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

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

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Post-Doctoral Researcher

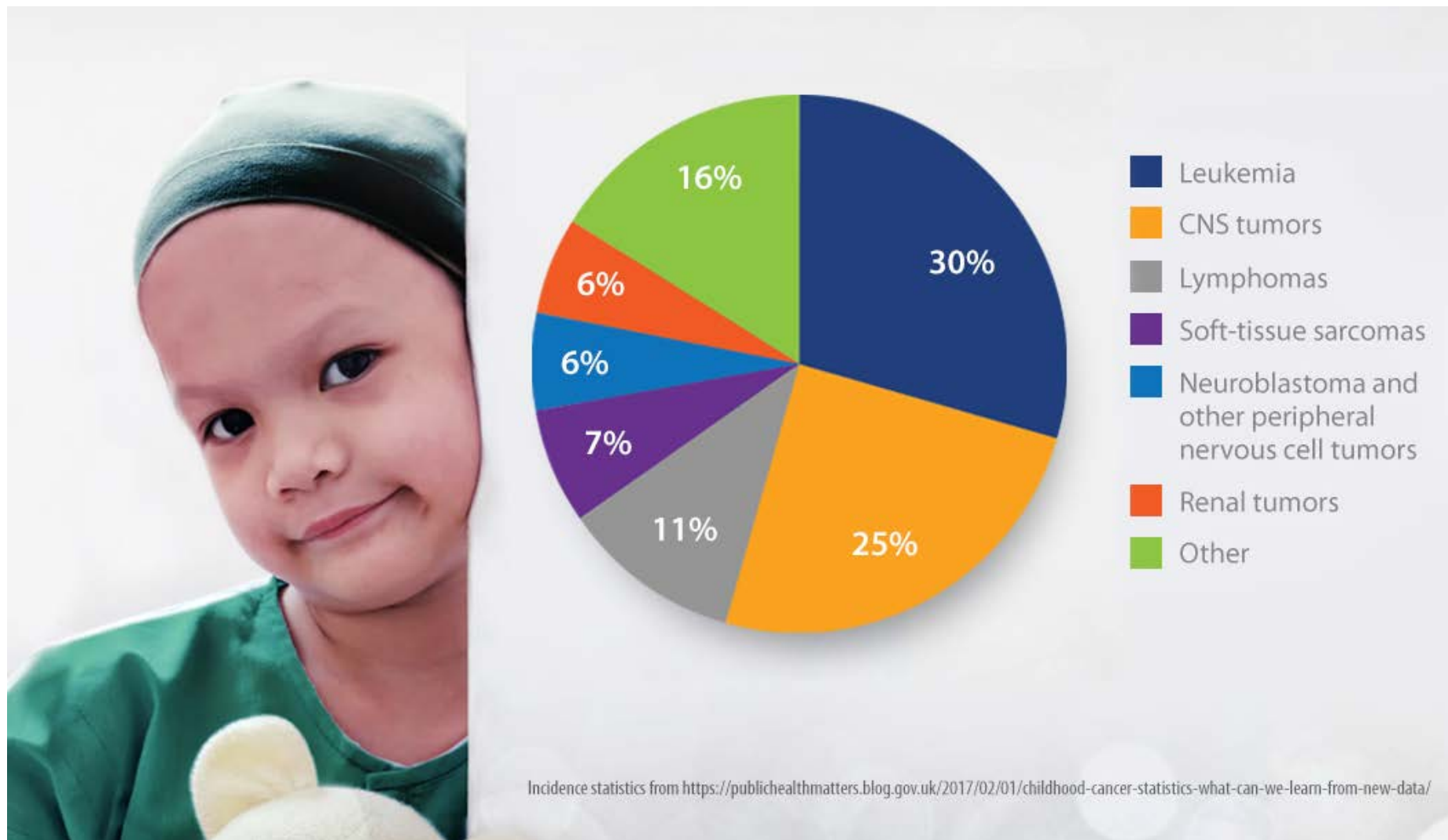
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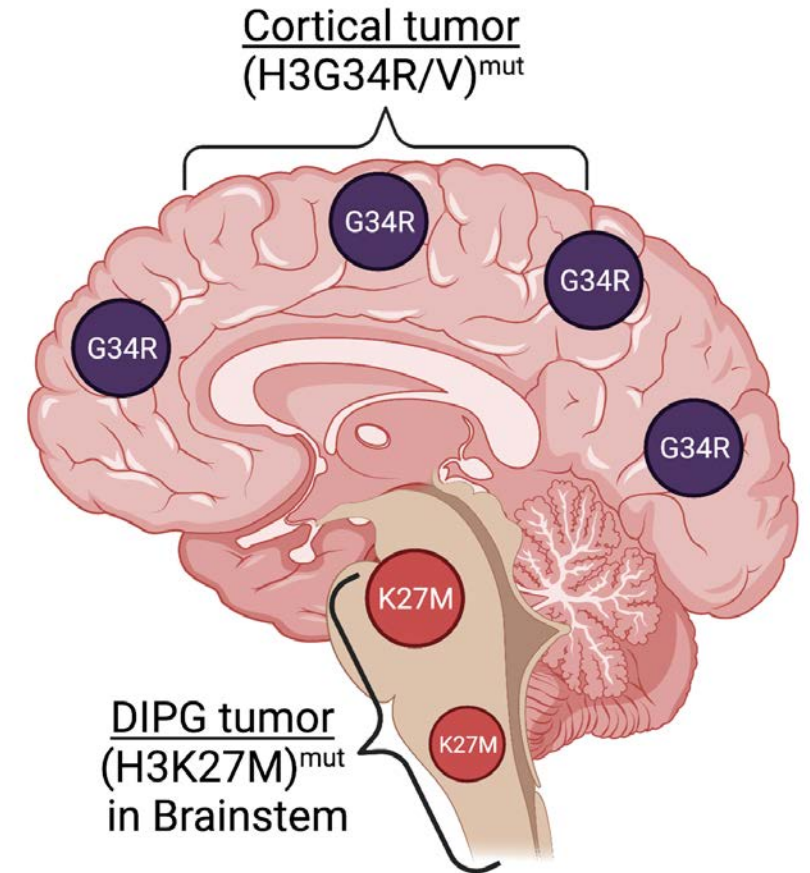
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Childhood cancers incidence



