

Terapia con cellule CAR-T anti-B7-H3 nella leucemia mieloide acuta: evidenze precliniche a sostegno della traslazione clinica

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AIEOP MEDICI
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HILTON GARDEN INN

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

Definition

Clonal expansion of immature myeloid progenitors



Heterogeneity

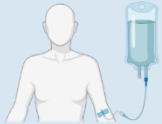
Genomic



Different mutations (SNPs, insertions, deletions or genome rearrangements)

Therapeutic options

Chemotherapy



"7+3" regimen (cytarabine for 7 days + anthracycline for 3 days)

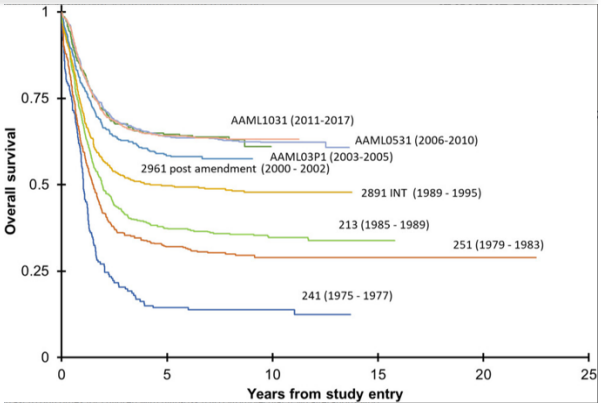
Hematopoietic Stem Cell Transplantation



Targeted Therapies



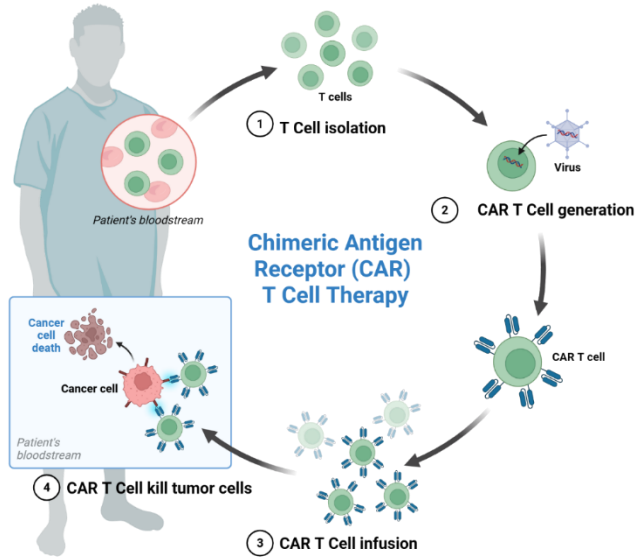
Development of drugs against specific genetic lesions (FLT3 inhibitors, IDH1/IDH2 inhibitors, BCL2 inhibitor)



Overall survival
<70% in children

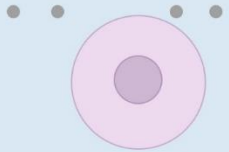
Pediatr Blood Cancer. 2023 Jul 21;70(Suppl 6):e30584

