Cellule CAR-T anti-B7-H3 per il trattamento del medulloblastoma: un confronto dei domini co-stimolatori 4-1BB e OX40 in un costrutto di terza generazione.

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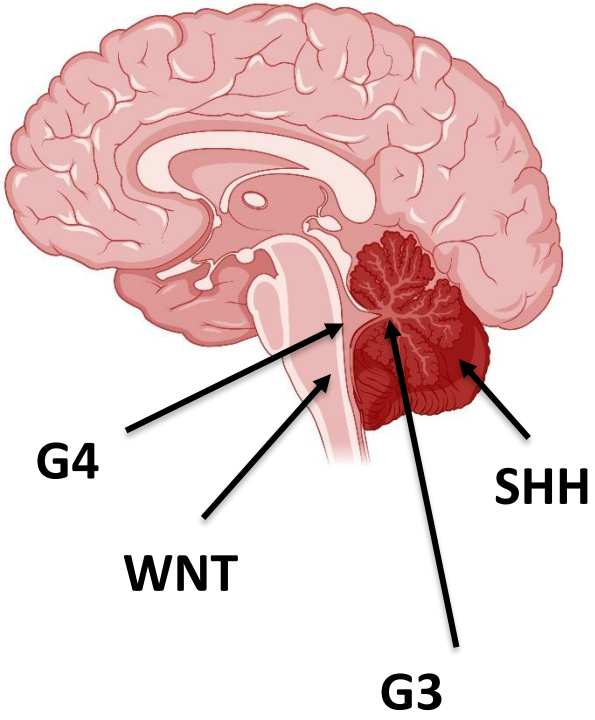
Medulloblastoma Classification



WNT 10%

Prognosis:
GOOD
Histology:
CLASSIC
Metastasis:
LOW

SHH 30%

Prognosis
INTERMEDIATE
Histology:
DESMOPLASTIC
CLASSIC
Metastatic **LOW**

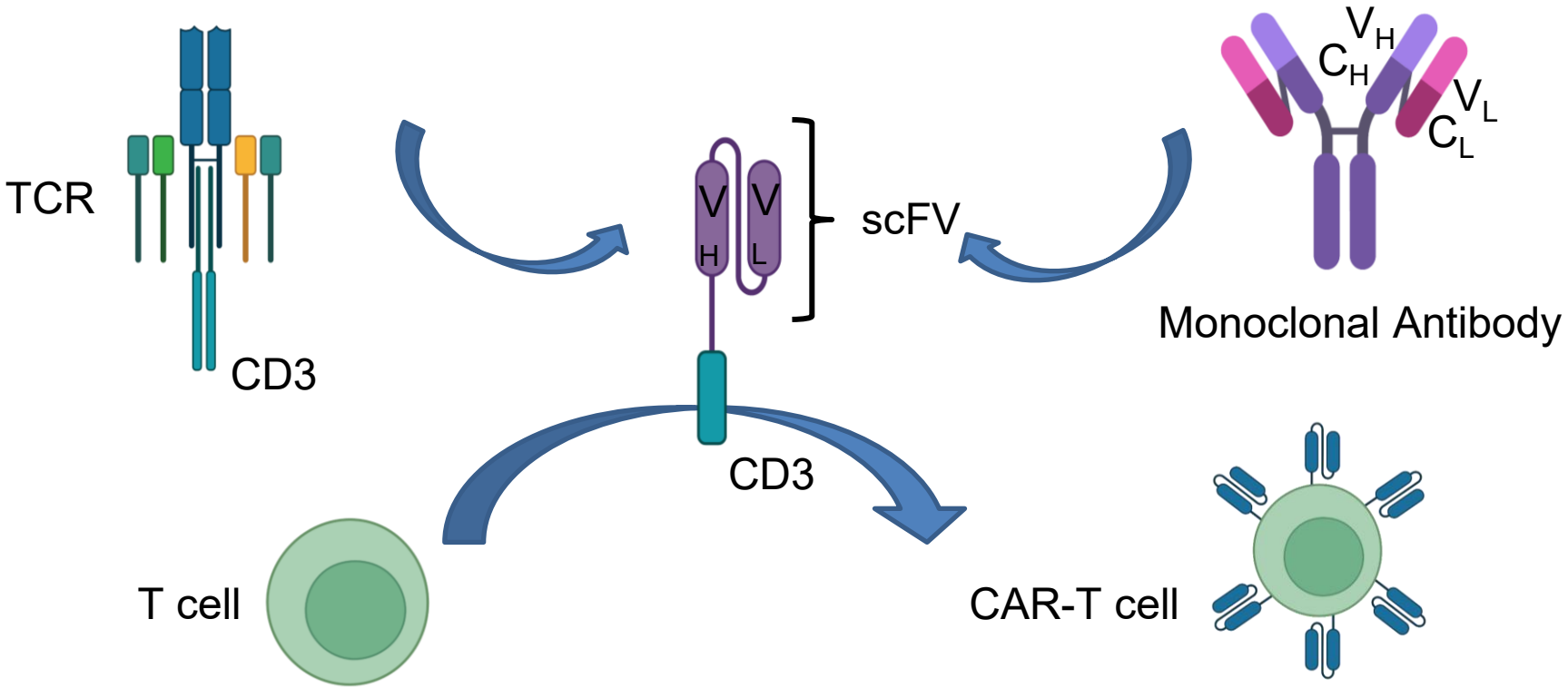
Prognosis:
INTERMEDIATE
Histology:
CLASSIC
Metastasis:
HIGH

