CANCER-MUTATION-SPECIFIC T CELLS: NOVEL IMMUNOTHERAPY APPROACH FOR LOW MUTATIONAL BURDEN PATIENTS


Background Immune checkpoint inhibitors, such as anti-PD1 antibodies, have revolutionized cancer immunotherapy. Their success demonstrates that a patient’s own T cells recognize and treat cancer. However, anti-PD1 therapy is most effective in the treatment of cancers with high mutational burden, ~5% of all malignancies. Therefore, an alternative strategy is necessary to target cancer with lower mutational burden. Importantly, the efficacy of PD-1 blockade is associated with the recruitment of new T cells from the blood rather than the activation of pre-existing tumor infiltrating lymphocytes (Yost K.E., et al. Nat. Med. 2019).

Methods Our approach is to prime and expand T cells from the blood to cancer-specific mutations ex vivo.

Results We can generate T cell populations reactive to as few as 8 and as many as 40 cancer-specific mutant proteins in a single production run. In vitro, these T cells have mutation-specific cytotoxicity and do not kill the normal cells. These T cells express homing receptors that allow them to infiltrate the tumor and express high levels of TNFa and IFNg, both of which are associated with effective tumor cytotoxicity and pro-inflammatory modification of the tumor microenvironment. The predominant immunophenotype of these cells is consistent with central and effector memory, CD4+ and CD8+ T cells, with almost no regulatory or exhausted T cells.

Conclusions We believe these T cells can be used as a cellular therapy in conjunction with, or as an alternative to, immune checkpoint inhibitors to treat lower mutational burden cancers that comprise most patients’ tumors.