B7-H3 as promising target in AML CAR-T therapy



B cell malignancies

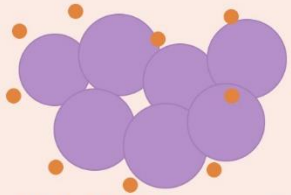
Normal tissues



Limited B7-H3 expression

Restricted expression in most normal tissues

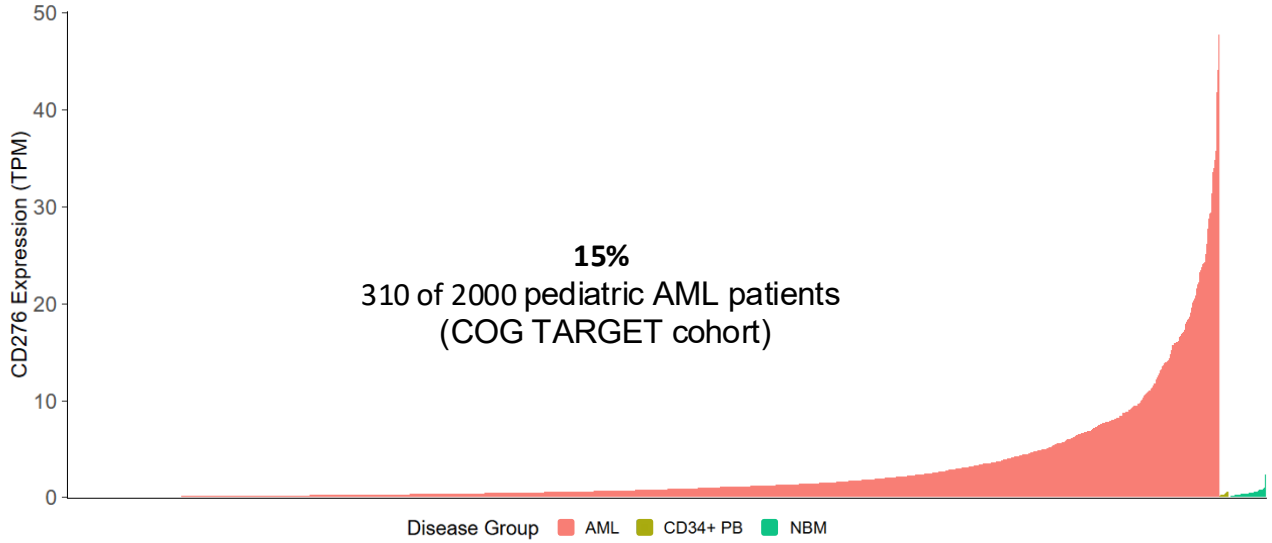
AML & leukemic stem cells



High B7-H3 expression

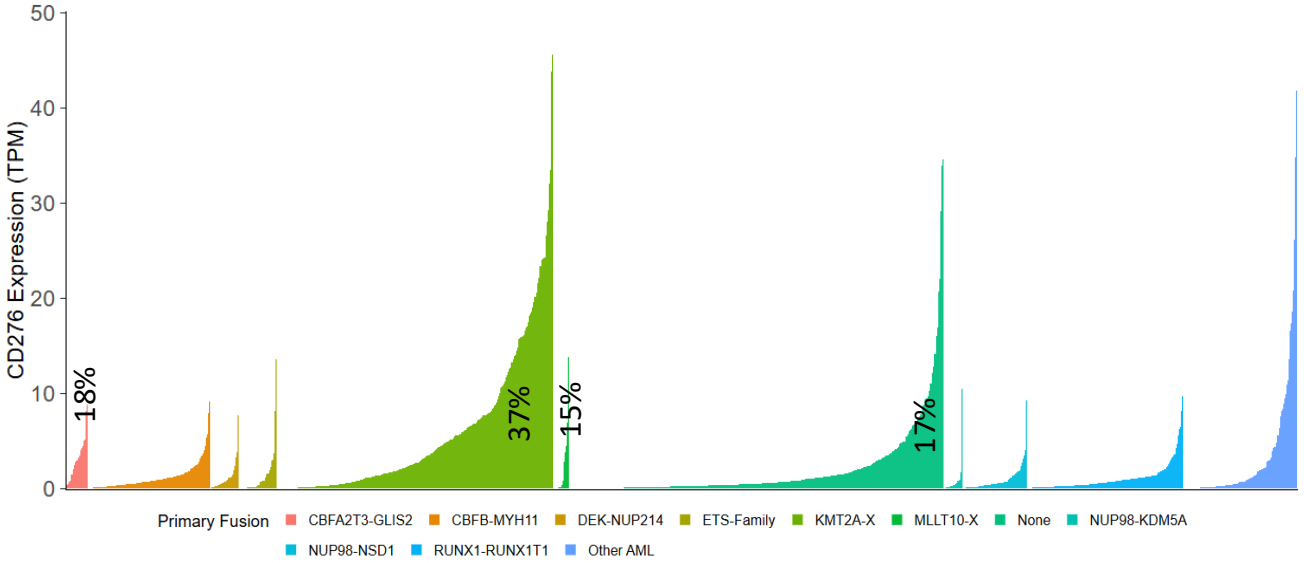
Enriched in AML subsets and leukemic stem cells

