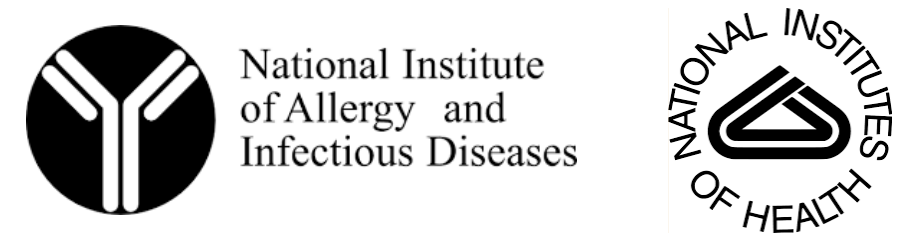


A long-acting form of recombinant human IL-7 shows biologic effect in both a pre-clinical model and a clinical study of Idiopathic CD4 Lymphopenia

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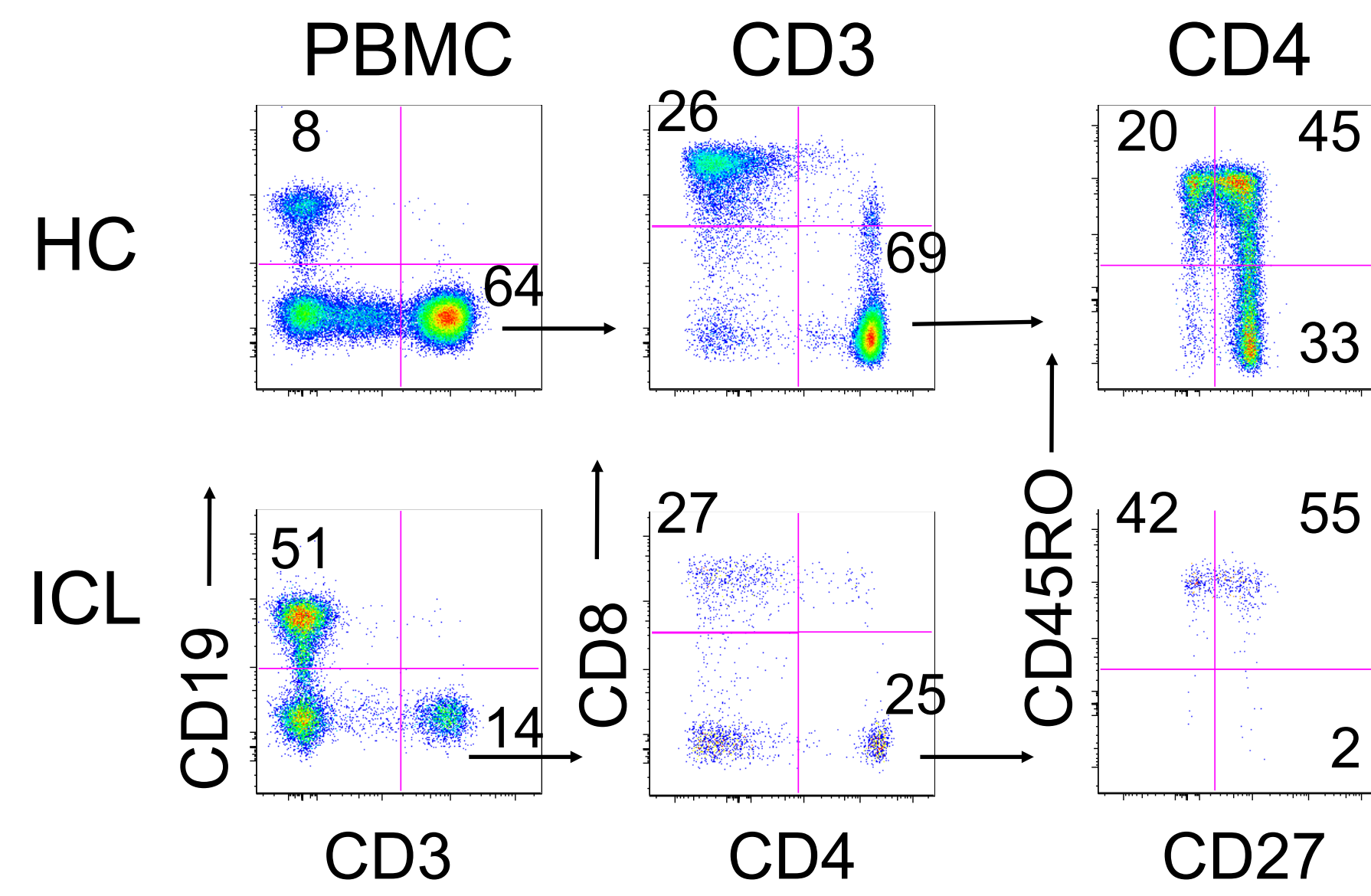
INTRODUCTION

Patients with Idiopathic CD4 Lymphopenia (ICL):

