Accelerating Cancer Immunotherapy: Optimization of an EGFRvIII-Based Cancer Vaccine via Computationally-aided Analysis of Proteasome Processing for Improved Glioblastoma Prognosis

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Cancer vaccines are a revolutionary field of cancer therapeutics that aim to utilize the body's natural defenses to treat cancer. Through this research, I optimized an effective anti-cancer vaccine based on the EGFRvIII mutation in glioblastoma by computationally and experimentally evaluating survival data with optimal proteasome processing and MHC antigen presence. Mass Spectrometry (MS) was conducted on amino acid-substituted variations of the LEEKKGNYVVTDHC (LEEK) peptide that were fed to the human proteasome, and peptides bound to MHC on U87 glioma cell lines were evaluated for immunogenic matches. By analyzing existing mouse survival and tumor volume data, I noted that tyrosine and alanine substitutions of the peptide vaccine performed consistently better than other variants. Several repetitions of MS demonstrated large amounts of processing of tyrosine and alanine-substituted peptides at 2606 Da and 973 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, 973 Da processed fragment, 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. A successfully optimized EGFRvIII-based cancer vaccine can potentially be applied to improve long-term prognosis for glioblastoma patients. Furthermore, this method of analysis can be used to improve other biomarker-based immunotherapeutic treatments.

Awards Won:

First Award of $5,000