

SITC 2019

Gaylord National Hotel
& Convention Center

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NATIONAL HARBOR, MARYLAND



Society for Immunotherapy of Cancer



Licensing of Th/Tc17 CAR-T cell Persistence and Function by STING Agonist in Breast Cancer

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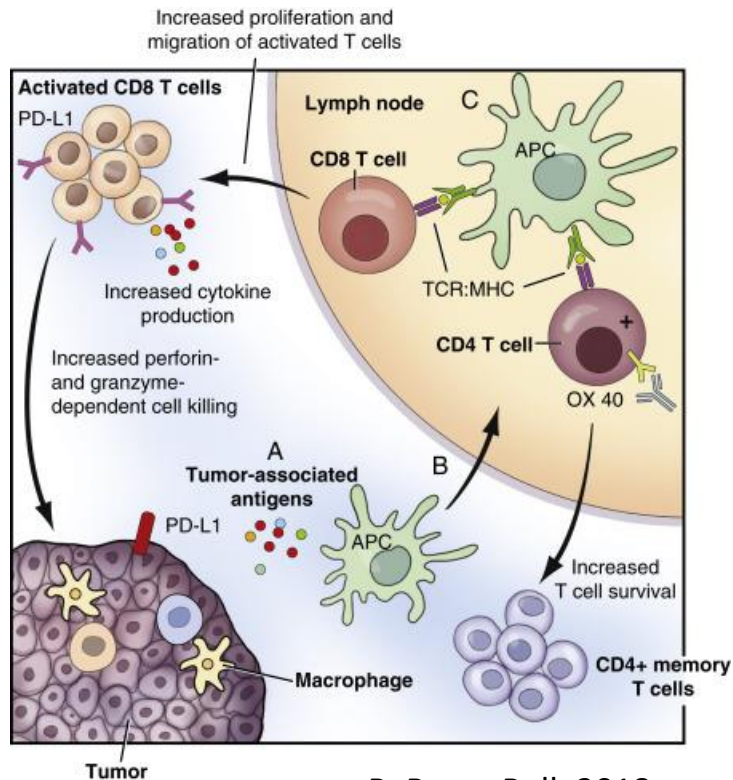
Society for Immunotherapy of Cancer

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I have no actual or potential conflict of interest
in relation to this study.

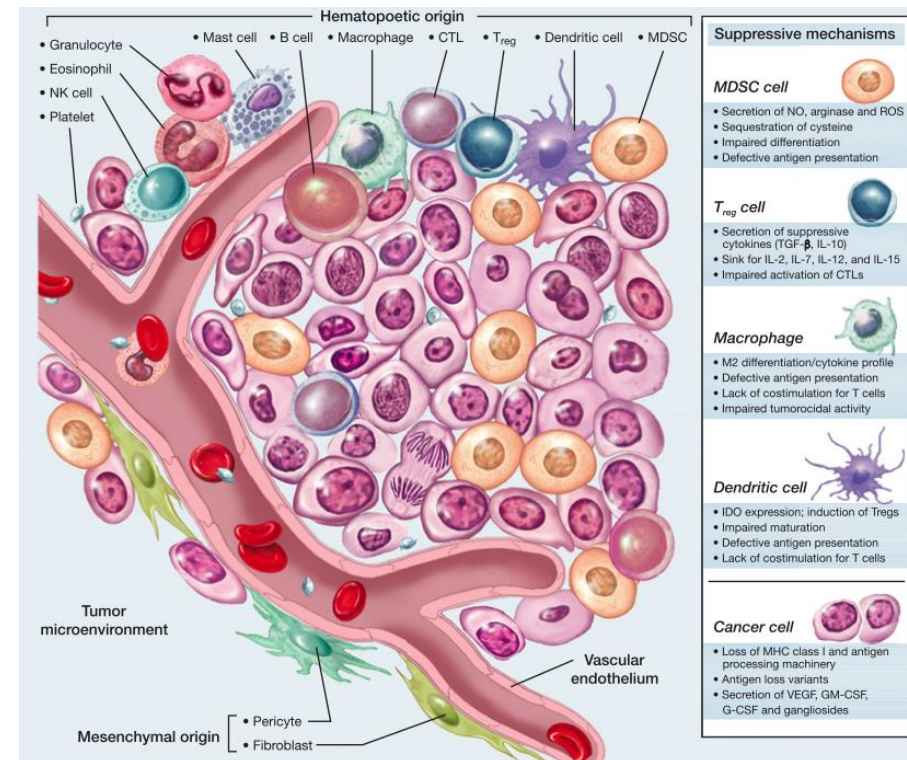
T cell function is impaired in tumor microenvironment (TME)

