CALIFORNIA STATE SCIENCE FAIR
2014 PROJECT SUMMARY

Name(s)

Mimi Lu

Project Number

34561

Project Title

Inhibition of Jak2 and PKC Induces Synergistic Apoptosis in Glioblastoma

Abstract

Objectives/Goals

The Epidermal Growth Factor Receptor (EGFR) signaling pathway is commonly mutated in glioblastoma, a type of brain cancer (Huse & Holland, 2010). I investigated combination treatments of clinically feasible drugs to induce apoptosis in glioblastoma in vitro (cultured cell lines) by inhibiting proteins in the EGFR signaling pathway.

Methods/Materials

Cell Culture: Immortalized (LN229) and primary (GBM34) cell lines were provided by the Weiss Lab at the University of California, San Francisco. The cell lines were cultured using Dulbecco#s Modified Eagle#s Medium (DMEM) and harvested for cell viability assays, fluorescence activated cell sorting (FACS) analysis, and western blotting.

Cell Viability Assay: Cells were stained with the chemical compound WST-1 and analyzed using a microplate (ELISA) reader. Data was analyzed using Microsoft Excel.

Fluorescence Activated Cell Sorting (FACS) Analysis: Cells were stained with the antibody Annexin V-FITC and analyzed using a BD FACS Calibur flow cytometer. Data was analyzed using FlowJo and Microsoft Excel.

Western Blotting: Protein was extracted from cultured glioblastoma cell lines. Proteins and their phosphorylated counterparts were detected using specific antibodies and recorded on autoradiography film.

Results

The chemical compound PP242 induces apoptosis, or programmed cell death, in cultured glioblastoma cells by inhibiting the key proteins Jak2 and PKC. Due to metabolic liabilities, PP242 is unable to be used in the clinic, but the combination treatments of the clinically feasible drugs Tarceva + AZD1480 and Lapatinib + Ruxolitinib successfully inhibit the same significant proteins as PP242 and mimic its cytotoxic effects.

Conclusions/Discussion

Each drug alone is only able to block a single portion of the pathway, but when combined, the combinations of Tarceva + AZD1480 and Lapatinib + Ruxolitinib inhibit Jak2 and PKC and induce cell death. Thus, this dual blockade of Jak2 and PKC by the two drug combinations may offer a novel treatment for glioblastoma, an incurable brain cancer.

Summary Statement

My project involves the investigation of how combination drug treatments induce apoptosis in glioblastoma, a type of brain cancer, through the inhibition of proteins in the EGFR signaling pathway.

Help Received

Used lab equipment at the University of California, San Francisco under the supervision of Dr. William Weiss and Robyn Wong.