Functional Comparison of LV19.20 Bispecific CAR T-Cells Manufactured Under Distinct Cytokine Priming Conditions

Thomas, Jordan (School: University School of Milwaukee)

CAR T-cell immunotherapy has proven to be effective in treating relapsed, refractory B-cell malignancies, such as non-Hodgkin's lymphoma (NHL). Nevertheless, limitations have emerged from IL-2 manufactured CAR T-cells, and IL-2 primed CAR T-cell therapy resulted in long-term progression-free survival in only 30-40% of patients. Therefore, based on the promise of IL-7 and IL-15, IL-7/-15-primed CAR T-cells will exhibit greater functional capacities compared to IL-2-primed CAR T-cells, which will lead to improved immunotherapies to treat patients suffering from B-cell malignancies. During this experiment, the Berkeley Lights LightningTM was used to measure various cellular parameters, such as cell differentiation status , polyfunctionality, and cytotoxic kinetics for the same cell to test and compare the efficacy of the generated products that were expanded using different priming conditions against CD19 expressing Raji cells. Regarding the transduction efficiency of LV20.19, a mean of 50% of transduced T-cells were found in the final cultures. 43% of IL-2 primed CAR T-cells displayed active cytotoxicity and 88% secreted IFNγ+, compared to IL-7/IL-15 primed CAR T-cells' 36% cytotoxicity and 58% secretion of IFNγ+. In both priming groups, CAR T-cells began cytotoxic activity as early as 3h and as late as 16h, and time needed to cause Caspase-3-activity ranged. This study elucidated the biological impact of different interleukins, which, in this case, were IL-2 and IL-7/IL-15, on LV20.19 CAR T-cells. Finally, this study provided a breakthrough regarding the importance of production of CAR T-cells, and thus, will aid overall efficacy of CAR T-cell immunotherapy against refractory B-cell malignancies and relapse.