Docket #: S19-046

Reducing neurotoxicity in CD19-directed immunotherapy

Background
The development of CAR-T and T-cell engaging BiTE therapies has been a breakthrough for patients with B-cell lymphomas, where T-cell targeting of CD19 has been the focus of multiple FDA-approved treatments. However, uptake of these novel treatments has been limited by a toxicity profile that requires strict observation and management for signs of neurotoxicity.

Technology
Stanford researchers have identified a key contributor to CD19 CAR-T and BiTE-mediated neurotoxicity, unlocking a potential mechanism for the well-documented adverse event profile associated with CD19 targeting therapies. Single cell analysis revealed that the CD19 antigen is also expressed on pericytes of the central nervous system (CNS) and vascular smooth muscle cells; further, administration of CD19-targeting therapies can disrupt the blood brain barrier (BBB) to further expose the vulnerable cells, with greater disruption from CAR-Ts like axicabtagene ciloleucel that use a CD28 co-stimulatory domain.

In collaboration with University of Pennsylvania, the inventors are developing strategies to spare CD19-binding on pericytes and vascular smooth muscle cells, including novel CAR-Ts or bispecific antibodies with an inhibitory domain to specifically prevent activity on non-target cells.

Applications

- B-cell lymphomas
- CD19-targeted therapies, including CAR-T

Advantages

- Improved safety relative to currently approved CD19-targeting therapies
- Reduction in off-target activity for CD19-targeting therapies

Publications

- K.R. Parker, D. Migliarini, E. Perkey, … H.Y. Chang, A. D. Posey, Jr., A. T. Satpathy Single-Cell Analyses Identify Brain Mural Cells Expressing CD19 as Potential Off-Tumor Targets for CAR-T Immunotherapies *Cell* 2020.

Patents

- Published Application: 20230039520

Innovators

- Ansuman Satpathy
- Howard Chang
- Kevin Parker

Licensing Contact

Minxing Li

Licensing and Strategic Alliances Manager

Email