Docket #: S25-003

Treating Cognitive Impairment from Cancer Immunotherapy by Chemokine Receptor Inhibition

Stanford researchers in Prof. Michelle Monje's lab have developed a method for treating cognitive impairment (aka brain fog) caused by cancer immunotherapy. This method involves the use of CCR3 chemokine receptor inhibitors to mitigate central nervous system (CNS) immune dysregulation and restore cognitive function.

Cancer therapies, including immunotherapy, often lead to persistent cognitive impairments, commonly referred to as "brain fog," characterized by deficits in attention and memory. Current treatments for these cognitive symptoms are largely ineffective, as they do not address the specific molecular mechanisms underlying immune-mediated cognitive dysfunction. The lack of targeted therapies to mitigate these cognitive deficits highlights a significant unmet need in the field.

Stanford researchers have developed a method that utilizes CCR3 chemokine receptor inhibitors, such as SB-328437, to treat cognitive impairment caused by cancer immunotherapy. This innovative approach directly targets CNS immune dysregulation, which is a key underlying mechanism of cognitive dysfunction in these conditions. By blocking the CCR3 receptor, this method effectively reduces microglial reactivity and normalizes oligodendroglial homeostasis, thereby restoring cognitive function. This solution is superior to current treatments as it addresses the specific molecular pathways involved, with evidence from mouse models demonstrating significant improvements in cognitive performance and cellular health.

Figure

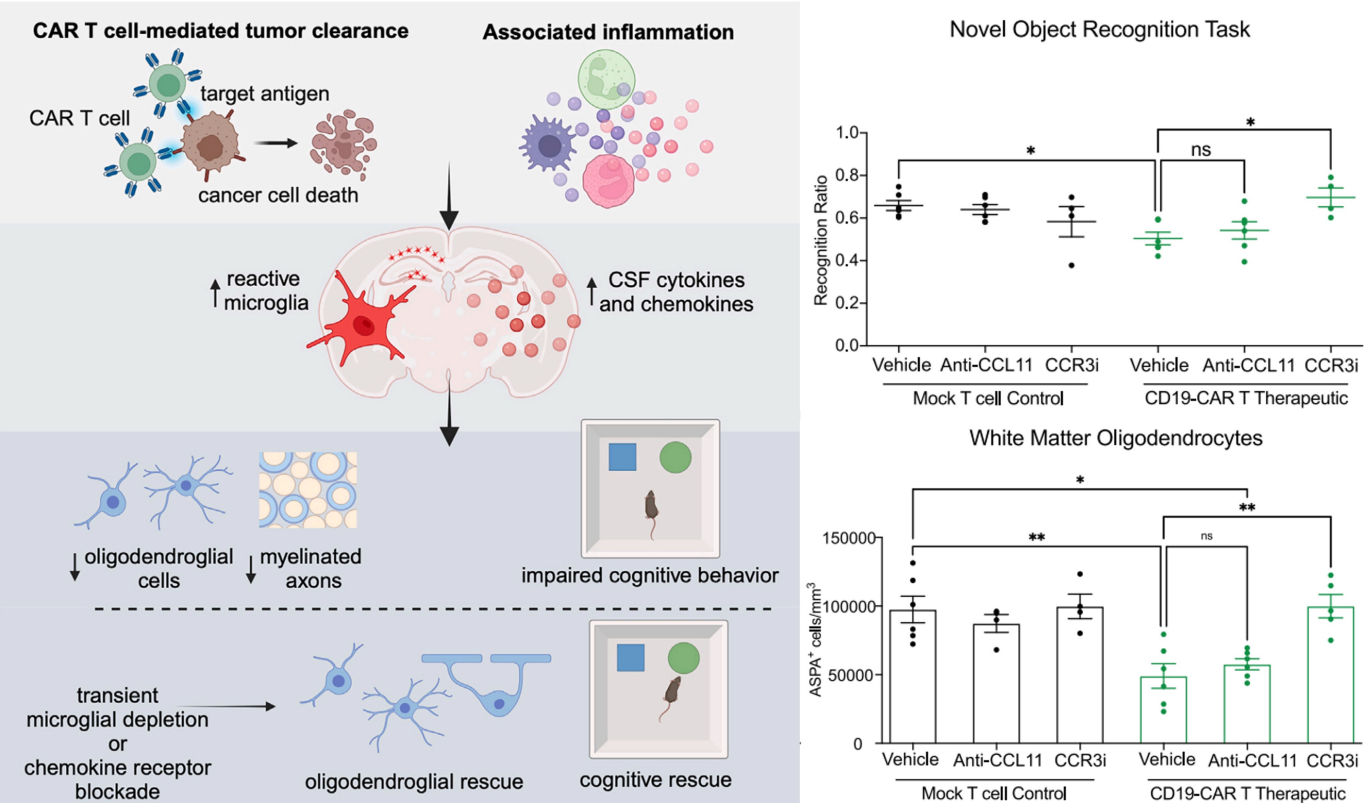

Figure Description: CAR T cell therapy can cause cognitive impairment in mouse models with CNS and non-CNS cancers by inducing persistent neuroinflammation, thereby disrupting oligodendroglial homeostasis and hippocampal neurogenesis, which can be rescued by microglial depletion or CCR3 blockade.

Stage of Development

Proof of concept - in vivo data using patient-derived xenograft models in mice

Applications

- **Cancer Therapy:** Treating cognitive impairment in patients undergoing immunotherapy
- **Neuroinflammation Management:** Targeting CNS immune dysregulation to restore neural cell function and cognitive performance

Advantages

- **Targeted Treatment:** CCR3 chemokine receptor blockade directly addresses immune-mediated cognitive dysfunction, unlike non-specific anti-inflammatory agents
- **No Existing Alternatives:** Currently, no therapies restore cognition after cancer treatments syndromes

Publications

- Geraghty, A. C., Acosta-Alvarez, L., et al. (2025). Immunotherapy-related cognitive impairment after CAR T cell therapy in mice. *Cell*, 188.

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