CALIFORNIA SCIENCE & ENGINEERING FAIR
2018 PROJECT SUMMARY

Name(s)
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Project Number
S0510

Project Title
Identifying the Mechanisms of Liver Cancer Cell Drug Resistance

Abstract

Objectives/Goals
This project was designed to understand potential mechanisms of drug resistance in human liver cancer cell lines.

Methods/Materials
The liver cancer drug, Tetrandrine (TET), was used to screen the most drug-resistant and drug-sensitive liver cancer cell line. Both cell lines were treated with 6 micro-molars TET and underwent bulk RNA sequencing. The drug-resistant cell line was treated with 20 micro-molars TET and underwent single-cell RNA sequencing. Sequencing data analysis was conducted on my laptop on Linux server and RStudio.

Results
Data analysis from the bulk and single-cell RNA sequencing revealed the top up-regulated genes and pathways the cell lines had after drug treatment. The unfolded protein response (UPR) was up-regulated in both the drug resistant and drug-sensitive cell line from both the bulk and single-cell RNA results. Additionally, from the bulk-RNA sequencing, it was found that IRE1 signaling was up-regulated only in the drug-resistant cell line while PERK signaling was up-regulated only in the drug-sensitive cell line.

Conclusions/Discussion
These results reveal that selective UPR activation is linked to drug resistance in liver cancer cells. UPR leads to the activation of the PERK and IRE1 signaling pathways. As previous literature has concluded that IRE1 signaling leads to cell proliferation while PERK signaling leads to cell death, I concluded that these two antagonistic pathways are possible mechanisms of drug resistance and drug sensitivity, respectively. As liver cancer has a very heterogeneous and poorly understood genetic landscape, the identification of UPR and its downstream signaling pathways (IRE1 and PERK) will shed light into the mechanisms of liver cancer cell drug resistance and help develop effective approaches to sensitize liver cancer to drug treatment.

Summary Statement
Using RNA sequencing technologies, I found that the up-regulation of IRE1 signaling in the unfolded protein response is a possible mechanism of liver cancer cell drug resistance.

Help Received
I designed and performed the experiment, and I analyzed the results. My mentors, Dr. Xiwei Wu and Dr. Juan Du, taught me the procedures of culturing and treating cells, and using computer software to analyze RNA sequencing data.