In lymphoid organ



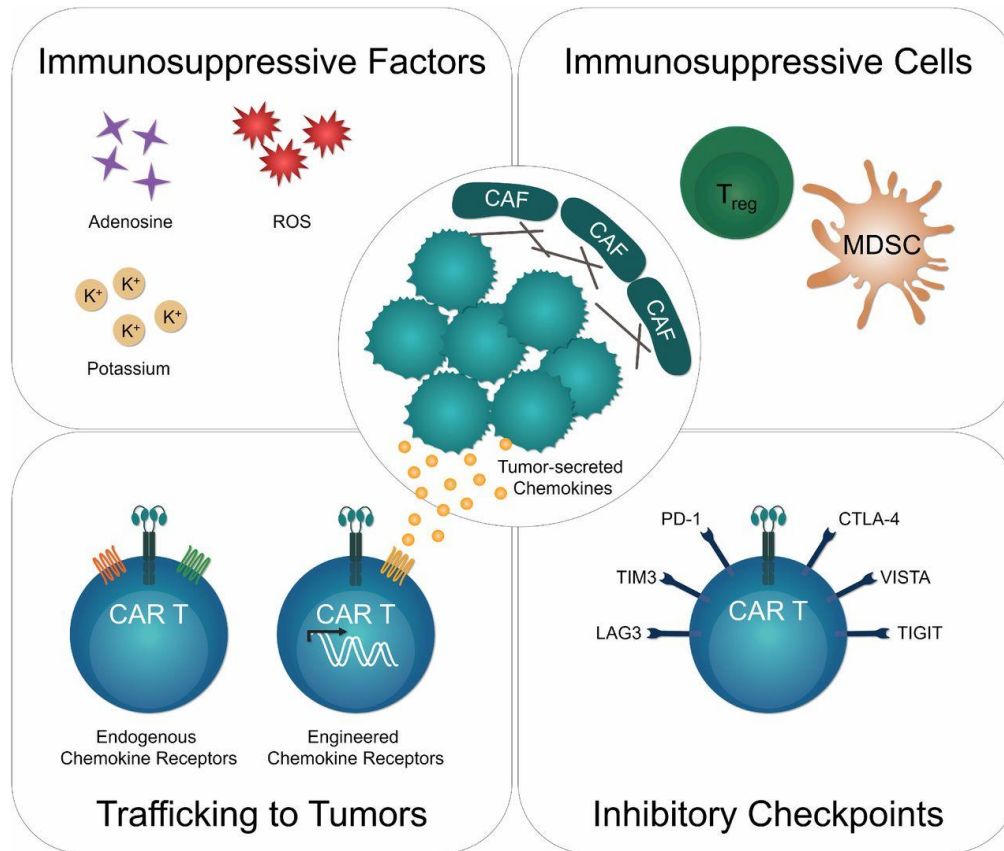
R. Bryan Bell, 2018

In solid tumor microenvironment



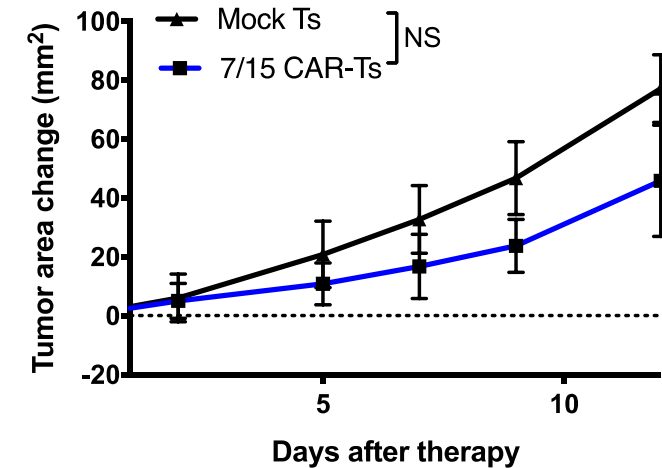
Kerkar, S.P., et al, Cancer Research 2012

