A CAR-T cell targets and kills GPC3 expressing cancers such as hepatocellular carcinoma (HCC). The CAR construct works by using an anti-GPC3 scFv region to enable T cell targeting of GPC3 expressing cancer cells and T-cell activation by incorporating co-stimulator and intracellular signaling regions. GPC3 is a tumor associated antigen over-expressed on about 90% of HCCs. GPC3’s low or absent expression on normal adult tissues makes it an attractive target for therapy. Co-expression of the chemokine receptor CX3CR1 enhanced infiltration of the CAR-T cells into the tumor tissue as evidenced by more than 100 fold greater tumor cell killing in a mouse xenograft model compared to GPC3 alone or untransfected T cells. With the addition of the CX3CR1 construct, the anti-GPC3 CAR-T cells may be one of the first therapies to show promising results in solid carcinomas.

COMMERCIAL OPPORTUNITY

- The American Cancer Society estimates that in 2018 there will be 42,220 patients who develop liver cancer and 30,200 liver cancer patients will die. The mortality rate for liver cancer is increasing. GPC3 is specifically expressed in hepatocellular carcinoma (HCC), ovarian clear cell carcinoma, melanoma, squamous cell carcinoma of the lung, hepatoblastoma, nephroblastoma (Wilms tumor), yolk sac tumor, and some pediatric cancers.

- The addition of expression of CX3CR1 to the GP3 CAR-T cells was due to a recent Moffitt study using primary patient tumor specimens where it was found that infiltrating lymphocytes (T and NK) within the tumor tissue were absent of CX3CR1, a key chemokine receptor for lymphocytes, and had possibly been downregulated by the tumor cells in order to evade the immune system.

- The marketplace is attractive for CAR-T development, as Novartis received approval in August 2017 for Kymriah, its anti-CD19 CAR-T therapy for pediatric B-cell ALL. The trial had an overall response rate of 82.5% (52/63). Although the list price for Kymriah is $475,000 for a one-time treatment, Novartis has said only those patients who respond by the end of the first month will need to pay. In October 2017, Gilead’s Yescarta, an anti-CD19 CAR-T, was approved for large B-cell lymphoma and is listed at $375,000. In 2017, Gilead acquired Kite Pharma for $11.7B, and in 2018, Celgene acquired Juno Therapeutics for $9B. Juno was also developing a CD-19 CAR-T therapy.

TECHNOLOGY

GPC3 is over-expressed in about 90% of HCCs compared to normal liver as shown by a Moffitt study (37 HCC vs. 21 normal tissue samples). GPC3-CX3CR1 CAR-T cells effectively kill GPC3+ HepG2 liver cancer cells in vivo in a human xenograft mouse model when compared with untransduced T cells. The killing efficacy is demonstrated by the mean of luminoscores of images of luciferase in 5 treated and five control mice. At week 3, GPC3+ liver cells with the untransduced T cells demonstrate a mean value of over 2000 X 10^3 photon flux units vs almost zero for the GPC3+ liver cells with the anti-GPC3/CX3CR1 CAR-T cells.

PUBLICATION/PATENT

- Provisional Patent filed on March 19, 2019 for Dr. Wei