# BISPECIFIC ANTIBODIES ACTIVATE AUTOLOGOUS LEUKEMIA-REACTIVE T CELLS IN ACUTE MYELOID LEUKEMIA

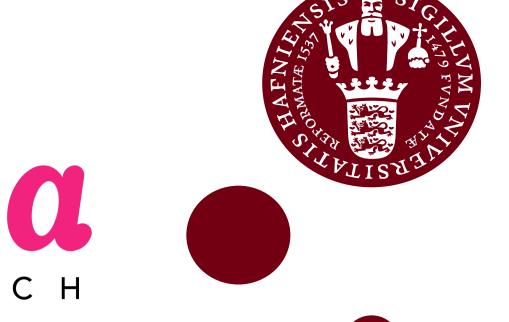
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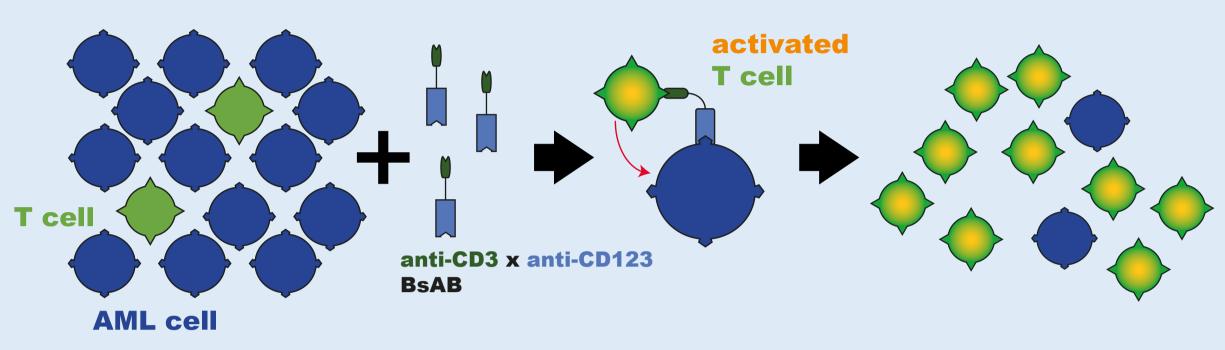




### **Background**

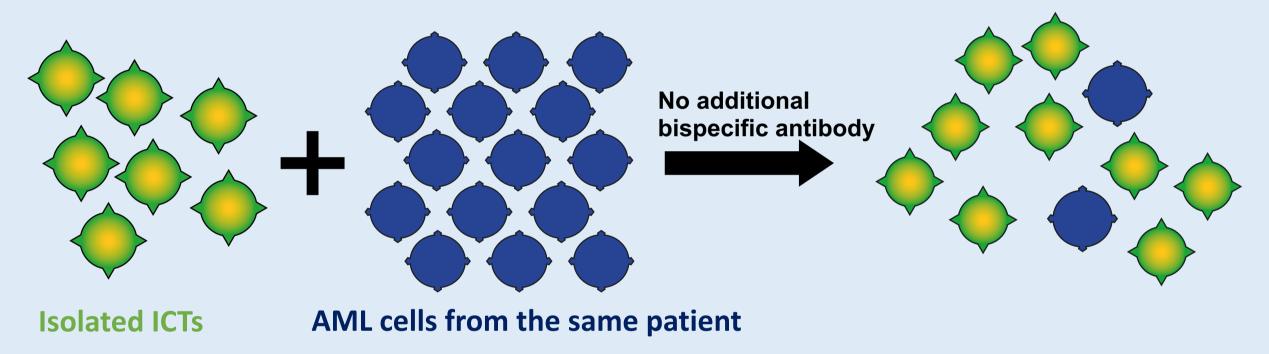
### 1) Immunocoaching:

Adding a bispecific antibody to AML bone marrow mononuclear cells activates endogenous T cells, which leads to AML cell killing and T cell expansion.