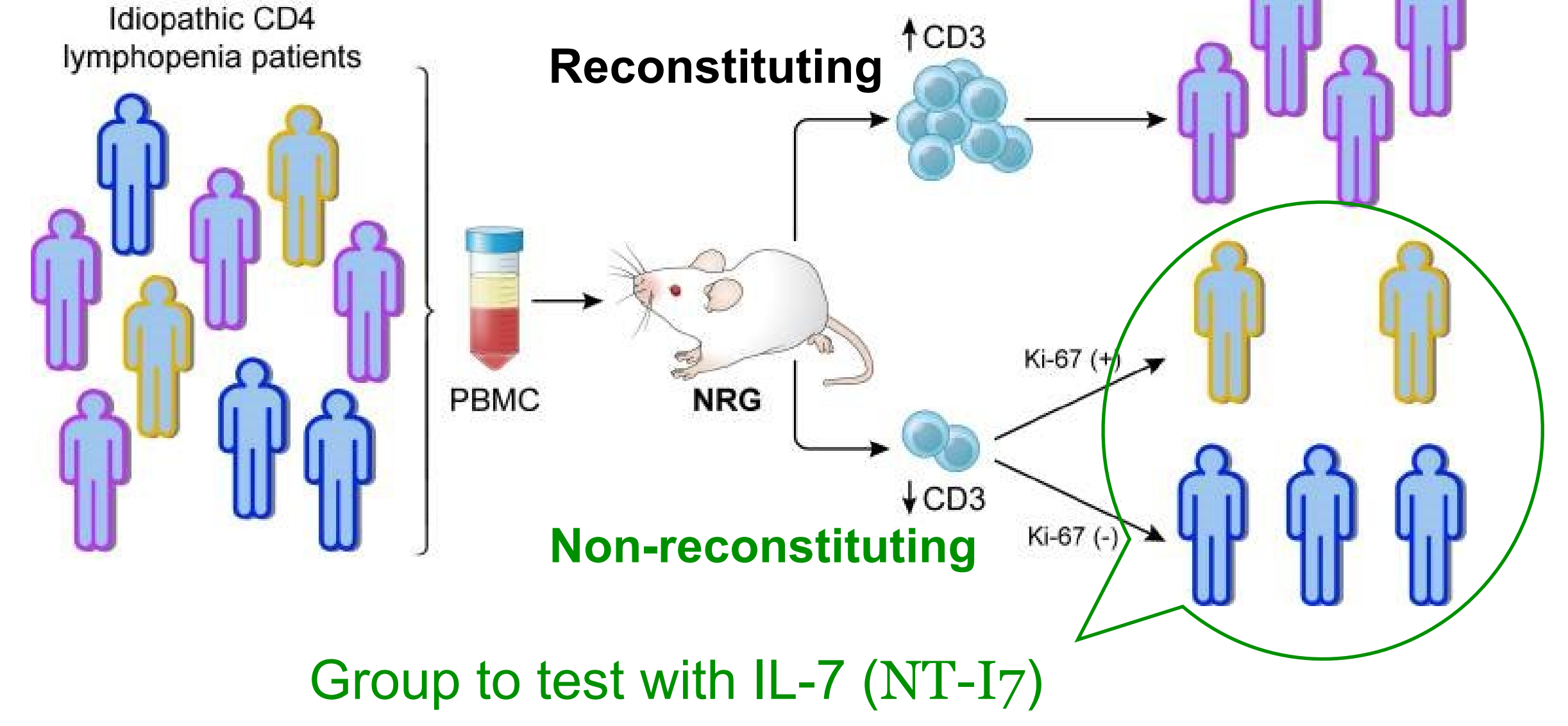
- Have low numbers of CD4 T cells in blood
- 60% of patients also have low numbers of CD8 T cells
- Most develop opportunistic diseases and/or autoimmunity

IL-7 is a homeostatic cytokine critical for T cell proliferation and survival

Example ICL PBMC phenotype



ICL pre-clinical model (Pérez-Díez et al, JCI-Insight, 2019)