Factors Associated with Poor CAR T cell Function Against Solid Tumors



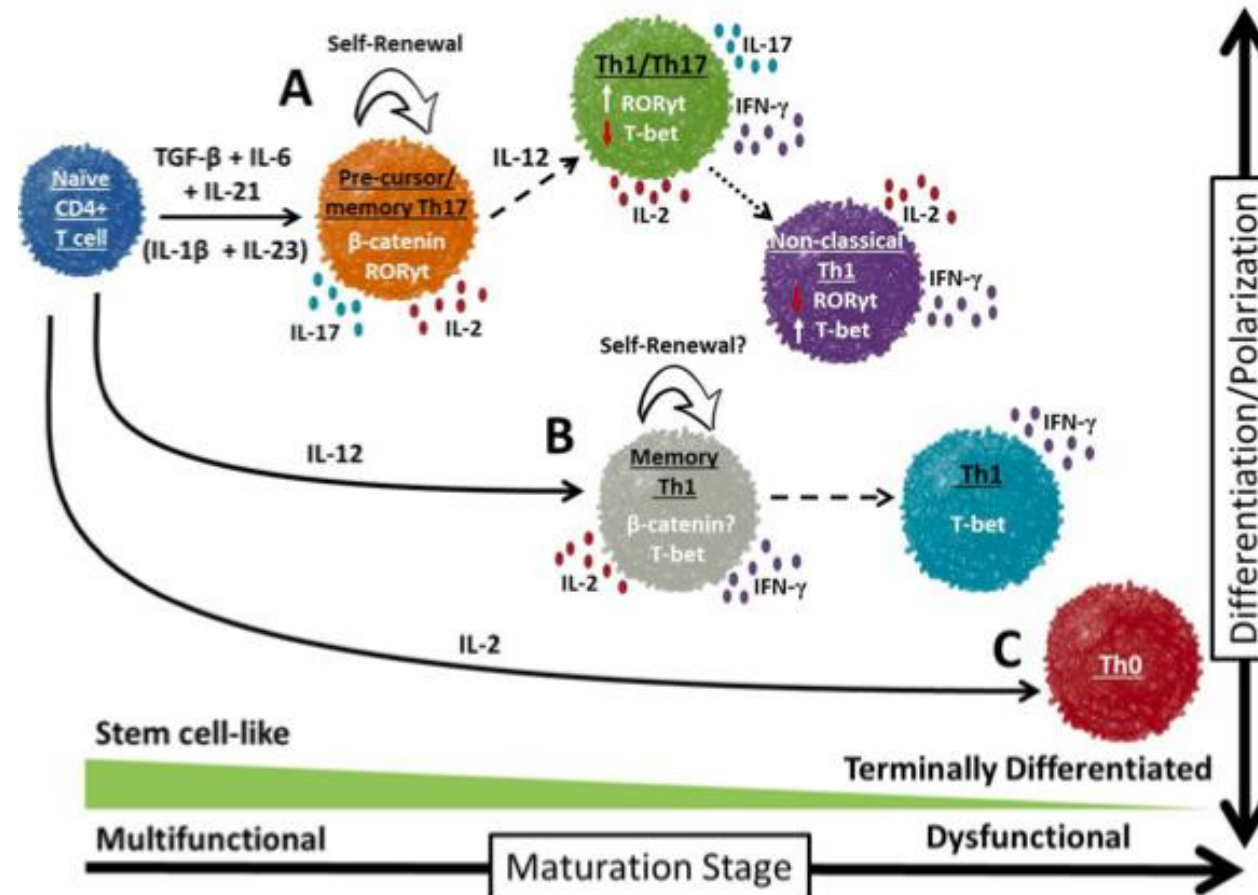
Srivastava and Riddell, Journal of Immunology 2018

Her2+ breast tumor growth in FVB-Neu mice



Current method for CAR-T culture using IL-7/15 fails to induce robust tumor growth control in **immuno-component** mice due to poor persistence

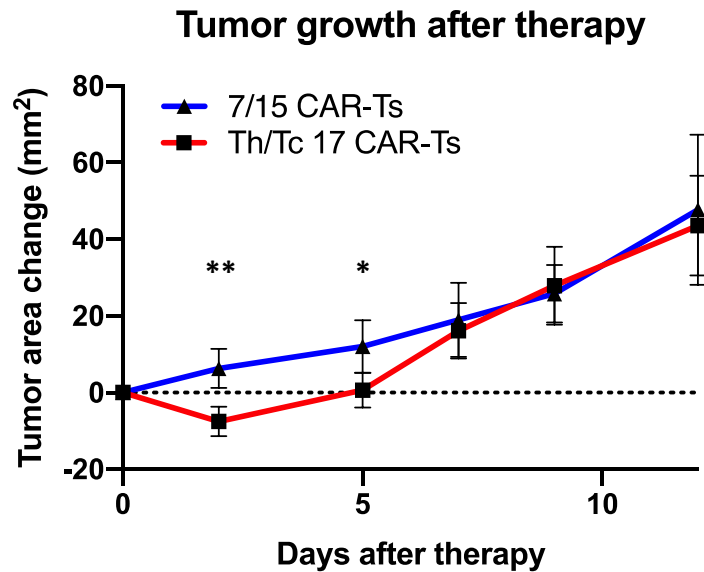
Th17 cells show enhanced persistence in vivo



