CALIFORNIA STATE SCIENCE FAIR
2016 PROJECT SUMMARY

Name(s)

Jerry Chen; Amy Jin

Project Number

36672

Project Title

Combating the Obesity Epidemic: Gene Knockdown and Drug Repurposing to Discover Therapeutic Targets and Novel Treatments

Abstract

Objectives/Goals

The objective was to determine genes associated with obesity in humans, test them through wet lab experimentation, and conduct virtual screening on protein models to find potentially effective drug treatments.

Methods/Materials

The GIANT Consortium's GWAS for body mass index was combined with the UCSC Genome Browser to determine the genes related to obesity. dsRNA expressing E. coli were acquired from the Ahringer RNAi feeding library and fed to N2 wild-type C. elegans. The C. elegans were stained for lipid content using Oil Red O. Lipid content was quantified by analyzing microscope images with ImageJ. SWISS-MODEL was used to create protein structure models, and AutoDock Vina was used to screen compounds from multiple databases to determine drugs that could potentially be repurposed as obesity treatments.

Results

A list of 80 genes was compiled as potential driver genes for obesity. The C. elegans orthologs were found for the five most promising gene candidates and were suppressed in wet lab. Gene knockdown for four of the five yielded 20-70% decreases in fat content. The virtual screening resulted in candoxatril, cyanocobalamin, dutasteride, and icatibant as the four drugs that are most likely to be effective obesity treatments.

Conclusions/Discussion

The 80 genes that were compiled included a few genes previously studied with relation to obesity, confirming our process and implying that the rest of the list is also highly likely to have some association with obesity. This hypothesis was also confirmed through our wet lab procedure, from which we determined that the genes were indeed related to fat content. By virtually screening FDA-approved drugs against protein models for the genes that were found, we identified potential drug treatments that are likely to be not only effective but also safe.

Summary Statement

We developed a novel end-to-end drug discovery pipeline that starts with publicly available genomics datasets and returns a promising set of drug targets and leads, generating valuable insight into obesity genetics in the process.

Help Received

Prof. Stuart Kim of Stanford allowed us to use his lab for wet lab experimentation, and Biff Mann, a graduate student in the lab, helped us design the gene knockdown experiment. Prof. Susan Strome of UCSC provided us with the RNAi E. coli.

Preliminary