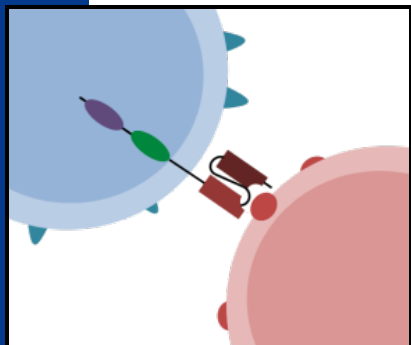


Olfactory Receptor Targeting Chimeric Antigen Receptor Expressing T cell (CAR-T) for Solid Tumors



A chimeric antigen receptor-expressing T cell that targets and kills cancer cells expressing the olfactory receptor OR2H1 or OR5V1 are being developed to target multiple solid cancers including prostate, liver, and renal cancer. The CAR constructs work by using novel anti-OR2H1 or anti-OR5V1 scFv regions to enable T cell targeting of OR2H1 or OR5V1 expressing cancer cells and T-cell activation by incorporating co-stimulator and intracellular signaling regions. OR2H1 is over-expressed in prostate and renal cancers, and has been found to be normally expressed in only the testes and the nose. OR5V1 is over-expressed in liver and renal solid cancers, and has been found to also be normally expressed in only the testes and nose. The OR2H1 scFv was recovered from a phage library, while the OR5V1 scFv sequences were derived from an antibody expressed by B cells found in ovarian tumors.

COMMERCIAL OPPORTUNITY

- Prostate, renal, and liver cancer are solid tumors with limited immune therapeutic options. The ACS 2020 estimates for the number of new cases of prostate, renal, and liver cancer are 191,930; 73,750; and 42,810, and the estimates of the number of deaths for prostate, renal, and liver cancer are 33,330; 14,830; and 30,160.
- The marketplace is attractive for CAR-T cell therapies, as Novartis received approval in August 2017 for Kymriah, its anti-CD19 CAR-T therapy for pediatric B-cell ALL with an ORR of 82.5%. 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 is also developing a CD-19 CAR-T therapy. Kymriah had annualized sales of \$243M in 2019, and Yescarta had sales of \$456M in 2019. Also CMS in 2018 set Medicare Part B reimbursements for CAR T-cell therapies at \$500,000 for Kymriah and \$400,000 for Yescarta in the outpatient setting.

TECHNOLOGY

For the OR5V1 antibody, a protocol was used to separate, activate and immortalize B cells from freshly dissociated advanced serous ovarian carcinomas from patients with tertiary lymphoid structures (TLS). Freshly resected stage III/IV ovarian carcinomas from naive patients are routinely obtained through an IRB approved protocol. Tissues are mechanically dissociated and cryopreserved. B cells can be purified from every dissociated ovarian carcinoma and can be immediately activated with CD40 agonists plus IL-21 and immortalized using EBV. OCT blocks can be generated for histological analysis and identification of TLS through IHC analysis, using CD19 and CD3 antibodies. Before cryopreservation, IgG can be purified from immortalized B cells with resins that selectively capture IgG of IgA (Thermo) and sent to CDI Laboratories for determination of their specificities using *HuProt* proteome arrays, which contain >80% of the human proteome

PUBLICATION/PATENT

- Provisional patent application filed June 17, 2020 for Dr. Jose Conejo Garcia.

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LICENSING OPPORTUNITY

