1122 VIDUTOLIMOD, AN IMMUNOSTIMULATORY VIRUS-LIKE PARTICLE, REDUCES PROLIFERATION BUT ENHANCES THE ACTIVATION OF TUMOR-SPECIFIC T CELLS

[1]Travis D Fischer*, [1]Caitlin D Lemke-Miltner, [2]George J Weiner. [1]*University of Iowa, Iowa City, IA, USA*; [2]*Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA, USA*

Background One approach to enhancing the anti-tumor T cell response is to alter the tumor microenvironment (TME) through intratumoral injection (IT) of immunostimulatory agents such as Vidutolimod (**Vidu**). Vidu is a virus-like particle (VLP) composed of a TLR9 agonist (CpG-A, known as G10) encapsulated by the Qβ bacteriophage capsid. IT Vidu shows considerable promise in early phase clinical trials. The immune response to Vidu is initiated by induction of IFNa production by pDCs within the TME. This effect is dependent on coating of Vidu with antibodies against the Qβ capsid. This is followed by a series of changes in the TME that ultimately result in an enhanced anti-tumor T cell response. Mouse models have shown that the efficacy of IT Vidu depends on the presence of both CD4+ and CD8+ T cells. Most studies to date exploring the impact of Vidu on T cells have focused on the overall T cell population.

Methods The current studies were designed to further assess the complex mechanisms by which Vidu induces an anti-tumor T cell response through use of the well-established OT-1 mouse model that allows for analysis of the tumor-specific T cell population. OT-1 mice contain CD8+ T cells with a transgenic TCR that recognizes the ovalbumin (OVA) peptide SIINFEKL sequence (OVA257–264) presented on MHC Class I. Prior to culture, OT-1 splenocytes were labeled with CellTrace Violet in order to monitor proliferation over time. OT-1 splenocytes were then cultured with EL4 cells (an OVA-negative T lymphoblast cell line) or E.G7-OVA (OVA-expressing EL4 derivative cells).

Results Minimal proliferation or evidence of T cell activation was seen when OT-1 CD8+ T cells were cultured with EL4 cells regardless of the addition of Vidu and anti-Qβ antibodies. OT-1 CD8+ T cells cultured with E.G7-OVA cells showed both proliferation and activation as indicated by increased intracellular IFNγ and surface PD-1. Addition of Vidu and anti-Qb antibody reduced OT-1 CD8+ proliferation but enhanced production of IFNγ and expression of PD-1. The increase in IFNγ and PD-1 expression was strongest in the dividing OT-1 CD8+ T cell population. Preliminary results of ongoing *in vivo* studies are consistent with these results.

Conclusions Vidu reduces proliferation but enhances phenotypic markers of activation expressed by tumor-specific CD8+ T cells (OT-1 cells) when co-cultured with cells expressing OVA, their target antigen. Markers of activation are most notable in dividing OT-1 CD8+ T cells.

Ethics Approval Mouse studies were approved and performed according to guidelines established by the University of Iowa Institutional Animal Care and Use Committee (IACUC) under the approved Protocol #1011236.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1122