Background

- Worldwide infection rates for HPV are estimated to range from 9% to 13%, equaling 20 million women affected in the US alone [1].
- Human papillomavirus (HPV) cancers are uniquely antigenic with ubiquitous and essential expression of viral proteins E6 and E7 [2].
- It has been shown that anti-tumor T cells responses after adoptive T cell therapy in HPV-positive tumors target non-viral antigens rather than viral antigens, suggesting vaccines alone may be insufficient to treat cervical cancer [3].
- TCRs can be used as a biomarker to identify underlying immunity to specific antigens [4]. We have identified 1,331 TCRs which are increased in tumor specimens incubated the HPV antigens.
- We hypothesize that the radiation therapy may synergize with vaccine treatments to stimulate T-cell mediated anti-tumor.

Objective

- We are investigating the effect of PDS0101, an E6/7 HPV16 T-cell activating immunotherapy delivered subcutaneously, combined with the standard of care chemoradiation for patients with locally advanced squamous cell cervical cancer.
  - Characterize antigen-specific populations.
  - Identify HPV responsive T-cells using TCR sequencing.
  - Determine if previously identified population of HPV-reactive T-cells correlate with treatment outcome in patients treated with vaccine and chemoradiation.

Methods

- This project is a part of the IMMUNOCERV trial. The criteria of inclusion of this trial are patients with locally advanced squamous cell cervical cancer with either lymph node metastasis or tumors of >5 cm.
- Subjects
  - 8 patients to date have completed treatment and have been evaluated with post-treatment PET (Positron Emission Tomography) scan to evaluate response.

Results (Cont.)

- Cervical Swabs are collected at each timepoint (T) shown in Figure 1.
- Genomic DNA from Cervical Swab was isolated using Isohelix™ Xtreme DNA Isolation Kit.
- Isolated genomic DNA was amplified in a bias-controlled multiplex PCR.
- The CDR3 regions of human TCR-β chains were sequenced using immunoSEQ assay (Adaptive Biotechnologies, Seattle, WA).
- Analyses were performed to assess the diversity of TCR in each timepoint (T0, T1, T2, T3, 4, T4B, T5).
- Detected T cells clones with TCR-β sequences expected to generate functional TCRs (productive rearrangements).
- Evaluated differential abundance at T4 and T4B by using IMMUNOSEQ analyzer.

Results

- HPV type impacts TCR expansion. (A) (B) TCRs expanded from T4 to T4B in PDS03 and PDS05. (C) TCRs did not expand from T4 to T4B in PDS06. The differences were HPV type; HPV16 (PDS03 and PDS05) and HPV18 (PDS06).

References