G4 35%

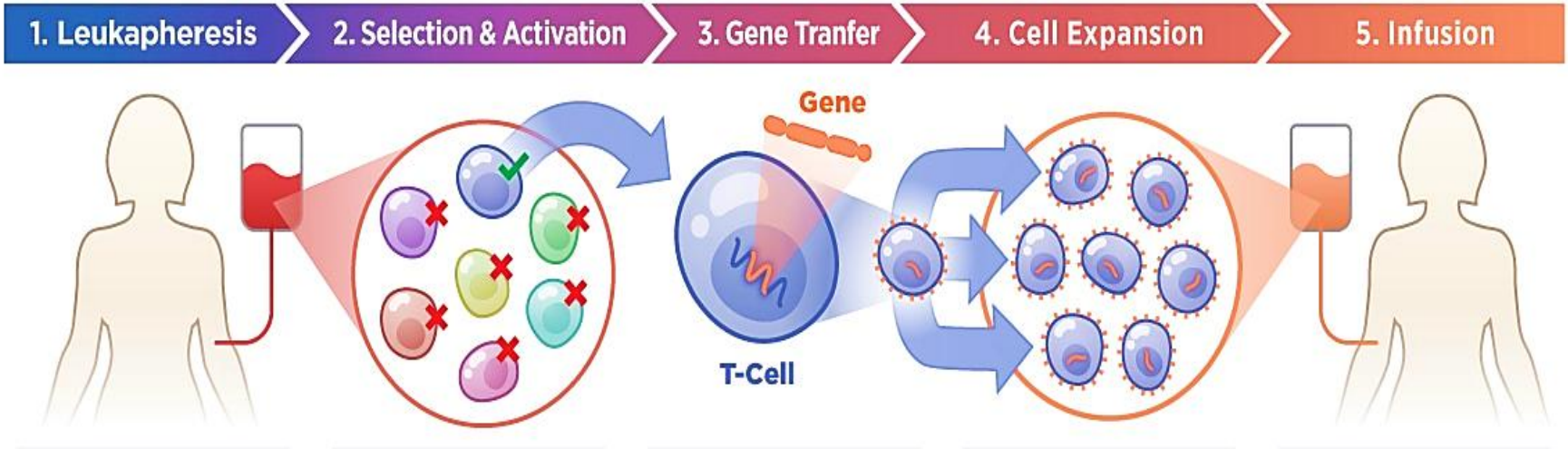
Prognosis:
POOR
Histology:
CLASSIC
Metastasis:
HIGH