B7-H3 expression in AML



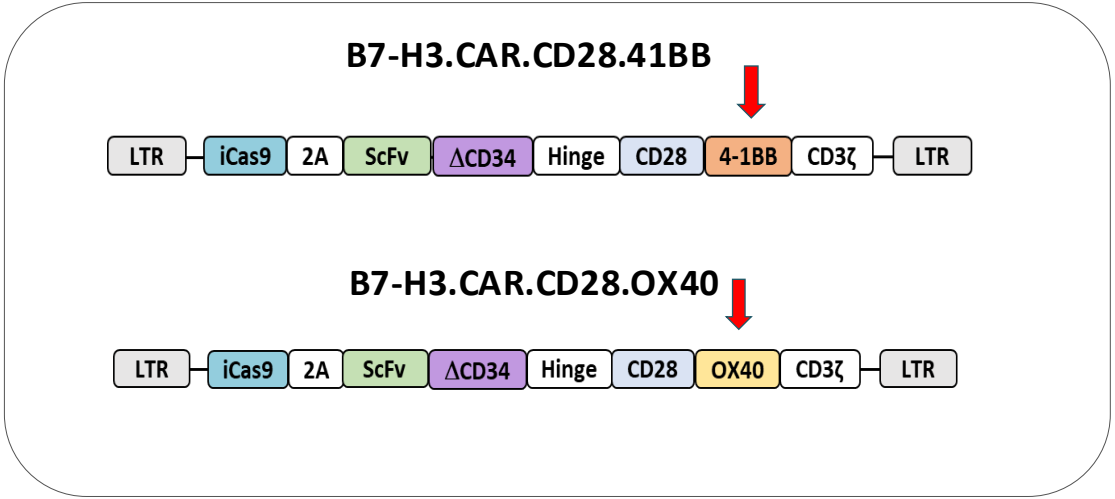
Thanks to
Prof Meshinchi database
"Meshinchi Lab DataViz"

B7-H3 expression in AML

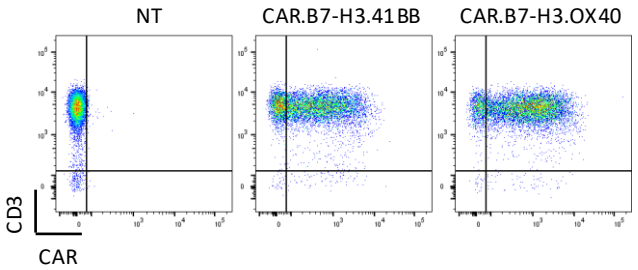


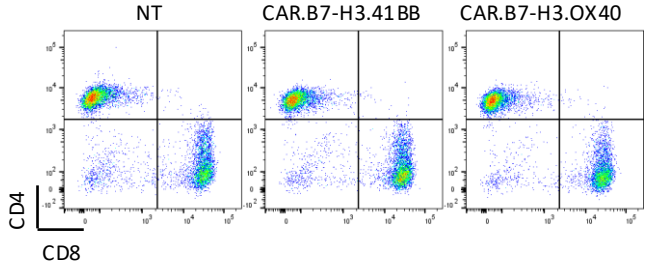
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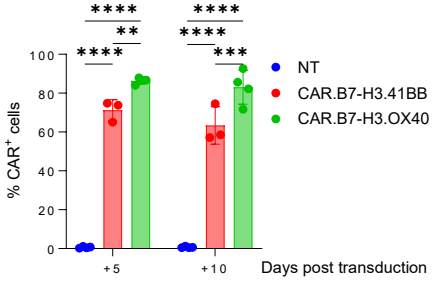
B7-H3 as promising target in AML CAR-T therapy

