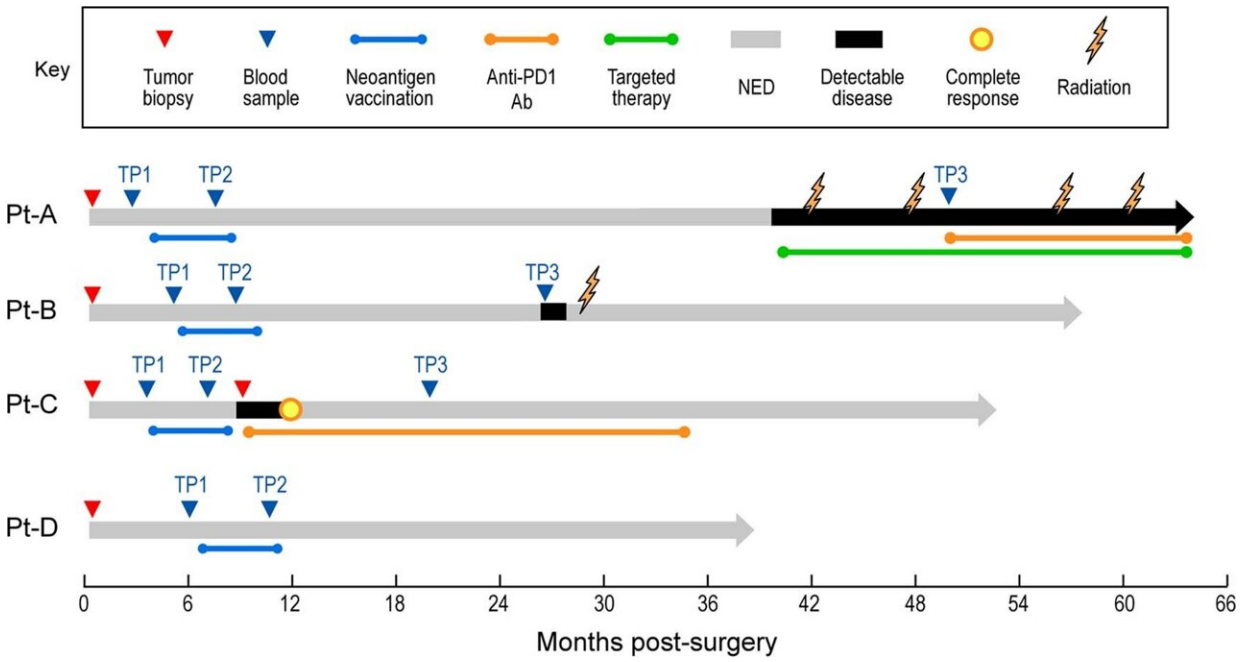
What makes some immune cells better at killing melanoma

July 27 2021, by Natalia Mesa



Extended Data Fig. 1: Clinical course of patients with melanoma analyzed for single-cell sequencing and TCR specificity. Schematic representation of the clinical histories of the four patients with melanoma profiled in this study. Triangles indicate the time of collection of tumor biopsies (red) analyzed with single-cell sequencing or of peripheral blood samples (blue) used for isolation of tumor-reactive T cells at serial time points (TP). NED, no evidence of disease. Credit: DOI: 10.1038/s41586-021-03704-y

T cells rely on surface proteins called T cell receptors (TCRs) to bind to

and destroy viruses, cancer cells, and other invaders in the body. T cells that infiltrate tumors, however, can have varied, sometimes ineffective responses. How the molecular structure and function of TCRs correlates with T cell behavior is not fully understood.

In a new study published in *Nature*, Giacomo Oliviera, associated researcher and institute member Catherine Wu, and colleagues at the Dana-Farber Cancer Institute and the Cancer Program at the Broad Institute of MIT and Harvard take an in-depth look at the relationship between TCRs and T cell phenotypes. Using single cell RNA (scRNAseq) sequencing and TCR sequencing (scTCRseq) of CD8+ T cells, coupled with the detection of surface proteins, the researchers set out to study the transcriptomic and molecular profiles of melanoma tumor-invading T cells and their TCRs. They found that most T cells with tumor-specific TCRs bore the molecular signs of "exhaustion," a state of decreased function following chronic antigen exposure. Higher circulating levels of these tumor-invading, exhausted T cells in the blood correlated with persistent disease. These findings highlight the importance of restoring normal T cell function for a productive, effective immune response in cancer therapies.

In the video presentation above, Oliveira describes the research that led to the identification of the properties of antitumor T cells and highlights how such findings can pave the road to the development of novel therapeutic strategies that aim at generating T cells with potent antitumor TCRs and functional cell states.

More information: Giacomo Oliveira et al, Phenotype, specificity and avidity of antitumour CD8+ T cells in melanoma, *Nature* (2021). DOI: 10.1038/s41586-021-03704-y

Provided by Broad Institute of MIT and Harvard