Liminatus Pharma LLC

GCC CAR-T

Pre-Clinical Study of GCC CAR-T Cells

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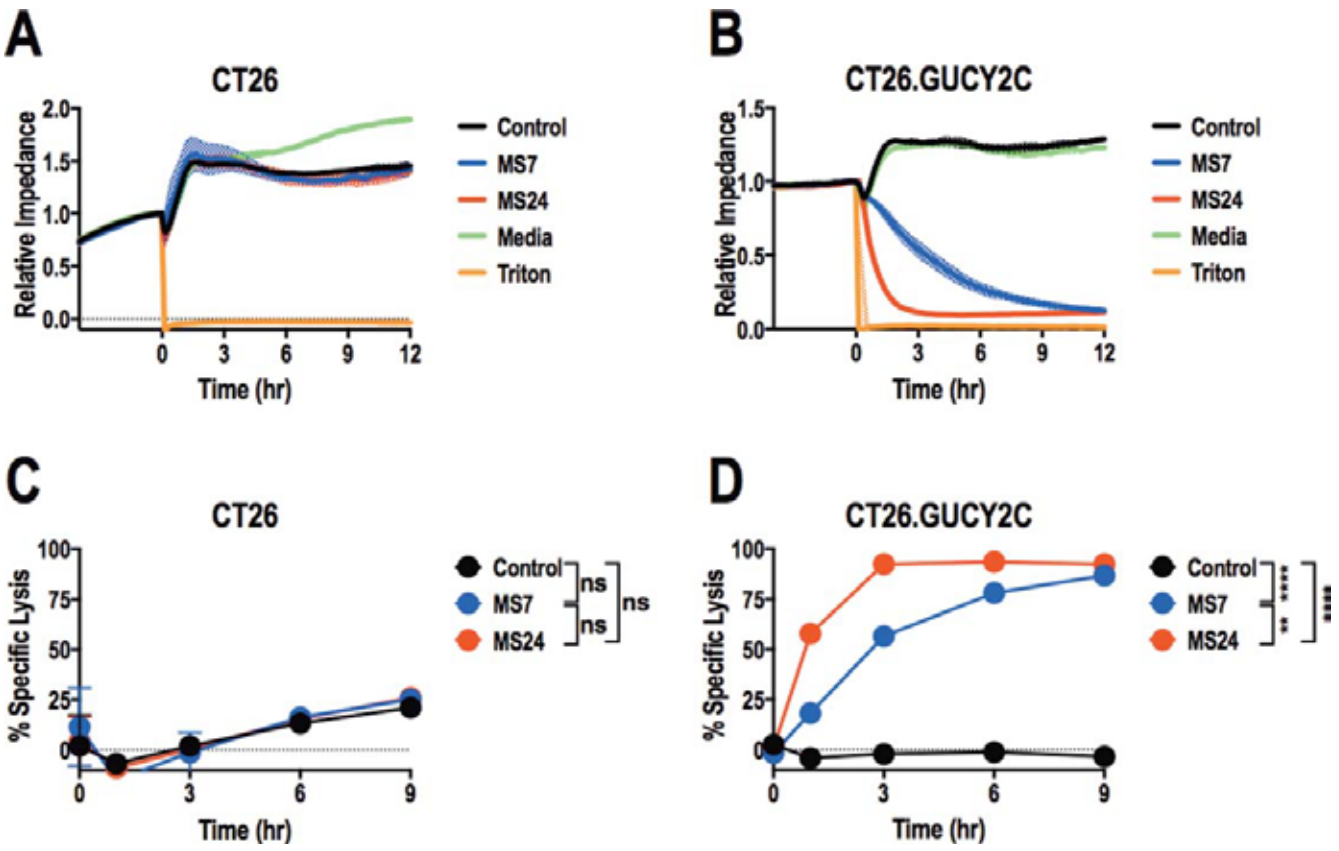
Preclinical results show that GUCY2C directed CAR-T cells kill GUCY2C-expressing mouse colorectal cancer cells, reduce the number of metastatic tumors, and increase the survival rate of mice harboring metastatic GCC-expressing colorectal tumors. GUCY2C-directed T cell efficacy against metastatic tumors was achieved in syngeneic mice without immune damage to normal tissues, including intestine.



