May 15th, 12:15 PM - 12:30 PM

Therapeutic Efficacy of B7-H3 CAR T Cell Therapy In Pediatric High-Grade Gliomas with H3G34R/V Mutation.

Monika Yadav
Children's Mercy Kansas City

Siddharth Subham
University of Kansas Cancer Center

John Szarejko
Children's Mercy Kansas City

Douglas Myers
Children's Mercy Kansas City

David Akhavan
University of Kansas Cancer Center

See next page for additional authors

Authors

Monika Yadav, Siddharth Subham, John Szarejko, Douglas Myers, David Akhavan, and Viveka Nand Yadav

Therapeutic Efficacy of B7-H3 CAR T cell therapy in Pediatric High-Grade Gliomas with H3G34R/V mutation

Monika Yadav, PhD

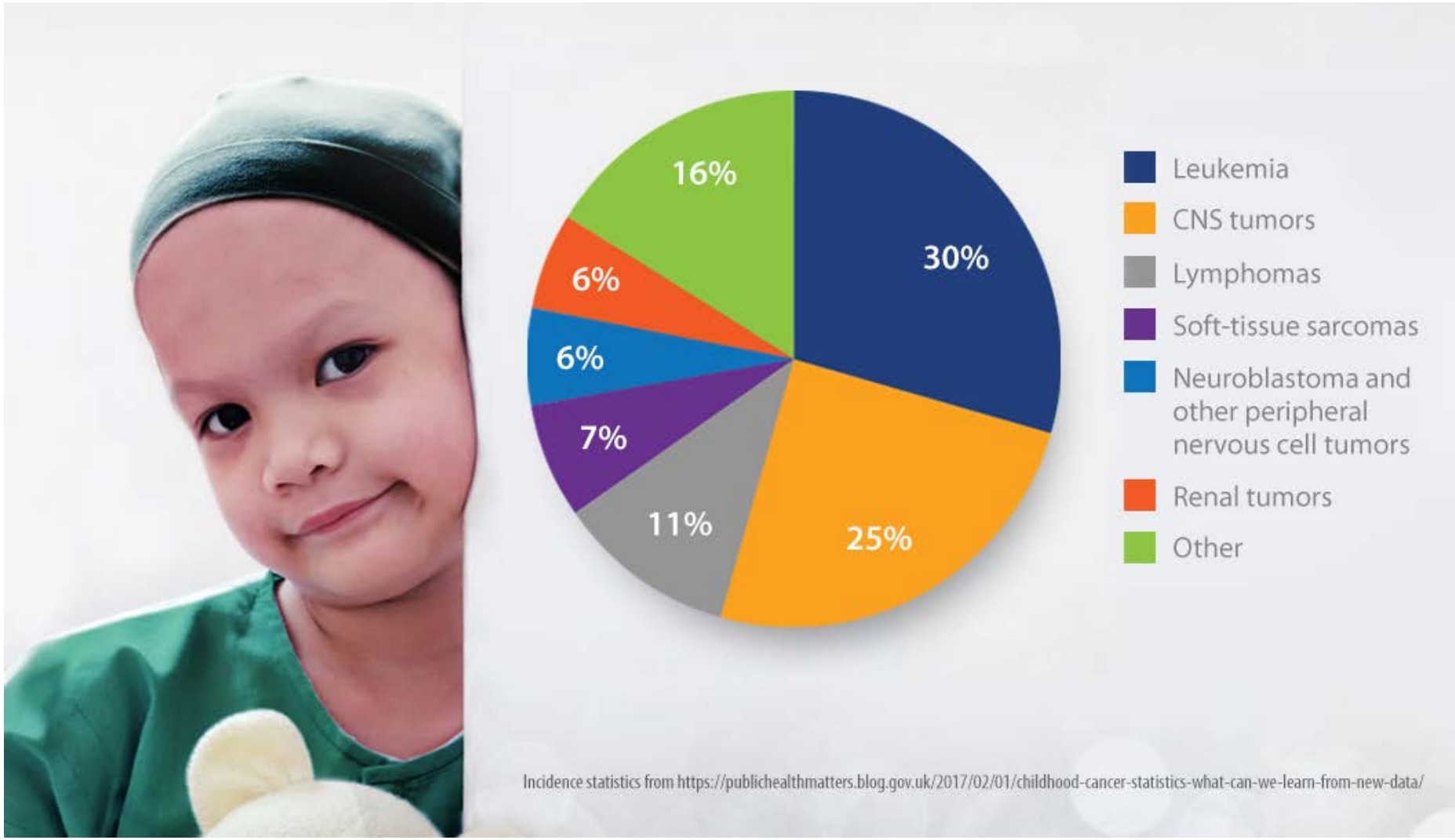
Post-Doctoral Researcher

Yadav Lab

Department of Pediatric Hematology/Oncology

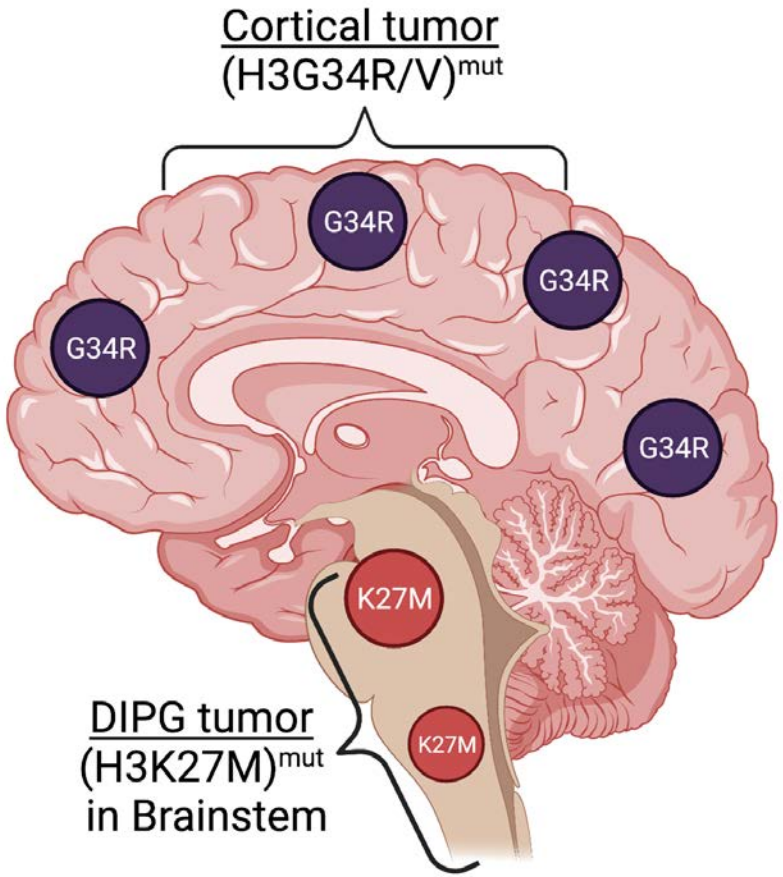
Children's Mercy Research Institute

Childhood cancers incidence



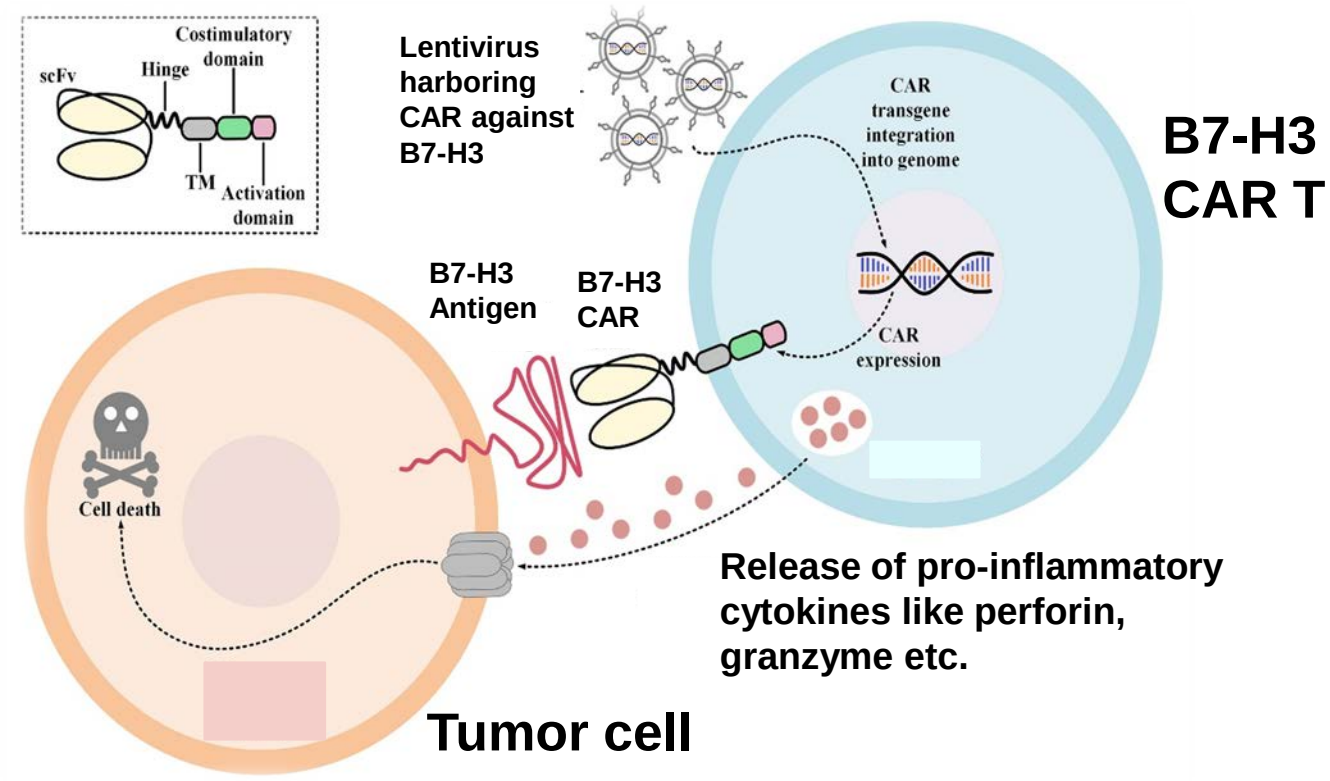
Pediatric high-grade gliomas (pHGGs)

- pHGGs are among the most devastating malignant brain tumors.
- It represent the leading cause of cancer-related death in children.
- These tumors often carry mutations in the H3F3A gene, which encodes histone H3.3 proteins.
- DHG (Diffuse hemispheric gliomas) HG34R/V mutations-occurs in upto 15% of HGGs of adolescents and young adults.



