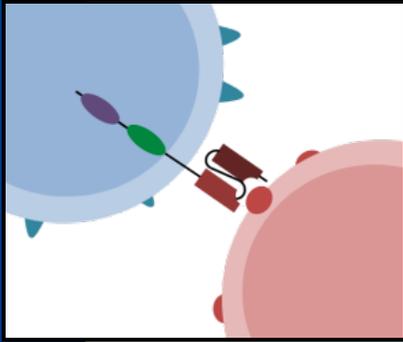


Lung Cancer Brain Metastases Targeting CAR-T Cell Constructs with Phage Display Derived Peptide Oligomers



A chimeric antigen receptor-expressing T cell that targets and kills lung cancer brain metastases. The CAR construct works by using novel phage display-derived peptide oligomers as a substitute for the scFv region to enable T cell targeting of lung cancer brain metastases and T-cell activation by incorporating co-stimulator and intracellular signaling regions. The oligomers were generated through in vitro and in vivo selection methods using cell lines and xenograft mice. The specific binding of peptide oligomers to lung cancer brain metastases has been confirmed through flow cell sorting techniques.

COMMERCIAL OPPORTUNITY

- The American Cancer Society estimates that in 2018 in the US there will be 234,030 new cases of lung cancer and about 154,050 deaths from lung cancer, and about 20 to 40% of the patients with non-small cell lung cancer will go on to develop brain metastases. Lung cancer-derived metastatic brain tumors are the most common type of brain metastases.
- The average survival time with brain metastases is usually less than a year, but when only isolated metastases (oligometastases) are found and can be treated, over 60 percent of people may survive for two years or longer.
- 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 is also developing a CD-19 CAR-T therapy.

TECHNOLOGY

Two strategies were used for phage display screening to isolate lung cancer derived metastatic brain tumors binding peptides. In the in vitro screening method, the phage library was applied to lung cancer cells. Phage peptides that were NOT bound were collected. The collected peptides were applied to normal brain tissue, and again peptides that were NOT bound were collected, and applied to lung cancer derived metastatic brain tumor cells. After washing away non-binding peptides, phage peptides were collected and amplified, and the peptides were collected and sequenced. In the in vivo strategy, NSG mice have lung cancer brain mets injected into the intracranial cavity. After maximal tumor growth, the phage library was injected into the tail vein and after 24 hours, the intracranial tumors were collected and the phage peptides were harvested. These phage peptides were amplified and reapplied to new mice with intracranial tumors for 4 total rounds. After 4 rounds, the peptides were collected and sequenced. Results of flow cytometric analysis of peptides showed that for each peptide, as the concentration of peptide goes up, there was a right shift indicating binding to the brain met cells, with minimal binding to the lung cancer primary cells. For example, at a concentration of 150 nM LBM2 peptide, there was 50% binding to the brain met cells, and no discernible binding to primary lung cancer cells.

PUBLICATION/PATENT

- Provisional patent application was filed on October 17, 2018 for Drs. Liu and Abate-Daga.

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LICENSING OPPORTUNITY



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