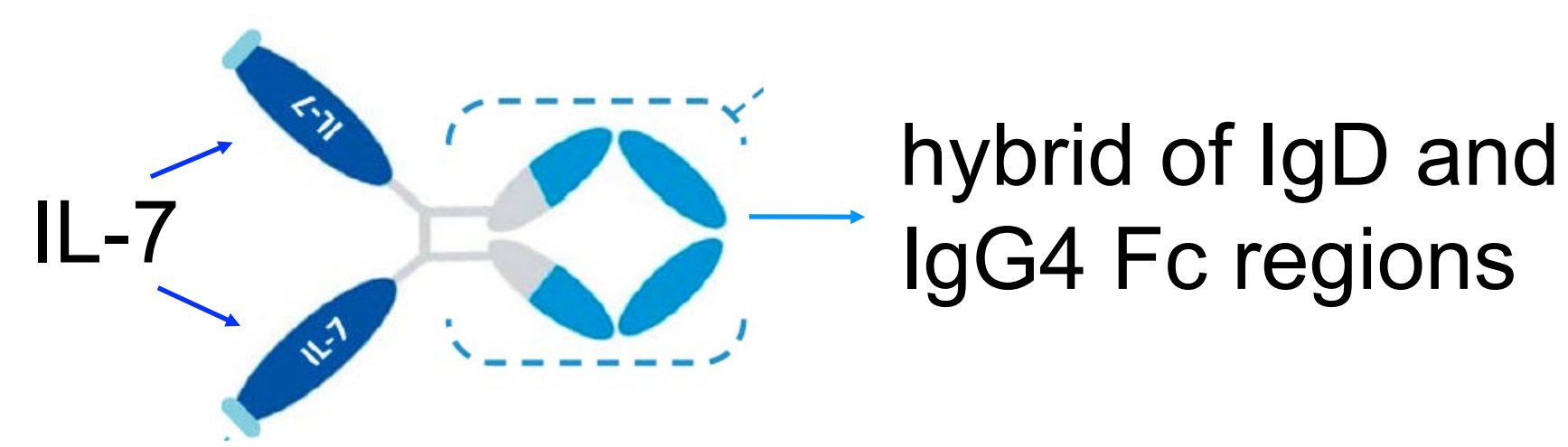


Hypothesis: IL-7 treatment can improve reconstitution and restore lymphocyte numbers in both the pre-clinical and clinical setting

METHODS

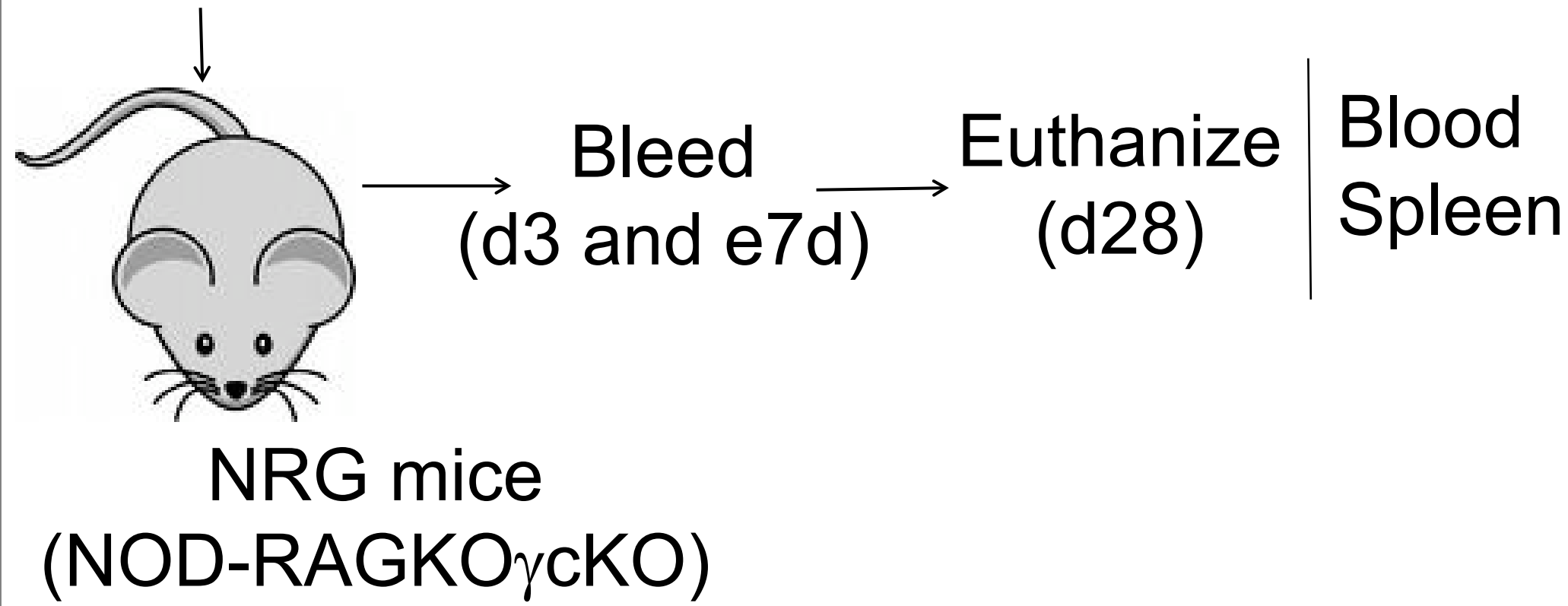
NT-I7 (efineptakin alfa)

A potent, stable and long-acting IL-7 fused to a hyFc platform (rhIL-7-hyFc)



Humanized mouse model

Healthy Control (HC) or **NR ICL PBMC** +/- NT-I7 (IL-7), s.c., day 0



Compare ICL +/- IL-7:

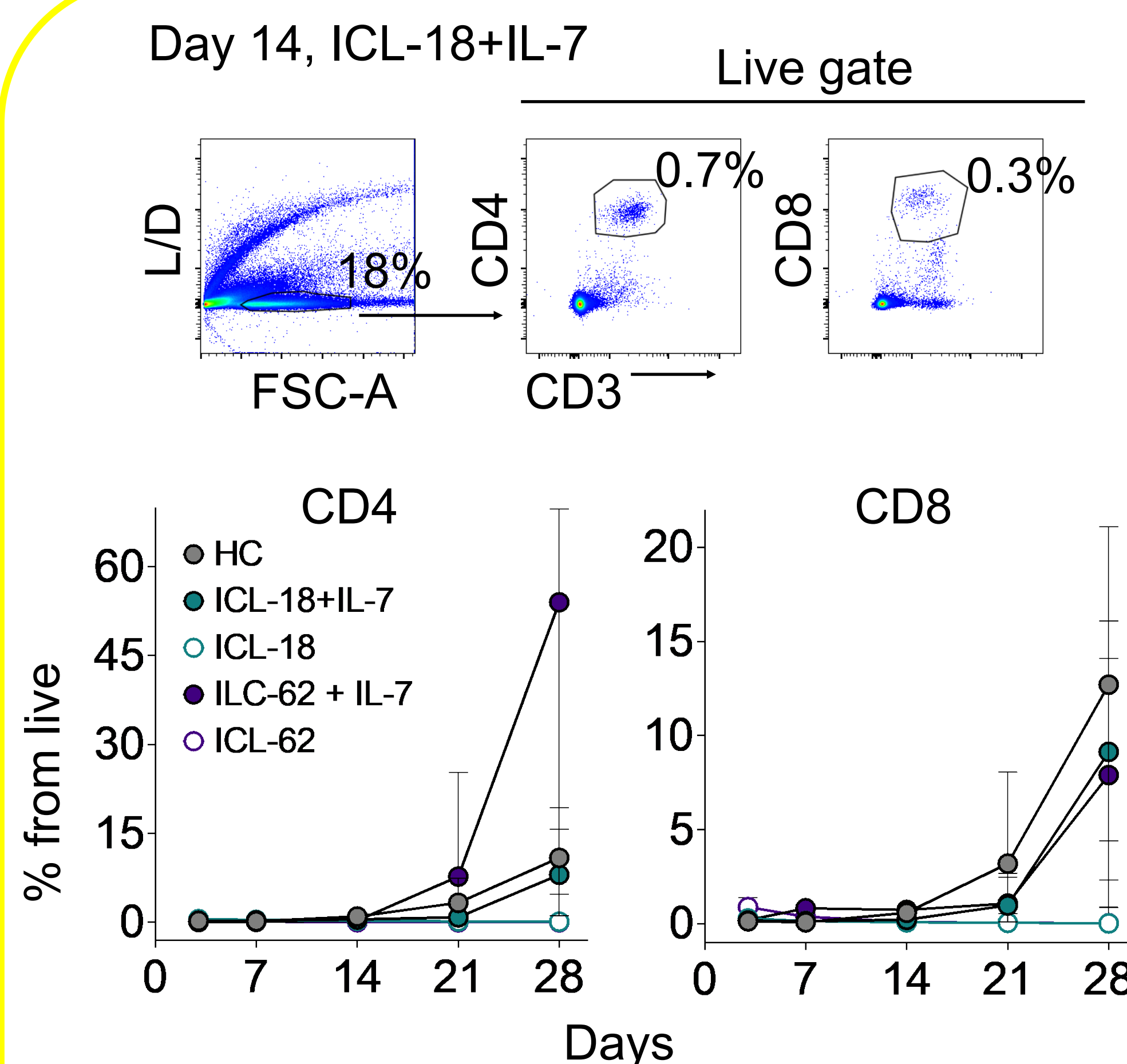
- CD4 and CD8 T cell reconstitution
- Graft versus host disease (GvHD)
- IL-7Rα expression
- TCR clonality

Clinical Study on an ICL patient

-Patient received two doses of NT-I7 (400 µg/kg) three months apart.

