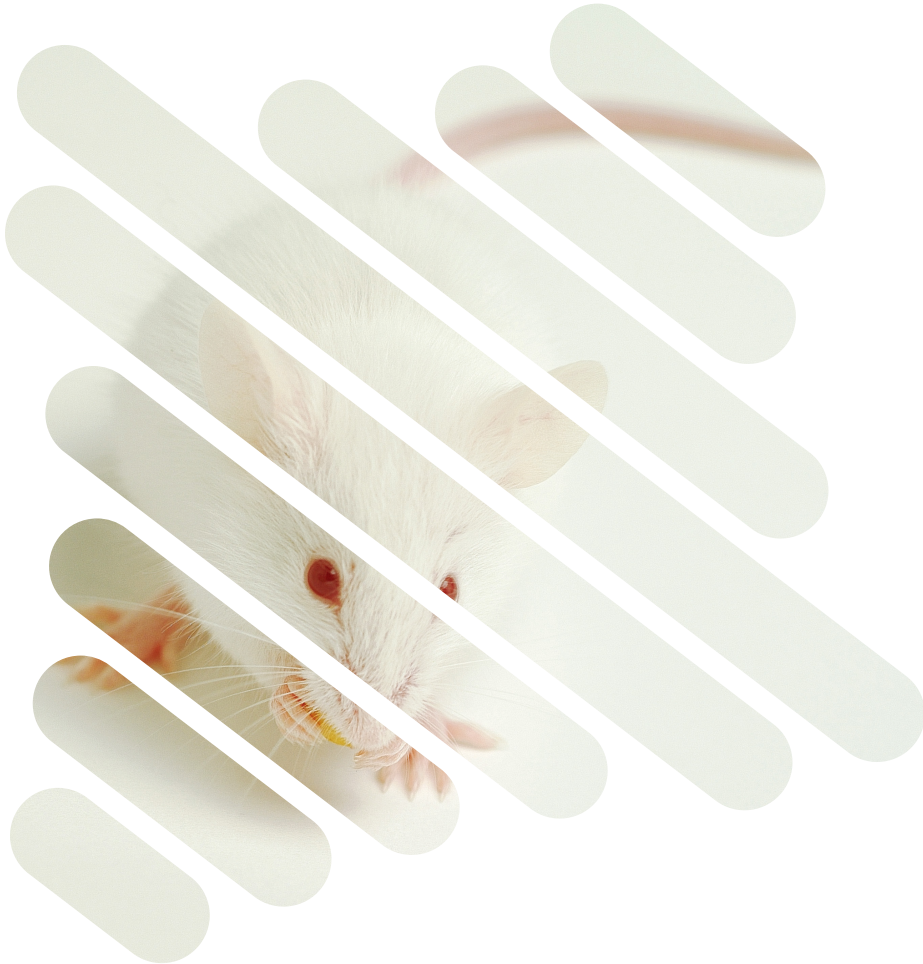
IDMO

Our Business is Life Itself



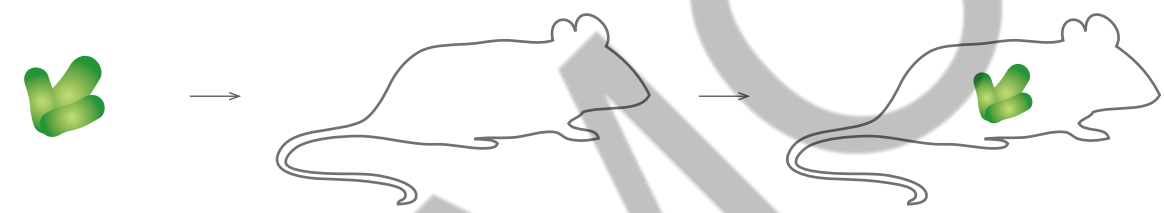
HuNPI Mice

The humanized Immune reconstitution mice model

HuNPI Introduction

Traditional immune system for humanized mice models are transplanted into human PBMC(Peripheral blood mononuclear cells) in the Immune-deficient mice，limited by degree of immunodeficiency for mice model and mature human hematopoietic cells or immune cells lack the ability to self-renew for a long time. So such a model is difficult to maintain the stability of human cells and the subsequent applications are very limited.

IDMO purified the CD34 + hematopoietic stem cells from human umbilical cord blood and transplanted the cells into the NPI mice，the HuNPI mice were prepared by this process. Because the transplanted HSC can differentiate into various cells of the immune system and can maintain the stability of the immune system for a long time in mice. So，This is a valuable, real humanized immune system mice model and has a wide range of application prospects.

