V90lec13 were evaluated with a 4-hours Calcein-AM assay or with a 40/60-hours real-time cell assay against HER-2+ breast cancer cell lines. The concentration of cytokines produced upon the 20-hours co-culture of effector with target cells was assessed with a multiplex assay by flow cytometry analysis. The in vivo biodistribution of the fluorophore-conjugated HER2xCD3 bsAb was monitored in tumor bearing NSG mouse model.

Results HER2xCD3 binds efficiently to CIK cells with the ScFv of CD3 and to cancer cells with the ScFv of HER-2 in a dose-dependent manner. The specific combination of HER2xCD3, TRS or TRS V90lec13 with CIK cells significantly enhances their anti-tumor activity against several breast cancer cell lines, compared to CIK cells alone, even at a very low effector/target ratio (0.1:1). Interestingly, TRS-resistant tumor cell lines show to be sensitive instead to HER2xCD3 redirected CIK cell lytic activity. The increase of CIK cell killing is correlated to the dose of bsAb and it is functional even at very low concentrations. Moreover, redirected-CKI cells presents a proinflammatory and not a toxic cytokines profile. The bsAb HER2xCD3 arrives efficiently at the tumor site where reaches the maximum concentration after 8 hours of injection into mice.

Conclusions These results highlight the potentiality of using clinical grade mAbs or recombinant immunotoxins to improve the cytotoxic activity of CIK cells against HER-2+ tumor cells, opening new perspectives for adoptive immunotherapy to treat solid tumors.

REFERENCES

