

A First-in-Class CADM1-Directed CAR Platform for the Treatment of Small Cell Lung Cancer and Neuroendocrine Cancers.

Venkateshwar Keshamouni, Ph.D

Associate Professor

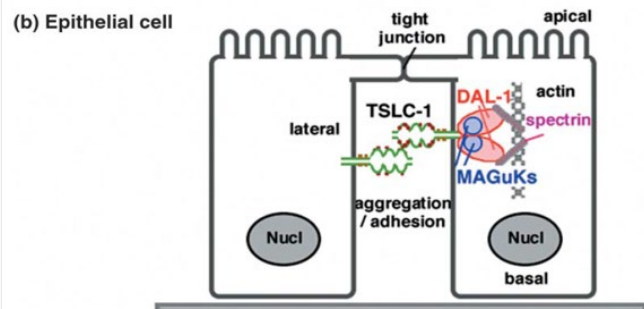
Department of Internal Medicine

Research Scientist

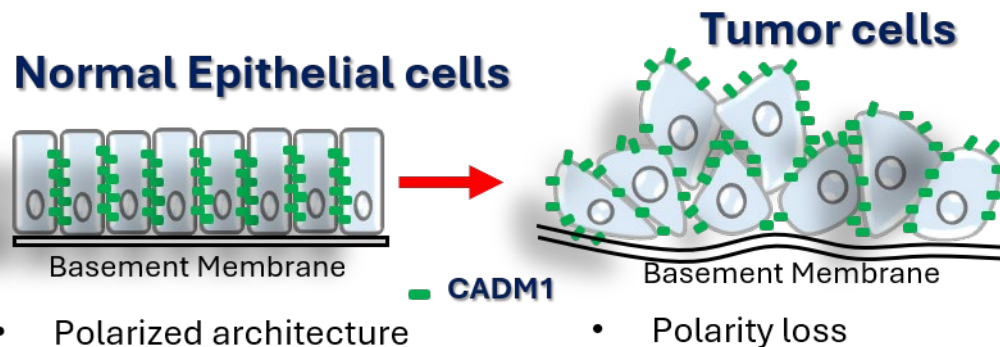
LTC Charles S. Kettles VA Medical Center