G3 25%

Chimeric Antigen Receptor (CAR) Structure

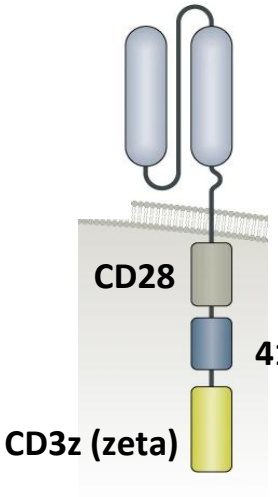


CAR-T cells Production Workflow



CAR T-cell development

THIRD GENERATION CARs



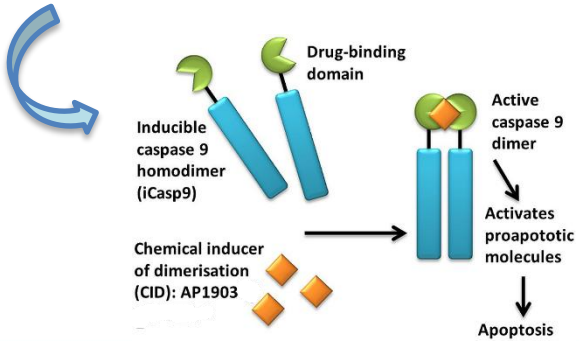
Cytotoxicity

Proliferation/cytokine production

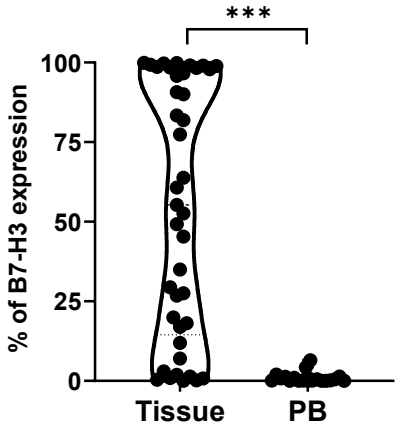
Survival

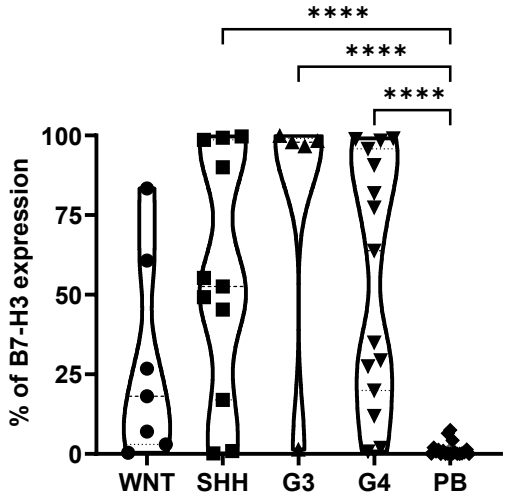
B7-H3.CAR.CD28.41BB

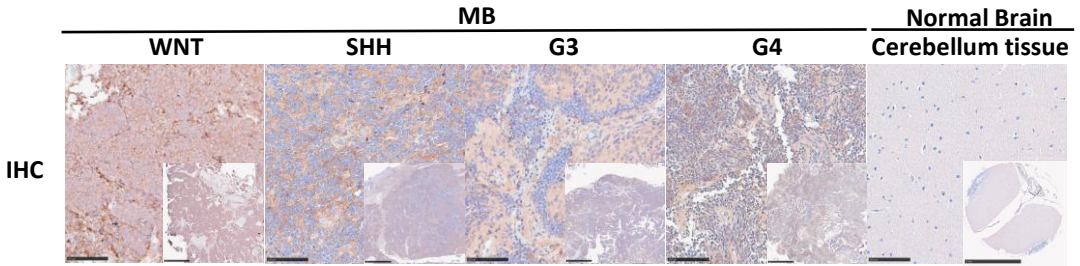
B7-H3.CAR.CD28.OX40



B7-H3 Tissue Expressions