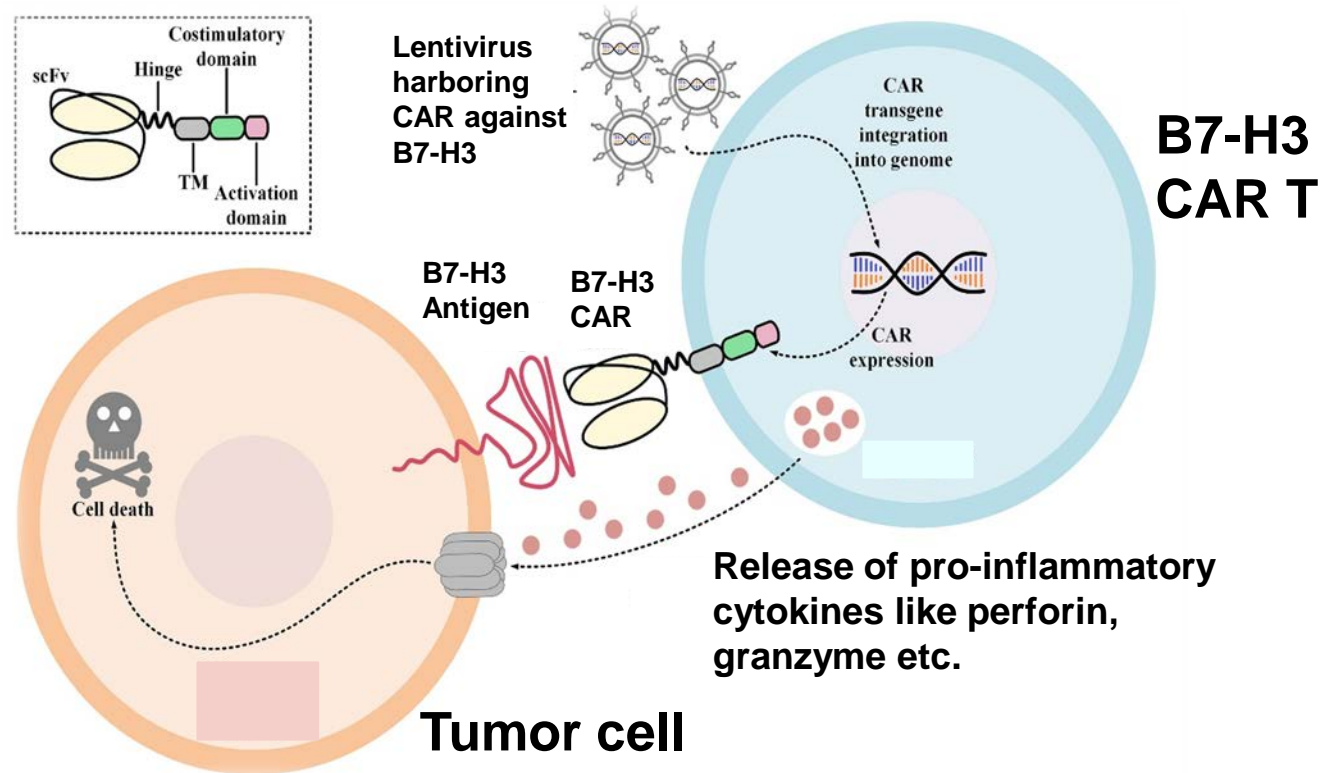
Pediatric high-grade gliomas (pHGGs)

- 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.