Ann Arbor, MI, USA

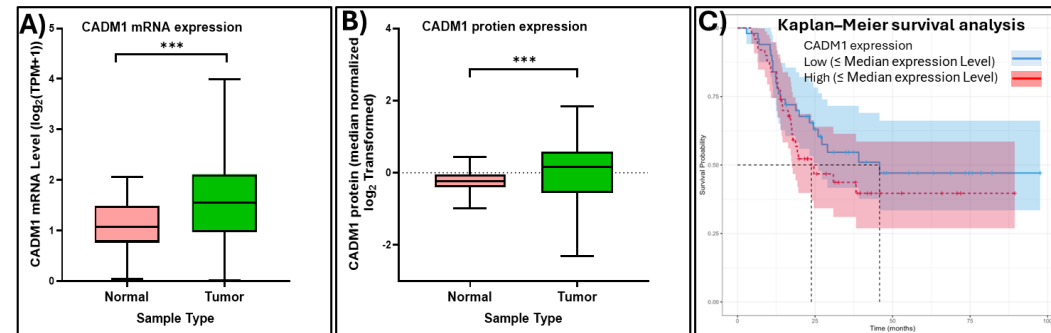
Cell Adhesion Molecule (CADM) -1



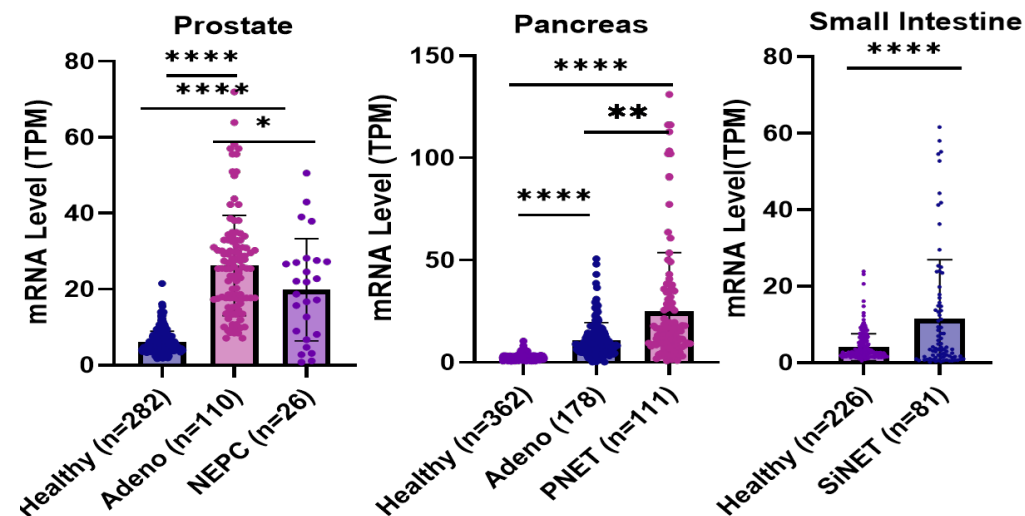
- Belongs to immunoglobulin superfamily.
- Mediates cell-cell contacts in