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# Siglec-15 is a Novel Immunomodulatory Protein and Therapeutic Target in Acute Lymphoblastic Leukemia

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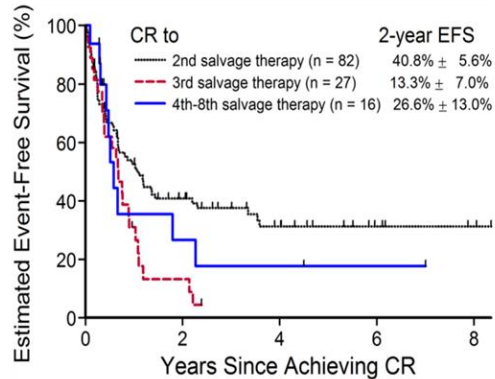
# Disclosures

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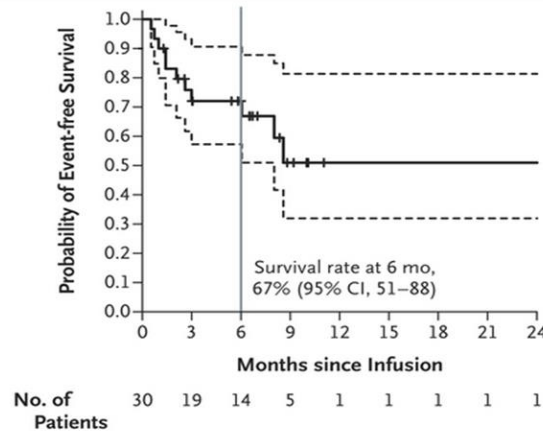
- <sup>3</sup>Authors are employees at NextCure Inc.
- All other authors have no financial disclosures or conflicts of interest with the presented material in this presentation.

