FOX CHASE CANCER CENTER
TEMPLE HEALTH

Personalized therapeutic Neoantigen-based cancer vaccines

(Ref. No. 550-PA)

Background

Normally, introns within messenger RNA (mRNA) are removed during their processing. However, in some cases, introns are retained, particularly when the SET Domain-Containing 2 (SETD2) gene is mutated, as it commonly in kidney cancer and other forms of cancer (e.g., liver cancer, mesothelioma, lung cancer, etc.). When SETD2 is mutated, the specific introns are retained and can be translated into non-self peptides in patients having cancer. By vaccinating patients against one or more peptides derived from aberrantly translated retained introns (ATaRIs) expressed in tumor cells, the immune system may attack the tumor, since the tumor should be the main anatomic location where these introns will be expressed as proteins. Such a vaccine may contain or encode peptide sequences or other forms of vaccine (such as mRNA or plasmid vaccines) which are expected to be aberrantly translated as a result of intron retention. Ideally, the peptide sequences would be derived from introns that are retained/translated across a plurality or majority of human tumors. The vaccine can be administered in combination with other immunotherapies, such as immune checkpoint blockade, for the purpose of immunizing patients against their tumors.

Summary of the Invention

Currently, neoantigen-based cancer vaccines are customized to each cancer patient. Previous neoantigen-based vaccine approaches require: a) either targeted or whole exome sequencing to identify mutations that result from single nucleotide variations in combination with informatics analyses to infer HLA restricted neoantigens; and b) RNAseq to identify highly expressed neoantigens. The bespoke vaccine needs to be customized to each individual patient for whom vaccine therapy might be considered, making the process cumbersome, laborious, and expensive. The invention greatly simplifies this process as the neoantigen-based vaccine contains multivalent antigens, with each antigen being immunogenic to many patients and all patients receiving at least some immunogenic antigens. The patients for whom the proposed vaccine is targeted have tumors that are genetically-defined whereby only one molecular feature needs to be known: SETD2 mutation status. This can be measured in CLIA-approved panel sequencing assays, whole genome sequencing assays, whole exome sequencing assays, or potentially with immunohistochemistry of the tumor. Therefore, the same vaccine might be effective for many patients, allowing for an off-the-shelf semi-personalized therapeutic vaccine. Such a vaccine may be indicated for many or all patients with cancers that harbor deleterious SETD2 mutations, not just SETD2-mutant kidney cancer.

Patent Status: A patent application has been filed.

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