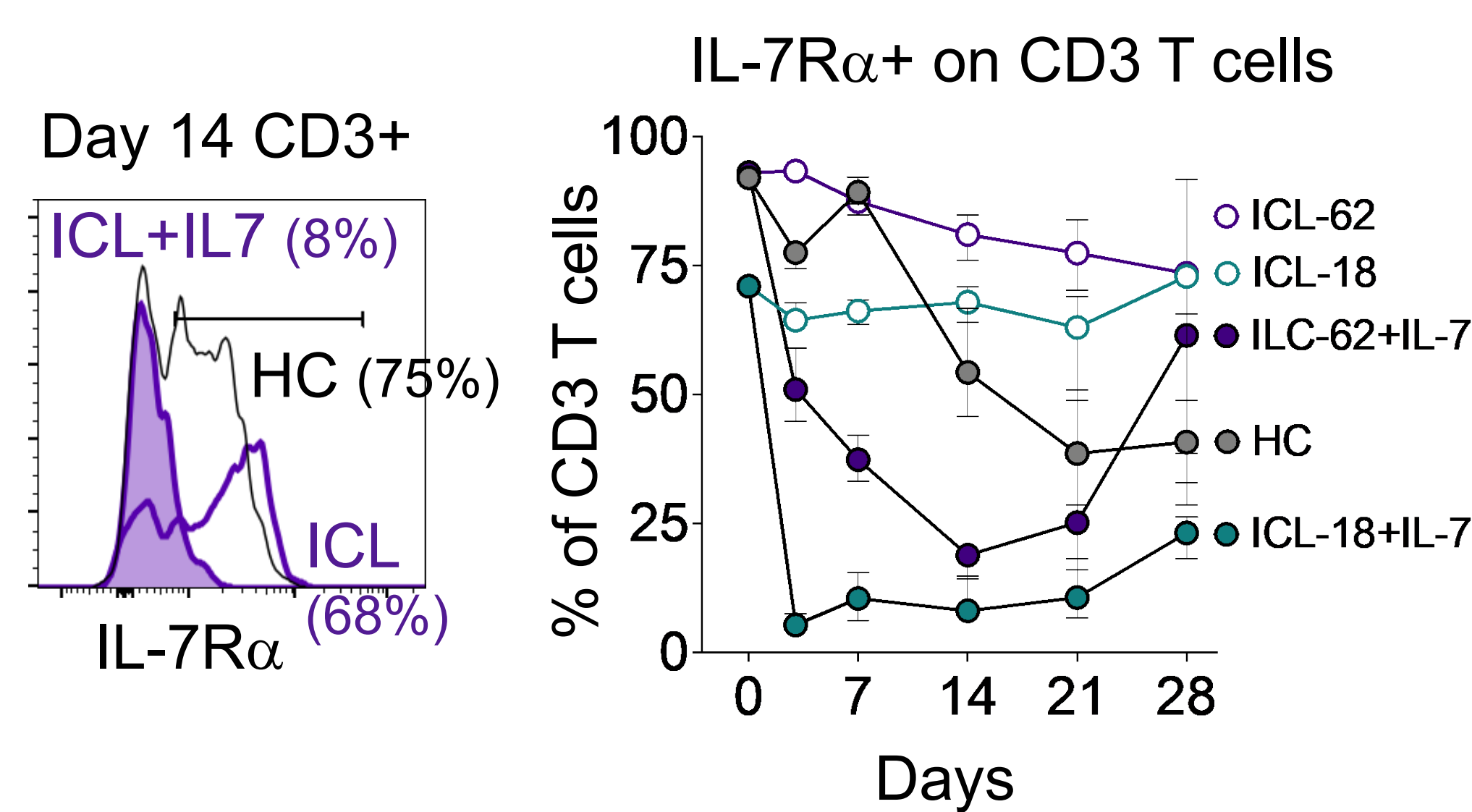
-Number of lymphocytes in peripheral blood was evaluated by flow-cytometry.

BLOOD humanized mice



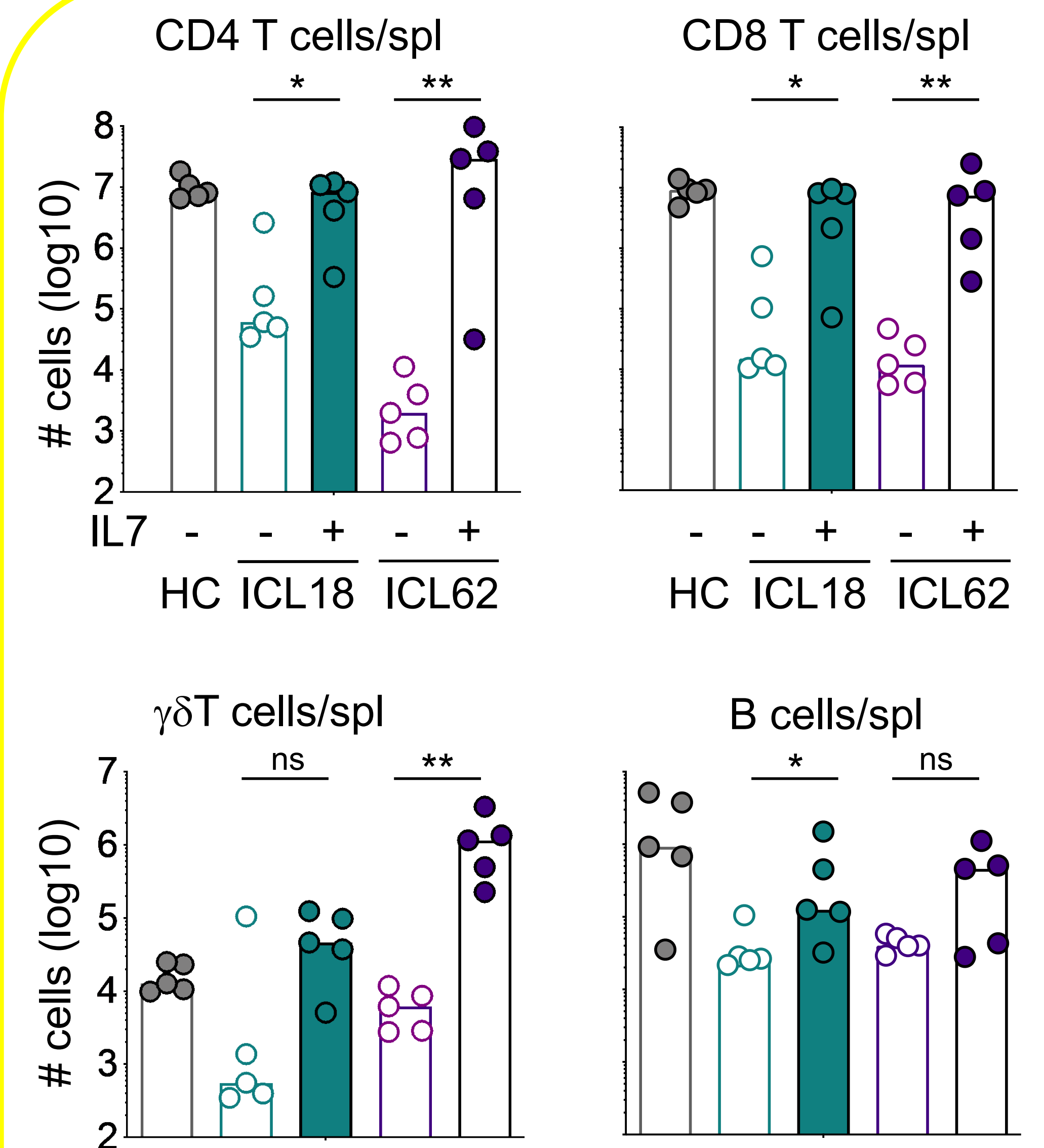
NT-I7 treatment induces expansion of ICL CD3 T cells in blood

