Comparing the Functional Capacity and Transcriptional Profiles of Chimeric Antigen Receptor (CAR) T Cells and Bispecific T Cell Engagers (BiTEs)

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Chimeric Antigen Receptor (CAR) T cells and Bispecific T cell Engagers (BiTEs) are two novel immunotherapy platforms. I hypothesized that the different mechanisms used by anti-CD3-CD19 BiTEs and anti-CD19 CAR T cells to initiate downstream signaling will lead to differential T cell functional capacity and transcriptional profiles. T cells were co-cultured with anti-FMC63 and CD19 beads at different ratios to determine bead-dependent changes. Spectral flow cytometry was performed to analyze T cell activation following bead engagement. The Bruker Cellular Analysis Beacon Optofluidic system was used to analyze differences in phenotype and functional capacity between T cells co-cultured with BiTEs or expressing a CAR. Functional analysis demonstrated expression of cytokines (IFN-?, TNF-??, Granzyme B) in a higher proportion of T cells co-cultured with BiTEs compared to CAR T cells. Transcriptional profiling revealed that the quantitative expression of cytokines, though more homogenous, was lower in T cells co-cultured with BiTEs, while a subset of CAR T cells demonstrated high expression of cytokines. CAR T cells showed greater polyfunctionality in cytokine expression, more durable target engagement, and had a higher proportion of CD8+ T cells to CD4+ T cells than T cells co-cultured with BiTEs. The low but homogenous expression of cytokines by T cells co-cultured with BiTEs and the polyfunctionality of CAR T cells suggest an important therapeutic role for both platforms. The more durable target engagement of CAR T cells compared to BiTEs needs to be balanced with the potential for greater cytokine release and toxicity. Additional functional assays are necessary to understand the impact of the tumor immune microenvironment in modulating the efficacy of both platforms.

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