epithelial tissues and in synaptic adhesions of neurons
- 80% of SCLC overexpress CADM1



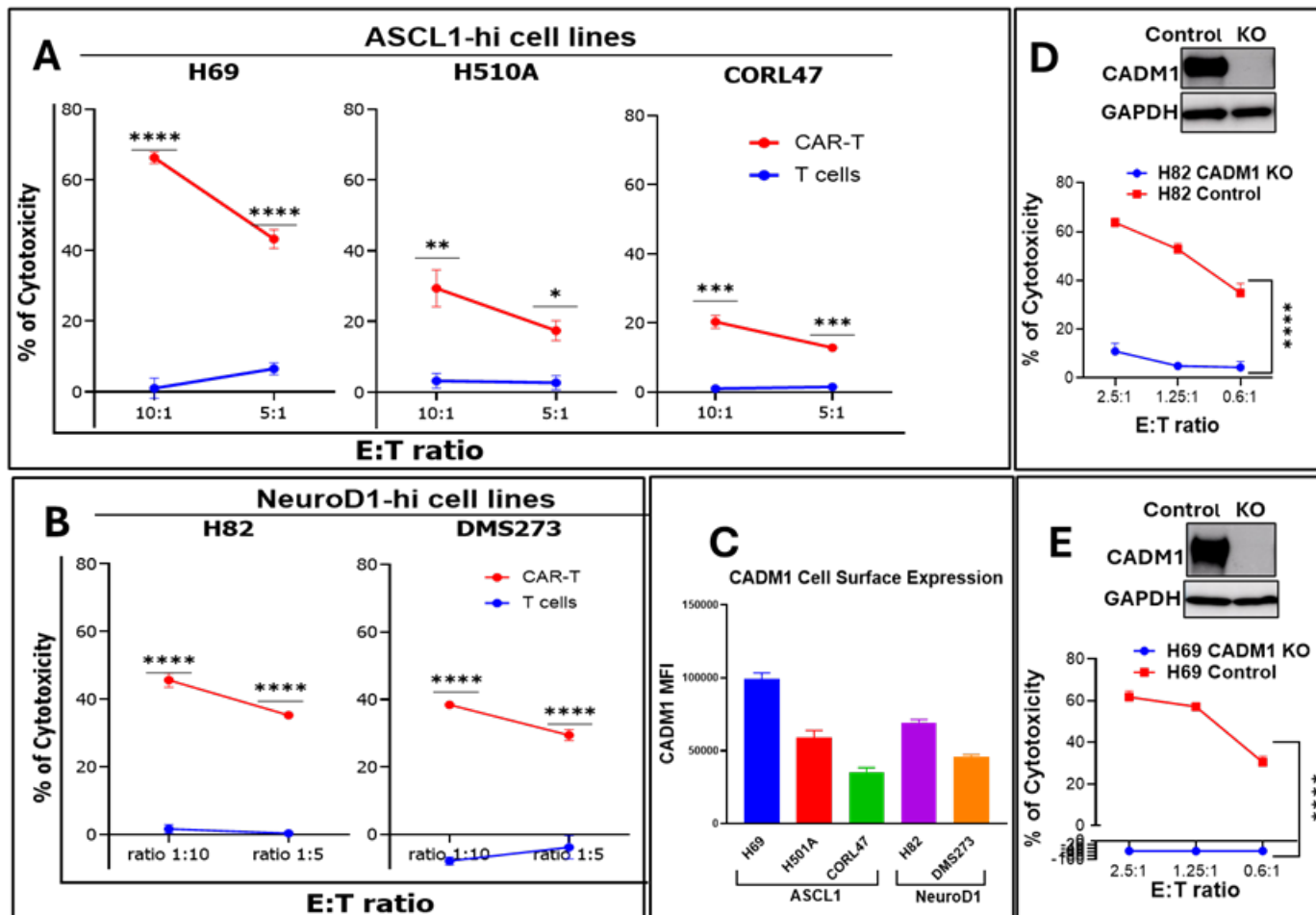
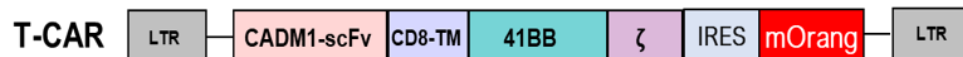
CADM1 Expression in Small Cell Lung Cancer



