With the advent of cancer immunotherapy, there has been a major improvement in patients' quality of life and survival. The growth of cancer immunotherapy has dramatically changed our understanding of the basics of cancer biology and has altered the standards of care (surgery, radiotherapy, and chemotherapy) for patients. Cancer immunotherapy has generated significant excitement with the success of chimeric antigen receptor (CAR) T cell therapy in particular. Clinical results using CAR-T for hematological malignancies have led to the approval of four CD19-targeted and one B-cell maturation antigen (BCMA)-targeted cell therapy products by the US Food and Drug Administration (FDA). Also, immune checkpoint inhibitors such as antibodies against Programmed Cell Death-1 (PD-1), Programmed Cell Death Ligand-1 (PD-L1), and Cytotoxic T-Lymphocyte-Associated Antigen 4 (CTLA-4) have shown promising therapeutic outcomes and long-lasting clinical effect in several tumor types and patients who are refractory to other treatments. Despite these promising results, the success of cancer immunotherapy in solid tumors have been limited due to several barriers, which include immunosuppressive tumor microenvironment (TME), inefficient trafficking, and heterogeneity of tumor antigens. This is further compounded by the high intra-tumoral pressure of solid tumors, which presents an additional challenge to successfully delivering treatments to solid tumors [1)].

Chimeric antigen receptor (CAR) therapy targeting CD19 has yielded remarkable outcomes in patients with acute lymphoblastic leukemia. To identify potential CAR targets in acute myeloid leukemia (AML), we probed the AML surfaceome for overexpressed molecules with tolerable systemic expression. We integrated large transcriptomics and proteomics datasets from malignant and normal tissues, and developed an algorithm to identify potential targets expressed in leukemia stem cells, but not in normal CD34+CD38- hematopoietic cells, T cells, or vital tissues. As these investigations did not uncover candidate targets with a profile as favorable as CD19, we developed a generalizable combinatorial targeting strategy fulfilling stringent efficacy and safety criteria. Our findings indicate that several target pairings hold great promise for CAR therapy of AML [2)].

1)
Guha P, Heatherton KR, O'Connell KP, Alexander IS, Katz SC. Assessing the Future of Solid Tumor Immunotherapy. Biomedicines. 2022 Mar 11;10(3):655. doi: 10.3390/biomedicines10030655. PMID: 35327456; PMCID: PMC8945484.
2)
Perna F, Berman SH, Soni RK, Mansilla-Soto J, Eyquem J, Hamieh M, Hendrickson RC, Brennan CW, Sadelain M. Integrating Proteomics and Transcriptomics for Systematic Combinatorial Chimeric Antigen Receptor Therapy of AML. Cancer Cell. 2017 Oct 9;32(4):506-519.e5. doi: 10.1016/j.ccell.2017.09.004. PubMed PMID: 29017060.