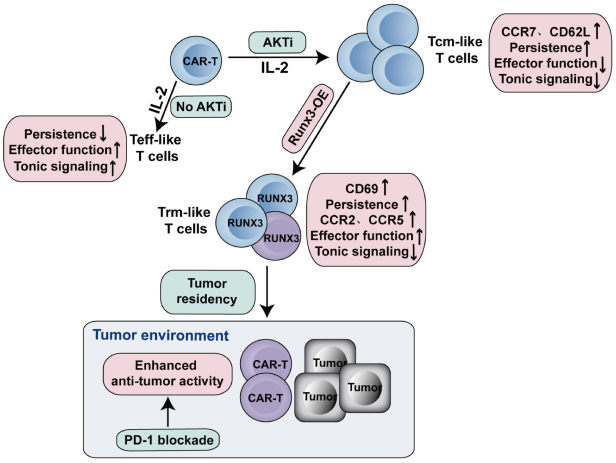
Runx3-overexpression cooperates with ex vivo AKT inhibition to generate receptor-engineered T cells with better persistence, tumor-residency and anti-tumor ability



Authors:
Jianghui Tang, Jianpeng Sheng, Qi Zhang, Yongtao Ji, Xun Wang, Junlei Zhang, Jiangchao Wu, Jinyuan Song, Xueli Bai, Tingbo Liang

Correspondence:
liangtingbo@zju.edu.cn

In Brief:
Runx3-overexpression cooperated with ex vivo AKT inhibition to generate CAR-T cells with both Tcm and Trm characteristics, which had enhanced antitumor activity and responded to PD-1 blockade well. While AKT inhibition promoted CAR-T cell central memory phenotype with prominently enhanced persistence, Runx3-overexpression promoted CAR-T cell tissue-resident memory phenotype and further enhanced persistence, effector function as well as tumor-residency. Runx3-overexpression also cooperated with AKT inhibition to repress terminal differentiation of CD8+CAR-T cells induced by tonic signaling, which contributed to CAR-T cell persistence as well.