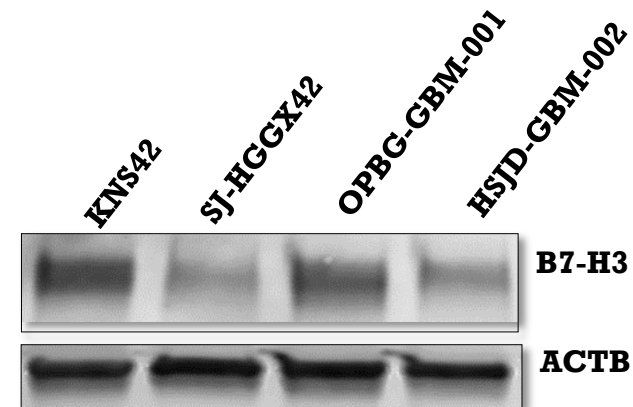
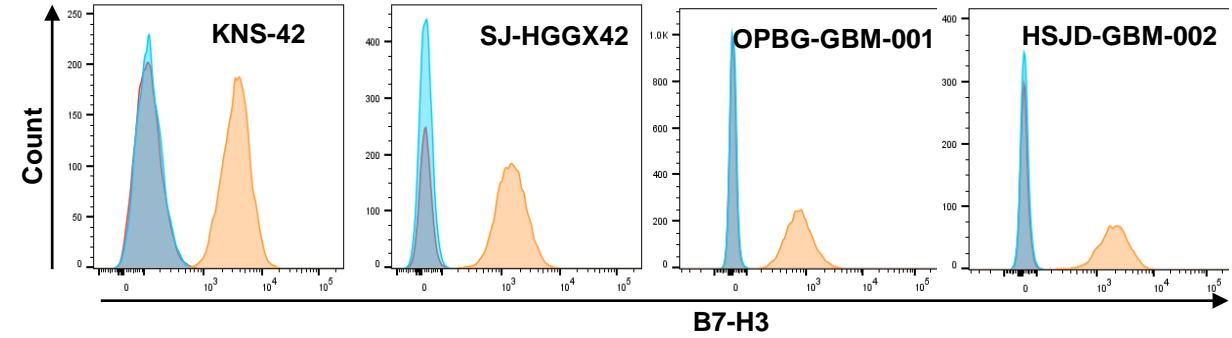
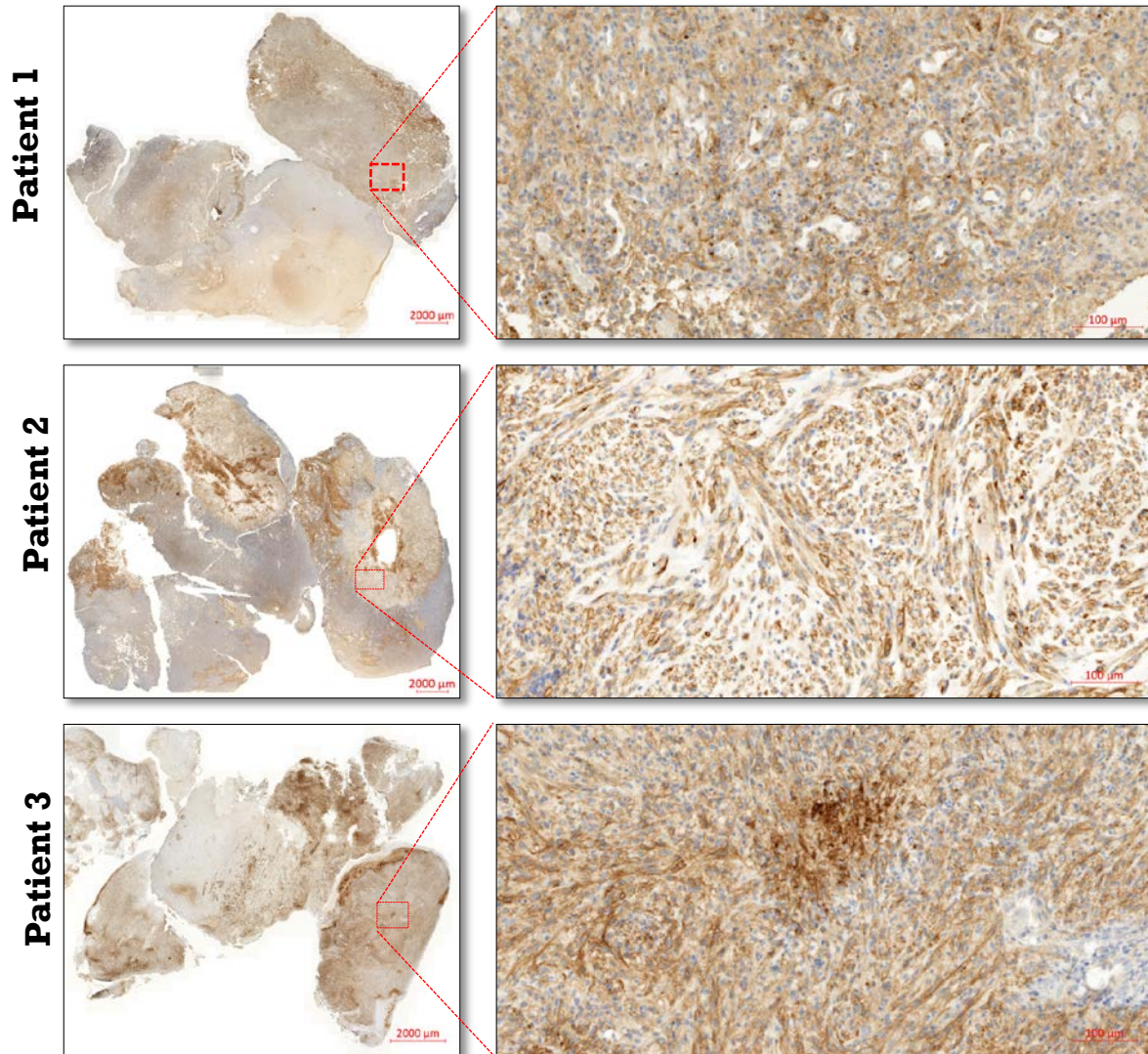


