MSC for CAR-T

CAR-T (chimeric antigen receptor T) cell therapy has achieved significant success in hematological malignancies but faces critical limitations in solid tumors: the immunosuppressive tumor microenvironment (TME) — characterized by regulatory T cells (Tregs), myeloid-derived suppressor cells (MDSCs), hypoxia and checkpoint molecules including PD-L1 — drives rapid T-cell exhaustion, limits CAR-T persistence, and reduces therapeutic durability. Antigen heterogeneity within solid tumors further enables immune escape[1]. Kyttaro holds patents covering the co-administration of mesenchymal stem cells (MSCs) with CAR-T cells specifically to overcome these limitations[2].

MSCs exert potent immunomodulatory effects on the TME through paracrine signaling, secretion of anti-inflammatory factors, and direct cell-cell contact. In preclinical models, co-administered MSCs remodeled the immunosuppressive TME, countered CAR-T exhaustion by reducing the suppressive signals that drive T-cell dysfunction, and addressed antigen heterogeneity-related immune escape through bystander immune activation[3,4,5]. Cytokine release syndrome (CRS) following high-dose CAR-T infusion is driven largely by macrophage activation[6]; the anti-inflammatory paracrine activity of MSCs is expected to attenuate this response.

Kyttaro's internal in vitro data show that combined MSC/CAR-T therapy achieves equivalent anti-tumor cytotoxicity at a substantially lower CAR-T cell dose, reducing CRS risk without compromising efficacy[7]. The approach may be applicable to glioblastoma and other solid tumor settings in which conventional CAR-T therapy is currently limited by TME immunosuppression, as well as to hematological malignancies in which improved CAR-T persistence can extend the duration of response.

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