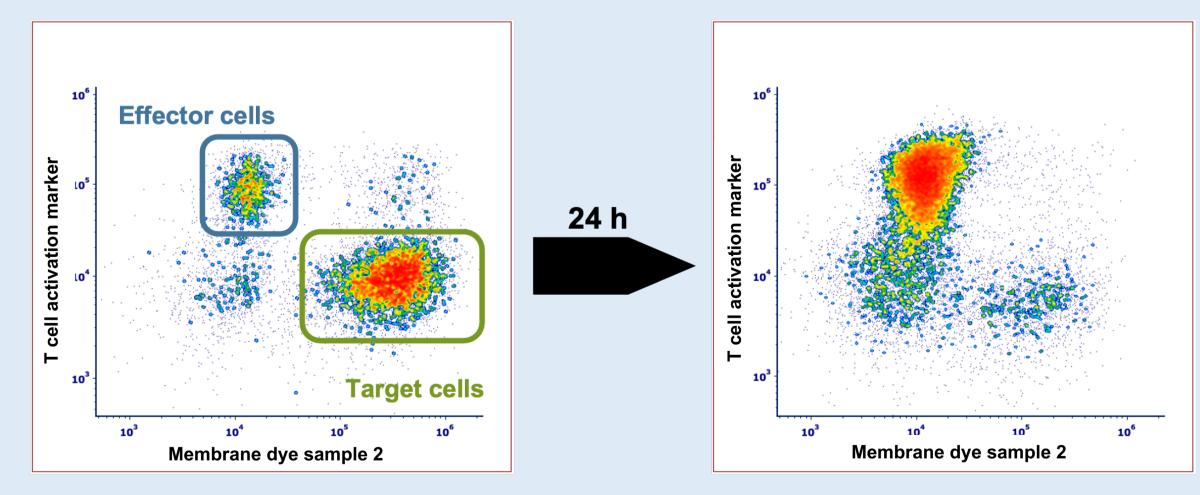
#### 2) ICT-mediated AML killing:

These "immunocoached" T cells (ICTs) are able to kill AML cells without additional bispecific antibody.

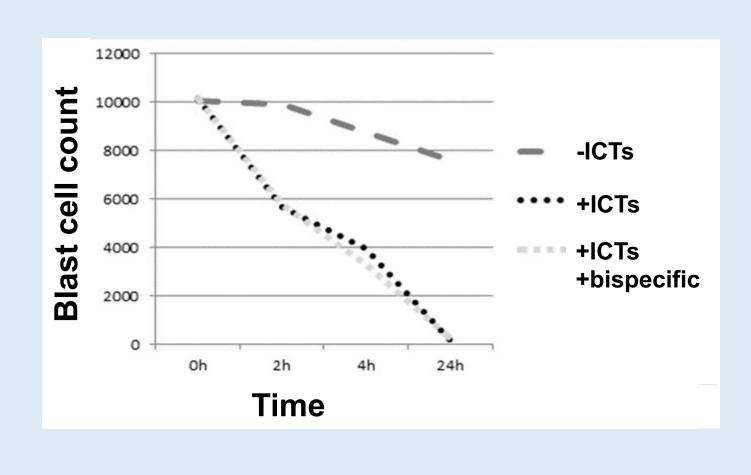


#### <u>In vitro:</u>

ICTs start killing endogenous AML cells within hours, depending on TCR-MHC interaction. T cells expand strongly upon restimulation with AML cells.



