GENETICALLY ENGINEERED MODELS (GEM)

NATURAL IMMUNO-DEFICIENT

WILD TYPE

NATURAL MUTANTS

MICE
Mutant inbred

NXG HSPC Mouse

Strain name: NOD-*Prkdc*^{scid}-*Il2rg*^{tm1}/Rj

Type: Inbred transgenic mouse, GEMM

Origin: Janvier Labs, in 2021

Colour and related genotype: Albino mouse

Grafted human cells: CD34 from blood cord

Treatment: Busulfan

Presentation of the model

Humanized CD34+ mice are the epitome of mice models in terms of surrogate models for humans. Application field ranges from immunology, oncology, infectious diseases and more. This innovative approach bridges the gap between *in vitro* studies and clinical trials, providing a platform for more accurate and translational investigations in immunology and regenerative medicine.

In that frame, NXG-HSPC mice are your best ally for all your research by relying on one of the best immunodeficient models and an optimized protocol allowing for the optimal development of multi-lineage human immune cells.

The NXG mouse model:

The NXG mouse is an inbred strain model on the NOD genetic background, sharing similarities with other strains like NSG, NcG, NOG (refer to the NXG technical sheet for greater details). It carries two crucial mutations: *Prkdc*^{scid,} known as "SCID," which inhibits T and B cell development, resulting in their absence; and *Il2rg*^{tm1}, a knockout of the interleukin-2 receptor subunit gamma gene, essential for various immune cells, causing severe immunodeficiency with the absence of T, B, and NK lymphocytic cells. Additionally, the NXG strain expresses the NOD variant of the *Sirpa* gene, promoting reduced phagocytosis of transplanted human cells due to cross-recognition with CD47 ligands on human cells.

All these factors contribute to establishing the NXG strain as one of the best performing models in the context of humanizing the immune system.

The humanization process:

The process of humanization involves injecting cord blood-derived human CD34+ cells into mice after inducing myeloablation. This technique allows for the development of a functional and multi-lineage human immune system within the murine host. The use of cord blood as a source of hematopoietic stem cells offers advantages such as accessibility, ethical considerations, and the potential for diverse immune cell populations.

Quality of the immune system engraftment is assessed between weeks 12-14 by flow cytometry. More than 85% of our mice successfully met the quality control threshold, exhibiting over 25% of human CD45+ cells in the peripheral blood.

NXG-HSPC mice stand as one of the most robust model of immune system humanized mice showcasing unparalleled homogeneity and unmatched robustness.

Services:

The scientific team at Janvier Labs is always available to assist you in optimizing the utilization of our NXG-HIS mice. Reach out to us to explore how we can contribute to the success of your experiments.

- Typically, our mice, along with a comprehensive report on human system engraftment and sanitary status, are shipped to customers around week 16 post-engraftment. But we can offer to liberate the animals sooner to accommodate your needs.
- Engraftment of CD34+ cells carrying a specific HLA from a donor can be a valuable tool for your research. We can routinely offer engraftment with HLA-A*02:01 donors but can accommodate additional requests.
- If specific percentages of the lymphoid and myeloid compartments are desired to tailor the use of NXG-HSPC mice to your research needs, we can selectively choose animals that best suit your requirements.

Main application and research fields

ONCOLOGY

IMMUNOTHERAPY

REGENERATIVE MEDICINE

IMMUNOLOGY

AUTO-IMMUNE DISEASES

INFECTIOUS DISEASES

HUMAN ORGAN TRANSPLANTATION

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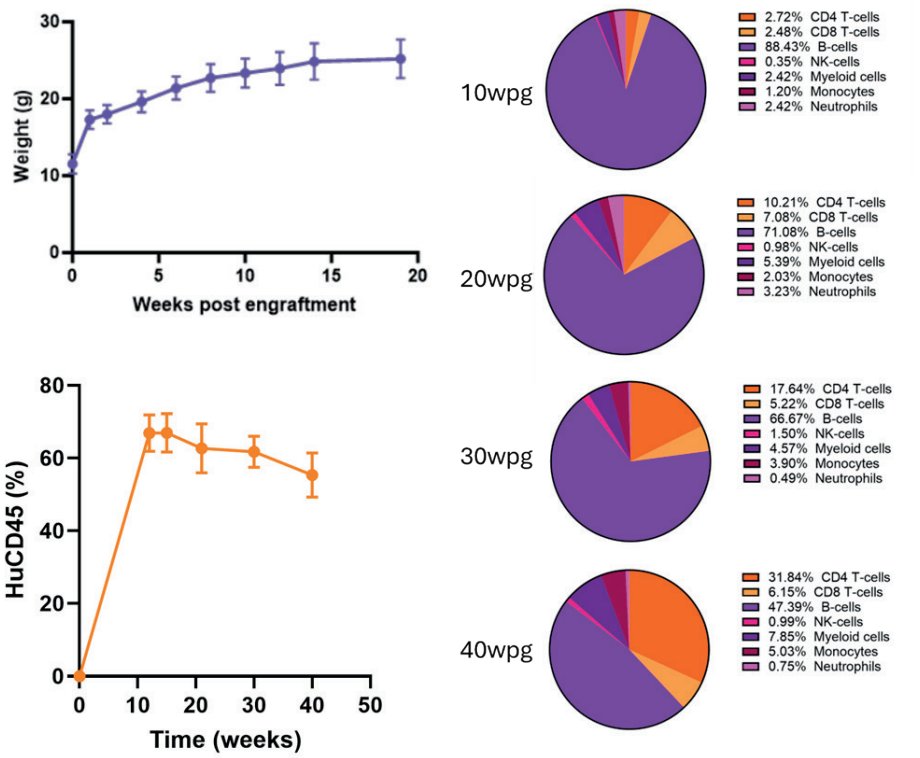
Peripheral blood and weight