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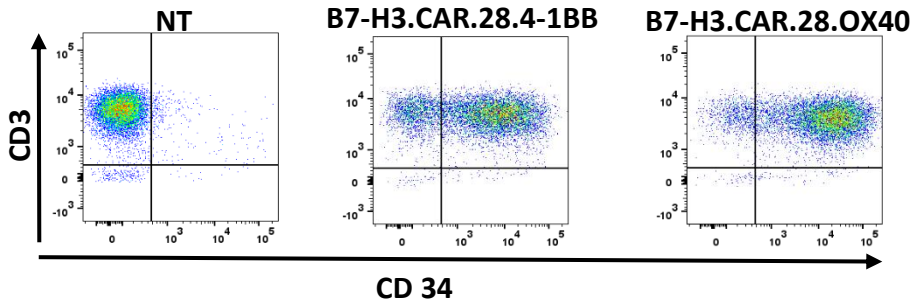
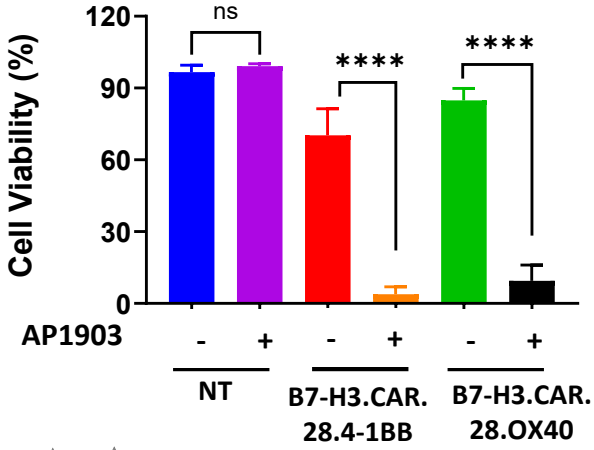
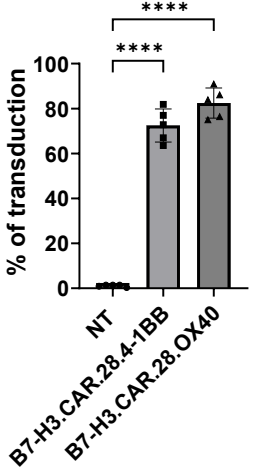
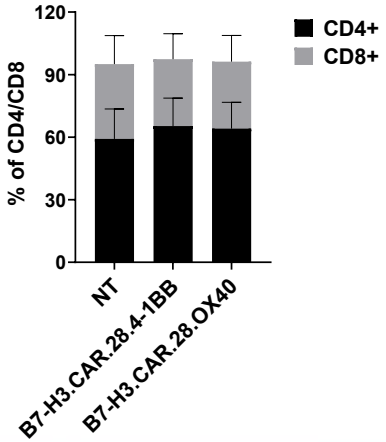
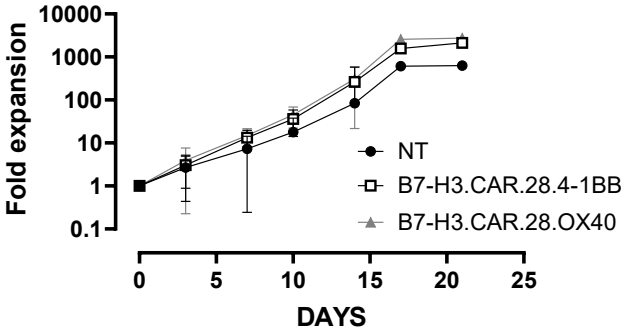
B7-H3.CAR T cells characterization











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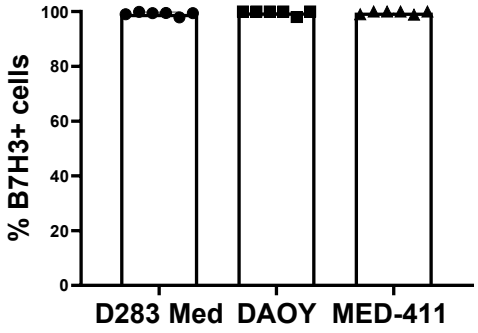
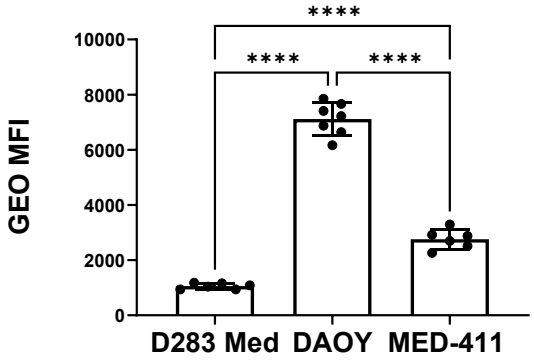
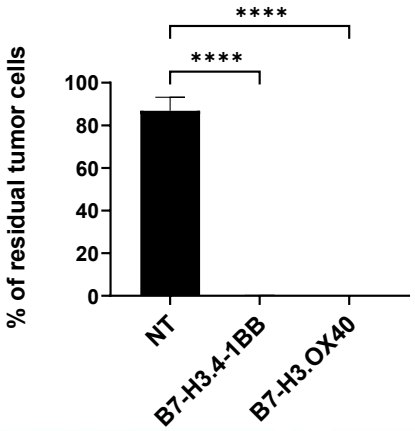
B7-H3.CAR T-cells *in vitro* anti tumor activity