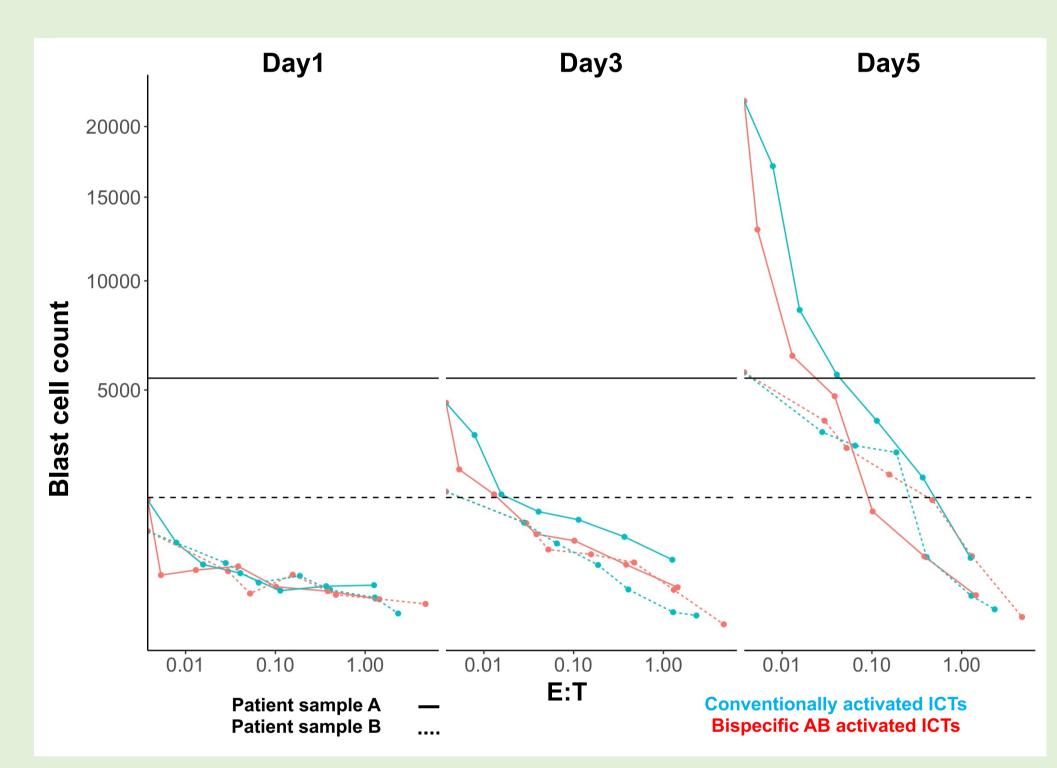
Adding a bispecific antibody does not enhance ICT-mediated killing of AML cells.