Approach

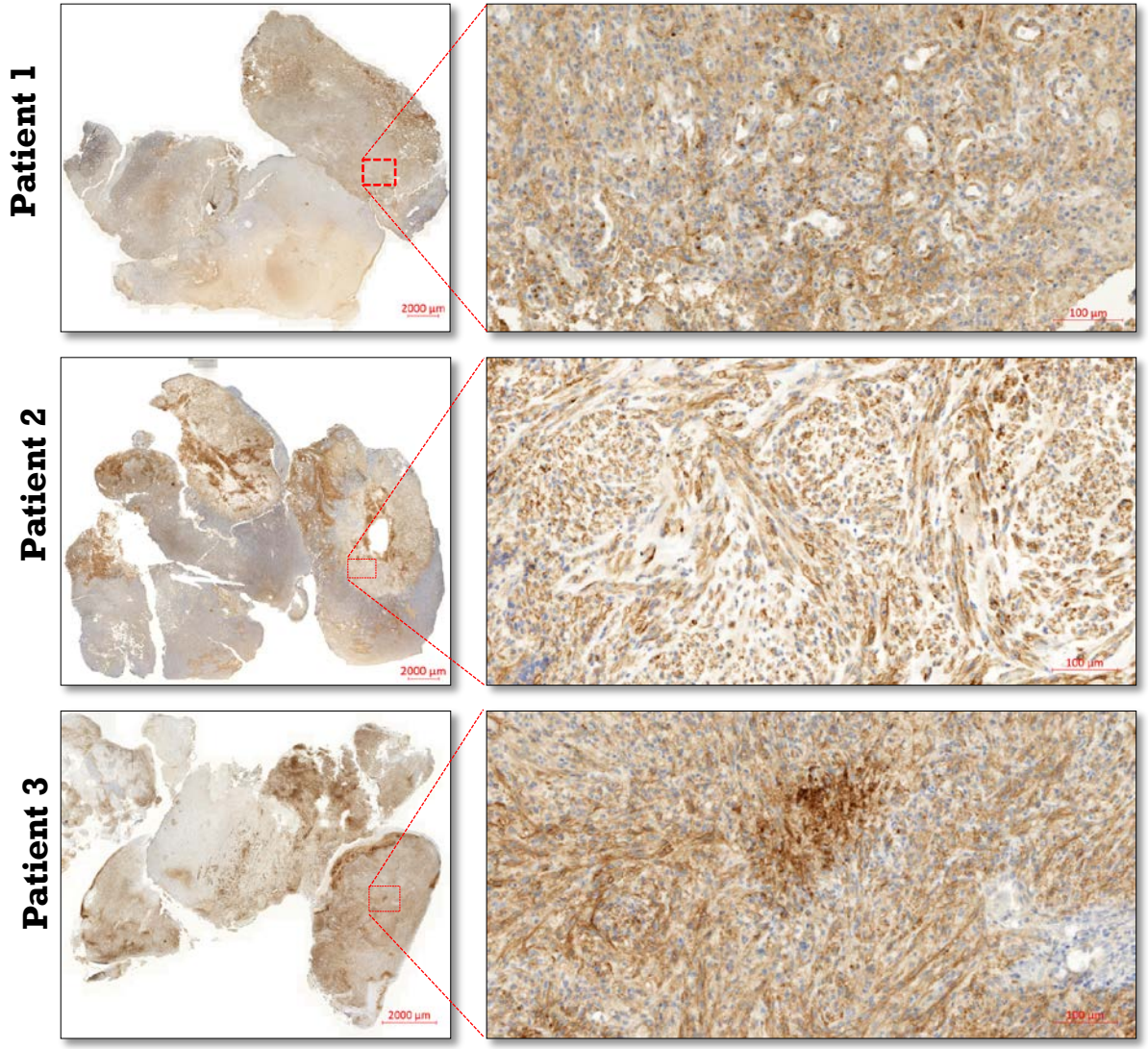
Chimeric antigen receptor (CAR) T cell-based immunotherapy therapy's success in childhood leukemia highlights its potential for effective pHGG treatment.

