CALIFORNIA SCIENCE & ENGINEERING FAIR
2019 PROJECT SUMMARY

Name(s)

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Project Number

S0511

Project Title

Gli Activation is a Key Mechanism of Resistance to EGFR-TKI in Lung Cancer

Abstract

Objectives

Lung cancer is one of the leading causes of cancer-related deaths worldwide. In recent years, the advent of targeted, biological therapies such as EGFR-TKI offers the most promising avenue for lung cancer treatment. However, because the benefits of EGFR-TKI are still modest in the entire lung cancer patient population, a greater understanding of biomarkers that can better predict resistance to EGFR-TKI is of significant clinical importance. Evidence shows that Hh pathway plays a critical role with a common property of the elevated Gli expression in human cancers. The goal of this project is to prove that Hh/Gli activation is a potential key control that accounts for the resistance of EGFR targeted therapy in lung cancer.

Methods

Gli expression was examined by RT-PCR and immunohistochemistry in lung cancer specimens. The Gli expression levels were correlated with responses to EGFR-TKI in those samples. RNAi and cDNA transfection was performed to manipulate Gli expression in lung cancer cell lines. Cell proliferation was evaluated by MTS assay. Protein expression was examined by Western blot. Lung cancer specimens from the UCSF Thoracic Oncology tissue bank were provided by Dr. Vivianne Ding. Human lung cancer cell lines were purchased from the American Type Culture Collection (ATCC).

Results

Correlation analysis showed that a high Gli level was significantly correlated with a poor progression-free survival in lung cancer patients with EGFR-TKI treatment. Inhibition of Gli sensitized lung cancer cells to EGFR-TKI treatment. On the other hand, over-expression of Gli rendered lung cancer cells even more resistant to EGFR-TKI treatment. Combination treatment of a Gli inhibitor and EGFR-TKI synergistically suppressed proliferation of lung cancer cells.

Conclusions

The data indicates that Gli activation may play a critical role in the resistance to EGFR-TKI in lung cancer. Gli may serve as an independent predictive biomarker for the EGFR-TKI treatment in lung cancer. Combinations of Gli inhibitor with EGFR-TKI are likely to enhance anti-tumor activity of the current available therapies for lung cancer, and to overcome the ineffectiveness of those single agent treatments.

Summary Statement

I found that Gli activation plays a critical role in the resistance to EGFR-TKI in human lung cancer.

Help Received

I did all experiments independently under supervision. My mentor provided advice and guidance throughout this project. A technician at the lab taught me about the standard lab procedures before my experiments. She also led me through the procedures for Western Blots and cell culture related