B7-H3

- 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



Construction of B7-H3 CAR T cells

A Design of CAR vectors

Human-B7-H3



Mouse-B7-H3



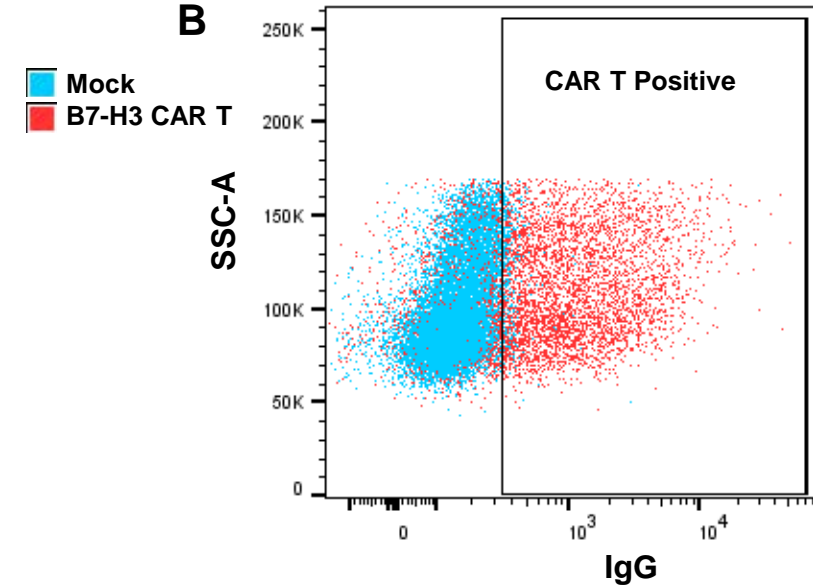