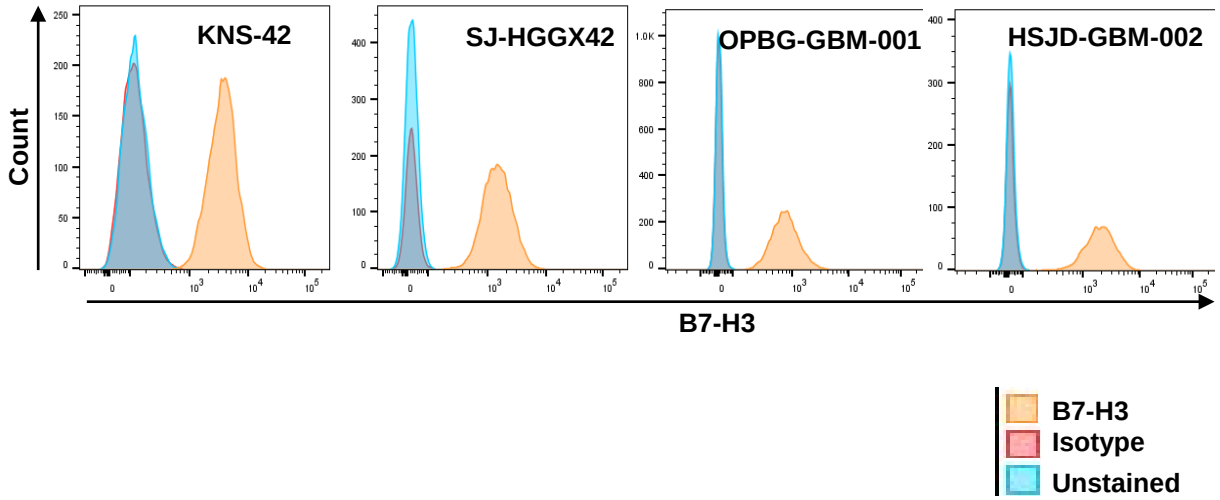


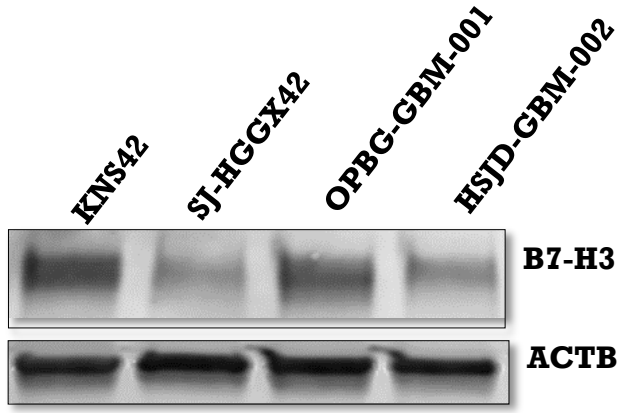
B7-H3

- B7 homolog 3 (B7-H3, also called CD276) contributes to several cancer-related processes including tumor metabolism, angiogenesis, invasion, and therapy resistance.
- B7-H3 is upregulated in several malignant cancers, but its expression is low in healthy tissues.
- Targeting B7-H3 can be a desired approach against advanced stage cancers through reshaping the immune ecosystem of solid tumors.

