Abstract: Adoptive T cell immunotherapy involves the isolation, ex vivo expansion and reinfusion of T cells, and is dependent on T cell engraftment and persistence for efficacy. Endogenous T cells undergo activation in nutrient-rich lymph nodes. In contrast, CAR-redirected T cells are activated in hostile territories in the tumor microenvironment. Consequently, competing for metabolites, the antigen-stimulated CAR T cells cannot generate sufficient energy to support bursts of proliferation and differentiation. IDH1 is one of the most frequently mutated metabolic genes in cancer. Mutations in R132 of IDH1 confer distinct physiochemical properties that catalyze the production of 2HG, which promotes central memory formation and limits effector differentiation during ex vivo culture. We hypothesize that IDH1R132-mediated production of 2HG optimizes the differentiation of CAR T cells, resulting in enhanced CAR T cell anti-tumor function. Our aim is to test the effectiveness of IDH1 for future therapeutic potential in patients with GBM and other rapidly growing tumors. “Fighting fire with fire” may be an effective strategy to arm CAR T cells for enhanced metabolic function and cytolytic activity in challenging settings.