A NOVEL SELF-ASSEMBLING VACCINE, VTX-067, TARGETING E6/E7 PROTEINS OF HUMAN PAPILLOMA VIRUS INDUCES T CELL IMMUNE RESPONSES AND INHIBITS HPV E6/E7 EXPRESSING TUMOR GROWTH IN A C57/B6 MOUSE MODEL

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Background Human papillomavirus (HPV) infection is associated with skin and mucosal papillomas or warts and cervical, anal and head and neck cancer. We developed a novel, broadly immune activating, self-assembling vaccine (SAV) that consists of a Mycobacterium tuberculosis heat shock protein 70 (MtbHSP70)-avidin (MAV) as an adjuvant that spontaneously self-assembles with biotinylated immunogenic peptides targeting the E6 and E7 proteins of HPV (VTX-067).

Methods Two biotinylated concatemerized peptides, each containing two immunogenic MHC class I and one class II epitopes derived from the tumorigenic HPV proteins E6 and E7, were used. MAV was self-assembled with peptides at a 1:5 molar ratio. To assess antigen-specific immune response, we vaccinated C57BL/6J mice (n=12) intradermally in a prime-boost-boost schedule every two weeks. Splenic and lymph node derived lymphocytes were isolated and antigen-specific T cell responses were analyzed using flow cytometry at 6 weeks post vaccination. To evaluate efficacy, we inoculated C57BL/6J mice (n=10) with the epithelial TC-1 cell line that constitutively expresses the E6 and E7 proteins of HPV (20,000 cells/mouse) and vaccinated with VTX-067 on days 3, 17 and 24. Tumor size was measured twice per week and survival determined based on growth of the tumor to a specific volume (2,000 mm³).

Results C57BL/6J mice vaccinated with VTX-067 generated significant CD8+IFNγ responses at the three highest doses of VTX-067 treatment: 130, 215 and 350 μg (p < 0.05, p < 0.0001 and p < 0.0001 respectively by ANOVA) and CD4+IFNγ T cell responses at vaccine doses 215 and 350 μg (p < 0.0001) compared to saline-treated groups. Mice vaccinated with VTX-067 at doses of 80, 130, and 215 μg survived significantly longer with markedly slower tumor growth than mice in saline control groups (p < 0.0001; log-rank followed by Mantel-Cox tests). VTX-067 vaccination resulted in a significant tumor volume reduction at any of the three highest doses of VTX-067 compared to mice in the saline control group. In the 215 μg group, four of the 10 mice were tumor-free at the end of the study.

Conclusions Overall, our study demonstrated that three dose levels of VTX-067 all provided significant antigen specific T cell responses, increases in overall survival and reduction of tumor volume. We believe these data, in addition to published work by our team on a Lassa Fever Virus vaccine, support the view that our self-assembling vaccine platform is potentially relevant to both infectious disease and cancer targets.

REFERENCE

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