Enriched B7-H3 expression in patient tumor specimen and pHGGs cell lines







Children's Mercy KANSAS CITY | Research Institute

Construction of B7-H3 CAR T cells

A Design of CAR vectors

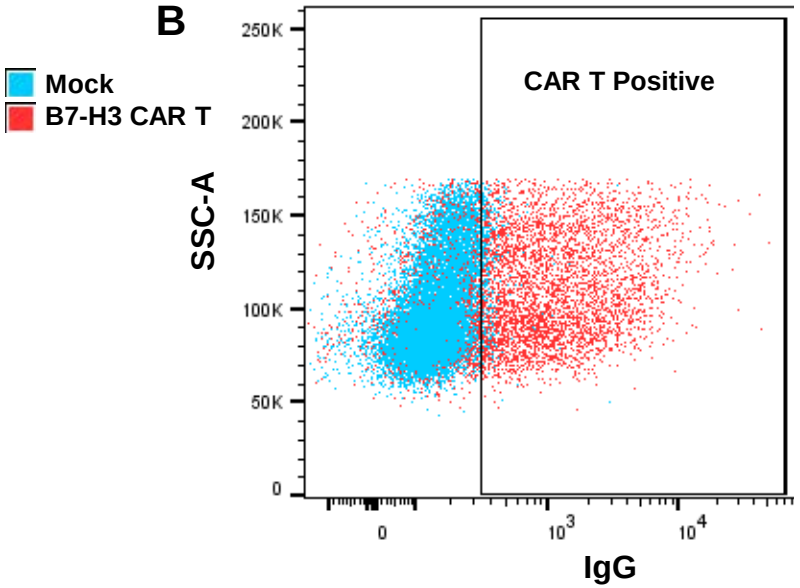
Human-B7-H3

Mouse-B7-H3

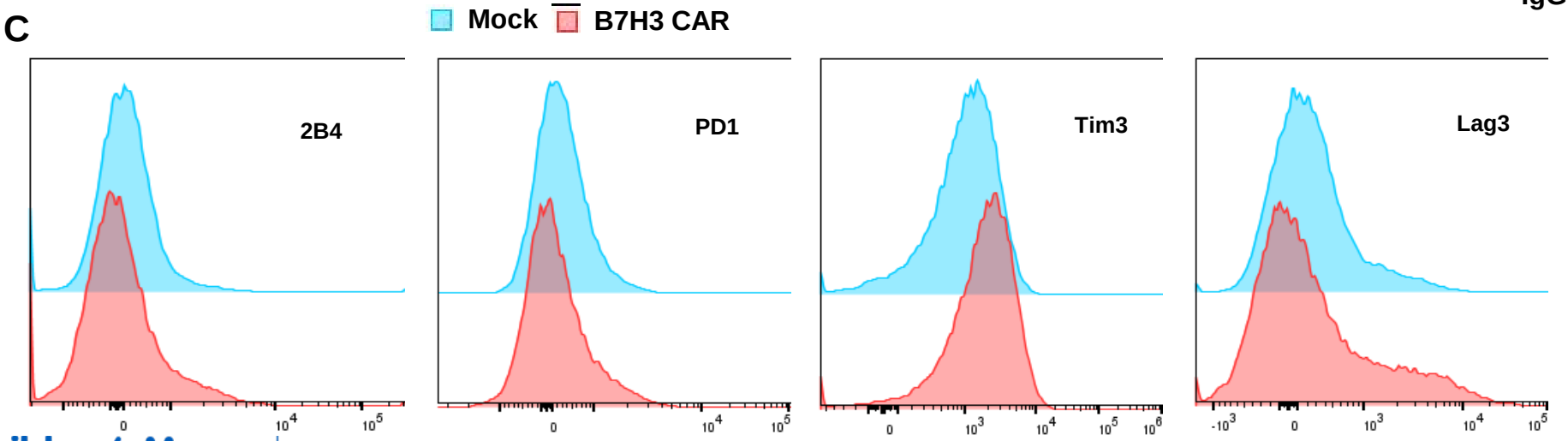
Human-B7-H3-GD2, Bi-specific CAR

Mouse-B7-H3-GD2, Bi-specific CAR

B

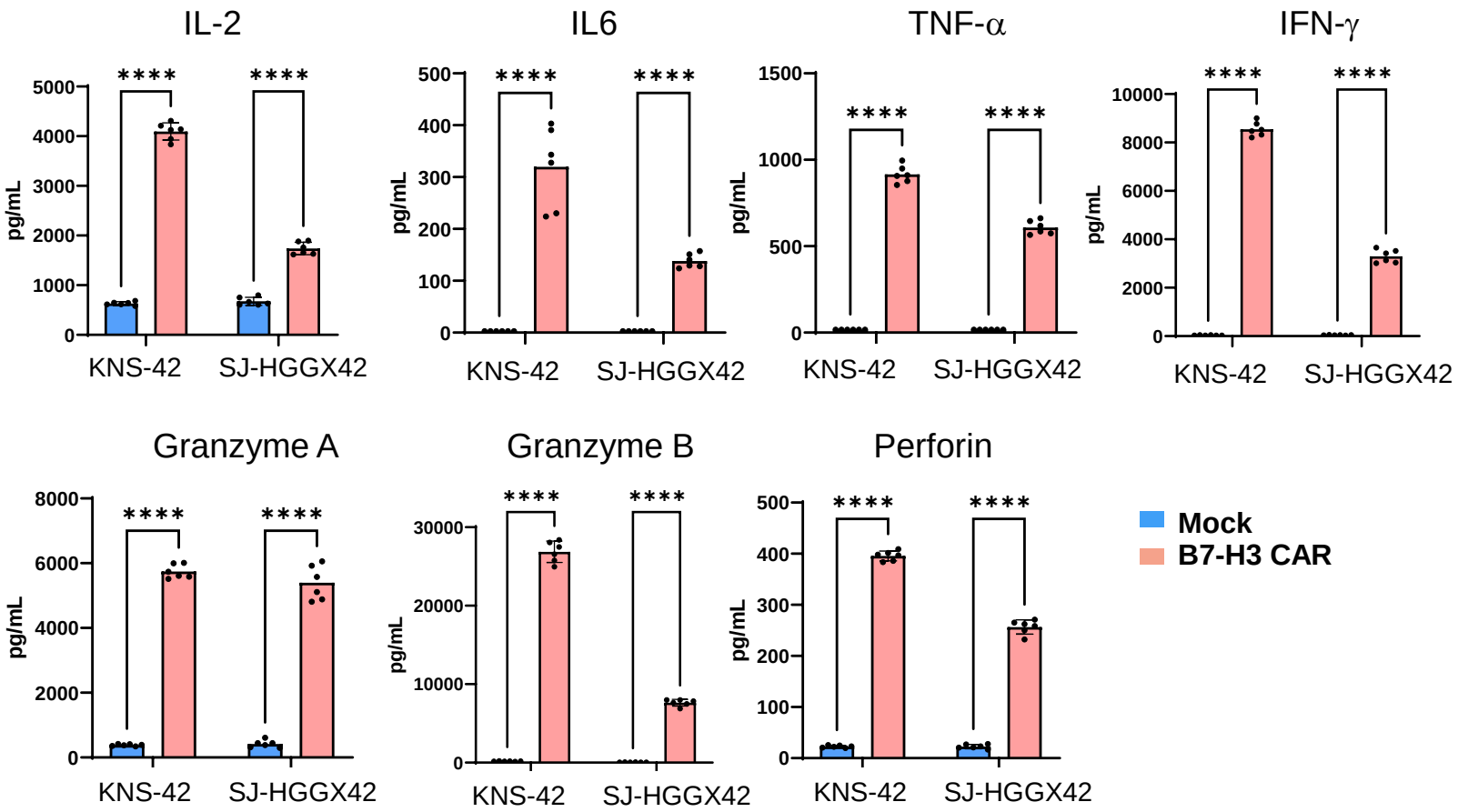