# Relapsed acute lymphoblastic leukemia remains a clinical challenge despite promising responses to immunotherapies

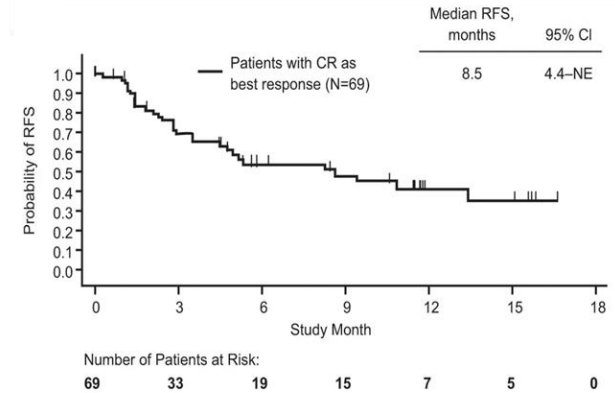
## Multiply R/R Pediatric B-ALL



## CTL019 in R/R Pediatric B-ALL



## Blinatumomab in R/R Pediatric B-ALL

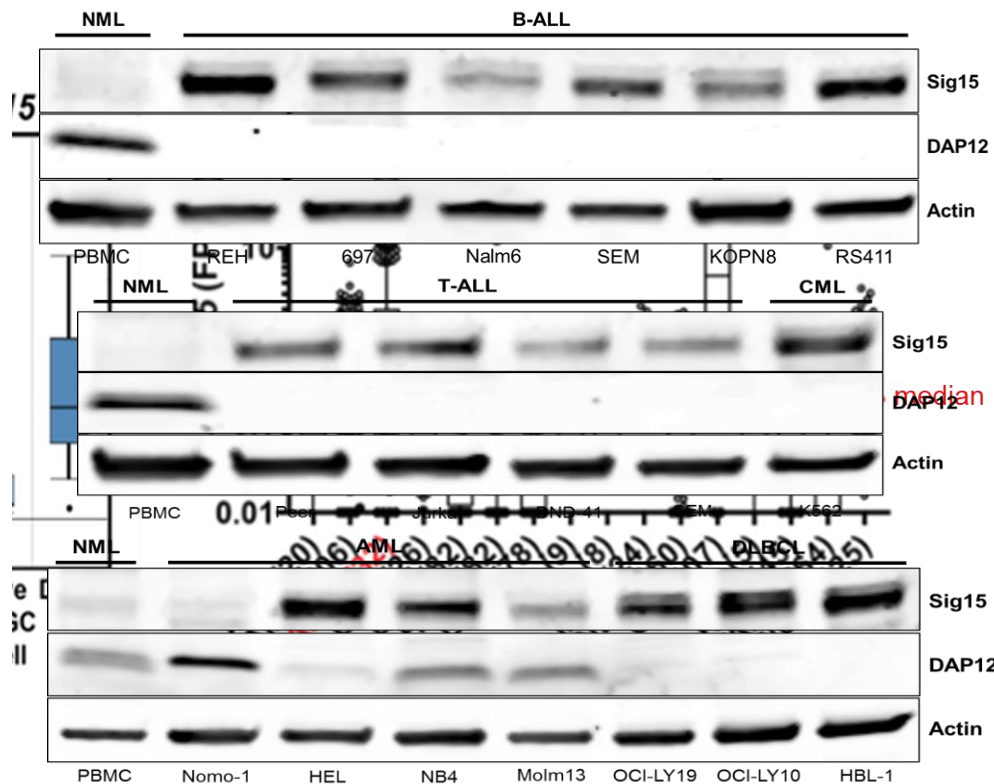
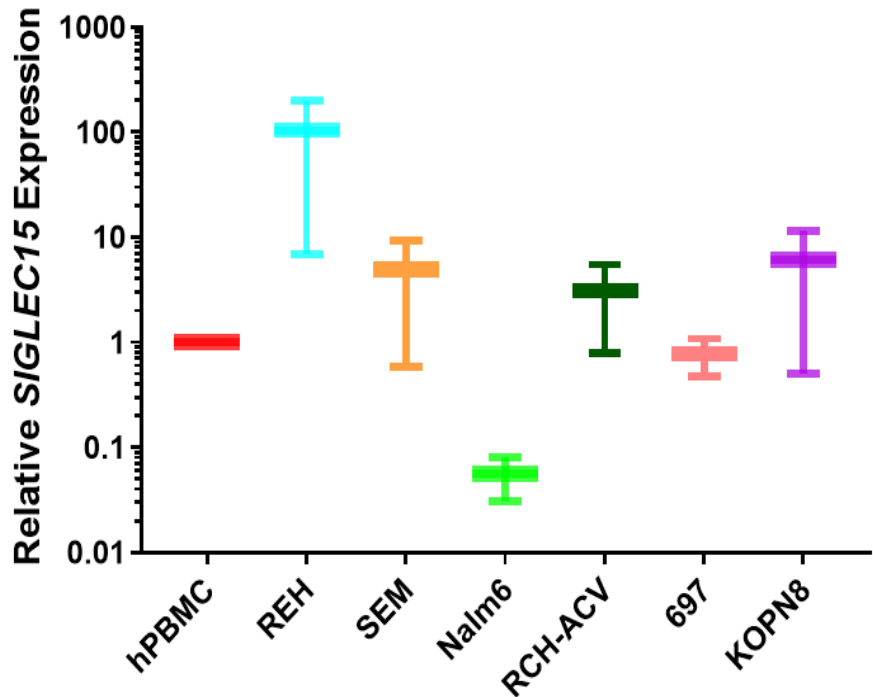


Sun, Malvar, Sposto et al., Leukemia 2018; 32(11):2316-2325.