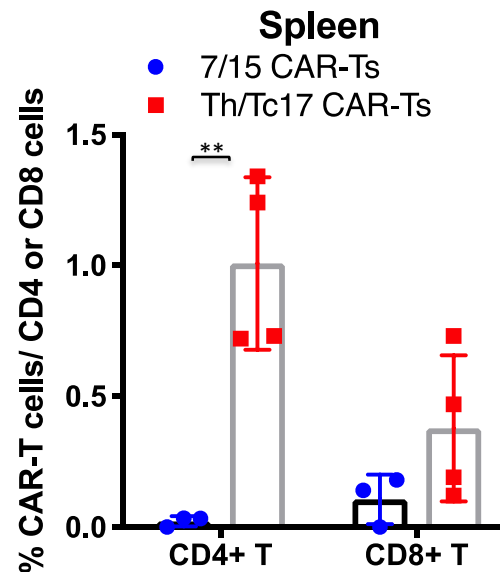
Paulos et al, Frontiers in Immunology, 2014

Th/Tc17 CAR-T have improved early tumor growth control correlated with enhanced persistence

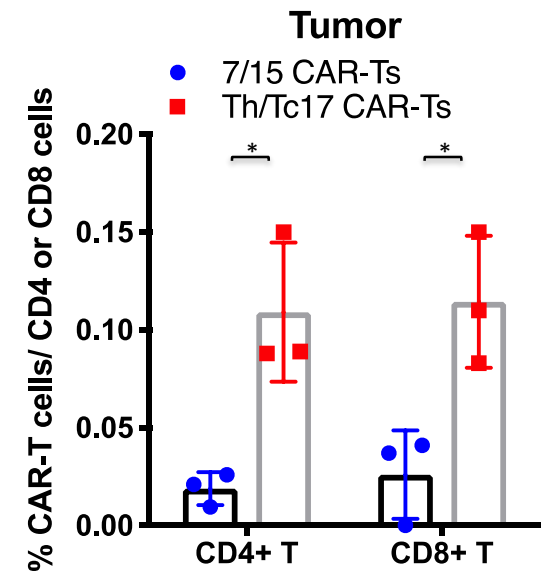
A.



B.

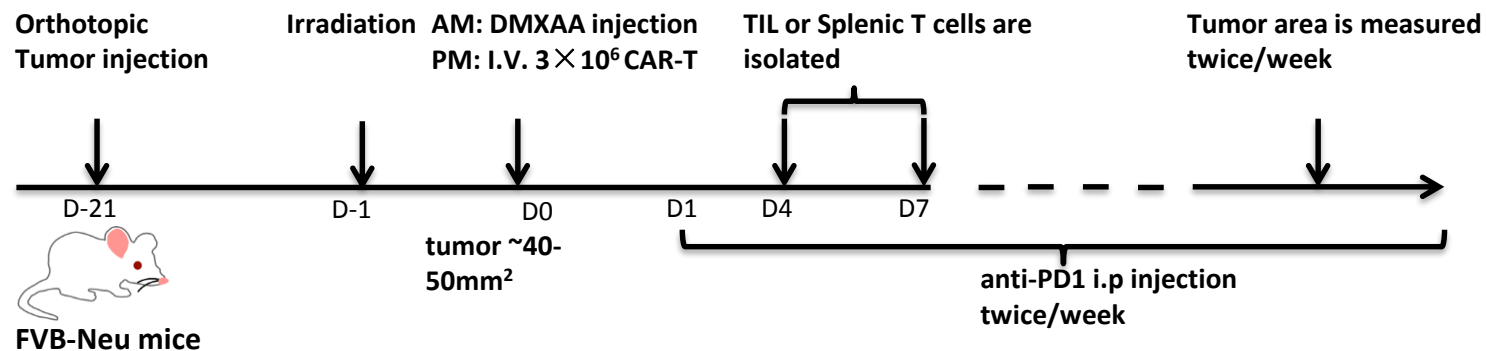


C.

