercholesterolaemia (HoFH) is a rare, severe condition from genetic mutations marked by extremely high levels of low-density lipoprotein (LDL) cholesterol, which causes health problems such as atherosclerosis. Gene therapy provides the potential for lifelong therapeutic benefits with a single treatment. CRISPR/Cas9 gene editing technology can conduct gene therapy by knocking down the PCSK9 or ANGPTL3 genes to decrease LDL cholesterol in circulation. We hypothesize that dual-gene editing can further decrease LDL. First, we built up a cell model for gRNA screening using the guide for PCSK9 (gPCSK9) as a positive control through transfection in N2a mouse cells. For editing the ANGPTL3 gene specifically, a highly efficient guide is vital. Then, we did ANGPTL3 guide RNA screening and found that a novel guide AB514 was successful in editing the ANGPTL3 gene with the highest efficiency. Finally, we co-transfected AB514 and gPCSK9 with SaCas9 into cells and the results showed that the ANGPTL3 and PCSK9 genes could be edited simultaneously. Our discovery of SaCas9/AB514/gPCSK9 editing capabilities for ANGPTL3 and PCSK9 genes may be applied to future research on mouse models and in a medical context to lower blood cholesterol as a cure for hypercholesterolemia.

We hereby certify that the above statements are correct and the information provided in the Abstract is the result of one year's research. We also attest that the above properly reflects our own work.

Team Leader's Signature: _____

Date: _____

Team Member 1's Signature: _____

Date: _____

Team Member 2's Signature: _____

Date: _____

In addition, all students must complete the ISEF Student Checklist (1A), Research Plan, Approval Form (1B), and Checklist for Adult Sponsor (1), and any other ISEF forms required for this type of project. See the International Rules and Guidelines for form requirements. Return COPIES of all of these forms to your Regional Fair Director with your Finalist Verification/Permission Form. **A signed copy of this form must be included in your notebook.**