Human-B7-H3-GD2, Bi-specific CAR



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

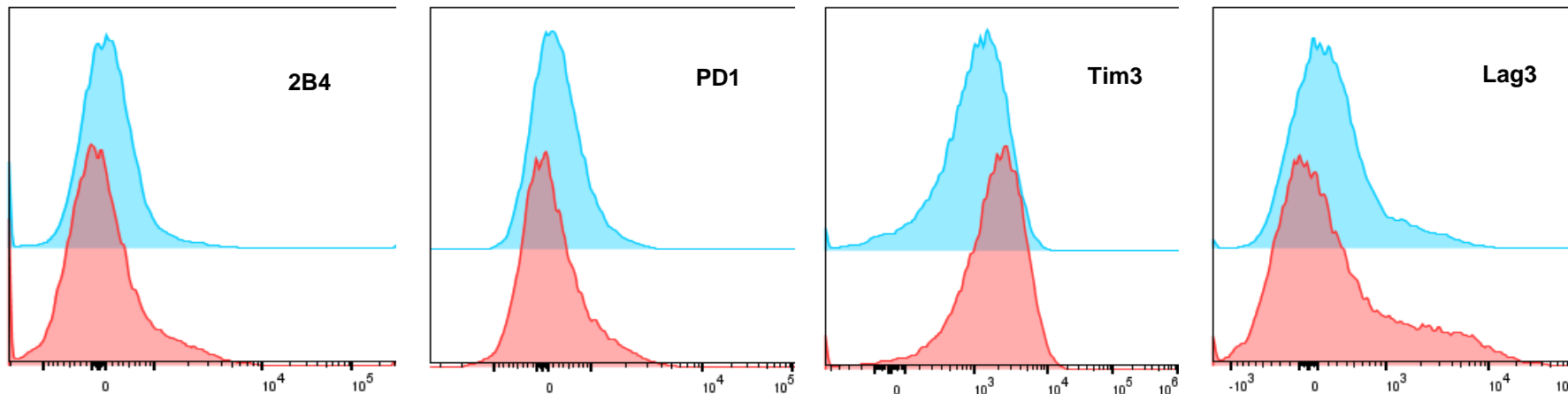


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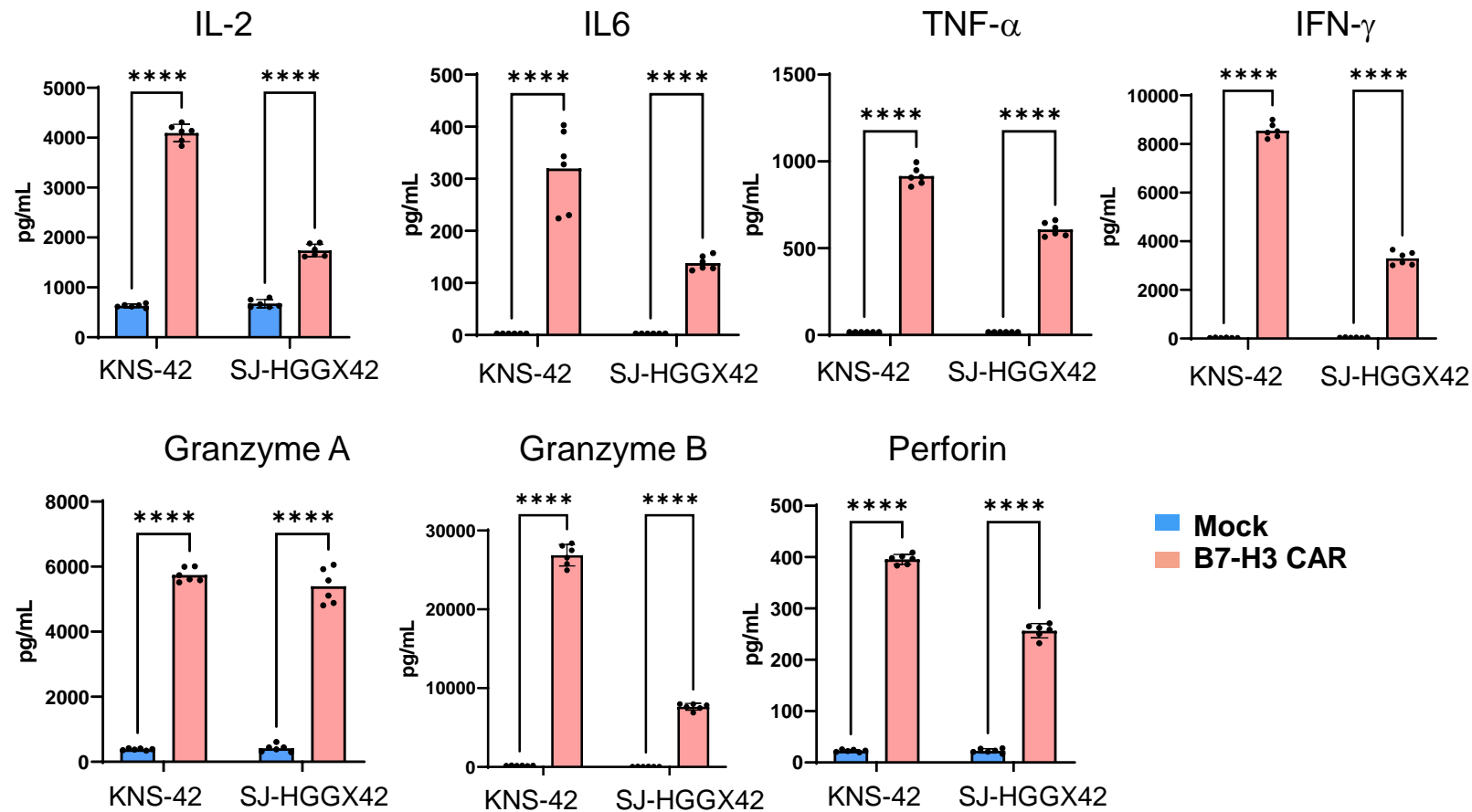


