CALIFORNIA SCIENCE & ENGINEERING FAIR
2018 PROJECT SUMMARY

Name(s)

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Project Number

38353

Project Title

Analyzing the Effects of Interferon Signaling as a Novel Approach to Neuroendocrine Prostate Cancer Therapy

Abstract

Objectives/Goals

Prostate tumors developed resistance to ADT through epithelial plasticity, and upon recurrence, develop into NEPC. NEPC has more aggressive characteristics and a higher chance of metastasis. PKC λ is a tumor suppressor, and its function is compromised in NEPC. We established that genetic inactivation of PKC λ effects interferon response. This might play a role in NEPC therapy.

Methods/Materials

We incorporated bioinformatics to analyze IFN expression in NEPC patients and statistically analyzed for IFN expression correlation with aggressive characteristics. Then, we ran a RT-qPCR to measure IFNɑ and IFNγ response in PKC λ knockout cells with a wild type control. We ran a RT-qPCR to measure IFNɑ and IFNγ response in non-IFN treated cells and cells treated with IFN for different time points in addition to wild type PKC λ expression and PKC λ KO cells. Another RT-qPCR was run with different cell lines and IFN treatment times, and was completed with successful results.

Results

IFN response is downregulated in metastatic tumors versus primary. RFS rate for patients with IFN downregulation is significantly lower than patients with upregulation or normal expression. These established a causal relationship between a patient exhibiting aggressive characteristics of NEPC with lower survival rate and a downregulation of IFN expression. PKC λ downregulation is correlated with IFN downregulation in the signaling pathway, thus the compromised PKC λ expression is most likely a result of IFN downregulation. IFN expression was higher in PKC λ normal function IFN treated cells, significantly lower in PKC λ KO without IFN stimulation, and restored to the wild type expression when treated with IFN with PKC λ KO.

Conclusions/Discussion

We found interferon signaling proteins to be a plausible biomarkers for the onset of NEPC in prostate cancer patients. We understand that the mechanism of NEPC resistance occurs in the transduction pathway of interferon signaling. Although PKC λ function was absent, when cells were artificially treated with interferon, the interferon expression was returned to wild type, indicating that the transduction pathway responds to PKC λ mediation. The results of this project presents the interferon pathway as a plausible route to restoration of the mechanism compromised in NEPC resistance.

Summary Statement

We identified IFNs to be an effective biomarker for the onset of neuroendocrine prostate cancer (NEPC), and transduction in the IFN signaling pathway to be where the mechanism of the onset occurs. Restoration of expression is effective.

Help Received

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