Real-time GUCY2C-specific CAR T cell-mediated cytotoxicity

Results are representative of two experiments (C and D); % specific lysis values for each CAR-T cell and target cell combination were calculated from the impedance data at the indicated time points. MS7 and MS24, but not control, CAR-T cells lysed GUCY2C-expressing, but not GUCY2C-deficient, CT26 mouse colon cancer cells. MS24 CAR T cells lysed GUCY2Cexpressing CT26 cells more rapidly than MS7 CAR-T cells (Oncoimmunology. 2016 Sep 2;5(10):e1227897. eCollection 2016).

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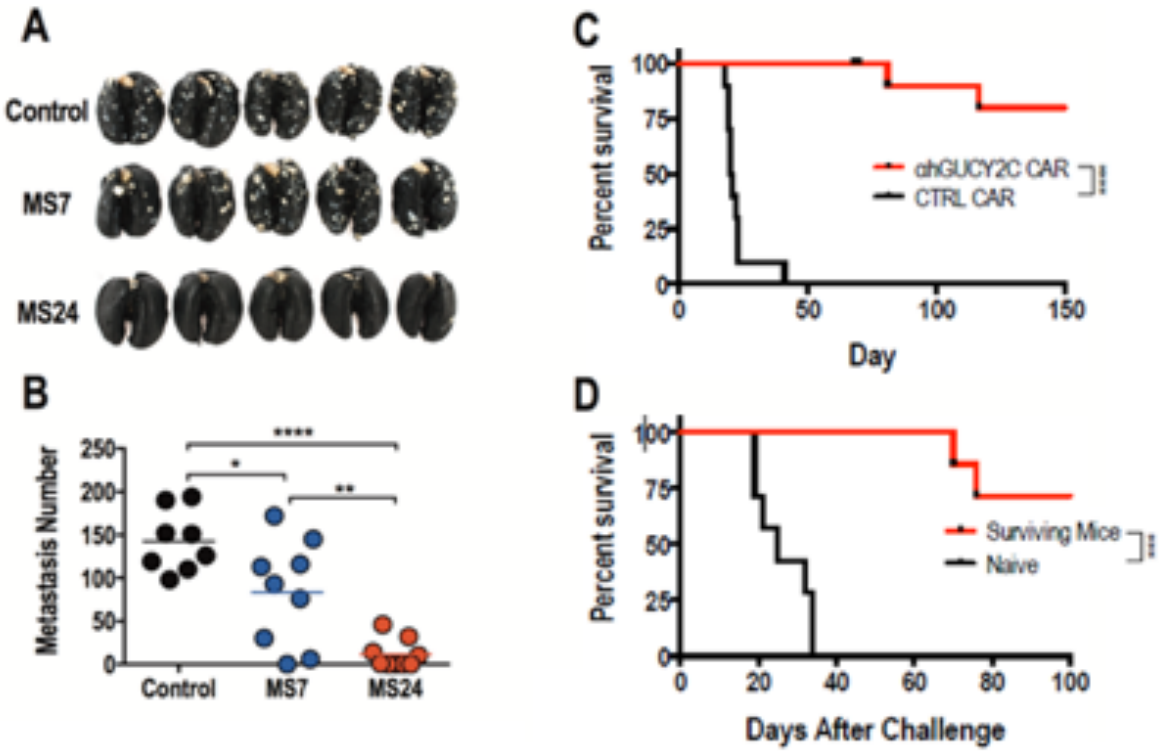

GUCY2C-specific CAR T cells oppose parenchymal colorectal cancer metastases

The number of tumors in lungs of mice treated with GUCY2C CAR-T cells was significantly reduced compared to mice treated with control CAR-T cells (A and B). Moreover, hGUCY2C CAR-T cell-treated mice (second dose administered on day 14) exhibited improved survival (C). Long-term surviving and naïve mice challenged with parental CT26 cancer cells exhibited identical death rates, indicating that long-term survivors did not produce a protective immune response to gp70 or other antigens expressed in CT26 cells (D). (Oncoimmunology. 2016 Sep 2;5(10):e1227897. eCollection 2016; Cancer Immunol Res. 2018 May; 6(5):509-516).