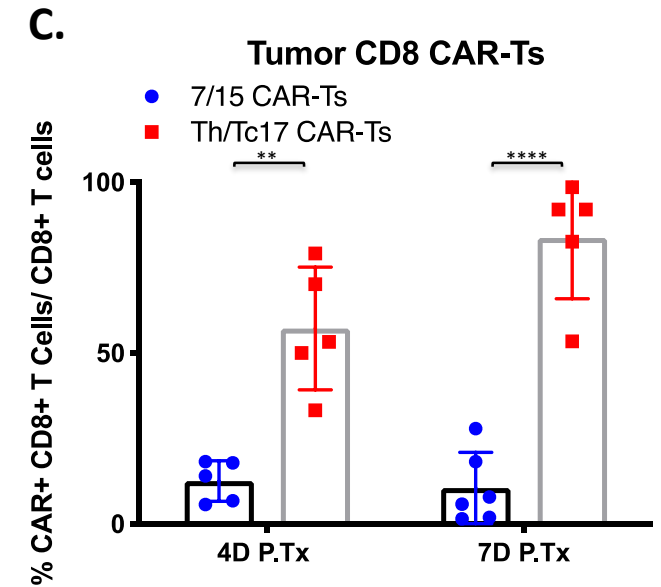
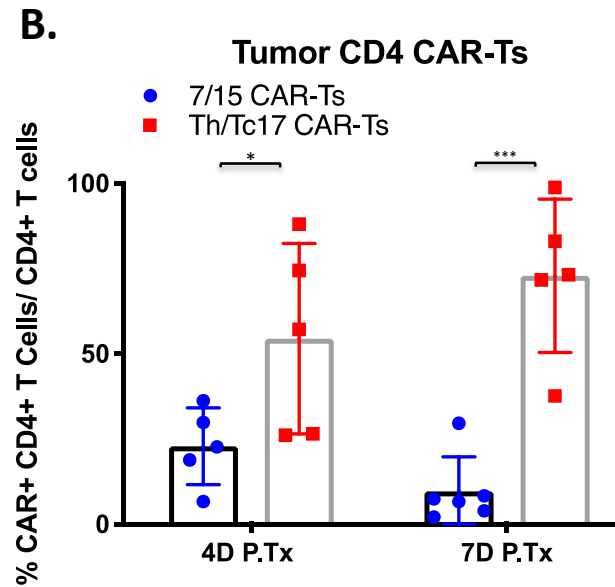
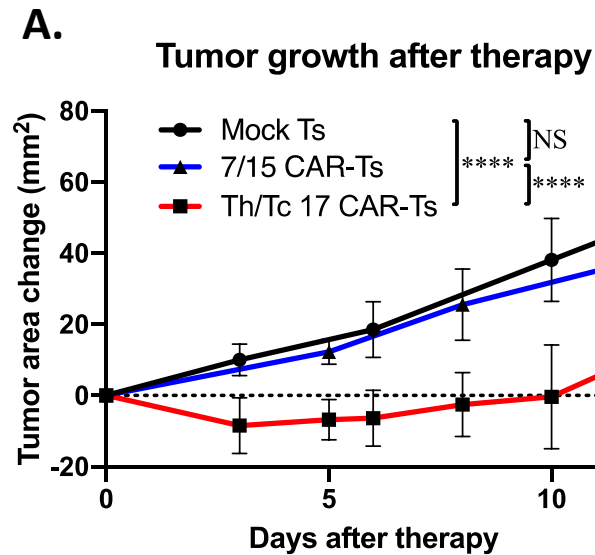


Modification of tumor microenvironment (TME) is required for better therapeutic effect

- STING agonist (DMXAA) enhanced therapeutic effect of Th/Tc17 CAR-T up to 7 days after therapy
- CAR-T cells in TME have increased PD-1 expression

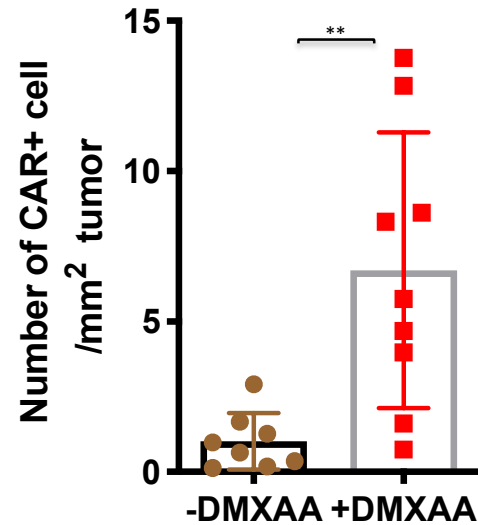


Combining DMXAA, Th/Tc17 CAR-T and anti-PD-1 leads to greatly enhanced persistence and improved anti-tumor control

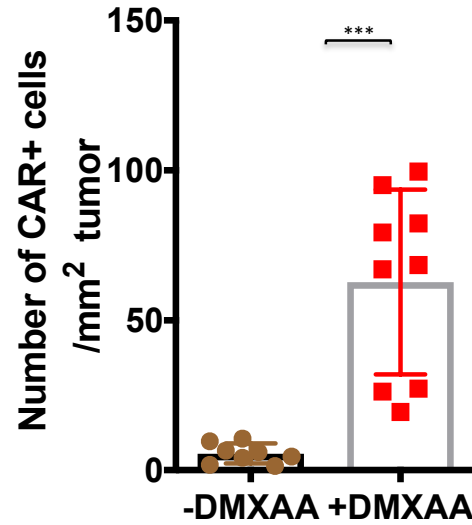


DMXAA treatment increases the number and function of Th/Tc17 CAR-T cells in the TME