IL-7Rα downregulation:



NT-I7 treatment downregulates IL-7Rα on ICL CD3 T cells for at least 2 weeks

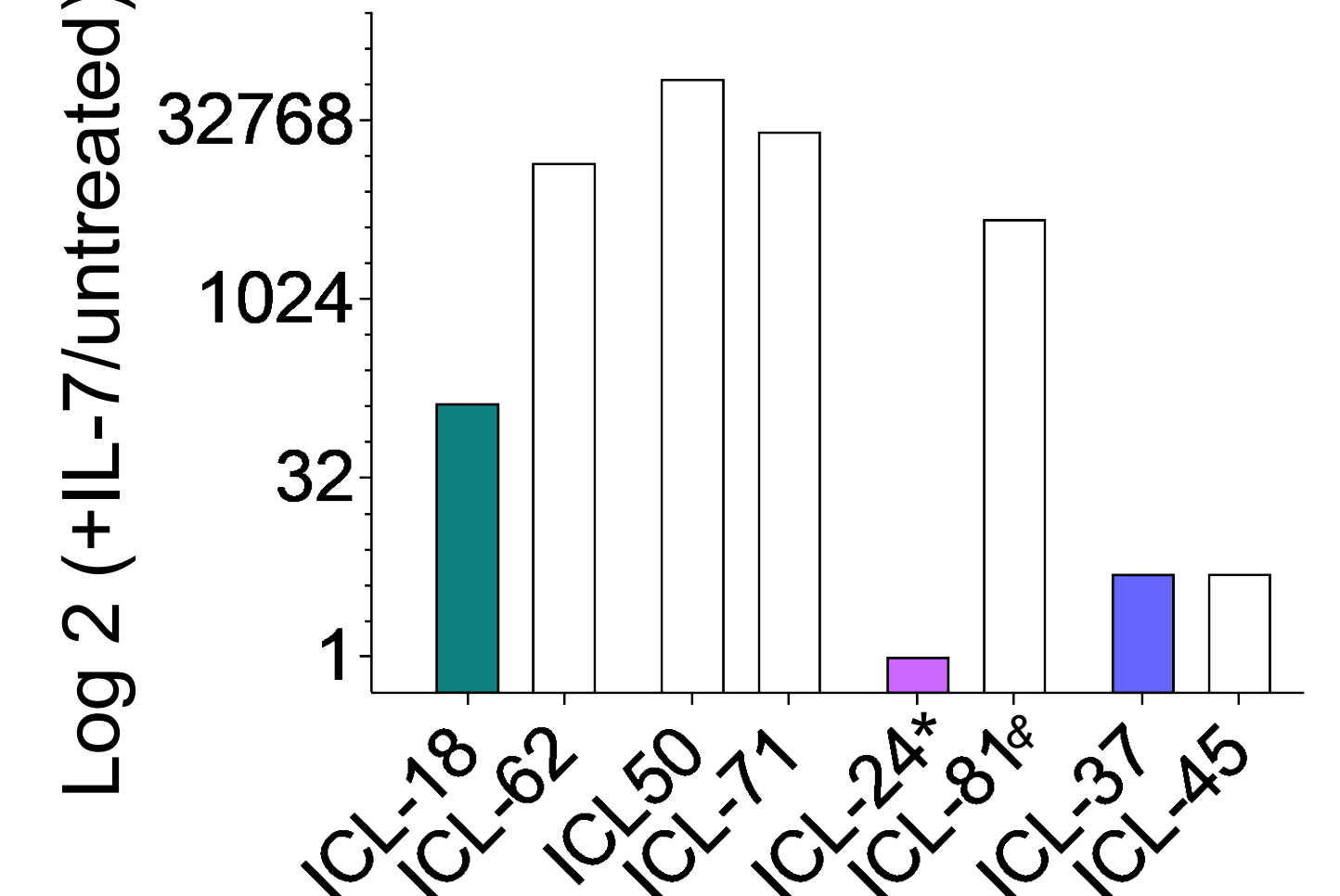
SPLEEN humanized mice day 28



*, p<0.05 and **, p<0.01 by two tailed Mann-Whitney test

In spleen, NT-I7 restores ICL lymphocyte reconstitution reaching similar levels to HC donors

Fold increase of CD4 T cells in spleen (all patients tested)



*This patient reconstituted well untreated mice
 &Patient treated in the clinic (shown on the left graph)

