Full Length Variant Survivin Polypeptide Vaccine

A new cancer vaccine consisting of dendritic cells transduced with a full-length double mutant survivin gene delivered via an adenoviral vector. The vaccine will target survivin expressing tumors. This protein is crucial to cancer cell function and is expressed in more than half of patients in twelve distinct types of cancer. Analysis of multiple myeloma patient derived T cells stimulated by this variant survivin vaccine ex vivo demonstrated a greater than 40-fold specific expansion and three times as many functional IFNγ producing T cells when compared with a control re-stimulation.

COMMERCIAL OPPORTUNITY

- The NCI designated survivin as a Top 25 cancer antigen due to its immunogenicity and expression in 90% of melanoma, MDS, ovarian and breast cancer patients and over 50% of patients in eight other cancer types. Survivin plays an essential role as an inhibitor of cancer cell death and promotes growth, metastasis, and treatment resistance of malignant cells.
- The growing market for cancer immunotherapy products is exemplified by worldwide annual revenue for Bristol Myers Squibb's Yervoy of $1.1 billion and Opdivo of $942 million in 2015. Additionally, Keytruda (Merck) generated $352 million in sales in the first nine months of 2015.
- The survivin vaccine market is attractive, as evidenced by two companies currently in clinical trials. DPX-Survivac is a survivin based vaccine produced by Immunovaccine Inc. that has been granted orphan drug status for treatment of ovarian cancer and is in Phase II trials for ovarian cancer, lymphoma, and glioblastoma. MimiVax LLC is generating a synthetic peptide vaccine (SurVaxM) that is currently in Phase I/II trials for multiple myeloma, glioblastoma, and glioma.
- In contrast to DPX-Survivac and SurVaxM, a full length variant survivin protein vaccine allows for the presentation of multiple peptide epitopes and recognition by a more diverse immune repertoire across all patient populations.

TECHNOLOGY

An antigen presenting cell displaying a variant survivin polypeptide was produced through transfection of dendritic cells (DCs) with a double mutant (T34A and C84A) full length survivin protein adenovirus construct and confirmed by Western blot. Co-culture of MM patient-derived DCs with CD4+CD25- peripheral T cells *ex vivo* resulted in a significant increase in both the frequency and absolute number of survivin-reactive CD4+ T cells, with a fold expansion range of 0-270x and median of 42x. Additionally, T cells expanded with DCs presenting this variant survivin protein were survivin specific by IFNγ ELISpot analysis when restimulated with survivin peptide pools, producing about three times as many spots as an irrelevant peptide control.

PUBLICATION

- Provisional patent application filed on May 7, 2015 for Drs. Locke, Altieri, and Gabrilovich

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