Background

- Human papilloma virus (HPV) is responsible for 72% of oropharyngeal, 70% of cervical, 90% of anal, and 71% of vulvar, vaginal, or penile cancers, causing significant morbidity and mortality worldwide. Innovative therapies are urgently needed for these malignancies, particularly in the largely incurable metastatic setting.
- The E7 oncoprotein is constitutively expressed in HPV-associated cancers, is necessary for initiation and maintenance of malignant transformation, and is genetically conserved in cancer (Mirabello 2017).
- Clinical proof of concept for HPV-targeted T cell therapy includes demonstration of complete regression of metastatic cervical cancer upon adoptive transfer of tumor-infiltrating T cells (Sweatman 2015; Stevanovic 2017).
- The E7 sequence, including that encoding the E71–22 peptide in CUE-101, is maintained in cancer and this epitope is immunodominant in humans (Ressing 1995).
- Immuno-STAT™ molecules are engineered to selectively modulate the activity of antigen-specific T cells in situ.

CUE-101 selectively expands HPV E71–22-specific CD8+ T cells from healthy human PBMCs

CUE-101 selectively binds antigen-specific T cells

CUE-101 selectively elicits effector cytokine production

CUE-101 murine surrogate (mCUE-101) inhibits tumor growth in the TC-1 syngeneic model

mCUE-101 expands antigen-specific CD8+ T cells in the tumor and the periphery

Antigen-specific TILs upregulate PD-1 expression

Conclusions

- CUE-101 demonstrates selective binding, receptor signaling, effector T cell cytokine secretion, and expansion of HPV16 E71–22 specific human CD8+ T cells.
- CUE-101 demonstrates reduced non-specific immune cell activation and cytokine secretion when compared to recombinant wild type IL-2.
- A murine surrogate of CUE-101 inhibits the growth of E7-expressing TC-1 syngeneic tumors, selectively expands antigen-specific CD8+ T cells in the tumor and periphery, and generates immunologic memory against TC-1 tumor cells.
- Enhanced in vivo combination efficacy was associated with increased expression of PD-1 on tumor antigen-specific CD8+ T cells resident in the tumor microenvironment.
- The novel mechanism of action of CUE-101, namely targeted activation of tumor-antigen-specific CD8+ T cells via delivery of reduced affinity mutant IL-2, supports its increased potential for anti-cancer efficacy and reduced toxicity relative to non-targeted forms of immunotherapy.

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