NT-I7 restores ICL lymphocyte reconstitution in 7/8 patients tested in the preclinical model

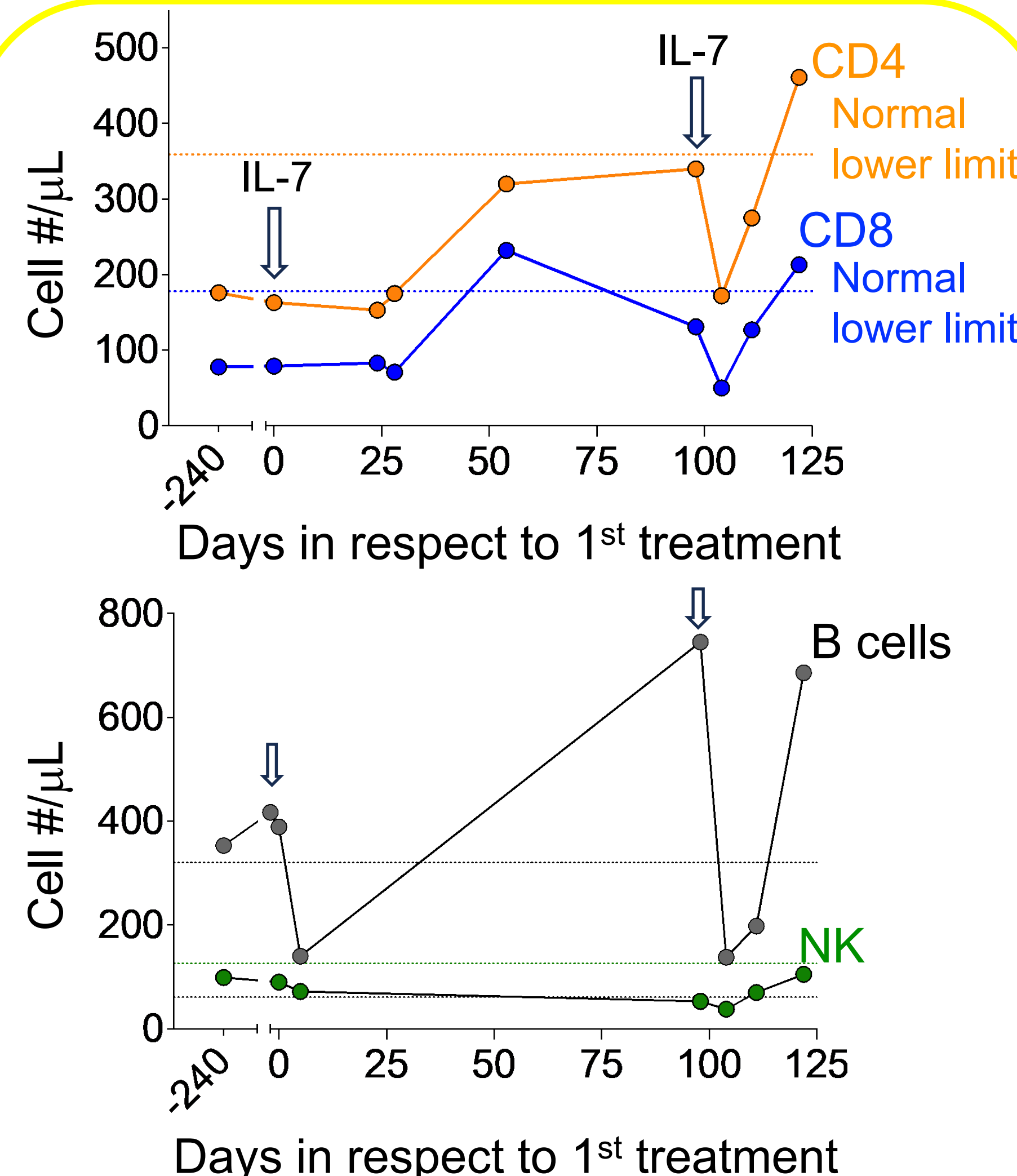
CONCLUSIONS

- A single treatment of NT-I7 (IL-7) restores ICL T cell reconstitution in the hPBMC preclinical model of ICL
- NT-I7 treatment increases TCR repertoire, without significantly increasing Graft versus Host Disease in the preclinical model of ICL
- NT-I7 treatment of an ICL patient was safe and increased lymphocyte numbers in blood, reaching normal levels for both CD4 and CD8 T cells