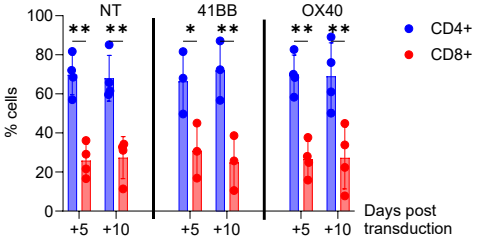


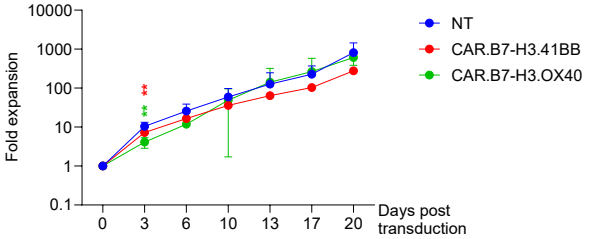
CAR.B7-H3.OX40 and 41BB show a comparable in vitro profile



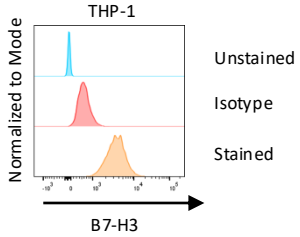


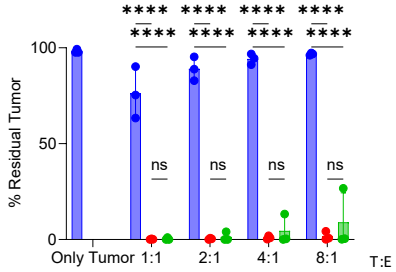


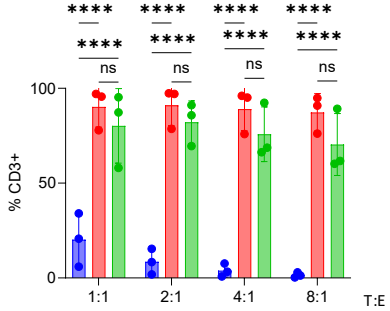


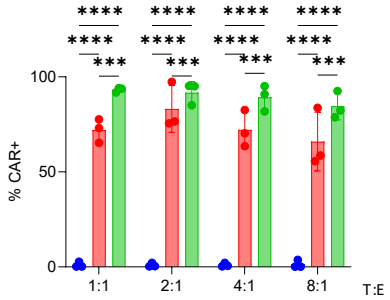


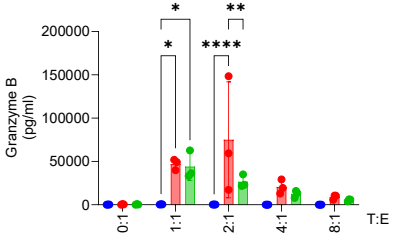
CAR.B7-H3.OX40 and 41BB display potent anti-leukemia activity