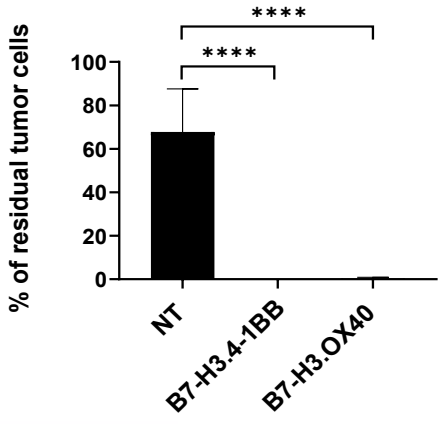




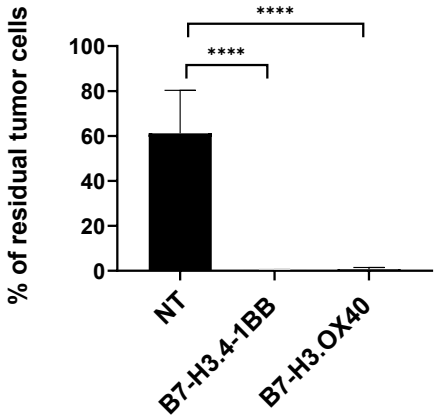
D283 Med (G3/G4)



DAOY (SHH)



MED-411 (G3)