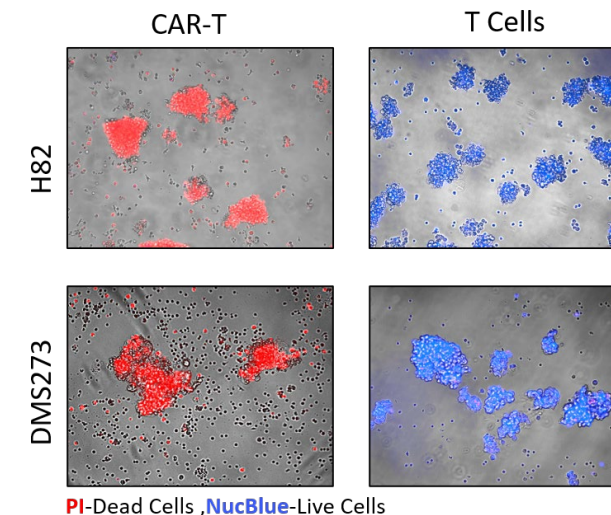
CADM1 in other neuroendocrine tumors



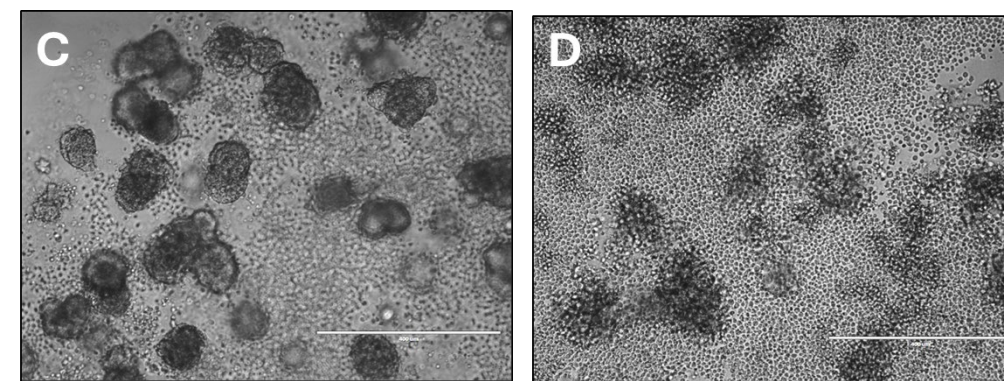
Antigen specific Cytolytic Activity of CADM1 CAR-T cells in 2D and 3D culture models



