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 rate 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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177 A SEVERE CYTOKINE RELEASE SYNDROME WITH RESPIRATORY FAILURE IN RECURRENT MESOTHELIOMA INDUCED BY EPCAM CAR-T CELLS INFUSION: A CASE REPORT

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Background With the development and maturity of chimeric antigen receptor T (CAR-T) cells therapy-related technologies, the application of CAR-T therapy has progressed from blood tumors to solid tumors, and its potential risks and side effects have been more widely recognized. As the most common complication of CAR-T therapy, cytokine release syndrome (CRS) is an inflammatory syndrome caused by the activation and proliferation of T-cell and the increased levels of multiple cytokines. Epithelial cell adhesion molecule (EpCAM) is overexpressed in a variety of tumors and has been used as one of the targets of CAR-T therapy. Case reports of severe CRS due to the use of anti-EpCMA CAR-T cell therapy are very rare.
Methods A 45-year-old malignant mesothelioma woman with EpCAM-positive whose disease progressed after chemotherapy was enrolled into our study (ChiCTR2000030274). The patient received a total of 1.8×107 autologous T cells which contained sequences encoding single-chain variable fragments (scFv) specific for EpCAM after cyclophosphamide lymphodepletion. After the infusion of CAR-T cells, the patient developed typical CRS reactions such as fever, hypoxemia, pulmonary edema, and elevated inflammatory factors. The patient's condition did not improve after the use of anti-inflammatory and antipyretic drugs. After administration of tocilizumab (4 mg/kg, day 6 and day 17) combined with glucocorticoid (40 mg q12h, decreasing gradually), the patient's general condition gradually improved, and chest computed tomography (CT) showed that pulmonary edema was absorbed.
Results The patient's CRS was successfully eliminated after the use of IL-6 inhibitor tocilizumab combined with glucocorticoid.
Conclusions Although EpCAM CAR-T 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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