

**Table S1** Comparison of structural differences dual-targeted CARs (Tandem CAR, Parallel CAR, and synNotch CAR).

Characteristics	Tandem CAR	Parallel CAR	synNotch CAR
Structure	Single chain with two scFvs	Two independent CARs on one T cell	Primary CAR + synNotch receptor
Target Recognition	Simultaneous binding to two antigens	Independent binding to two antigens	Sequential binding (Antigen A → Antigen B)
Signaling Pathway	Integrated CD3ζ + co-stimulation	Separate CD3ζ for each CAR	synNotch → Primary CAR activation
Activation Logic	OR-gated (either antigen activates)	OR-gated (either antigen activates)	AND-gated (both antigens required)
Potential Advantages	Compact design, easy manufacturing	Flexible antigen pairing	High specificity, reduced off-target toxicity
Limitations	Potential steric hindrance	Higher manufacturing complexity	Delayed activation kinetics