Conclusions We developed an engineering approach to enhance the in vivo persistence and antitumor efficacy of transferred T cells. Our targeted, two-hit strategy uses a single fusion protein to overcome a death signal prevalent in the TME of many cancers and on activated T cells, and to provide a pro-survival costimulatory signal to T cells. Our results suggest that this fusion protein can increase T cell function when combined with murine or human TCRs, and can significantly improve therapeutic efficacy in liquid and solid tumors, supporting clinical translation.

REFERENCES

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EVALUATING THE SAFETY OF TUMOR TREATING FIELDS (TTFIELDS) APPLICATION TO THE TORSO – IN VIVO STUDIES
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Background Tumor Treating Fields (TTFIELDS) are a noninvasive, antineoplastic treatment delivered locoregionally to tumor bed via low intensity (1–3 V/cm), intermediate frequency (100–500 kHz), alternating electric fields. This treatment modality has been shown to be cytotoxic to rapidly dividing cells, with highest efficacy demonstrated at different optimal frequencies depending on tumor cell-type. TTFIELDS therapy is FDA-approved for the treatment of newly diagnosed and recurrent glioblastoma (GBM), with the overall tolerable safety profile (EF-11 and EF-14 clinical trials) attributed to the low rates of mitotic events in normal, quiescent brain cells. Further evaluation of the safety profile of TTFIELDS is needed for treating cancer in different body regions where there are high rates of cellular proliferation, i.e. torso. Many solid malignant tumors may reside in the torso region – mesothelioma and non-small cell lung carcinoma (NSCLC) in the thoracic segment; pancreatic cancer, hepatocellular carcinoma, and gastric cancer in the abdomen; and ovarian cancer in the pelvis. Hence, we investigated the safety of delivering TTFIELDS to the torso of healthy rats at conditions previously deemed effective for treating the aforementioned cancer cell types.

Methods TTFIELDS were applied using the Novo-TTF100L system at frequencies of 150 or 200 kHz and intensities of 1–2 V/cm RMS to torsos of Sprague Dawley (SD) female rats for a duration of 2 weeks. Throughout treatment, animals underwent daily clinical examinations. Blood samples and comparative histological evaluation of major internal organs were performed at treatment cessation.

Results No significant differences were observed for the TTFIELDS treated groups in comparison to control groups for the following parameters: activity level, food and water intake, stools, motor neurological status, respiration, weight, complete blood count, blood biochemistry, and pathological findings.

Conclusions Although EpCAM CAR-T cells therapy is safe in general, serious complications still happen possibly requiring close monitoring and timely treatment. Our findings suggest that tocilizumab combined with glucocorticoid can be an effective therapeutic method for severe CRS caused by CAR-T cells therapy in solid tumor.

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