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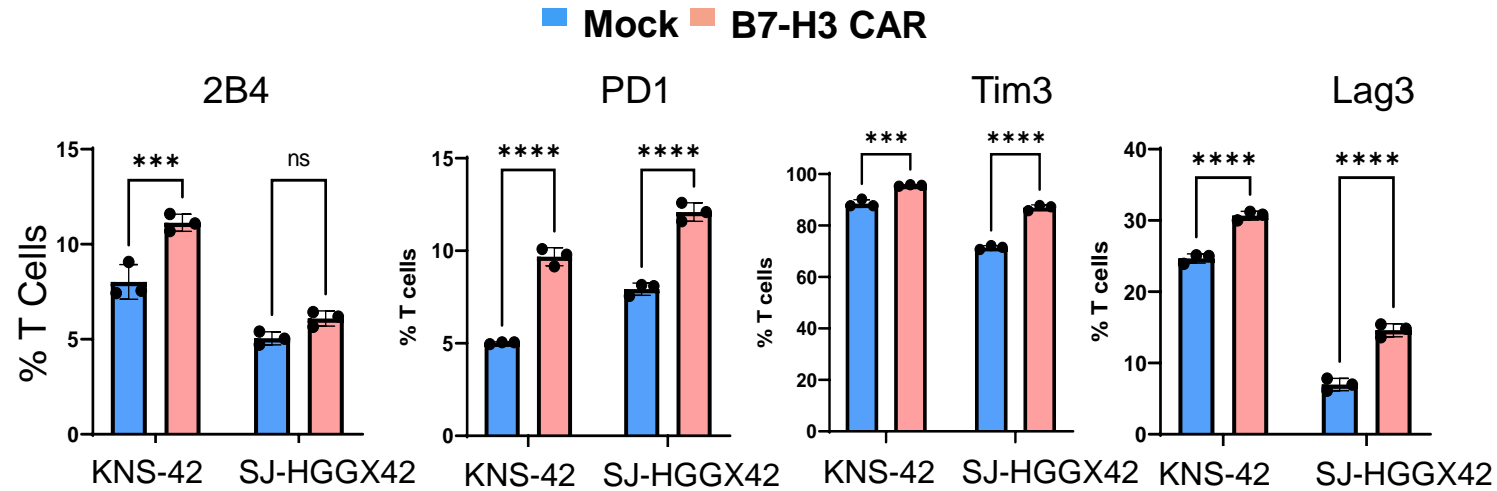
Mock B7H3 CAR



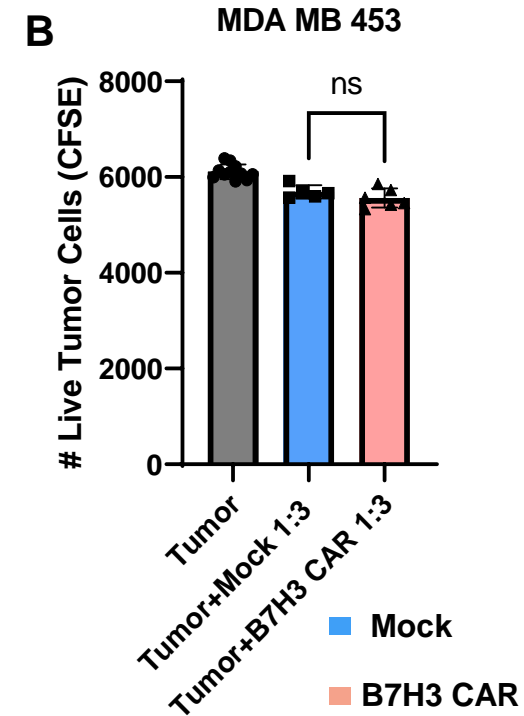
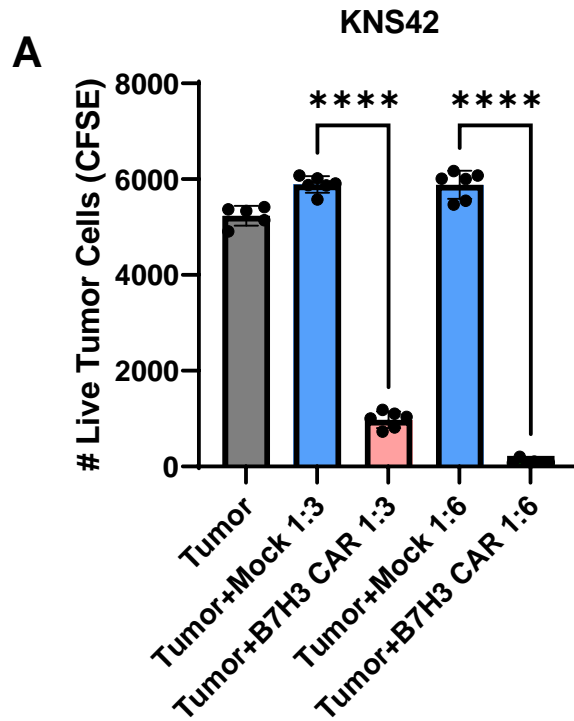
B7-H3 CAR T cells increased expression of T-cell activation and immune response markers