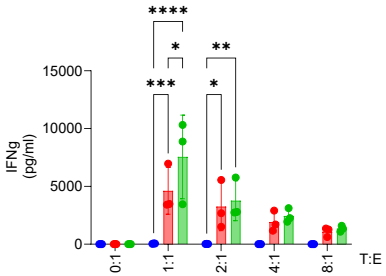


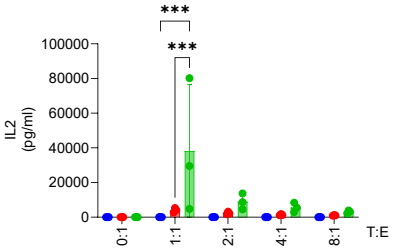


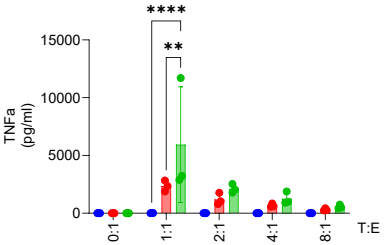








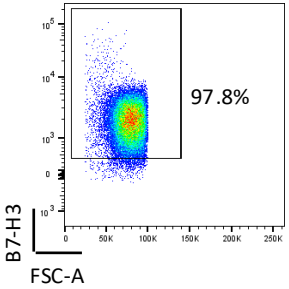


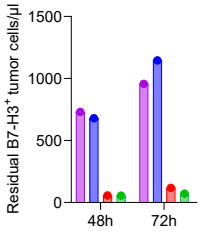


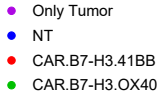
NT CAR.B7-H3.41BB CAR.B7-H3.OX40

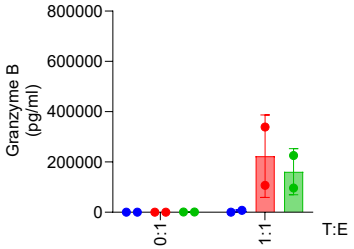
Anti-leukemia activity is preserved against patient-derived samples

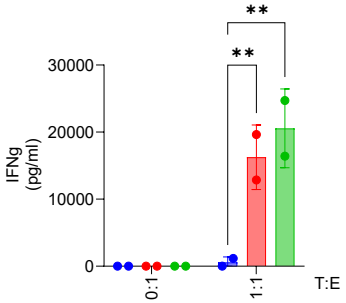
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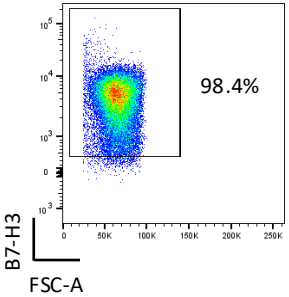


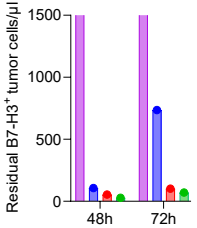


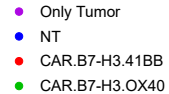


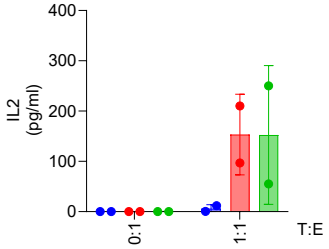


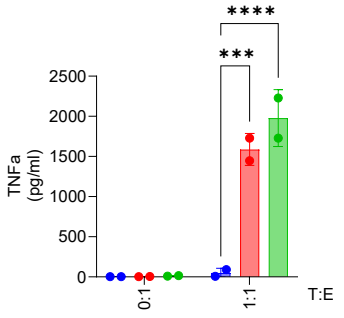
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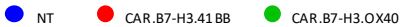




