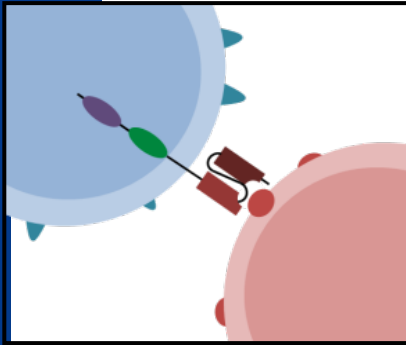


CAR-T Constructs with NKG2D Receptor Signaling Domains



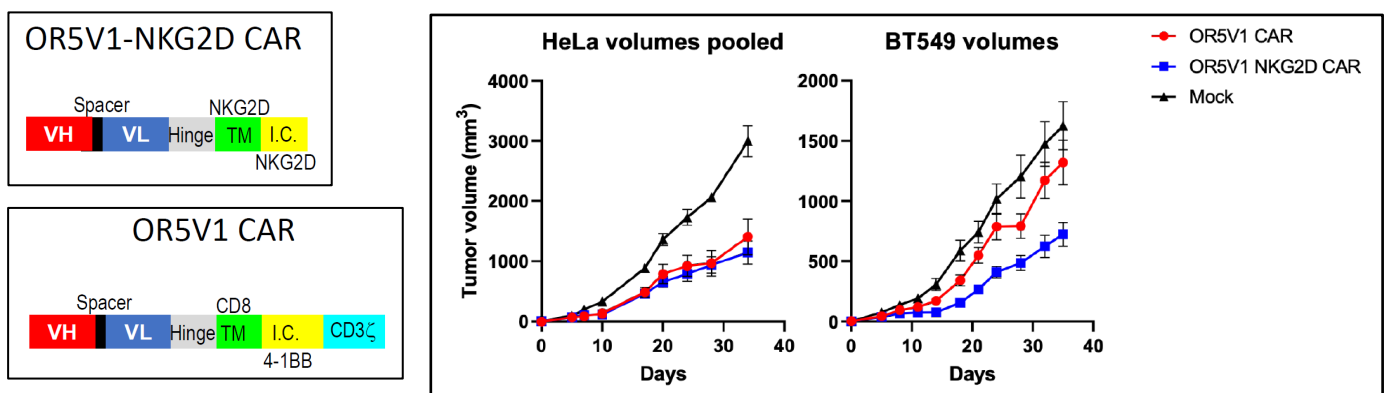
CAR-T constructs with wild-type intracellular NKG2D receptor signaling domains have been developed that show comparable or superior target cell killing without the classic second generation 41BB intracellular costimulatory domain and the CD3 ξ activation domain (see Figure below). Using CAR constructs with the NKG2D receptor signaling domains may lead to memory cell formation (memory cell certification) with increased persistence and migration leading to longer lasting target cell killing that may result in more durable responses. This new construct also may help solve the inability of many CAR-T cells to effectively attack solid tumors because these CAR-T cells may be insensitive to inhibition by PD1. This is because the NKG2D receptor signaling domain is not part of the TCR signaling apparatus that includes the 41BB and CD3 ξ domains. This type of construct may also be functional in gamma delta T cells and NK cells, in addition to CD8+ T cells, as all three of these cell types have the intracellular machinery for the NKG2D receptor signal transduction.

COMMERCIAL OPPORTUNITY

- The marketplace is attractive for autologous 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 July 2020, Gilead's Tecartus, an anti-CD19 CAR-T made by a different method than Yescarta, was approved for mantle cell lymphoma. In March 2021, Bluebird and BMS' Abecma, an anti-BCMA CAR-T, was approved for multiple myeloma. 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. In 2020, Kymriah had annualized sales of \$422M, and Yescarta had annualized sales of \$592M. 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

Figure shows tumor volumes in mouse models after treatment with OR5V1 or OR5V1-NKG2D CARs.



PUBLICATION/PATENT

- PCT application was filed in April 2022 for Drs. Guevara and Conejo-Garcia

CONTACT

Haskell Adler PhD MBA
Senior Licensing Manager
Haskell.Adler@Moffitt.org
(813) 745-6596

LICENSING OPPORTUNITY