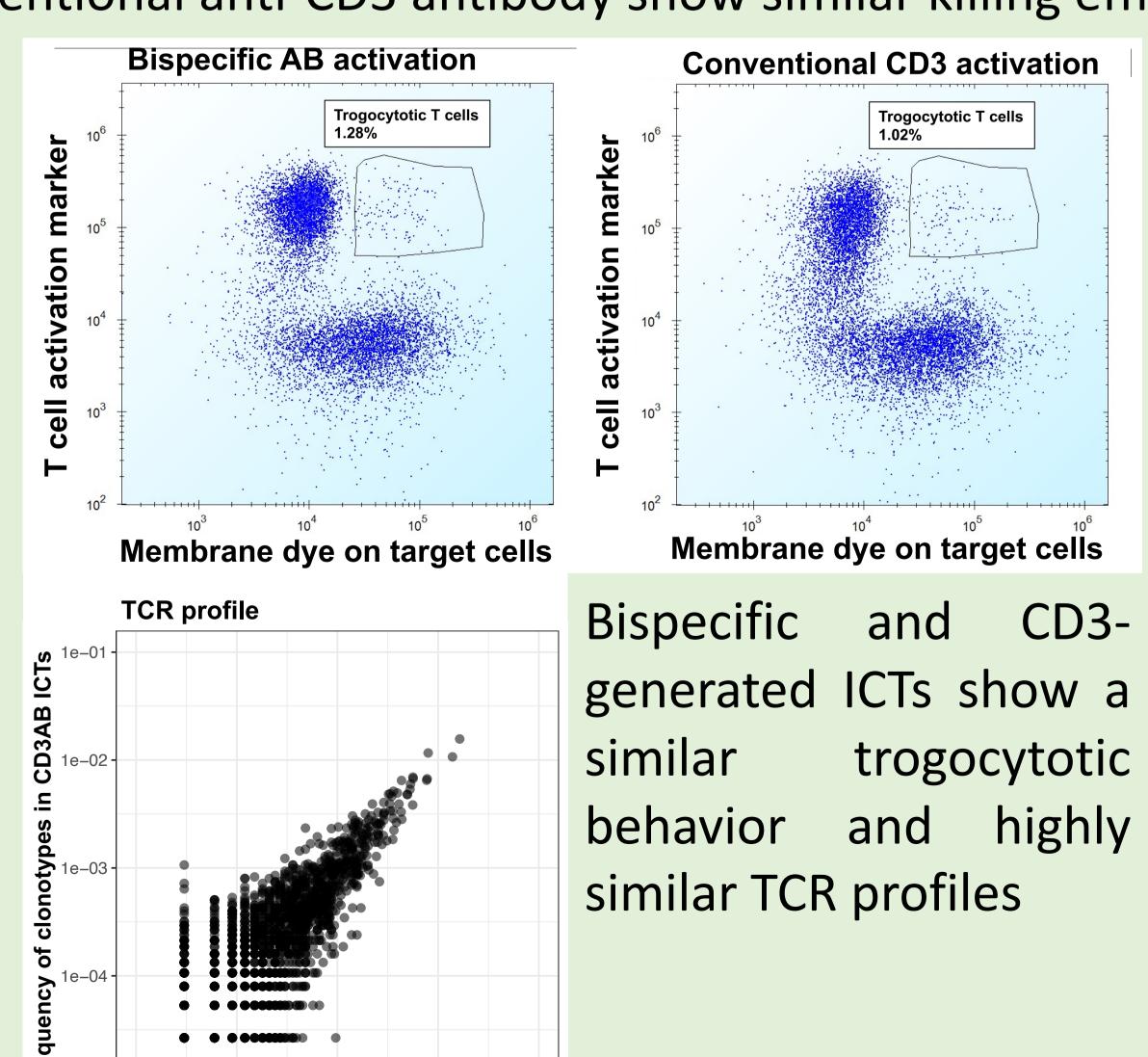
## WHAT IS THE MECHANISM BEHIND IMMUNO-COACHING OF AML BONE MARROW T CELLS?

Immunocoaching by bispecific antibodies works via CD3 stimulation, but is not dependent proximity mechanism.

### How different are bispecific immunocoached T cells from just anti-CD3 activated T cells?



T cells activated with either a bispecific antibody or a conventional anti-CD3 antibody show similar killing efficiency.