NXG-HSPC mouse model features. (A) weight evolution upon engraftment with HSPC cells (B) frequency of hCD45+ cells in the peripheral blood, among total number of CD45+ cells. (C) Evolution of immune cell distribution in the peripheral blood of NXG-HSPC. HSPC = hematopoietic stem and progenitor cells, Wpg = weeks post engraftment

Analysis of the tumor microenvironment in NXG-HSPC mice inoculated with MDA-MB-231 breast cancer cells.

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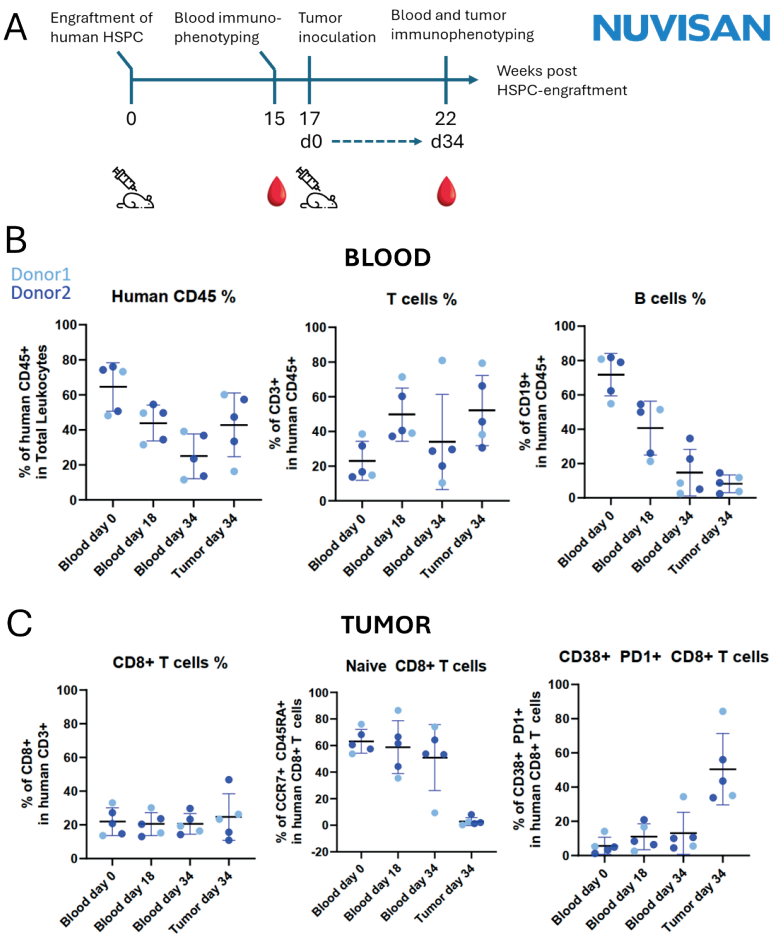

(A) Experimental design: immunophenotyping was performed in NXG-HSPC mice before and after sub-cutaneous inoculation of human MDA-MB-231 cells.

(B) Human immune cell frequencies evolution in the peripheral blood, and infiltration in the tumor of NXG-HSPC mice.

(C) Immunophenotyping of tumor infiltrating lymphocytes, and activation status.

Selected references

- *Carretero-Iglesia, Laura et al. "ISB 2001 trispecific T cell engager shows strong tumor cytotoxicity and overcomes immune escape mechanisms of multiple myeloma cells." Nature cancer vol. 5,10 (2024): 1494-1514. doi:10.1038/s43018-024-00821-1*
- *Kam, Ngar-Woon et al. "ENOX2 inhibition enhances infiltration of effector memory T-cell and mediates response to chemotherapy in immune-quiescent nasopharyngeal carcinoma." Journal of advanced research vol. 56 (2024): 69-86. doi:10.1016/j.jare.2023.04.001*

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