CALIFORNIA STATE SCIENCE FAIR
2016 PROJECT SUMMARY

Name(s)

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Project Number

S0532

Project Title

Accelerating Cancer Immunotherapy: Optimization of an EGFRvIII-based Cancer Vaccine for Improved Glioblastoma Prognosis

Abstract

Objectives/Goals

Glioblastoma multiforme accounts for 50% of all types of gliomas. Despite recent advances in treatment, survival rates for patients have remained abysmally low for the past several decades, with no curative treatment option currently available. However, cancer vaccines are a revolutionary, new field of cancer therapeutics that aim to utilize the body's natural defenses to treat cancer. The goal of this study was to optimize an EGFRvIII-based peptide for glioblastoma through characterizing the effects of amino acid substitutions immunologically by analyzing the proteasomal consequences of substitution and tumor-associated antigen (TAA) presence at the tumor site.

Methods/Materials

Peptide segments were digested with human 20S immunoproteasome for two hours in 37 C. After incubation, samples were analyzed using Mass Spectrometry. Peak molecular weights were subsequently computationally evaluated to determine significant molecular weights and noise from adducts. The algorithm was ultimately used to synthesize a method of digestion for the human immunoproteasome and identify TAAs unique to EGFRvIII-expressing gliomas. EGFRvIII- U87 cells were used as a control.

Results

Several repetitions of MS demonstrated large amounts of processing at ~2600 and ~1000 Da, which were then fully characterized using the graphical and computational methods I created. A peptide of identical molecular weight was detected in the tumor-associated antigen population, bound to EGFRvIII+ U87 MHC. Furthermore, the TAA peptide, as validated computationally and biologically, was found to be present in processed fragments of effective variations, but not present in ineffective variations. I also demonstrated the relationship between the production of key intermediate fragments by antigen presenting cells and survival data, leading to the discovery of the most efficacious vaccines.

Conclusions/Discussion

A successfully optimized EGFRvIII-based cancer vaccine can potentially be applied to improve long-term prognosis for glioblastoma patients. Furthermore, my discovery of unique immunoproteasome processing, creation of computational methods, and identification of tumor-associated antigens as a result of amino acid substitutions can potentially be used to improve other biomarker-based immunotherapeutic treatments.

Summary Statement

I worked on optimizing a cancer vaccine for glioblastoma, one of the deadliest forms of brain cancer, through experimentally and computationally analyzing proteasome processing and the tumor associated antigen population.

Help Received

Special thanks to Stanford University, Dept. of Neurosurgery for their support and guidance throughout my project.