

Cal Poly Humboldt

Digital Commons @ Cal Poly Humboldt

IdeaFest 2022

2022

CSF1R Inhibition Restores Cognition Following Immunotherapy

Selena Dutton

Cal Poly Humboldt, srd55@humboldt.edu

Follow this and additional works at: <https://digitalcommons.humboldt.edu/ideafest2022>

Recommended Citation

Dutton, Selena, "CSF1R Inhibition Restores Cognition Following Immunotherapy" (2022). *IdeaFest 2022*. 25.

<https://digitalcommons.humboldt.edu/ideafest2022/25>

This Poster is brought to you for free and open access by Digital Commons @ Cal Poly Humboldt. It has been accepted for inclusion in IdeaFest 2022 by an authorized administrator of Digital Commons @ Cal Poly Humboldt. For more information, please contact kyle.morgan@humboldt.edu.

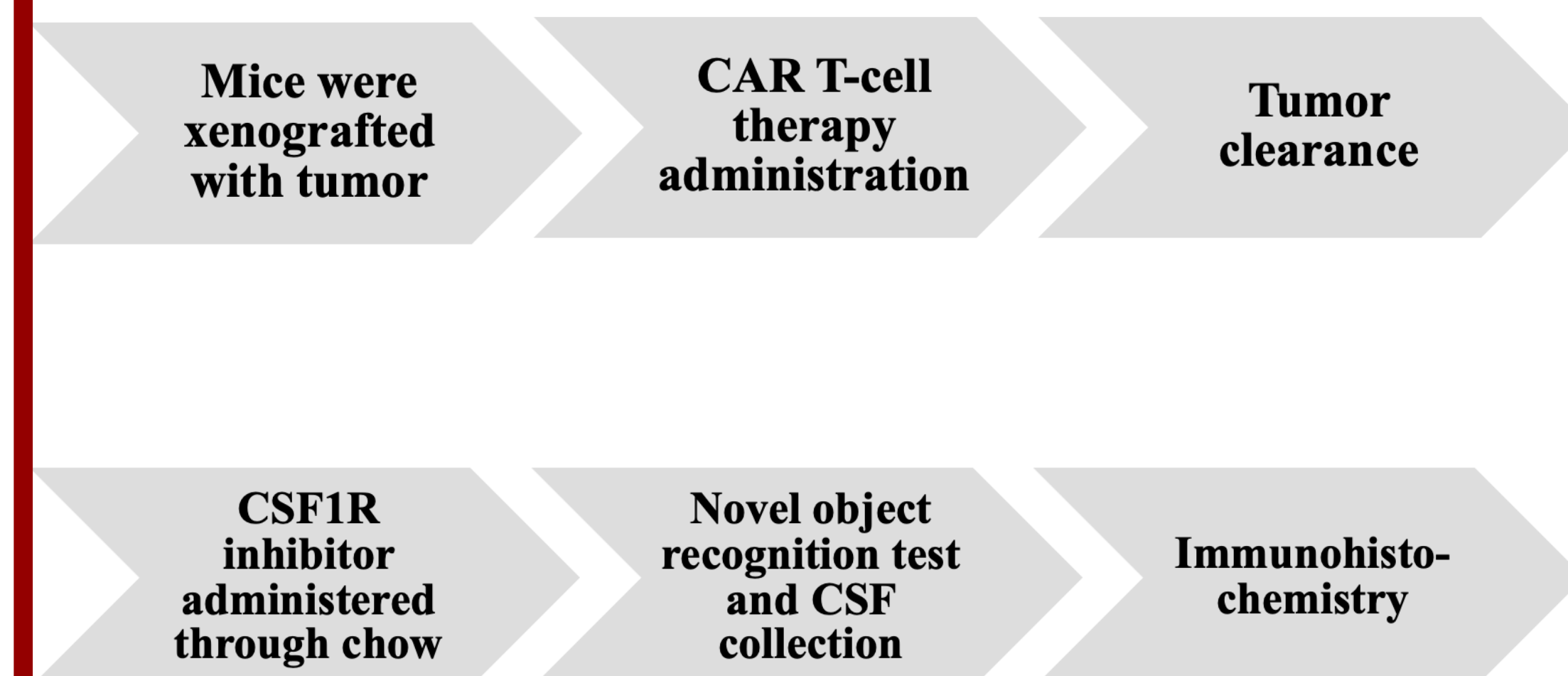
CSF1R Inhibition Rescues Cognition Following Immunotherapy