Cytotoxicity Against Tumor Cell Spheroids



Cytotoxicity against patient derived organoids



CADM1-CAR-T cells inhibit growth of SCLC (H82) xenografts,

Day 0
Tumor
inoculation
(tail vein)

↓

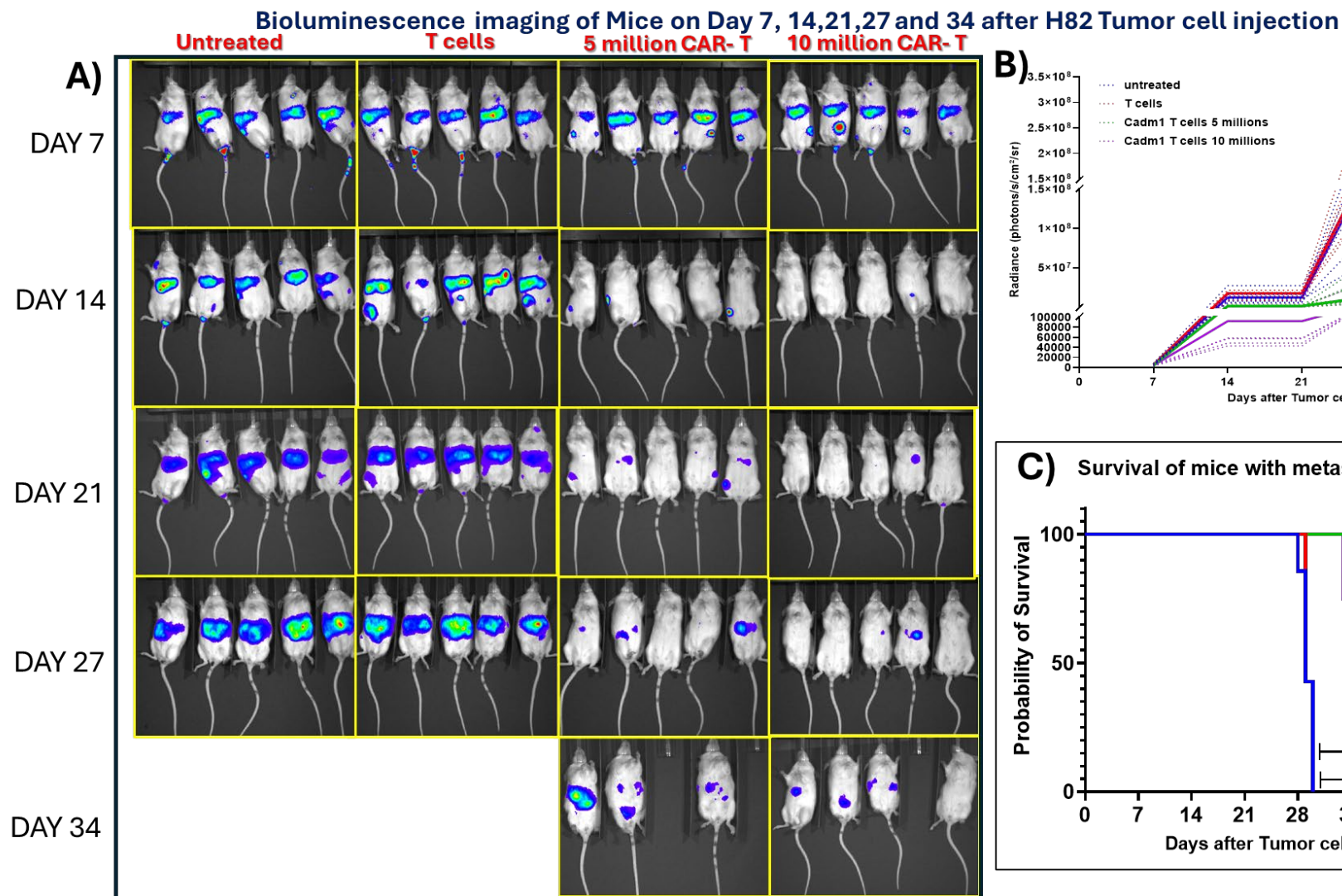
Day 07
T-cell infusion
(Retro orbital)