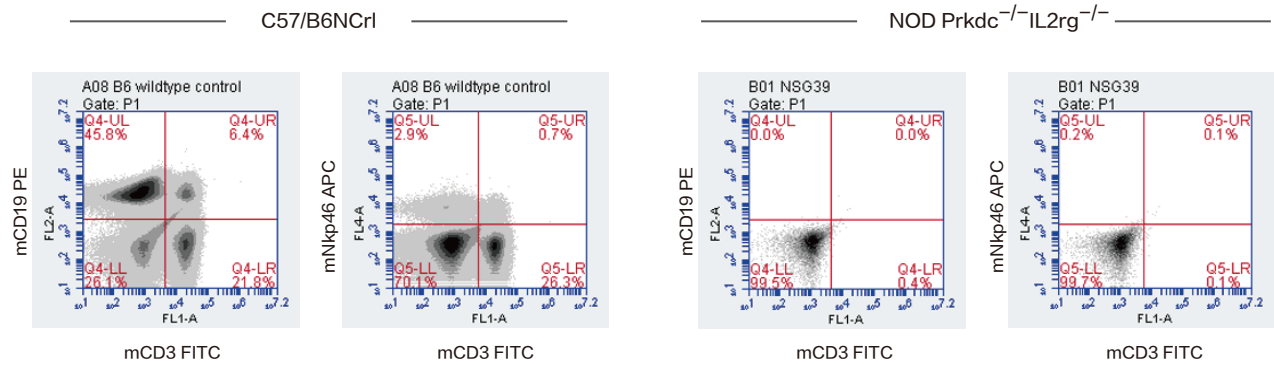


At present, each donor can produce 40 to 60 HuNPI mice and this number can meet the requirements of the user with the same batch of experiments. IDMO can provide a variety of mice models, including NPI，FRI（genetically modified mouse with damaged liver）and NPI derived mice （expressing humanized cytokines）.

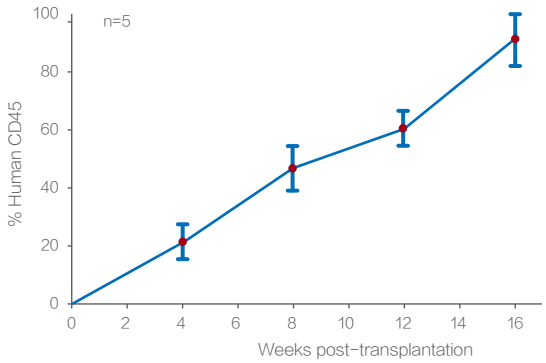
NPI

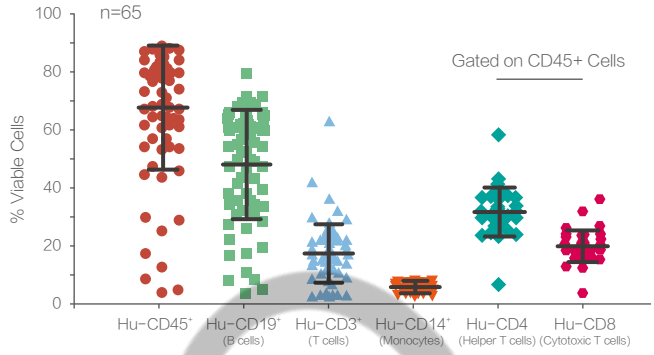
IDMO developed a mice model with NOD genetic background，Prkdc and IL2rg double gene knockout. NPI does not have mature T & B cells, and also missing NK cells , then it has severe immunodeficiency phenotype. So, This is the best carrier for transplanting HSC and constructing a humanized tumor tissue xenograft model.