Selena R. Dutton, Anna C. Geraghty, Michelle Monje

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

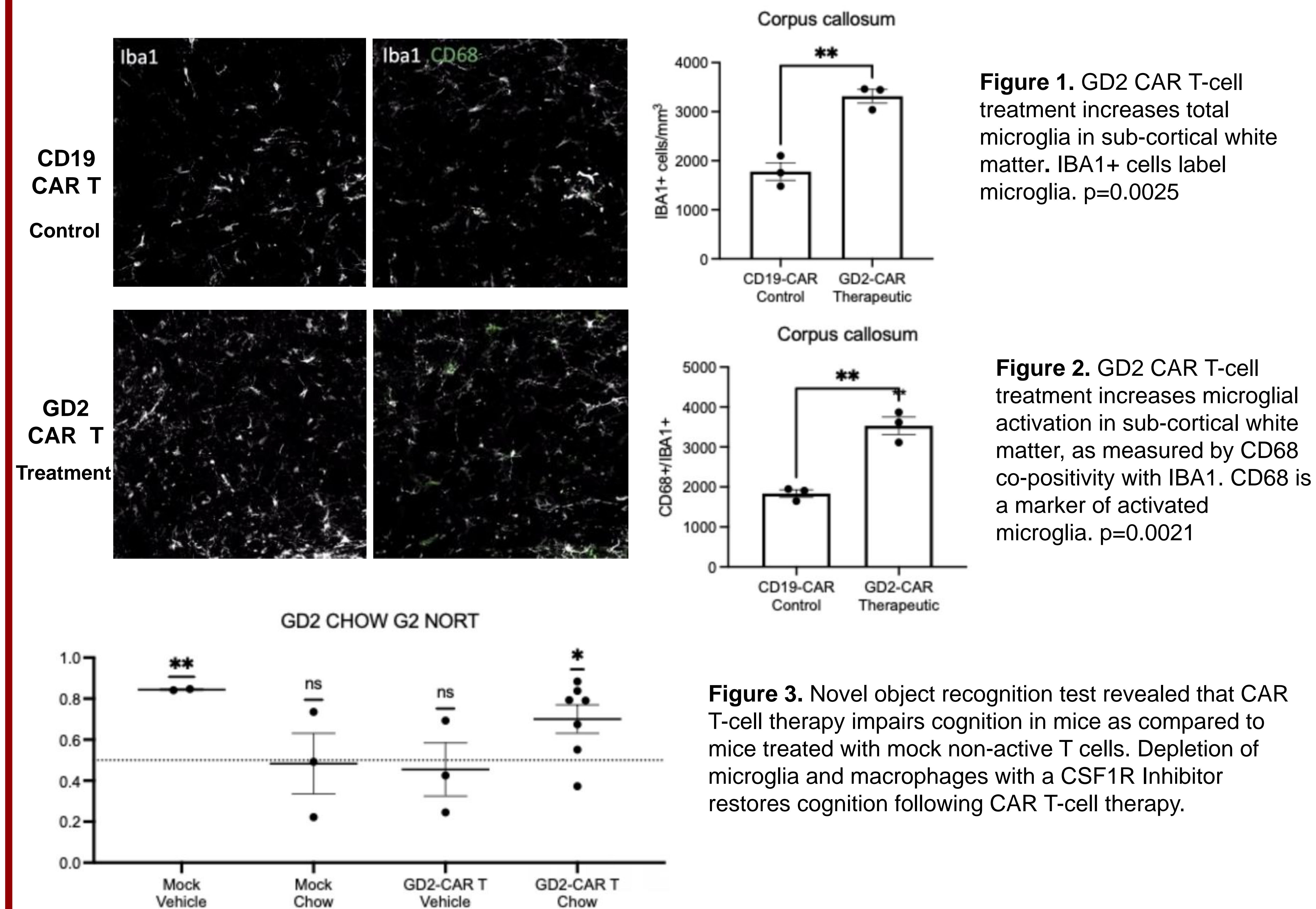
Methods



Literature cited

Geraghty AC, Gibson EM, Ghanem RA, Greenberg ME, Longo FM, Monje M. (2019). Loss of Adaptive Myelination Contributes to Methotrexate Chemotherapy-related Cognitive Impairment. *Neuron*. 103: 250-265.
 Green KN, Craspe JD, Hofsfield LA. (2020). To Kill Microglia: A Case for CSF1R Inhibitors. *Trends in Immunology*. 41(9).
 Hagan N, Kane JL, Grover D, Woodworth L, Madore C, Saleh J, Sancho J, Liu J, Proto J, Zelic M, et al. (2020). CSF1R signaling is a regulator of pathogenesis in progressive MS. *Cell Death and Disease*. 11(904).
 Leger M, Quiedeville A, Bouet A, Haelewyn B, Boulouard M, Schumann-Bard P, Freret T. (2013). Object recognition in mice. *Nature Protocols*. 8(12).
 Mount CW, Majzner RG, Sundaresh S, Arnold EP, Kadapakkam M, Haile S, Labanieh L, Hulleman E, Woo PJ, Rietberg SP, et al. (2018). Potent antitumor efficacy of anti-GD2 CAR T cells in H3K27M+ diffuse midline gliomas. *Nature Medicine*. 24(5): 572-579.

Results



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 microglia 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

Acknowledgments

Anna Geraghty, PhD
 Bridgett Blackman, PhD
 Jenny Cappuccio
 Michelle Monje, M.D., PhD
 CIRM Bridges 3.0 #EDUC2-12620

