CALIFORNIA STATE SCIENCE FAIR
2009 PROJECT SUMMARY

Name(s)
Sally Z. Gu

Project Number
S1811

Project Title
Rescuing a Failed Acute Myeloid Leukemia Drug (Troxatyl) using Biomarkers

Abstract

Objectives/Goals
This project presents a method of using deoxycytidine kinase (DCK) biomarkers to improve the efficacy of a failed cancer drug, Troxatyl (TRO), in acute myeloid leukemia (AML) treatments through patient selection with genetic biomarkers.

Methods/Materials
Clinical data of TRO in AML patients were obtained from RSQ Pharmaceuticals under proprietary agreements. This study extracted all known 133 SNPs on the DCK gene region from three publicly accessible databases (NCBI, ENSEMBL, and GENECARDS). Correlations between patient clinical responses and genetic biomarkers were obtained by using SPSS software and modules developed by RSQ. Based on these correlations, two haplotypes were generated from two identified SNPs. Finally, a link between two haplotypes with gene expression was established, and the results were verified by clinical data (not included in this study).

Results
TRO treatment has a genetic predisposition factor related to different patients' responsiveness to the drug. A single SNP on DCK is not sufficient to predict the drug responsiveness in AML patients; however, two SNPs, namely TROAML1 (C/G) and TROAML2 (C/T), on DCK's 5'-UTR region form two unique haplotypes that are directly correlated to TRO efficacy.

Conclusions/Discussion
50% of the heterozygous allele (C/G-C/T) patients (31.1% of total patients) and 100% of the minor homozygous allele (G/G-T/T) patients (2.5%) responded to TRO treatment. Thus, patients who have at least one allele of G-T will most likely respond to TRO treatment, because these patients produce higher amounts of dCK protein. This predicted G-T haplotype will cover 1/3 of all AML patients, and will increase the efficacy rate from 18% (the original efficacy rate) to 60%. A new clinical trial that selects patients using the aforementioned SNP biomarkers is needed for TRO to obtain FDA approval.

Summary Statement
This project applied a method of using biomarkers to improve the efficacy of Troxatyl, a failed leukemia drug, in order to gain FDA approval.

Help Received
Used software provided by RSQ Pharmaceuticals