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.

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176 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 These results demonstrate the safety of 150 and 200 kHz TTFIELDS when delivered to torsos of healthy rats, where there are normal tissues with high cellular proliferation rates. Overall, TTFIELDS delivery to the torso demonstrated safety and feasibility for the treatment of thoracic and other abdominal and pelvic cancers. TTFIELDS are currently being investigated in clinical studies for the treatment of solid tumors located in the torso, including locally advanced pancreatic cancer (PANOVA-3 Study, NCT03377491), ovarian cancer (INNOVATE-3 Study, NCT03940196), lung cancer (LUNAR Study, NCT02973789), hepatocellular carcinoma (HEPANOVA Study, NCT03606590) and gastric cancer.

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