Peripheral blood



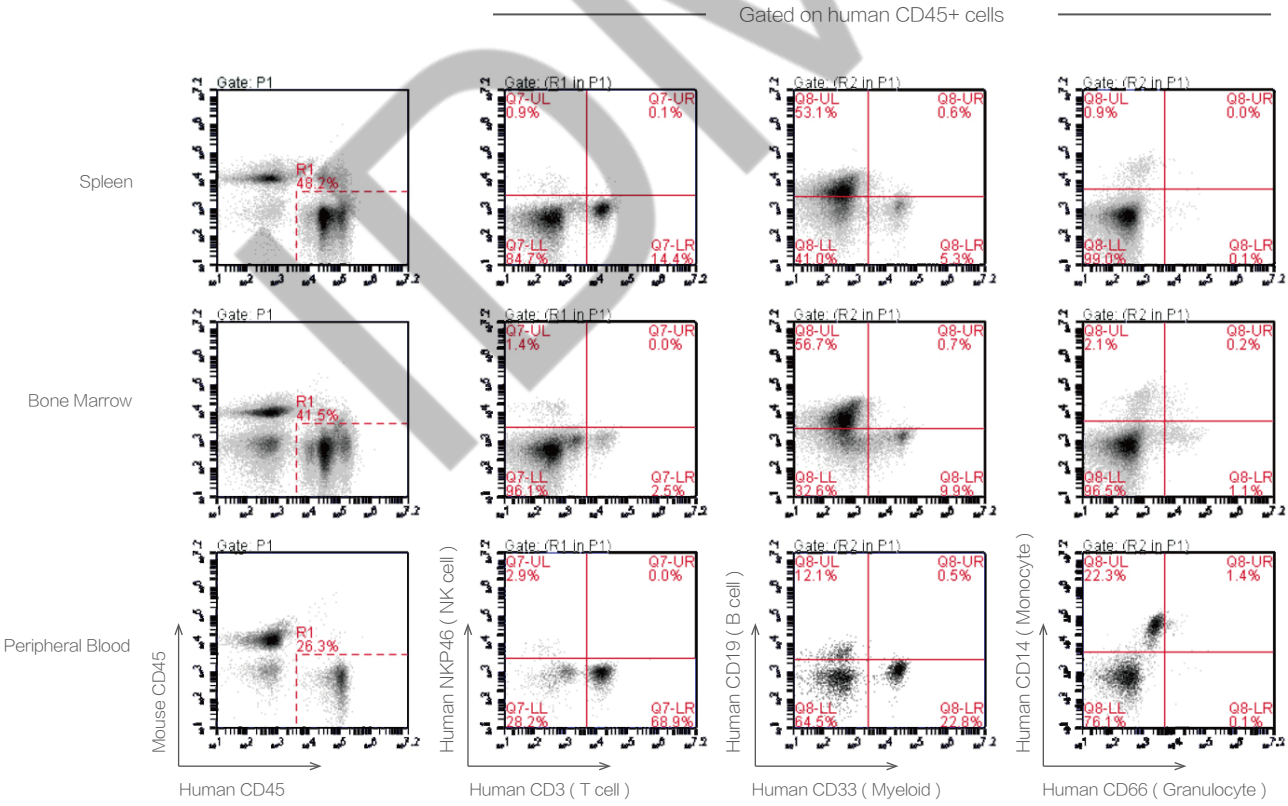
HuNPI





As time grows, The proportions of human lymphocytes reconstructed in HuNPI mice steadily increased, and the reconstructed immune system stabilized at 16 weeks. The percentage of lymphocytes in this reconstructed populations is as high as 80~90%.

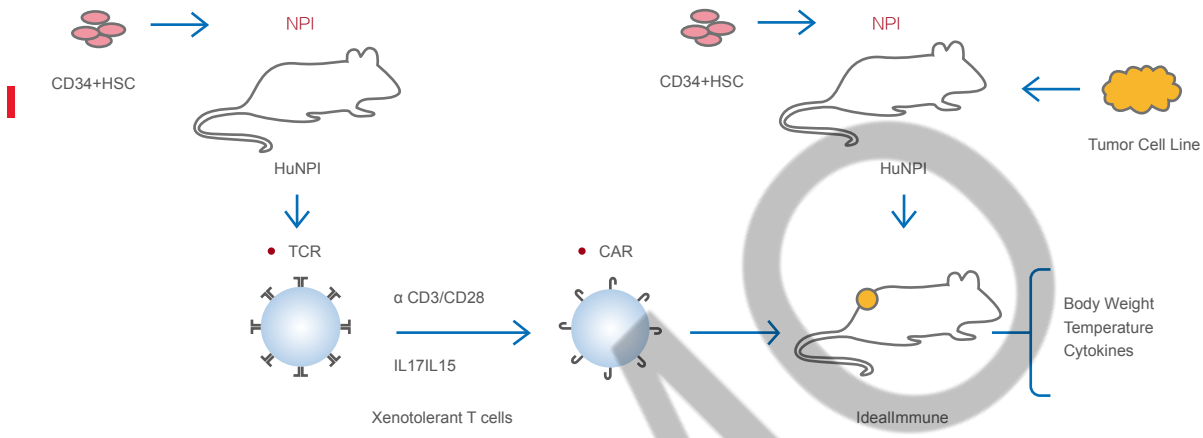
HuNPI reconstructed the type of lymphocyte very well and the ratio of CD4 and CD8 cells was 2: 1 in the Immune reconstructed T cell populations which is highly similar to the human immune system.