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



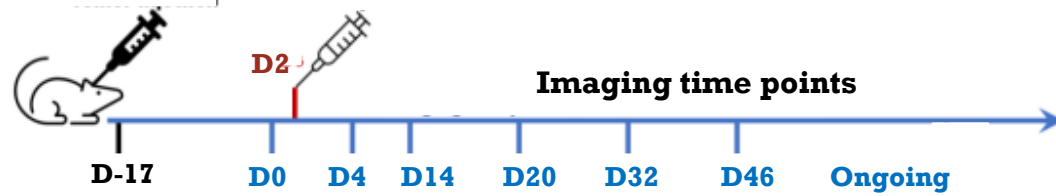
B7-H3 CAR T cells have antigen-specific cytotoxic potential against pHGGs cell lines



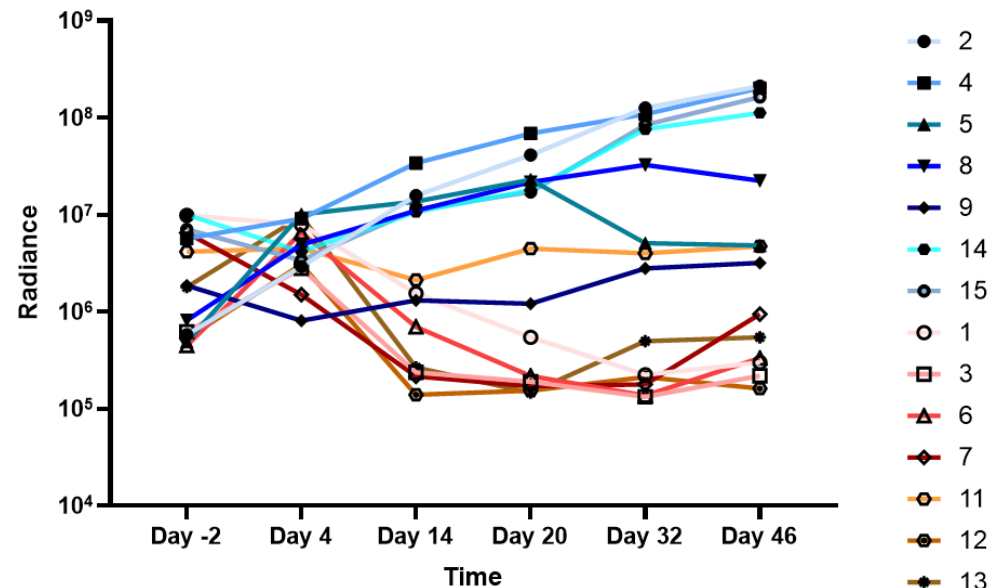
Anti-tumor effect of B7-H3 CAR T cells in xenograft NSG mice