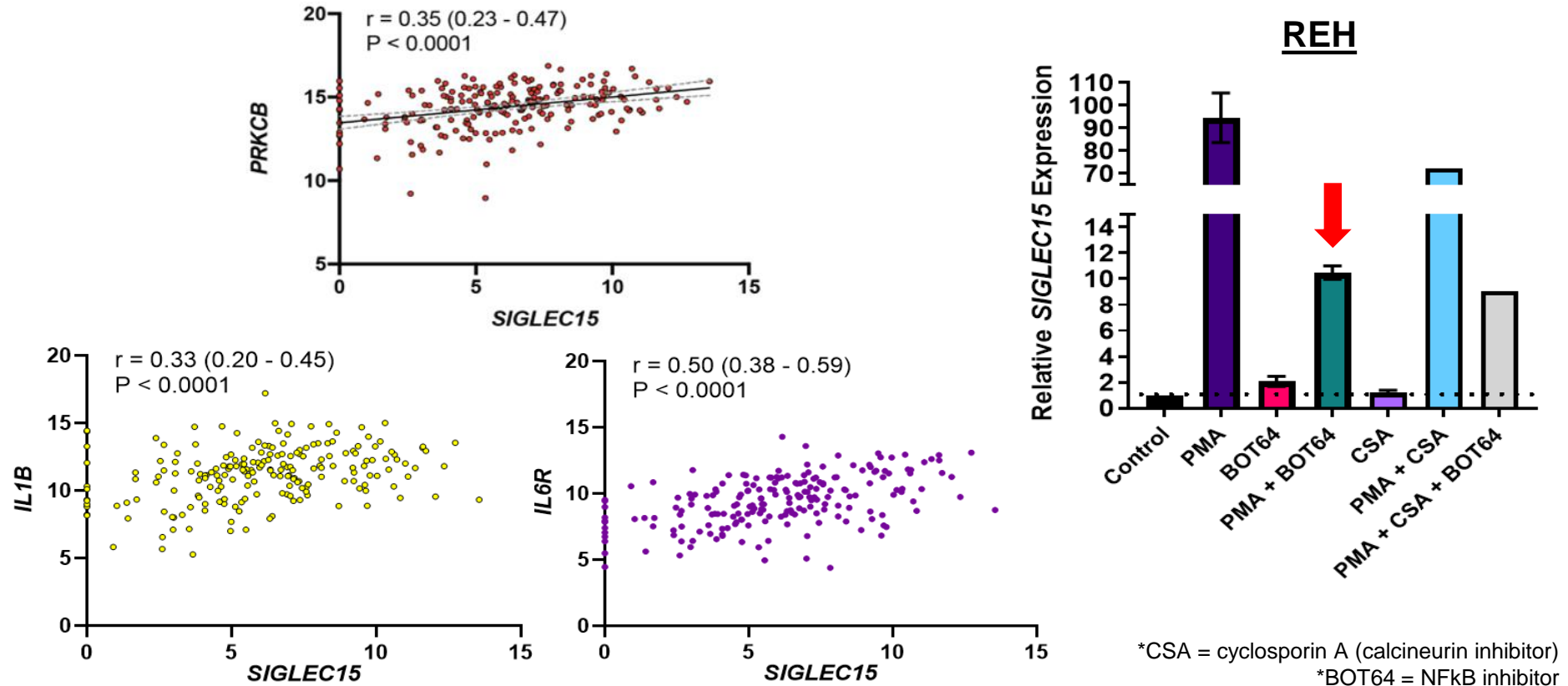
Maude, Frey, Shaw et al., N Engl J Med 2014; 371:1507-1517.

Locatelli, Zugmaier, Mergen et al., Blood Cancer J 2020; 10(77).