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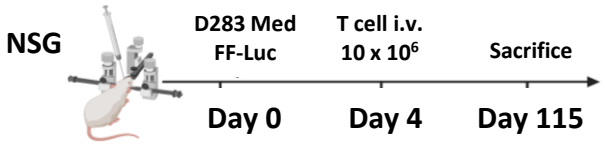
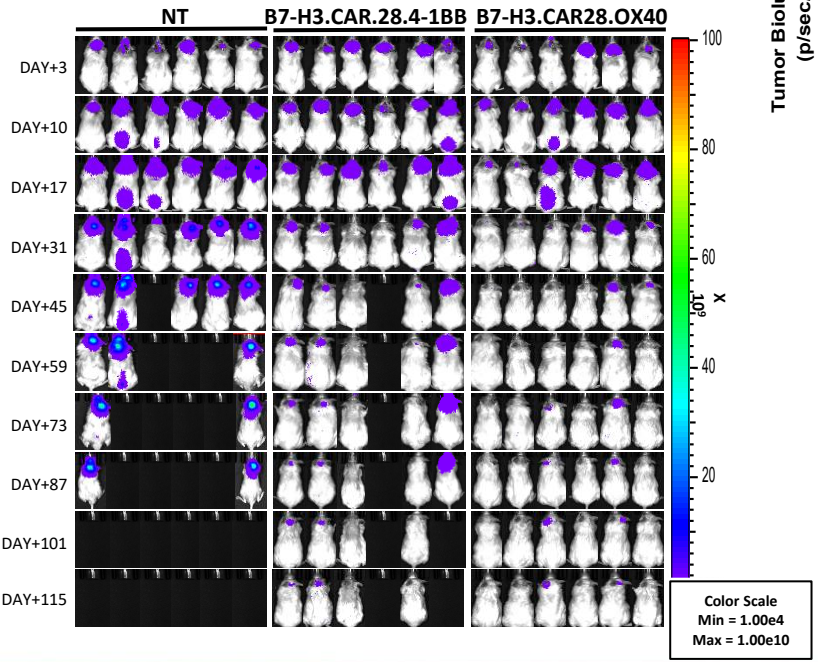
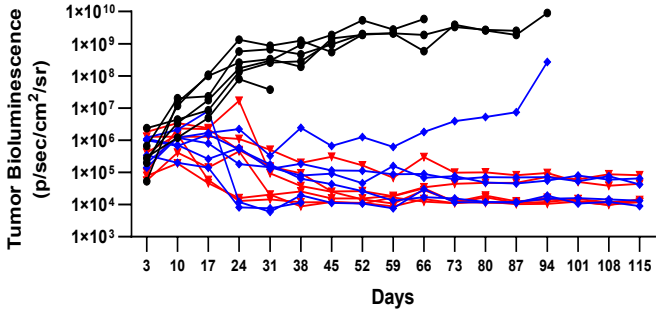
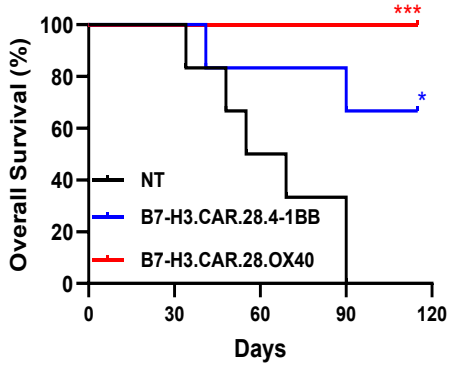
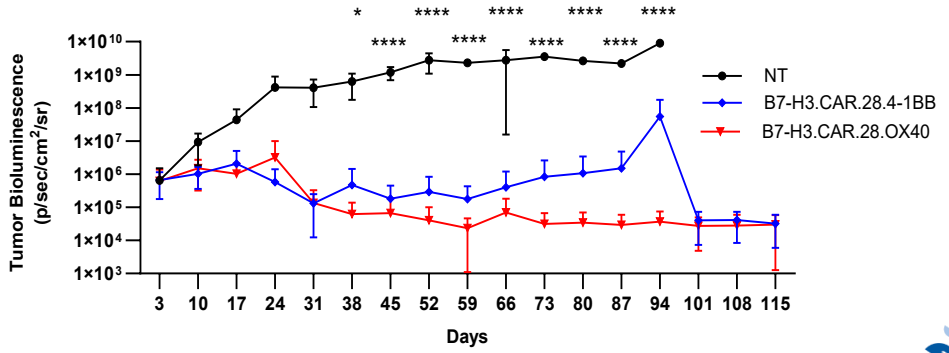
B7-H3.CAR T-cells vs D283 cell line *in vivo* anti tumor activity











