

A bioinformatics approach to cancer vaccines prioritization based cancer-testis antigens in melanoma

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Abstract

Peptide-based vaccines are a promising approach to cancer immunotherapy. Nowadays, several clinical trials using peptide-based vaccines have been carried in distinct tumor types, such as colorectal, lung cancer, and melanoma. Traditionally, these vaccines are synthesized based on tumor-associated antigens, such as cancer-testis antigens (CTAs). The CTAs are a large family of tumor-associated antigens with expression restricted in normal tissues (testis) and expressed in a broad number of tumor types. In addition, CTAs have been pointing out as important candidates due to low toxicity and high specificity. However, several attempts to use CTAs as vaccines were considered a failure, most likely due to a wrong candidate choice and/or absence of techniques to analyze the clinical risks. Consequently, it remains as an open challenge, with two main bottlenecks: i) properly prioritization of novel candidates, and then ii) how to combine these candidates effectively. Here, we present a multiple CTA vaccine to approach melanoma patients. First, we analyzed a large collection of CTAs in the TCGA cohort, in which was filtered candidates based on individual contribution to good prognosis and high T cell CD8+ correlation. As a result, we selected seven candidates, including INSL3, HSF5, GTSF1L, FAM209A, GPR31, SIRPD, and HEATR9. Next, we clustered patients into distinct groups based on the number of co-expressed CTAs. In total, four groups were obtained, named as Red (>5 co-expressed CTAs), Yellow (>2 to 4), Blue (>1 to 2), Grey (without expressed CTAs). Interestingly, the survival ratio has a significant improvement based on the number of co-expressed CTAs. Furthermore, it seems to be independent of other immune response drivers, such as mutation load. Finally, we evaluate the antigenic regions (epitopes) for each CTA protein. In short, the epitopes predictions were carried out using netMHC algorithms, considering a subset of high frequent HLA alleles based on population data. As a result, 40 and 27 high antigenicity regions were found to MHC I and II, respectively. Interestingly, a few peptides are associated with both CD4 and CD8 responses. In conclusion, these findings can be an interesting resource for a cancer vaccine protocol for melanoma.

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