# Siglec-15 is widely expressed in hematological malignancies



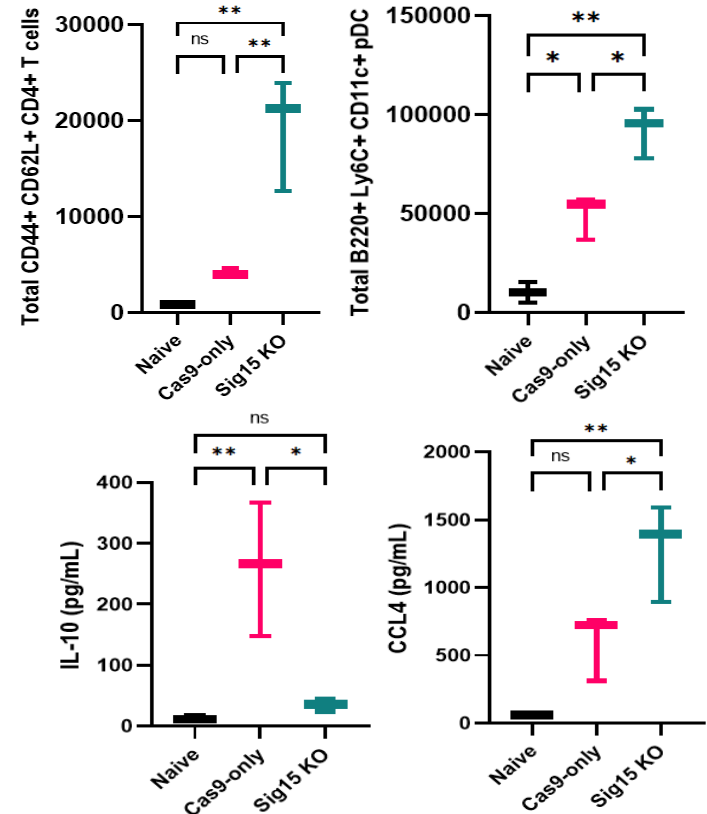
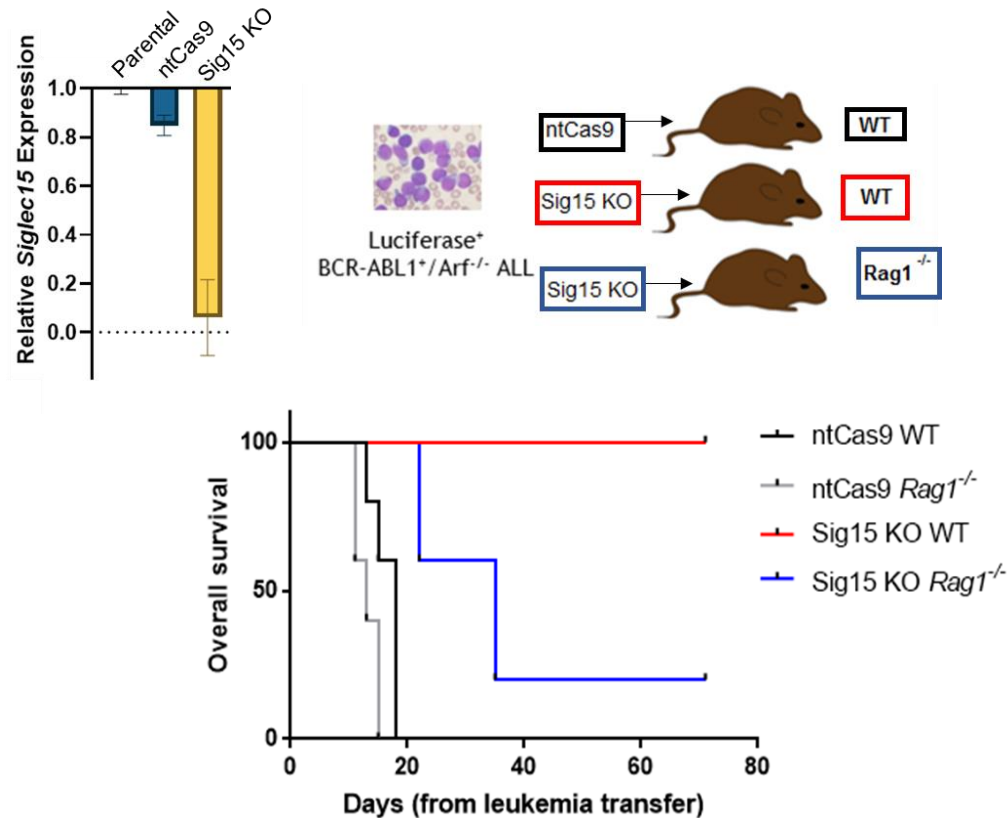
# Siglec-15 expression is regulated by NFκB activation in leukemia