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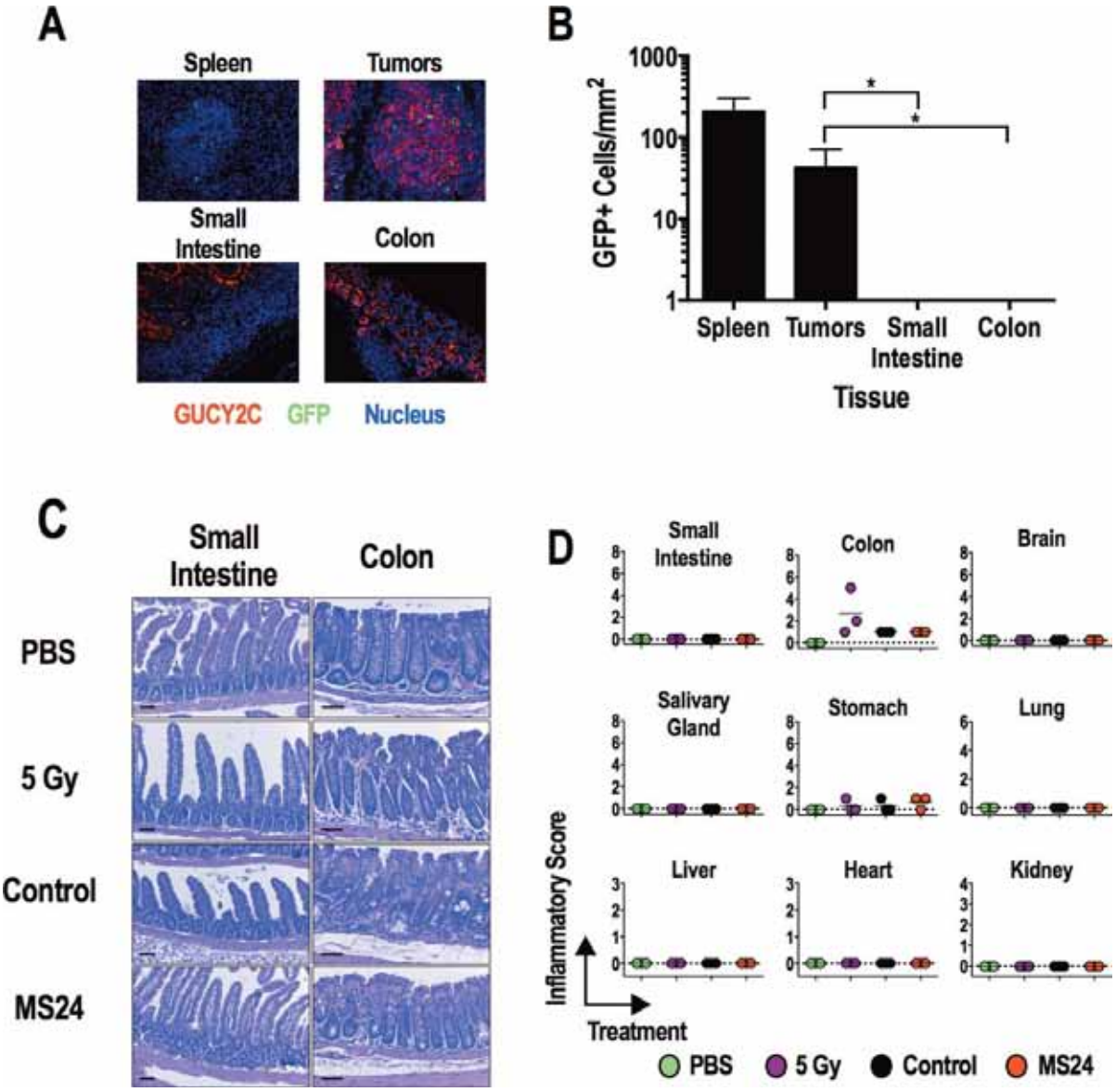

GUCY2C-specific CAR T cells do not induce tissue damage

MS24 CAR-T cells produce the greatest GUCY2C-dependent T cell activation, cytokine production, cytolysis, and antitumor efficacy without autoimmunity. Mice receiving MS24 CAR-T cells were healthy with no signs or symptoms of inflammatory bowel disease including failure to thrive, altered bowel habits, or rectal bleeding. MS24 CAR-T cells accumulated in GUCY2C-expressing CT26 lung metastases, mediating antitumor immunity, but were absent from intestines (A and B), producing no T cell-mediated damage quantified by histopathology (C and D) (Oncoimmunology. 2016 Sep 2;5(10):e1227897. eCollection 2016).