↓

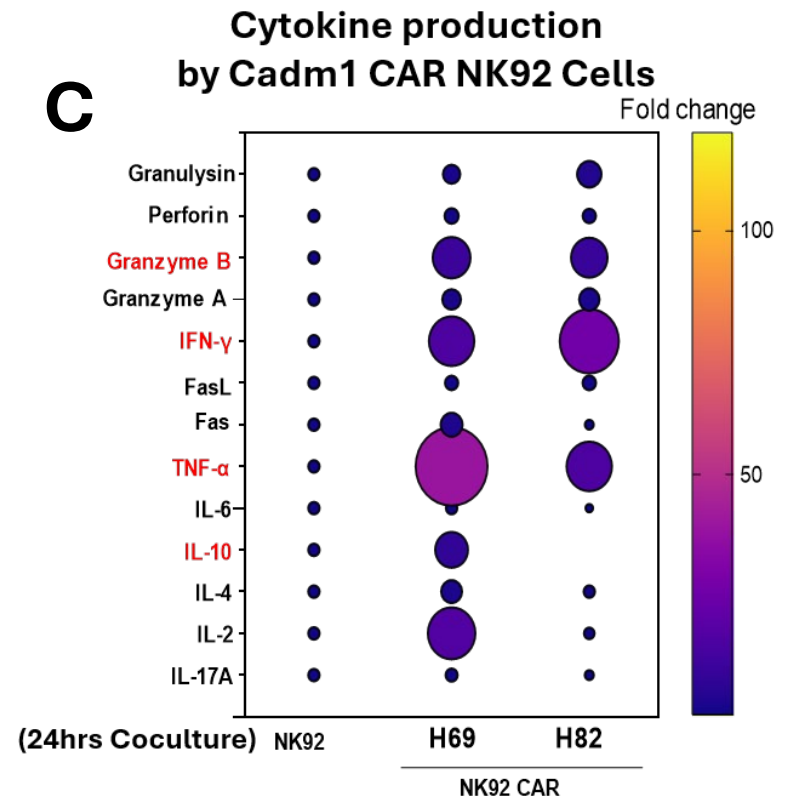
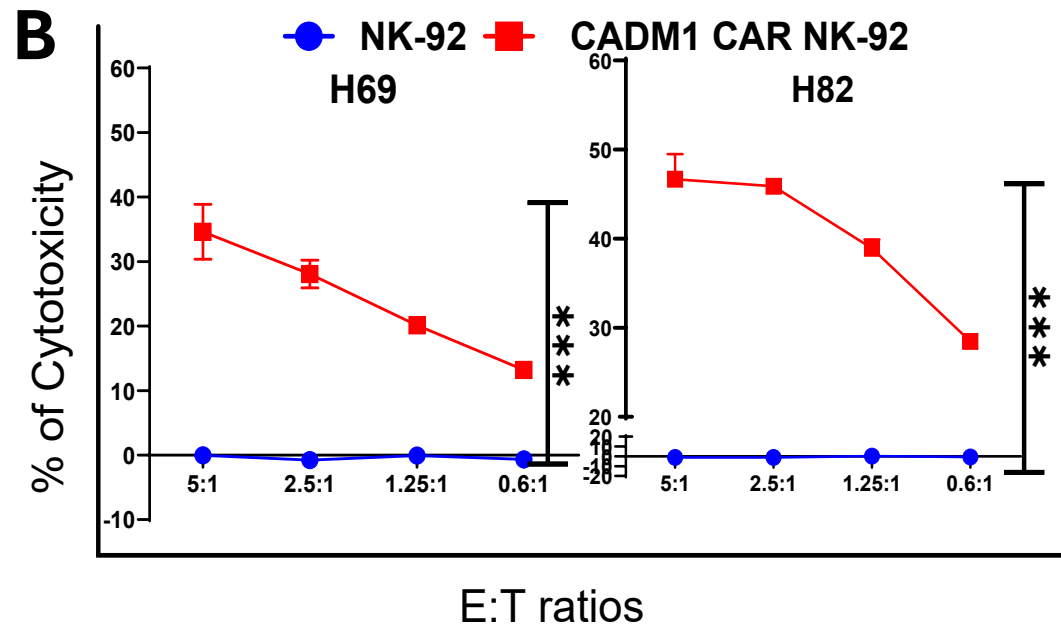
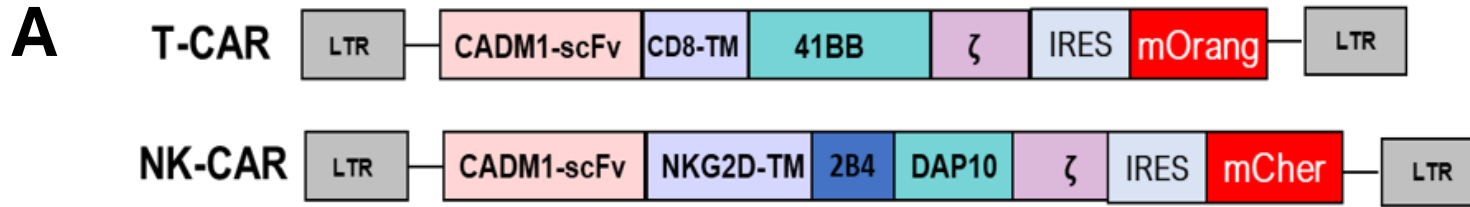
Weekly BLI