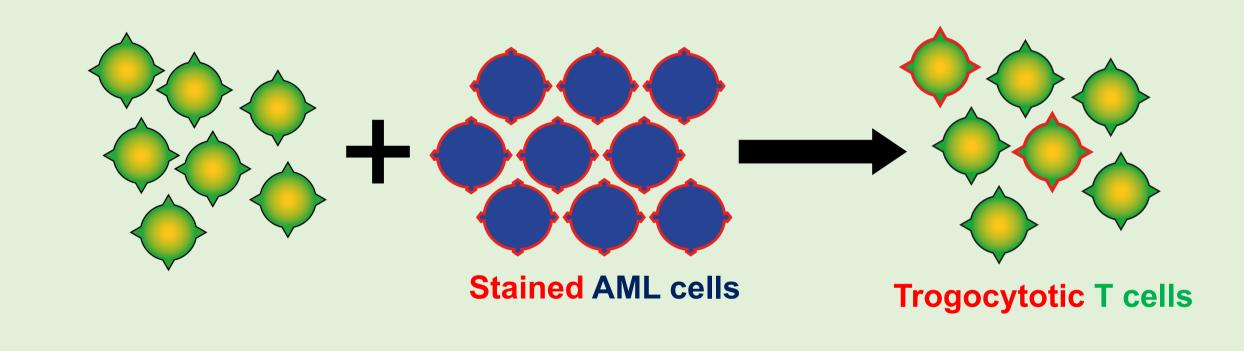
Frequency of clonotypes in bsAB ICTs

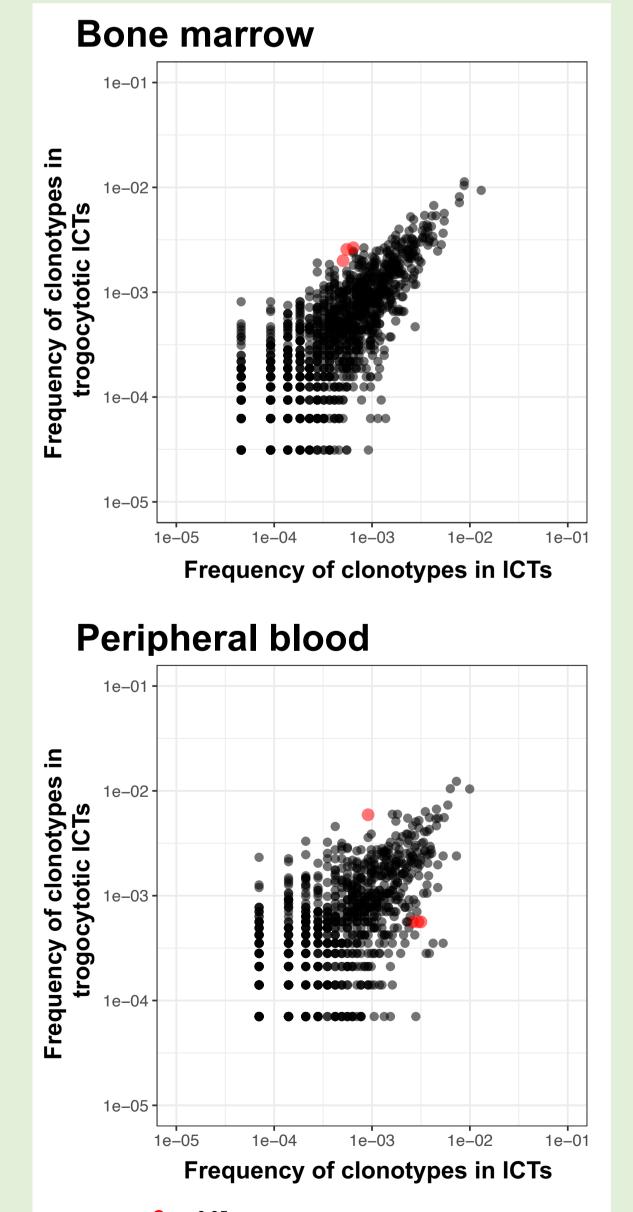
### WHICH ARE THE T CELLS THAT GET IMMUNO COACHED AND CAN MEDIATE AML CELL KILLING?

The bone marrow of AML patients contains T cells that are already targeted against AML cells.

### **How to find those T cells that directly target the AML cells?**

Trogocytosis: Transfer of plasma membrane from target cell to T cell. As ICT-mediated killing this process is depending on the TCR-MHC interaction.





Most ICT clones that are derived from AML patient bone marrow samples are also found in the trogocytotic population with very similar abundancies, arguing that most T cells in the AML bone marrow already are AML cell targeted.

In comparison, several ICT clones derived from the same patient's peripheral blood appear less frequent in the trogocytotic population.

### Next steps:

Repeated restimulation of ICTs with endogenous AML cells to see if we can obtain a clonal selection and thereby even more effective killing.



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