Towards next-generation CAR-T cell therapy for cancer

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Due to its ability to recognize antigens in an MHC-independent manner, T cells that are engineered to express chimeric antigen receptor (CAR) can be a viable option for the tumors with low mutational burden. Indeed, the second-generation CD19-targeting CAR-T cells with an engineered signaling domain demonstrated unprecedented anti-leukemic responses in patients with refractory B-cell cancer, and became the first approved gene therapy for cancer last year. In light of their clinical success, there has been an explosion of interest in CAR-T cells for cancer immunotherapy. However, the inability to control the activity of this potent live drug has resulted in severe treatment related toxicities and the constraint in targeting more than one antigen have limited its general application. Furthermore, various immune-suppressive mechanisms present in the tumor microenvironment often severely limits the anti-tumor activity of CAR-T cells against solid tumors, posing a major obstacle for more widespread application of this innovative therapy. In this talk, I will discuss our recent research efforts focusing on addressing these limitations of current CAR-T therapy.