Intracranial tumor injection

Intracranial CAR T cell injection



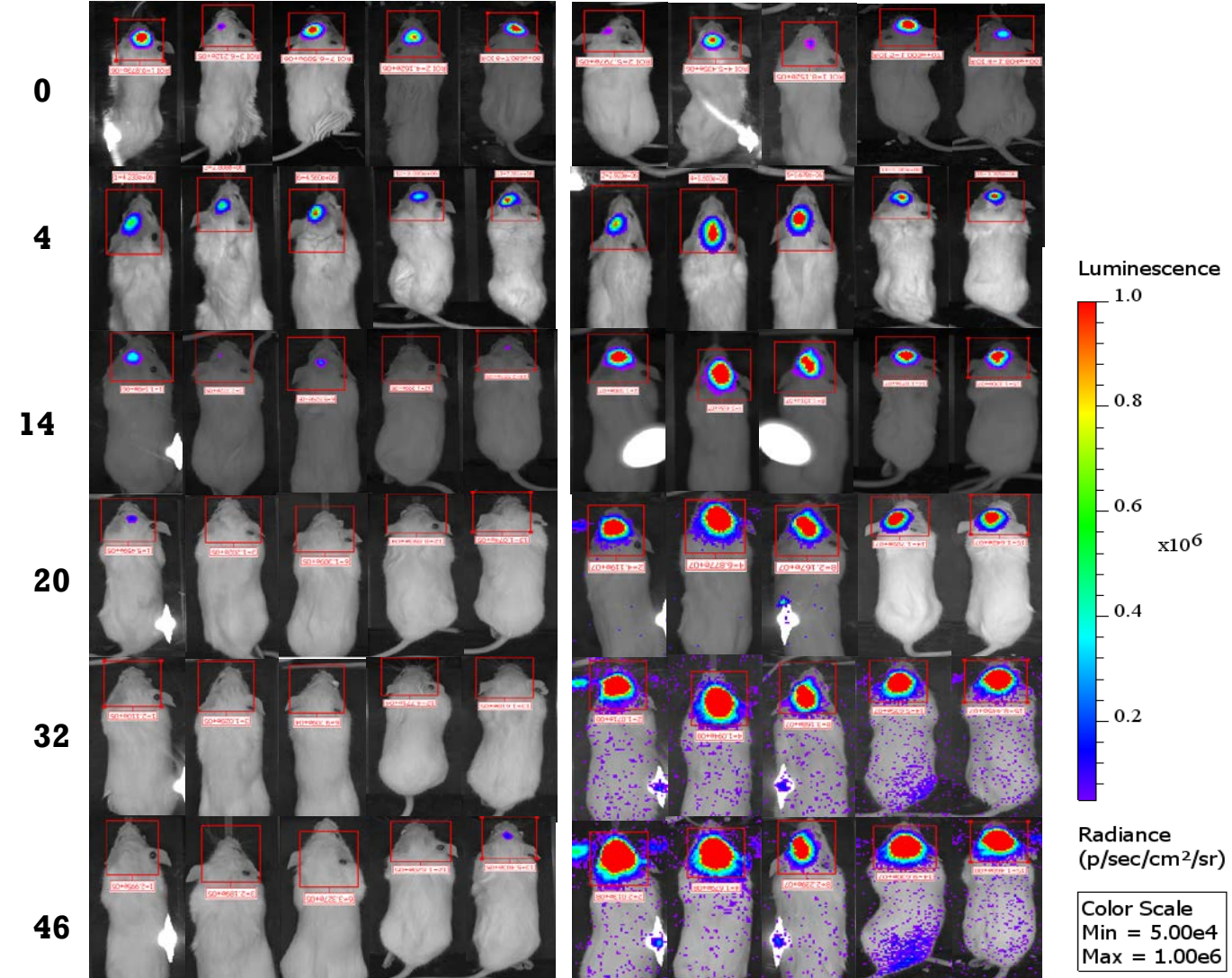
Total MAX Flux



DPT

B7-H3 CAR

CD19 CAR



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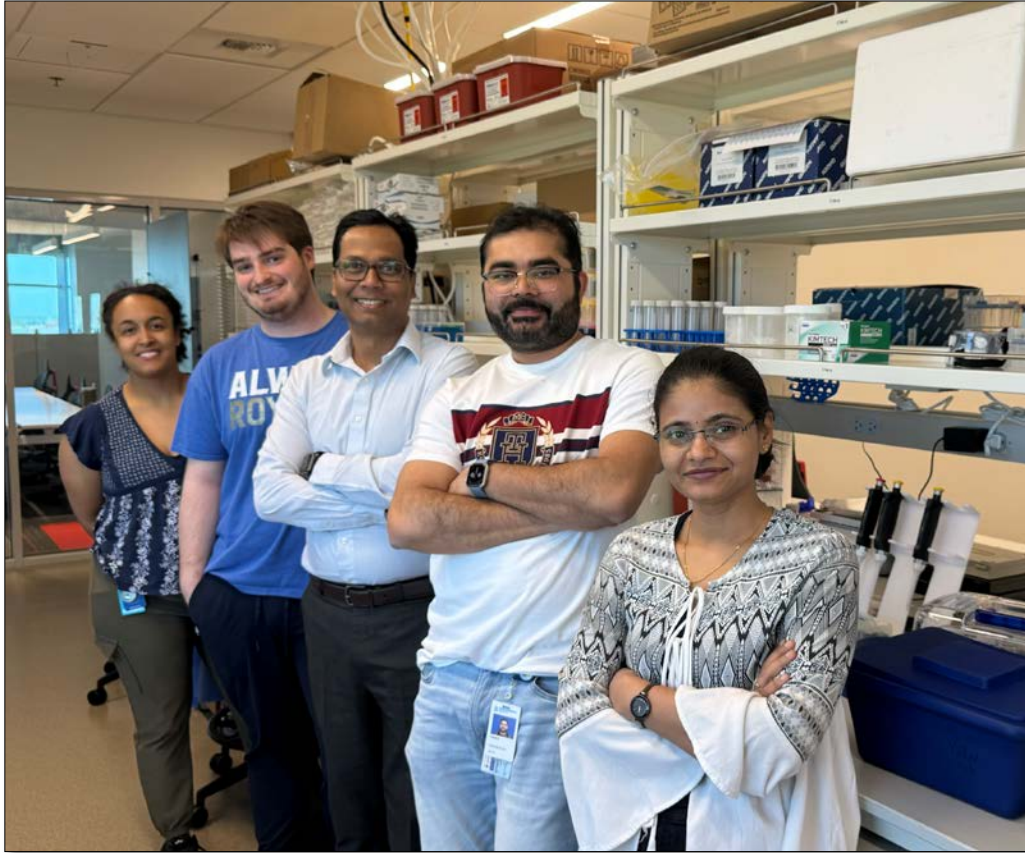
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Conclusion and Future Directions

- 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.



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Yadav Lab members

- Vivekanand Yadav, Ph.D (PI)
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- 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



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