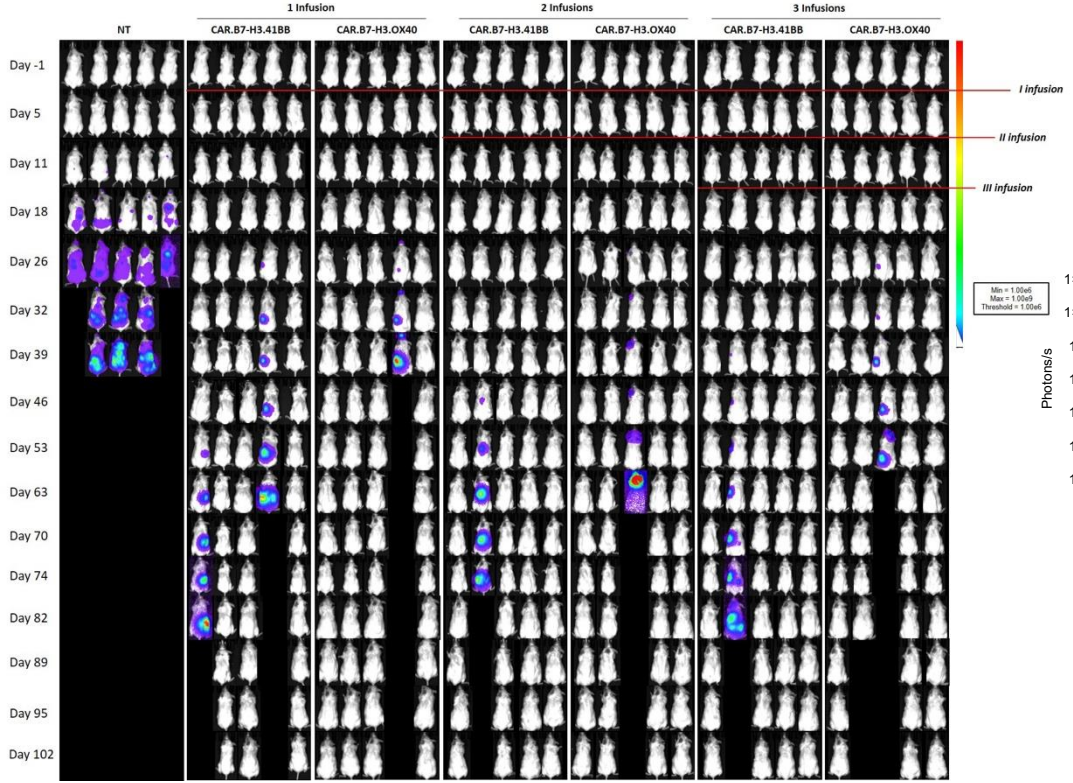


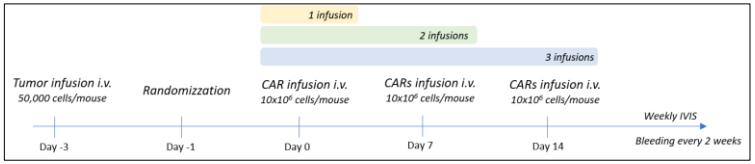


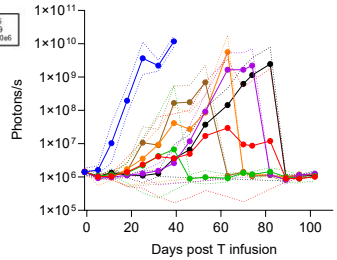


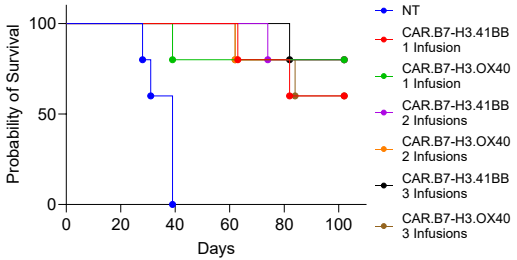


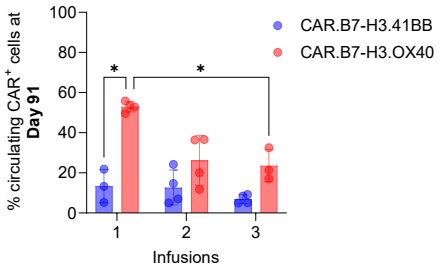
CAR.B7-H3.OX40 and 41BB retain in vivo anti-leukemia activity