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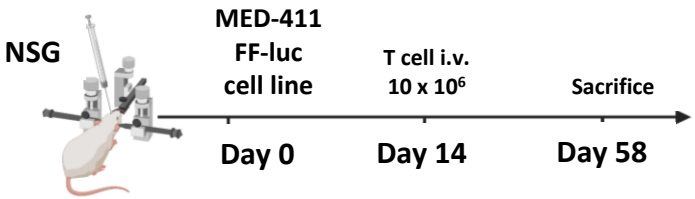
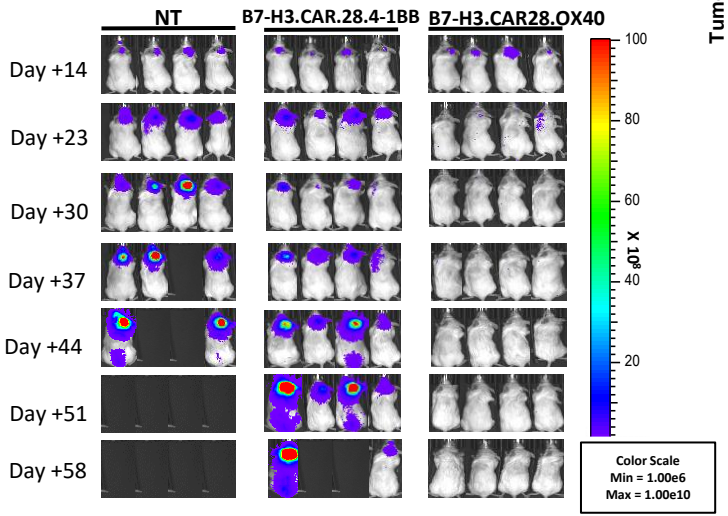
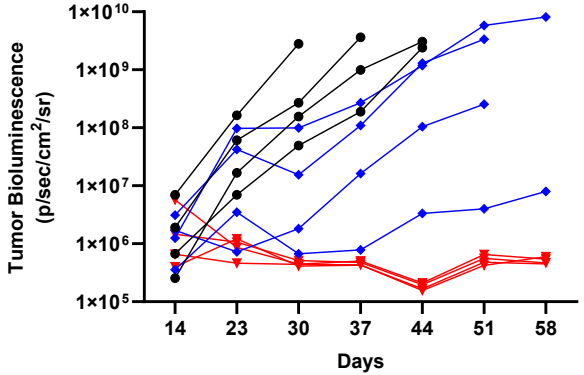
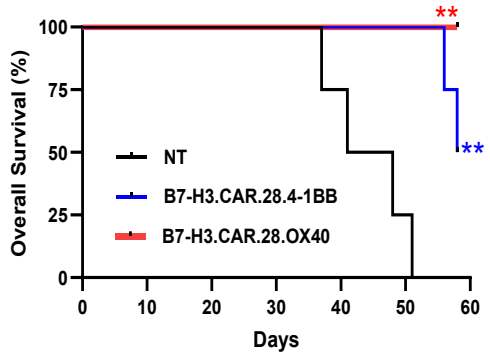
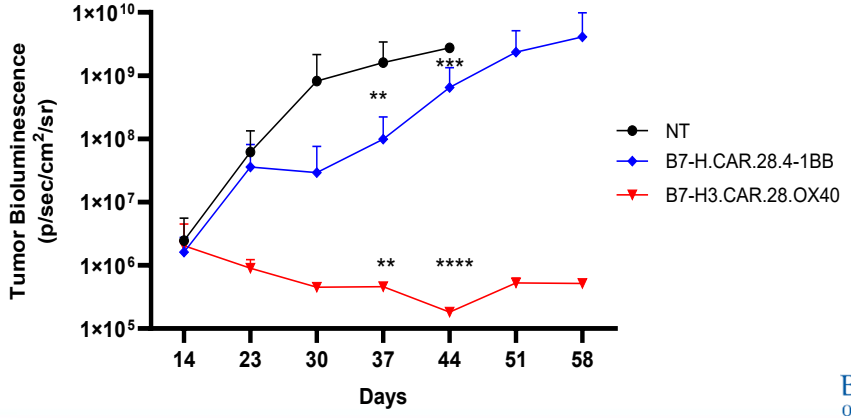
B7-H3.CAR T-cells vs MED-411 cell line *in vivo* anti tumor activity