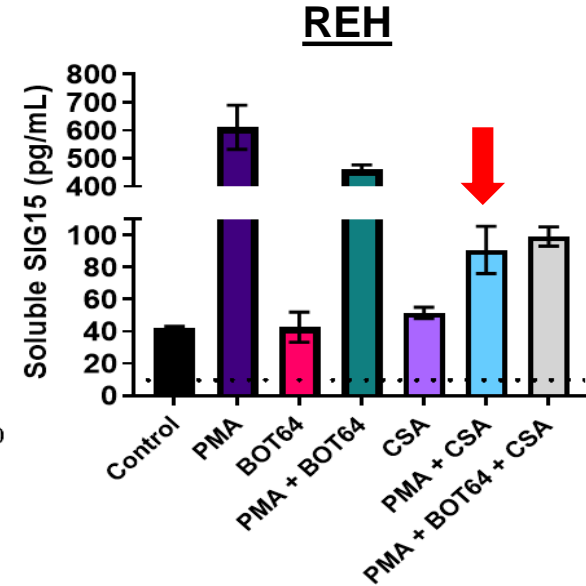
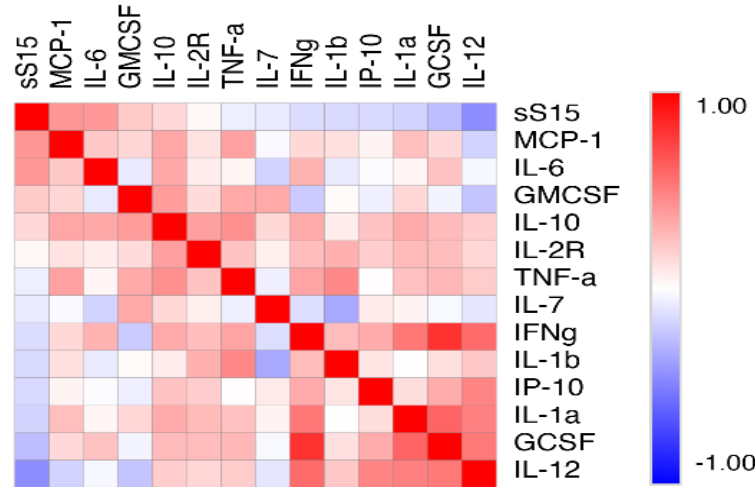
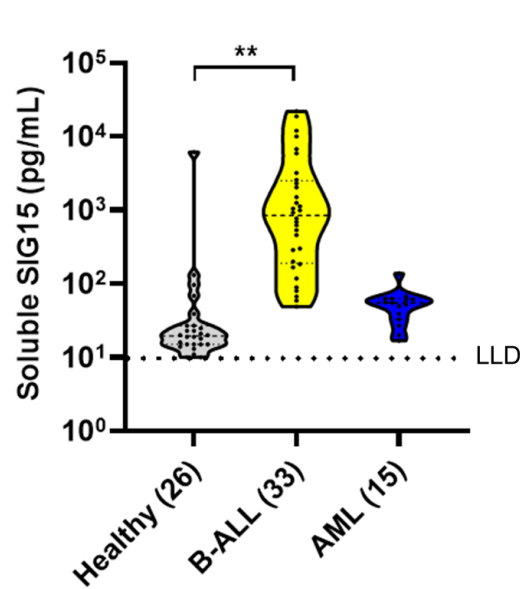
\*CSA = cyclosporin A (calcineurin inhibitor)

\*BOT64 = NFκB inhibitor

# Ablation of Siglec15 results in immune clearance of murine B-ALL



# Soluble Siglec-15 is higher in the plasma of pediatric B-ALL patients



\*CSA = cyclosporin A (calcineurin inhibitor)

\*BOT64 = NF $\kappa$ B inhibitor

# Conclusion

- Sig15 is expressed at higher levels in hematological malignancies such as ALL, AML, and DLBCL
- Sig15 knockout promotes lymphocyte dependent clearance of leukemia cells
- Sig15 expression is regulated by PKC and NFkB activation
- Soluble Sig15 is regulated by calcineurin activity and detectable at higher levels in the plasma of pediatric leukemia patients