C



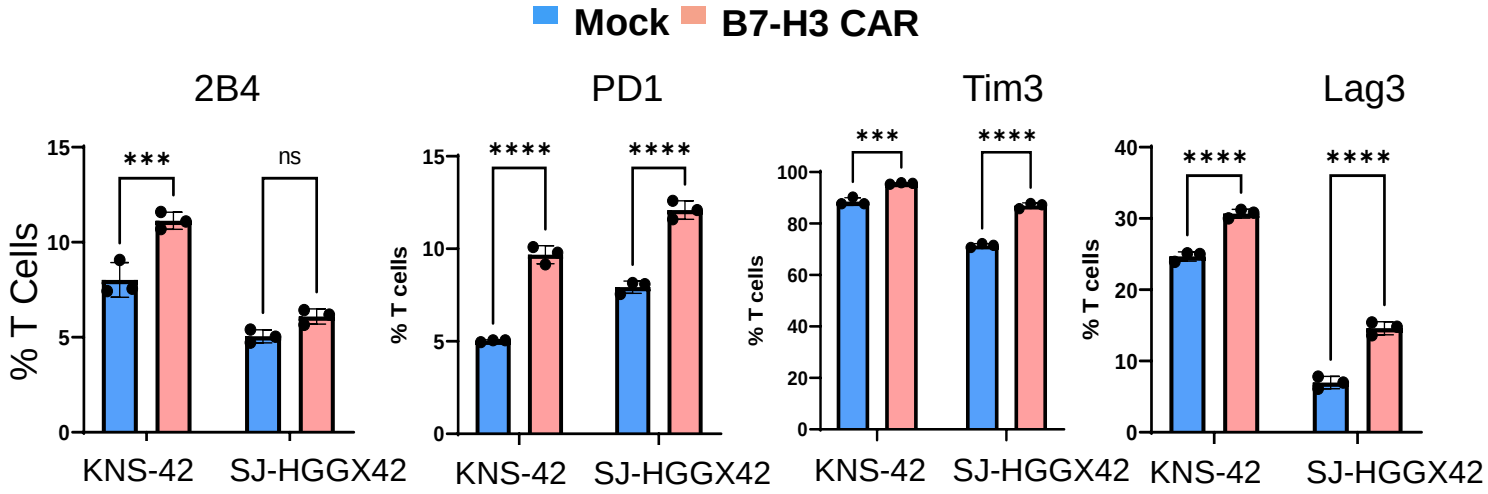
Children's Mercy KANSAS CITY | Research Institute

B7-H3 CAR T cells increased expression of T-cell activation and immune response markers

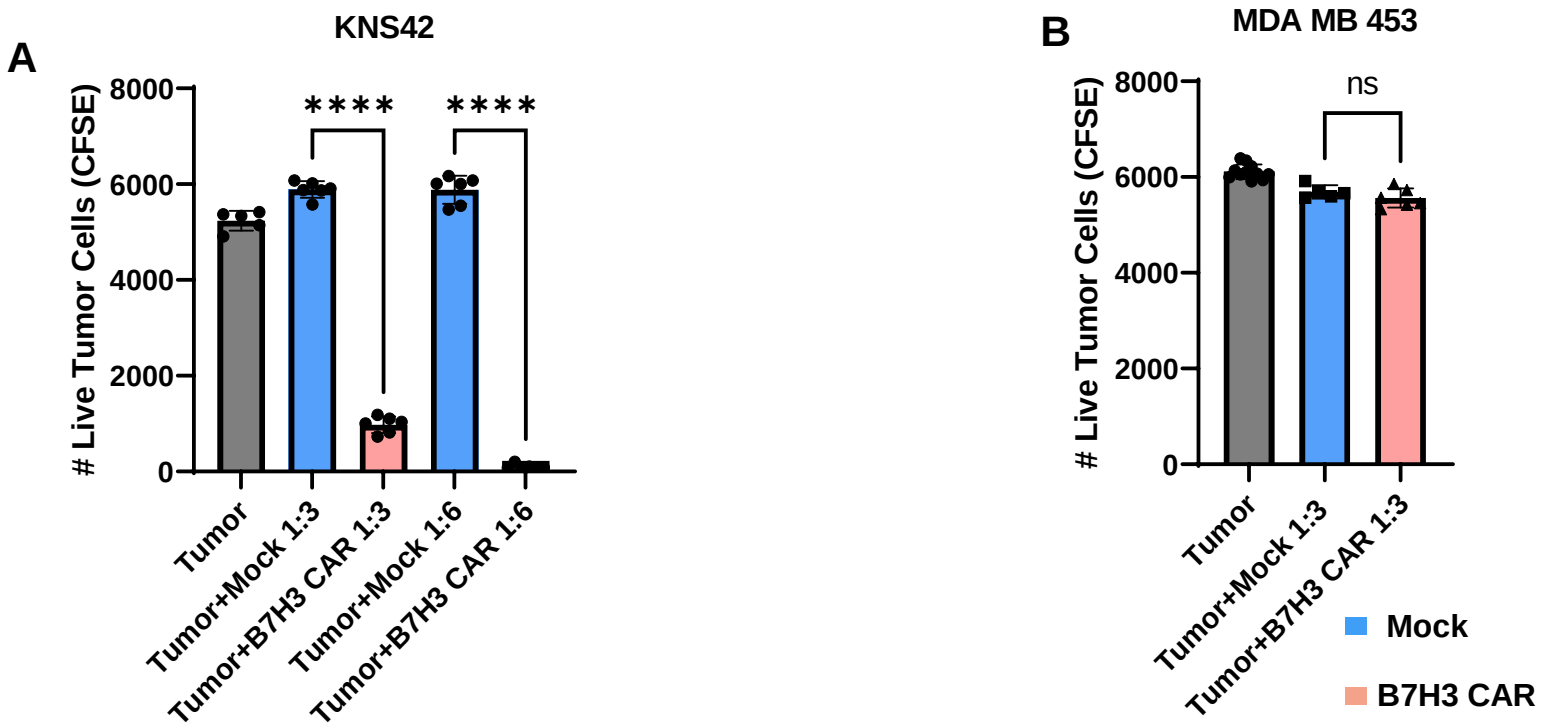


Children's Mercy KANSAS CITY | Research Institute

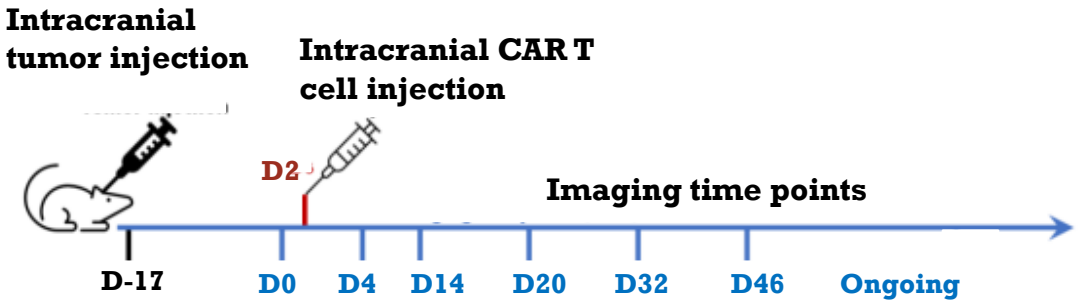
Elevated level of exhaustion markers observed on B7-H3 CAR T cells