Altogether, these data suggest NT-I7 has a potential therapeutic role in patients with ICL

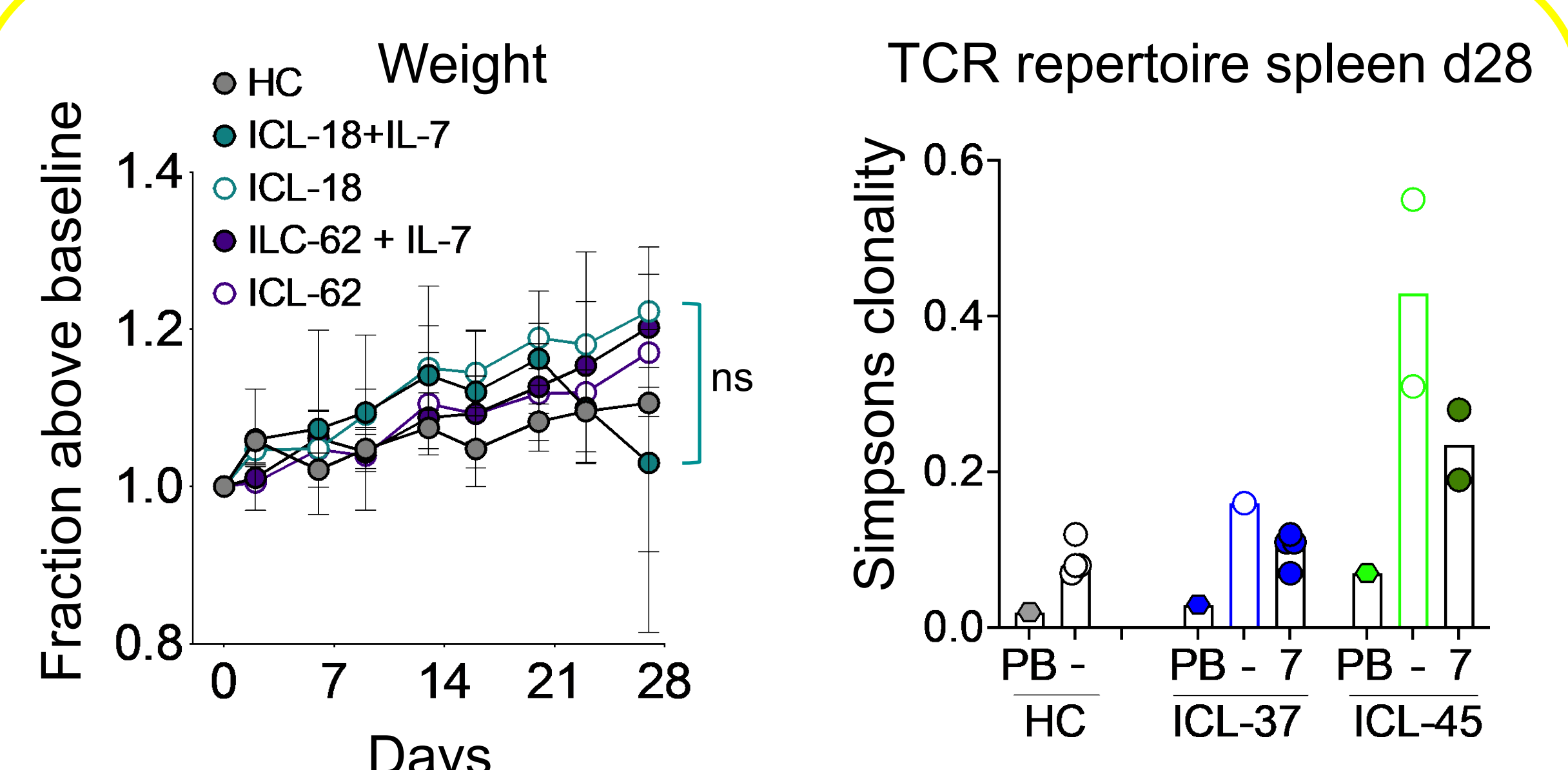
This work was supported by the Intramural Research Program of the NIH, NIAID

ICL-81 PATIENT lymphocyte counts after IL-7 treatment



NT-I7 treatment increased CD4 and CD8 counts as well as B lymphocytes in PBMC from an ICL treated patient

Graft versus Host Disease and TCR clonality in humanized mice



Despite T cell expansion, NT-I7 does not significantly increase GvHD

NT-I7 increases polyclonality of ICL T cells