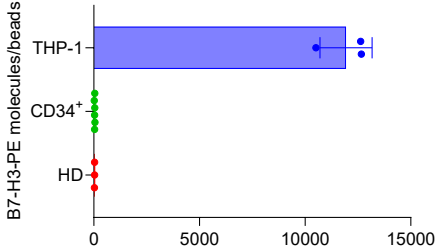


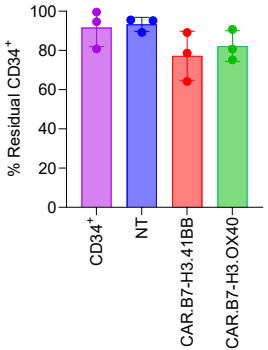


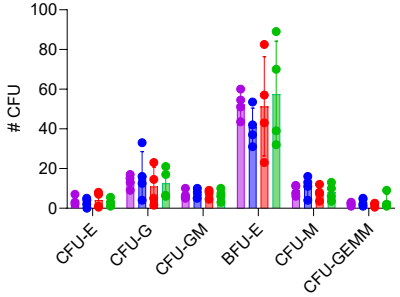




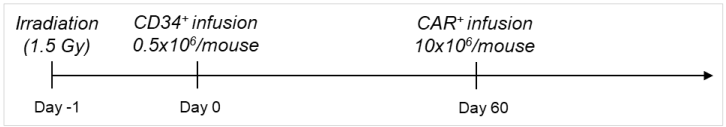
CAR.B7-H3.OX40 and 41BB preserve CD34⁺ viability and clonogenicity

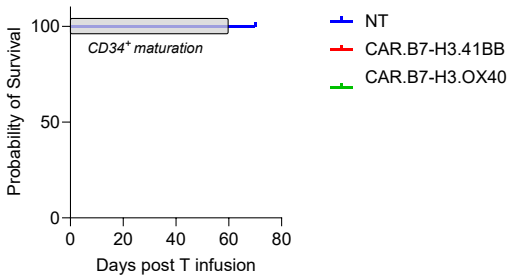


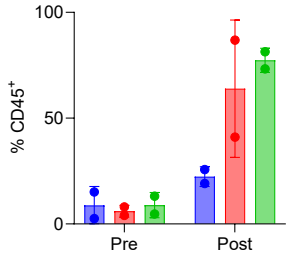


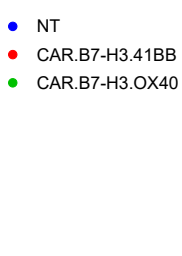


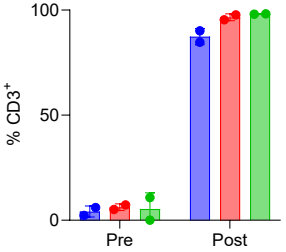
CAR.B7-H3.OX40 and 41BB preserve normal hematopoiesis in humanized model

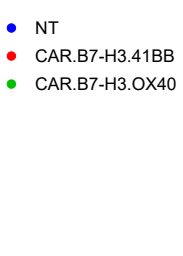


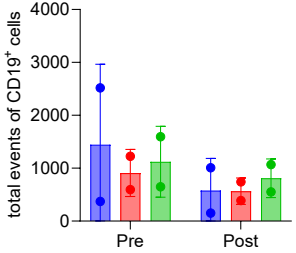


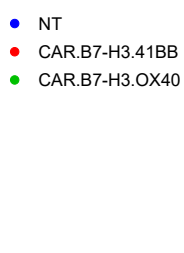


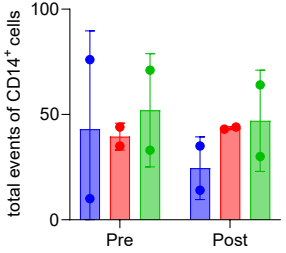


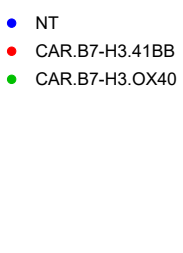












Take home messages

CAR.B7-H3.41BB and OX40 are two valid candidates for AML CAR-T therapy showing comparable therapeutic potential

- **Comparable phenotype**
  Transduction, proliferation, CD4/CD8 distribution
- **Comparable anti-leukemia activity**
  AML cell lines and patient-derived samples
- **Comparable in vivo efficacy**
  with CAR.B7-H3.OX40 cells displaying sustained CAR expression after infusion
- **Preserved safety profile**

Future perspectives

- Validating the performance of CAR.B7-H3.41BB and OX40 in PDX AML models
  Ongoing
- Evaluate B7-H3 expression in a larger cohort of AML patients (diagnosis and relapse)
  Ongoing

Thank you for your kind attention!

Onco-Hematology, Gene and Cell Therapy division, Bambino Gesù Children's Hospital

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