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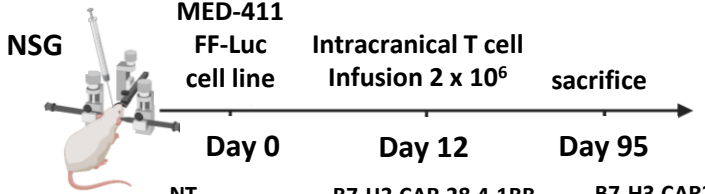
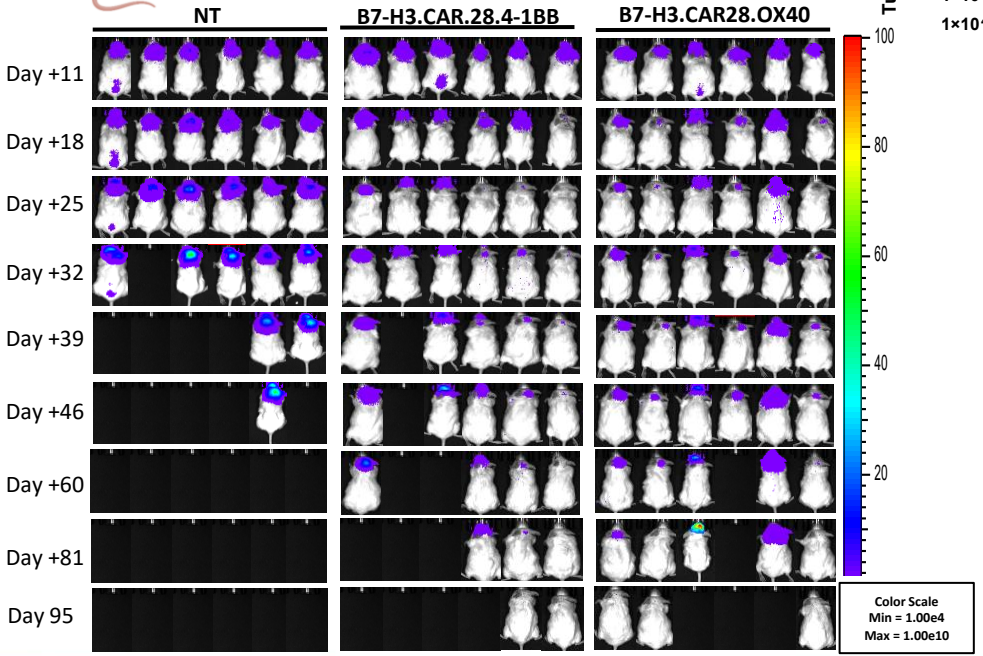
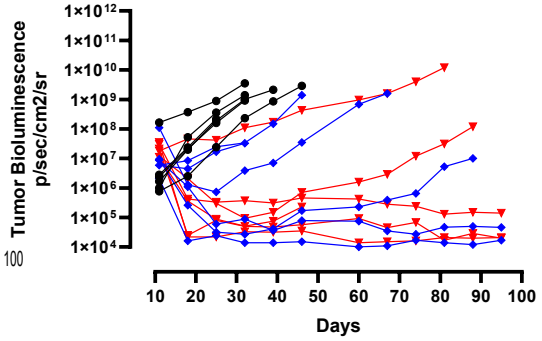
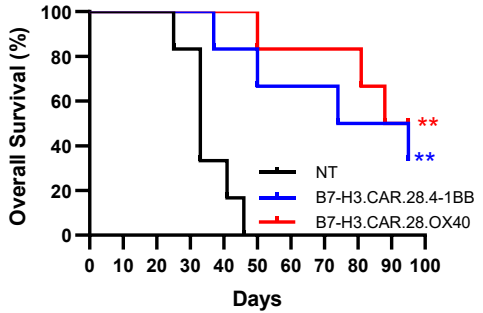
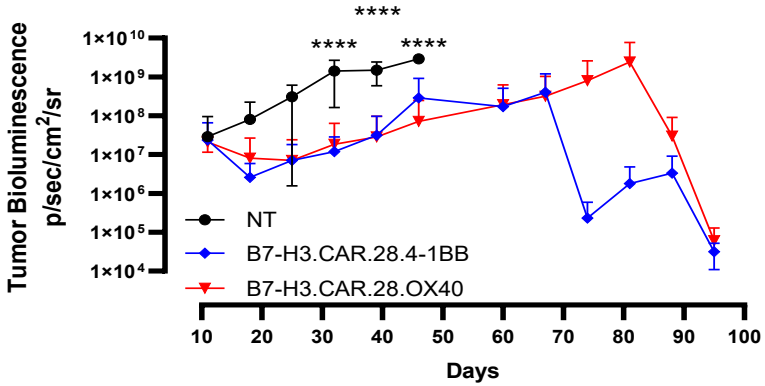
B7-H3.CAR T-cells intracranical administration with reduced dose











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Conclusions

- B7-H3.CAR.CD28.OX40 and B7-H3.CAR.CD28.4-1BB constructs are comparable in terms of transduction level, CD4/CD8 ratio and T cells proliferation.
- B7-H3.CAR.CD28.OX40 and B7-H3.CAR.CD28.4-1BB T-cells showed the same cytotoxicity in, *in vitro* assay against different Medulloblastoma cell lines.
- B7-H3.CAR.CD28.OX40 and B7-H3.CAR.CD28.4-1BB are comparable in terms of anti-tumor effect *in vivo* and Overall Survival.
- Based on these results we are starting to move to clinical application with a phase I clinical trial

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