



GENETICALLY
ENGINEERED
MODELS
(GEM)



MICE
Mutant inbred

NATURAL
IMMUNO-
DEFICIENT

NRG-HIS Mouse

WILD TYPE

Strain name: NOD-*Rag2^{tm1}*-*Il2rg^{tm1}*/Rj

Type: Inbred transgenic mouse, GEMM

Origin: Janvier Labs, in 2023

Colour and related genotype:
Albino mouse

NATURAL
MUTANTS

Grafted human cells:
CD34 from blood cord

Treatment: Irradiation



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, NRG-HIS 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 NRG mouse model:

The NRG or NOD *Rag2* γ c strain is a highly immunodeficient inbred model characterized by knockout mutations in the *Il2rg* and *Rag2* genes. The *Rag2^{tm1}* mutation disrupts recombinase activity crucial for B and T cell receptor formation, resulting in a total absence of T and B lymphocytes. The *Il2rg^{tm1}* mutation knocks out the gamma c chain, essential for the proper functioning of various immune cells, including NK cells, leading to severe immunodeficiency. The combination of *Rag2^{tm1}* and *Il2rg^{tm1}* mutations induces the absence of T, B, and NK cells.

The NRG strain also expresses the NOD variant of the *Sirpa* gene, reducing phagocytosis of transplanted human cells. In comparison to the NXG strain, the NRG strain is more resistant to irradiation, genotoxic products, and stress due to the replacement of the *Prkdc^{scid}* mutation with the *Rag2* knockout, enhancing its durability and stability for xenograft purposes.

All these factors contribute to establishing the NRG strain an attractive model for immune system immunization, especially in the frame of research related to radiotherapy or chemotherapy.

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.

Proper engraftment of the immune system engraftment is assessed between weeks 12-14 by ensuring that over 20% of human CD45+ cells are present in the peripheral blood.

NRG-HIS mice stand as one of the most robust model of immune system humanized mice while displaying a great resistance to genotoxic agents

Services:

The scientific team at Janvier Labs is always available to assist you in optimizing the utilization of our NRG-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 NRG-HIS 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

RADIOTHERAPY

INFECTIOUS DISEASES

HUMAN ORGAN TRANSPLANTATION

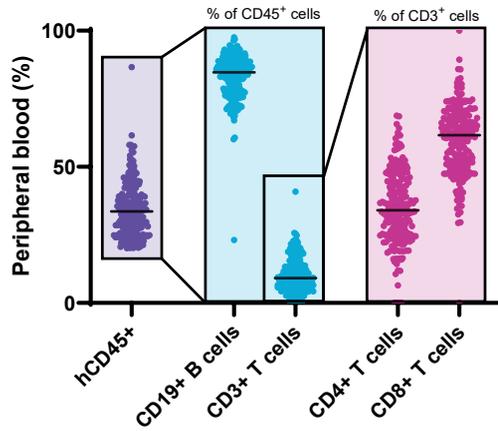
CHEMOTHERAPY



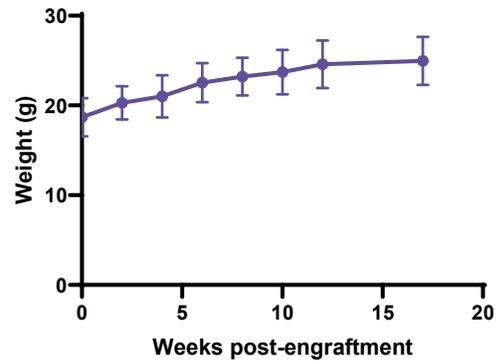


Peripheral blood and weight

Flow cytometry analysis of human cells 14 weeks after engraftment



Growth curve



Quality control allows to measure the relative humanization rate of humanized mice in the peripheral blood. The standardization of quality control is performed by flow cytometry of the different human populations: hematopoietic, lymphoid and myeloid. Each NRG-HIS is tested and analyzed before sending and use. NRG-HIS mice are produced with SOPF status. Each batch provided is supplied with a list showing the animal repartition according to the different CD34+ donors.

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