↓

Monitored
Overall survival



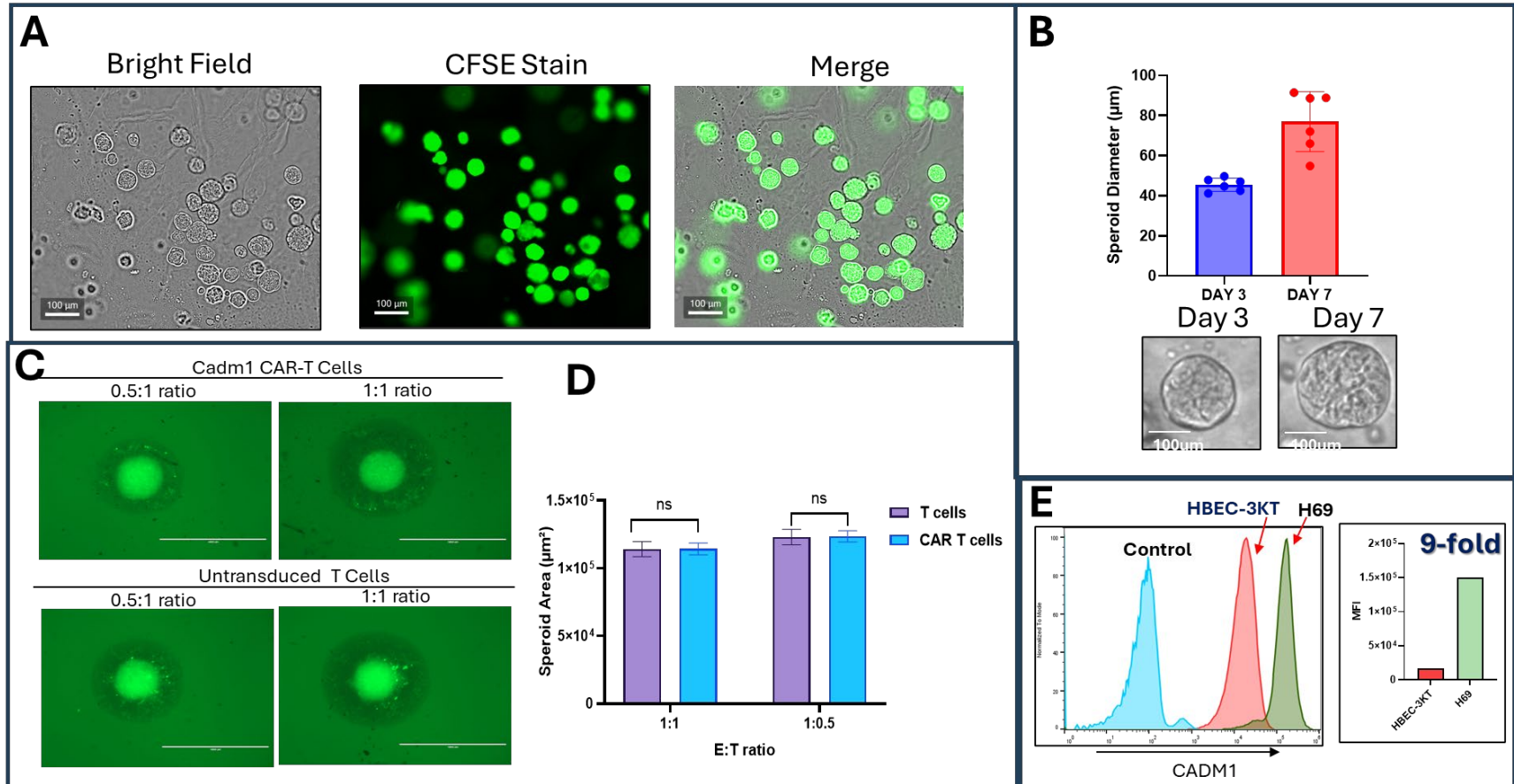
CADM1 Targeting CAR-NK cells



On-target, Off-tumor Toxicity in Normal Tissue Organoids

Toxicity is not just
“is antigen present or not?”
But a function of:

1. Where the antigen expressed?
2. With what accessibility?
3. At what density?
4. At what activation threshold?

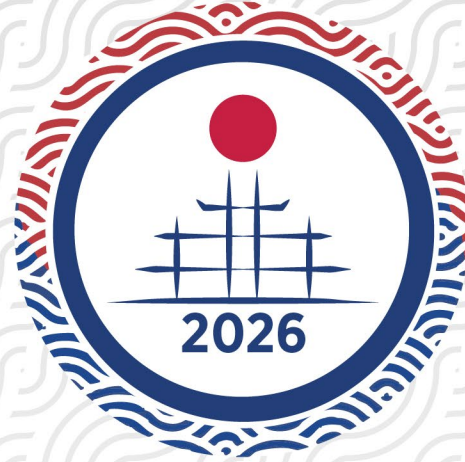


Other Co-Authors

- *Shiva Krishna Katkam*
- *Aravind Sivanesan*
- *Sergei Chuikov*

Collaborators

- *Navin Mahadevan*
- *Arul Chinnaiyan*
- *Qiao Yuanyuan*



Funding

- *NIH R01-HL-156998-01A1*
- *VA Merit CX002233*
- *Rogel Cancer Center*
(Thoracic oncology)

Thank You. ●