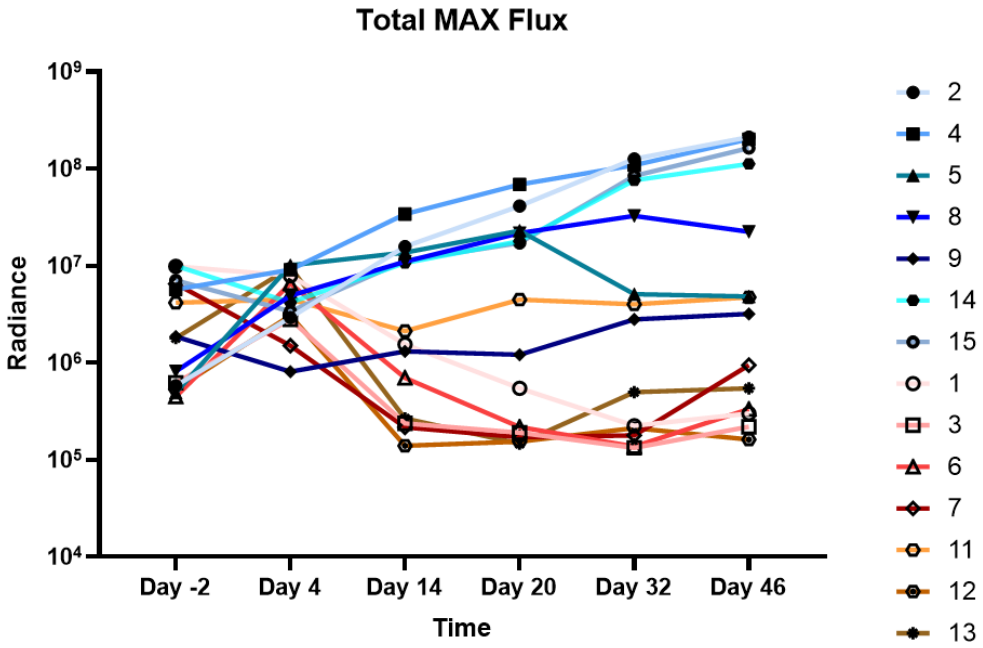


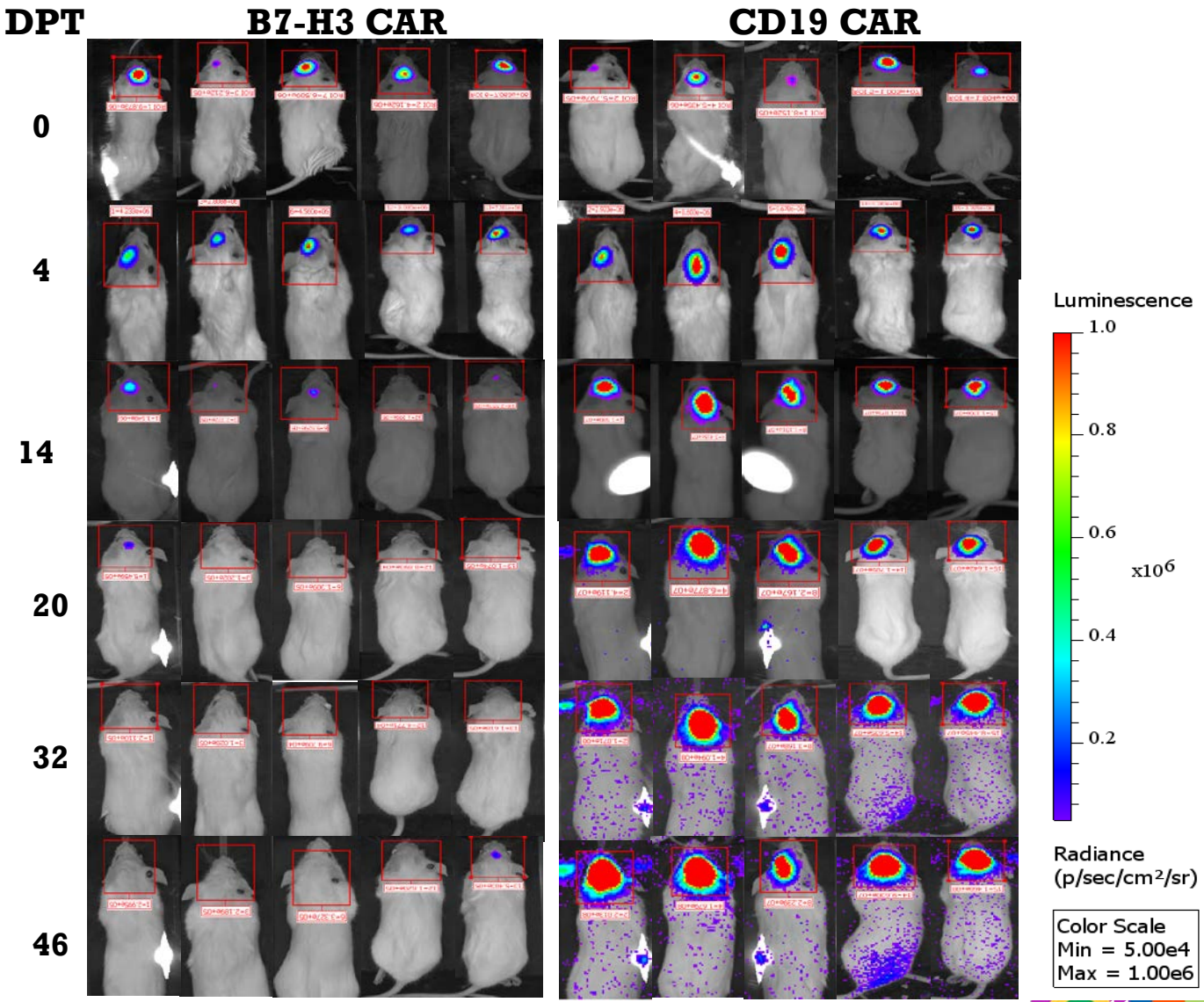
B7-H3 CAR T cells have antigen-specific cytotoxic potential against pHGGs cell lines