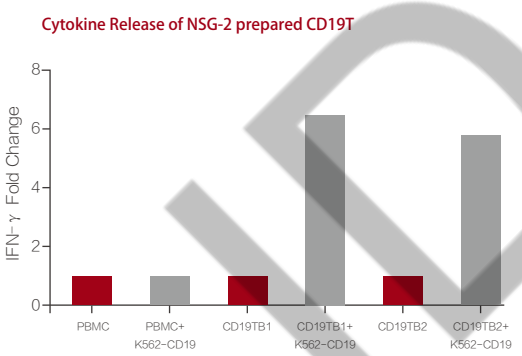
In the HuNPI different immune tissue can be detected in the reconstruction of the immune cell populations.

Functional verification of immune cells after HuNPI reconstruction

T cell proliferation capacity and killing ability

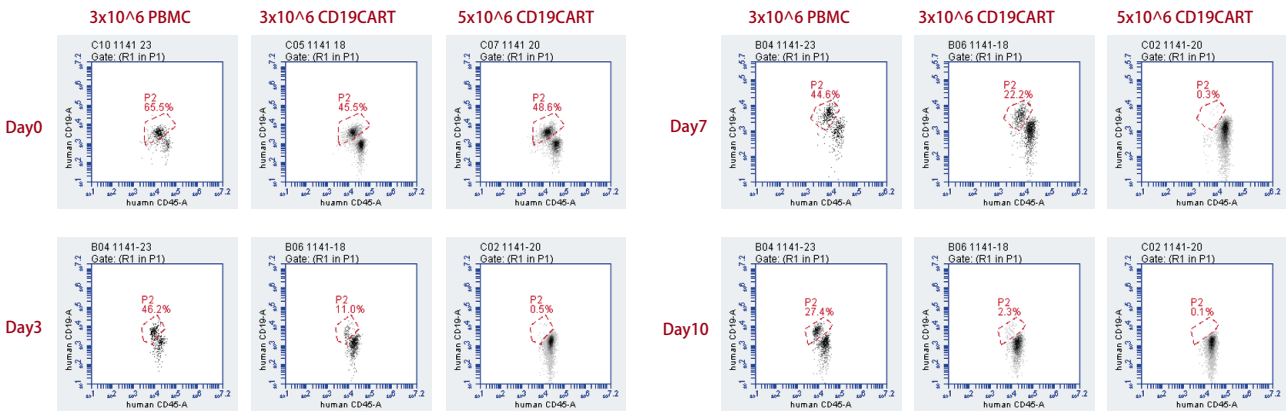


The reconstituted human T cells were harvested in HuNPI mice, transformed as CAR-T cells and cultured in vitro, then injected back into the HuNPI tumor - bearing mice which has the Same source of HSC donor, This can verify the functionality of reconstructed T cells.



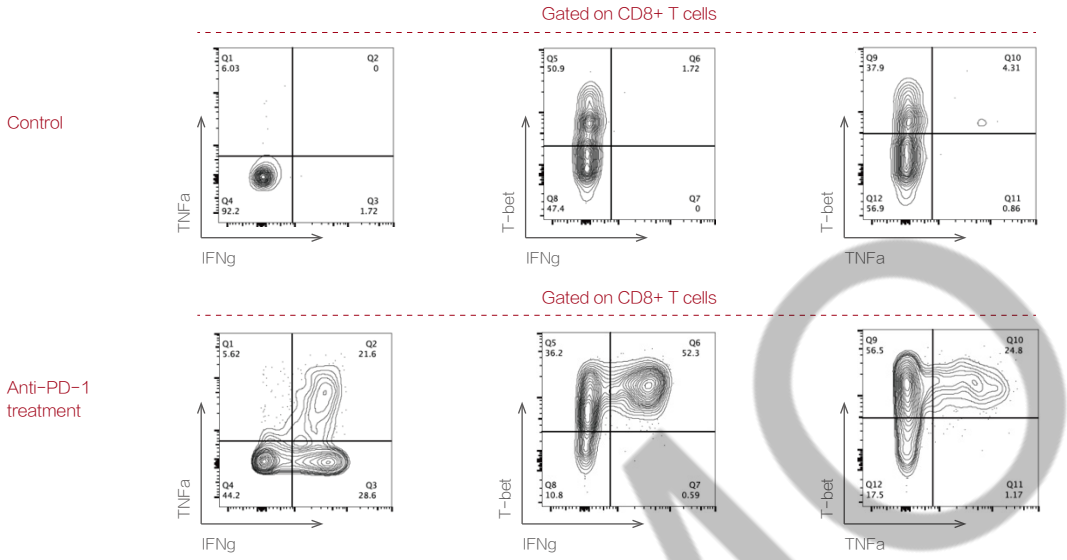
Mouse No.	CD4/CD8 Isolation	Transduced	Expansion D12
NPI-1	Yes	1.4E6	7.2E6
NPI-2	No	1.2E6	2.8E7