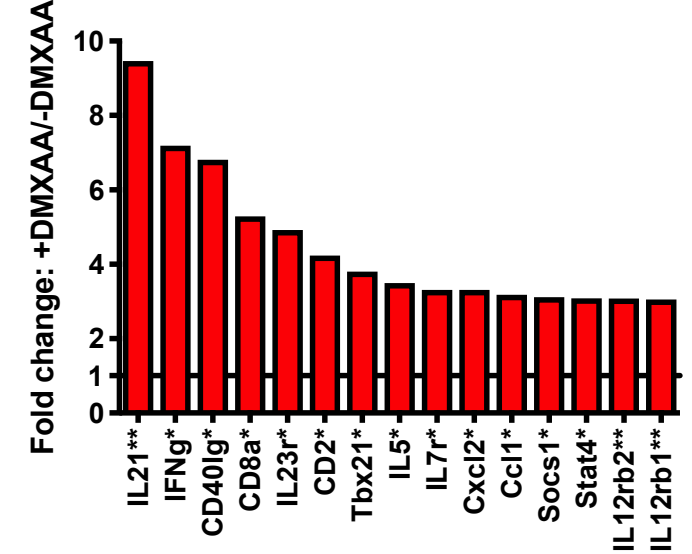
A. Number of CD4+ CAR-T



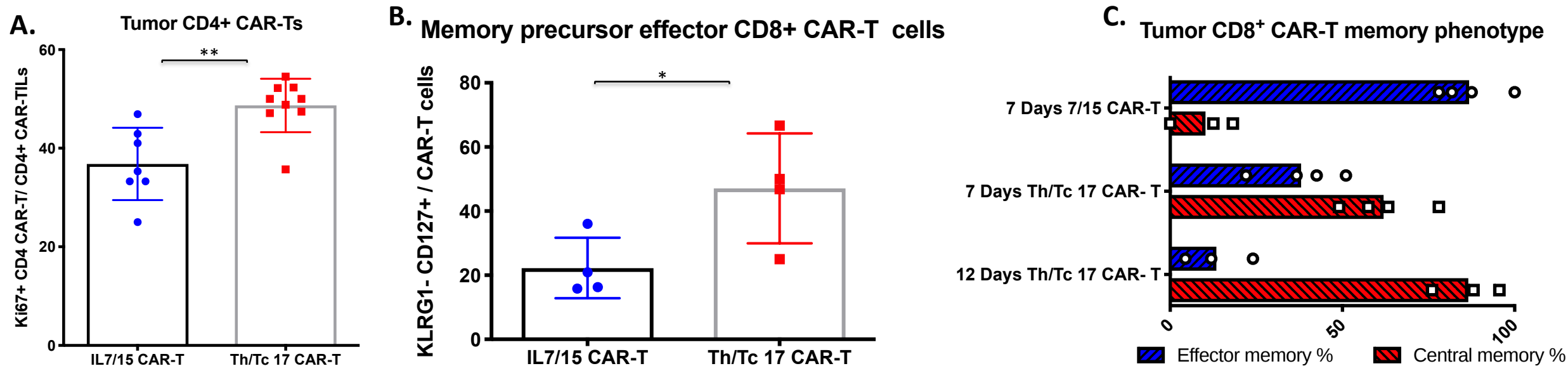
B. Number of CD8+ CAR-T



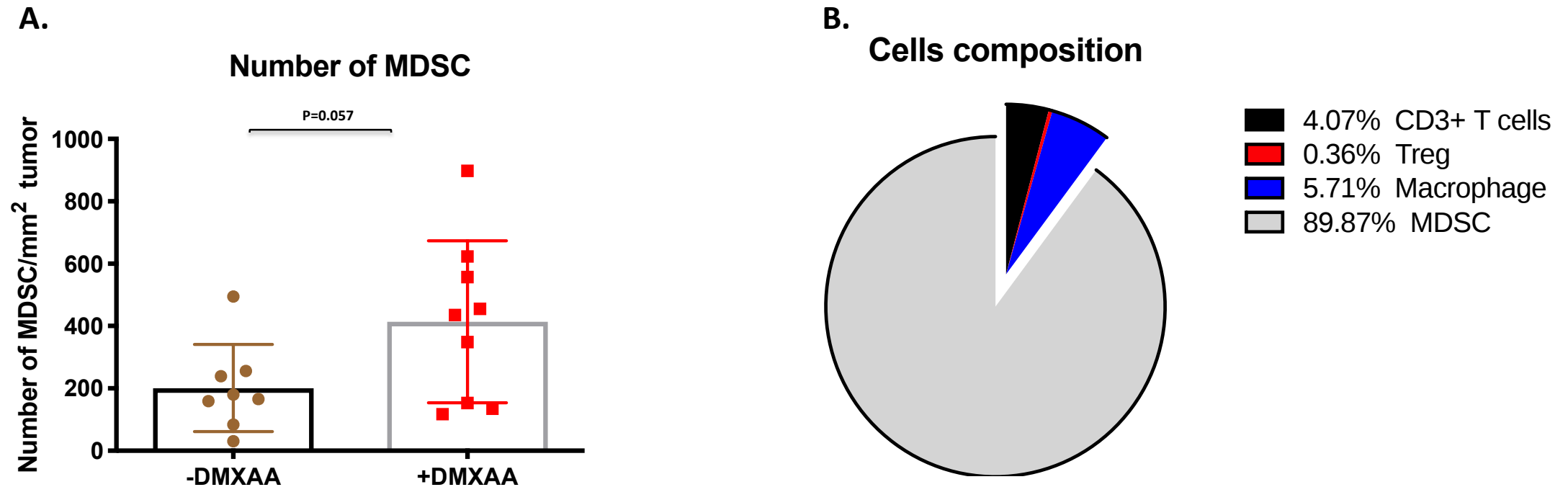
C. Gene expression change



STING Agonist + anti-PD-1 Enhanced Th/Tc17 CAR-T Cell proliferation and central memory generation

