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#### CSF1R Inhibition Restores Cognition Following Immunotherapy

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#### Introduction

 Patients that undergo CAR T-cell therapy often experience significant side effects, including cognitive decline.

 Chemotherapy related cognitive impairment mouse models show increased microglial activation and reduced myelin thickness •We seek to understand the long term cellular and neurological effects of CAR T-cell therapy



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# **CSF1R Inhibition Rescues Cognition Following Immunotherapy** Selena R. Dutton, Anna C. Geraghty, Michelle Monje

### Results



Vehicle

Chow

Acknowledgments

Chow

Vehicle

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Figure 1. GD2 CAR T-cell treatment increases total microglia in sub-cortical white matter. IBA1+ cells label microglia. p=0.0025

Figure 2. GD2 CAR T-cell treatment increases microglial activation in sub-cortical white matter, as measured by CD68 co-positivity with IBA1. CD68 is a marker of activated microglia. p=0.0021

**Figure 3.** Novel object recognition test revealed that CAR T-cell therapy impairs cognition in mice as compared to mice treated with mock non-active T cells. Depletion of microglia and macrophages with a CSF1R Inhibitor restores cognition following CAR T-cell therapy.

Institute for Stem Cell Biology and Regenerative Medicine



# Conclusions

•CAR T-cell therapy increases microglial activation in sub-cortical white matter, inducing myelin damage

•Damaged myelin may contribute to impaired cognition.

 Microglia/macrophage depletion with a CSF1R inhibitor reduces activation and rescues cognition.

## **Future Studies**

•Pre-depletion of microgla and macrophages with CSF1R inhibitors prior to CAR T-cell therapy

•Nuc-sequencing to understand transcriptional changes in multiple cell type following CAR T-cell therapy

