CD44v6-specific CAR-T cells: a promising therapeutic strategy for colorectal and thyroid cancer patients

Caterina D'ACCARDO – *University of Palermo*

Chimeric antigen receptor (CAR)-T cell therapy represents one of the most innovative immunotherapy approaches. The encouraging results achieved by CAR-T cell therapy in hematological disorders paved the way for the employment of CAR-engineered T cells in different types of solid tumors, such as colorectal cancers (CRCs)and thyroid cancers. This adoptive cell therapy is based on the use of T cells engineered to selectively recognize specific tumor-associated antigens (TAAs) in cancer cells. Immunotherapy outcomes are associated with several variables that consider the crosstalk between the tumor microenvironment (TME) and the immune system, including tumor mutational burden (TMB), and the presence of high levels of tumor infiltratinglymphocytes (TILs). We previously demonstrated that a subpopulation of cancer cells, called cancer stem cells (CSCs) express CD44v6 and are responsible for their migration and generation of metastatic tumors. Here, we engineered CAR-T cells to recognize CD44v6,and, by performing *in vitro*co-cultureassay, we examinedthe efficacy of CD44v6 CAR-T-cells to target CSCs. Our findings revealed that the engineered T-cellswere effectively able to kill CSCs expressing high levels of CD44v6. Given that the outcomes of immunotherapy in solid tumors are still unsatisfactory, based on our preliminary data, we'll proceed with a combinatorial approach between immunotherapy and target therapy inCSCs.