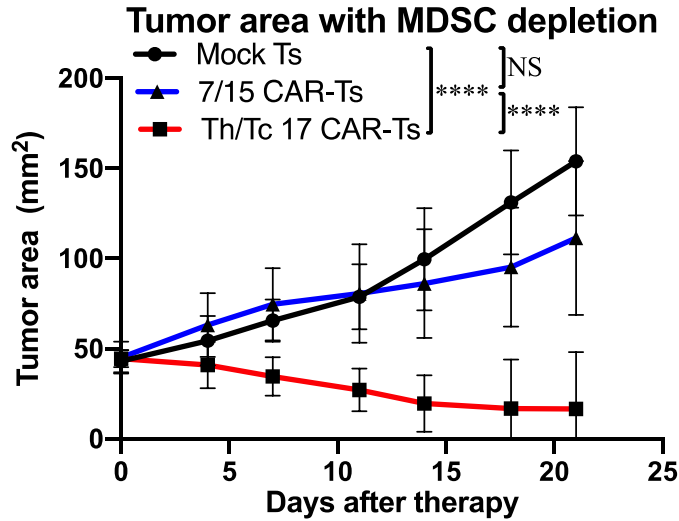


Therapeutic effect is lost due to accumulation of MDSCs

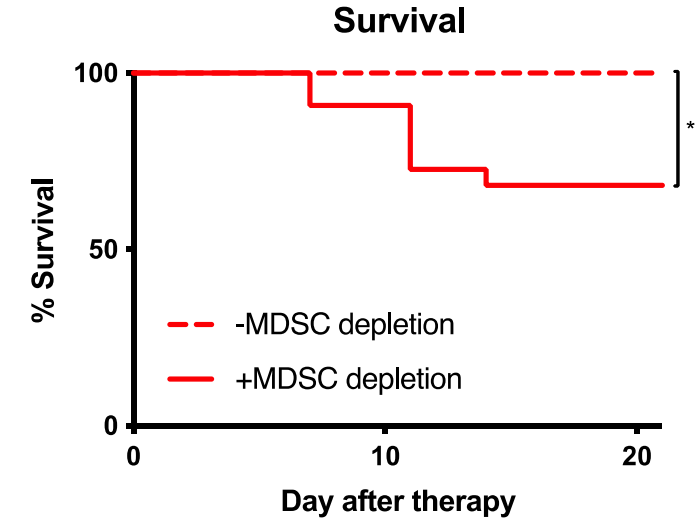


MDSC depletion leads to profound tumor remission with cytokine release syndrome

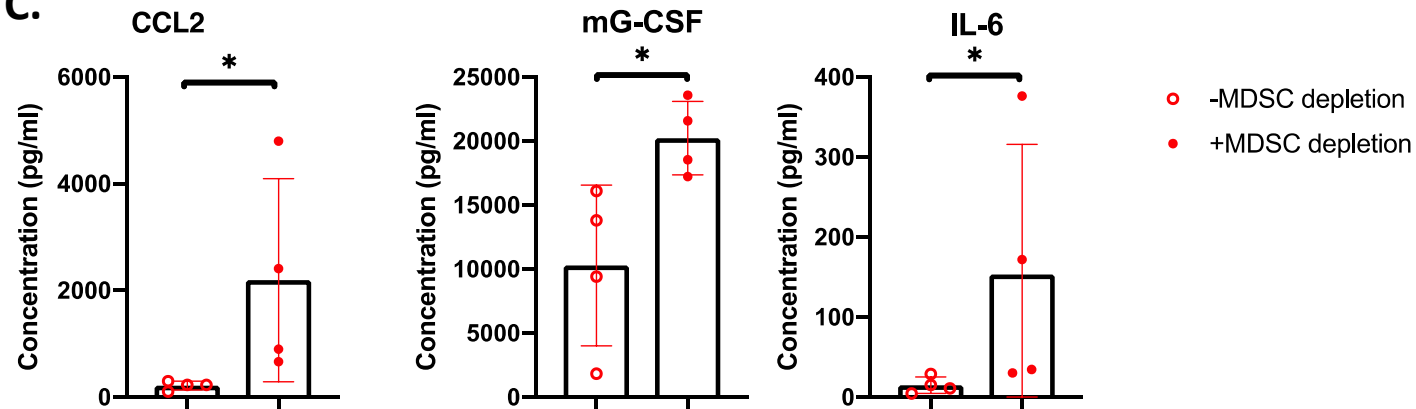
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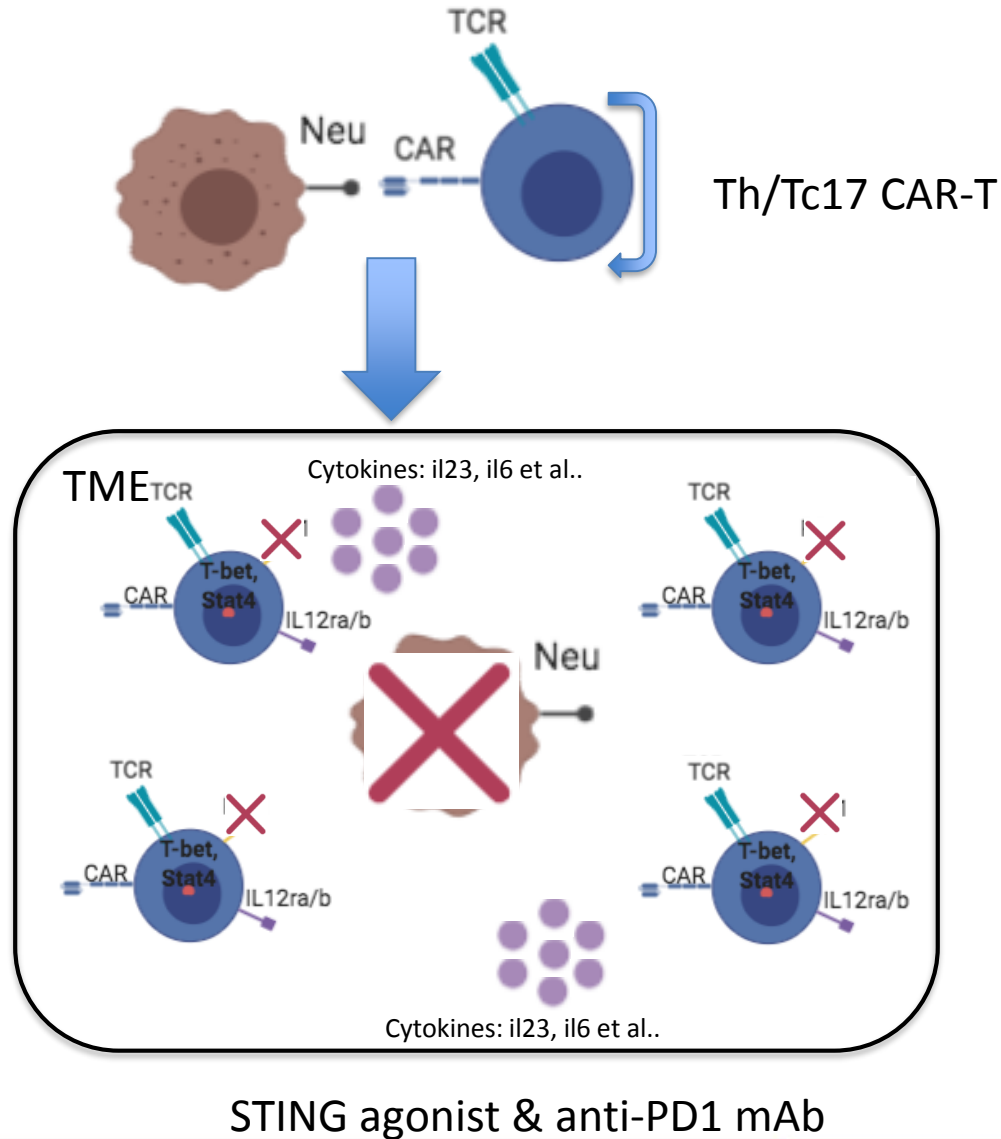
B.



C.



Proposed Model



- Th/Tc17 CAR-T cells have better persistence
- STING agonist enhances Th/Tc17 CAR-T cells expansion and function by modifying tumor microenvironment
- MDSC limits CAR-T function, but also protect host from immune related toxicity

MDSC depletion



MDSCs

Acknowledgment

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