CALIFORNIA SCIENCE & ENGINEERING FAIR
2018 PROJECT SUMMARY

Name(s)
Andrea Z. Liu

Project Number
S0514

Project Title
Repurposing FGFR Inhibitor AZD4547 for Neuroblastoma

Abstract

Objectives/Goals
The objective of my project was to determine the effect of the FGFR tyrosine kinase inhibitor AZD4547 on cell proliferation, induced apoptosis, and activated pathways in neuroblastoma. I predicted that the drug would inhibit some of the pathways that are active and produce a lower amount of the active phosphorylated form of the proteins than the no drug control.

Methods/Materials
Neuroblastoma cell lines SK-N-AS, SK-N-SH, SK-N-BE(2), and IMR32 were examined for drug sensitivity to AZD4547 (provided by AstraZeneca) by a confluence assay and an apoptosis assay conducted with the lab's IncuCyte. Three of the four cell lines were found to be more sensitive than the other, probably due to higher expression of FGFR1 and FGFR4 in the latter. To determine which pathways downstream of FGFR were inhibited by the drug, Western Blots were performed to detect the relative protein quantity of total proteins and active proteins. The intensity of phosphorylated protein versus total protein was compared to determine which pathway was affected by the drug.

Results
I found that AZD4547 treatment resulted in decreased cell confluence and increased rates of apoptosis. AZD4547 treatment also led to decreased phosphorylation of ERK, Akt, and S6K in sensitive cell lines, while the resistant cell line demonstrated reduced inhibition of phosphorylation. Furthermore, sensitive cell line demonstrated increased levels of p-STAT3 while resistant cell line demonstrated decreased or unchanged levels of p-STAT3, suggesting potential markers for AZD4547 response and mechanisms of resistance.

Conclusions/Discussion
My results demonstrate that AZD4547 has the potential to treat advanced stages of neuroblastoma. The fact that AZD4547 works effectively in only some types of neuroblastoma cell lines indicates that primary screening should occur before patients are treated.
I conducted these experiments alongside our lab's assistant, in part because I am too young to work by myself in the lab. I conducted the experiments in this portion of the experiment, while others in the lab conducted other scratch-wound and migration assays with the IncuCyte, while others are now conducting mice experiments to determine the drug's effect in mammals.

Summary Statement
I found that the drug AZD4547 was effective in inhibiting the activation of the FGF receptor pathway in neuroblastoma cells, limiting the cells' proliferation and inducing apoptosis.

Help Received
I discussed my ideas with the principle investigator I was working under, Dr. Peter Zage of UCSD, and he explained the mechanisms behind protein phosphorylation and the activation of downstream proteins. Anything else I didn't understand I asked Nikki, our lab assistant, and looked up online.