Anti-tumor effect of B7-H3 CAR T cells in xenograft NSG mice





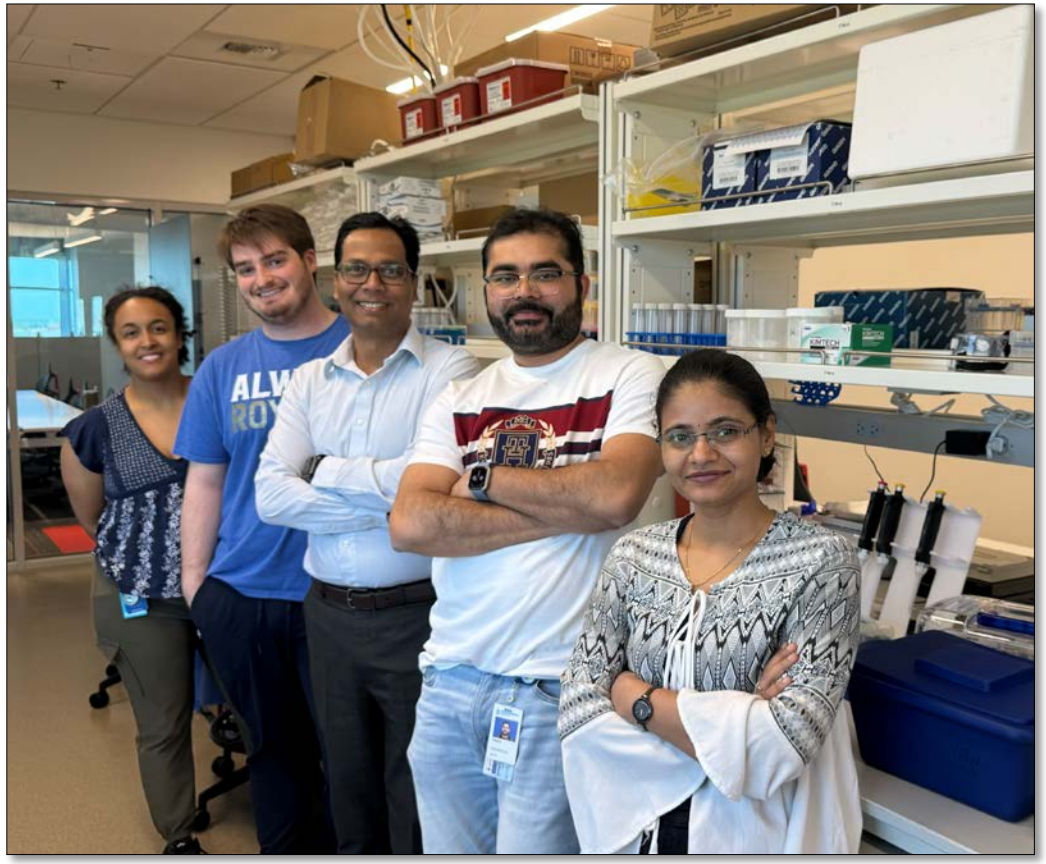


Children's Mercy KANSAS CITY | Research Institute

Conclusion and Future Directions

- Our results demonstrates anti-tumor activity of B7-H3 CAR-T cells *in vitro* and *in vivo*.
- We will test mouse-specific anti-B7-H3 and novel Bi-specific anti-B7-H3-anti-GD2 CAR T cells *in vivo* using our unique immunocompetent mouse model of pHGGs.
- The impact of CAR T cell function on the tumor microenvironment will be studied using our immunocompetent mouse model of pHGGs.

Acknowledgements



Yadav Lab members

- Vivekanand Yadav, Ph.D (PI)
- Garrett Gibson, B.S
- Adora T Klinestiver, M.S
- Mohammad Faisal Syed, Ph.D

Collaborators

CMRI

- Doug D. Myers, M.D
- John Szarejko, Ph.D

University of Kansas

- David Akhavan, M.D, Ph.D
- Siddhartha Shubham, PhD student
- John Jeppson, Ph.D

Children's Mercy KANSAS CITY | Research Institute

NOAH'S BANDAGE PROJECT
It's so much more than a bandage...