During this process, We find the reconstructed T cells in HuNPI mice ,which can proliferate effectively in vitro. After transforming it into CAR-T cells, This can produce specific killing effect to K562 cell line(human myeloid leukemia cell lines) which highly expressed CD19 . And CD19 CAR-T can also kill the reconstituted human B cells.

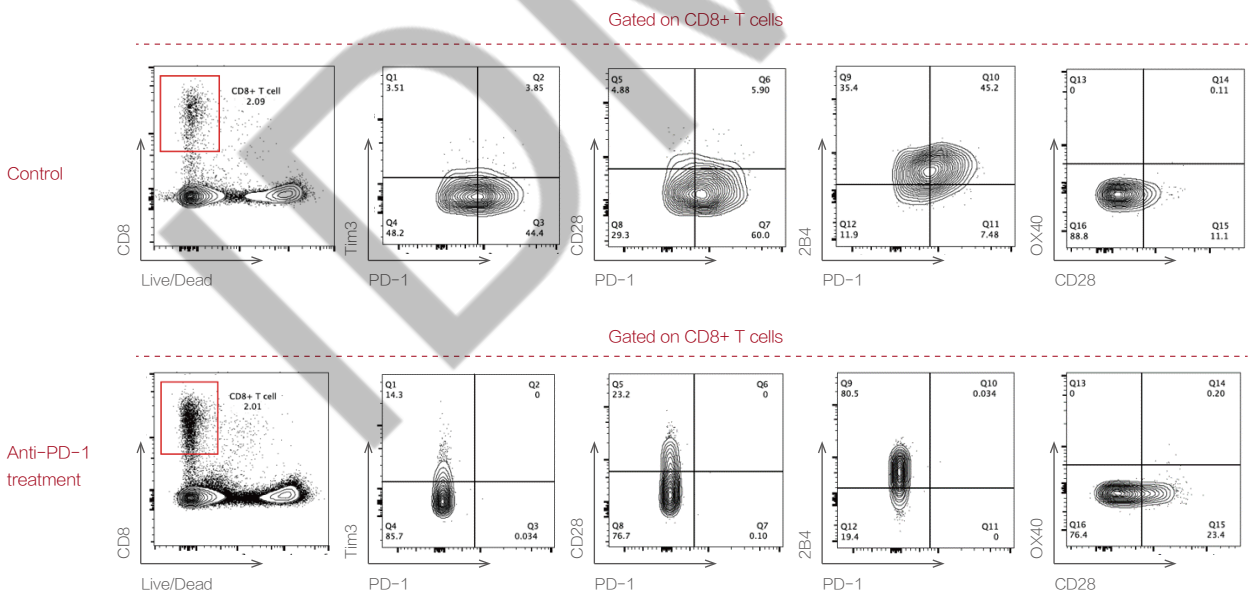


Expression and changes of checkpoint

Human tumor tissue was transplanted into HuNPI mice and constructed as tumor xenograft model. By evaluating the antibody drug of immunological checkpoint of can verify the functionality of HuNPI mice reconstructed T cells.



By detecting the release of inflammatory cytokines in the experimental and control groups, We found that CD8 cells released IFN (Interferon-Gamma) and TNF(alpha) after treatmented with PD-1 antibody and the Tc1 cells of T-bet positive expression have the killer ability.



CD8 cells were highly expressed in PD-1, Tim3, 2B4 and other immunological checkpoints in tumor tissue of the control group,but We did not detect PD-1 expression in CD8 cells in experimental group.

There is an interesting phenomenon after PD-1 suppressed, with the CD28 uptake, T cell activation at the same time, Tim3 also will be raised,but 2B4 is still high expression. This indicates that other tumor suppresses immune signaling pathways that may be activated.This phenomenon also confirms the consensus of the current tumor immunotherapy: relying solely on single-target antibody drugs for cancer therapy is far from enough, multi-target and drug combination therapy is the future of cancer treatment， and it's the real direction of development.