Design and Optimization of CAR T Cells and Their Application to Glioblastoma

Encouraging clinical experience with chimeric antigen receptor (CAR) T cells supports the notion that even immune privileged sites such as the brain may be amenable to CAR therapy. In the context of hematologic B-cell malignancies, CD19-CARs have been shown to accumulate in the cerebrospinal fluid (CSF) and reduce the incidence of metastatic disease in the central nervous system. However, brain tumors pose significant challenges for CAR T cell therapy, including heterogeneous antigen expression, immunosuppressive networks in the tumor microenvironment that limit CAR T cell function and persistence, and suboptimal T cell trafficking to the tumor site. This presentation will describe our clinical experience with CAR T cells for glioblastoma (GBM), one of the most common and aggressive primary malignant brain tumors, and our efforts to overcome therapeutic challenges.