

GENETICALLY
ENGINEERED
MODELS
(GEM)



MICE
Mutant inbred

NATURAL
IMMUNO-
DEFICIENT

NRG cKit HSPC Mouse

WILD TYPE

Strain name: NOD-*Rag2^{tm1}*-*Il2rg^{tm1}*-*Kit^{em1}*/Rj

Type: Inbred transgenic mouse, GEMM

Origin: Janvier Labs, 2023

Colour and related genotype:
Albino mouse

NATURAL
MUTANTS

Grafted human cells: CD34 from blood cord

Treatment: None



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 this context, the NRG cKit-HSPC mouse model is an excellent system, providing a consistent humanization rate over extended periods. This stability makes it well-suited for long-term experiments, such as studies involving hormone supplementation like oestradiol.

The NRG cKit mouse model:

The NRG-Ckit strain is a highly immunodeficient mouse model derived from a NOD background, featuring three key mutations: two Knock Out (KO) mutations in the *Il2rg* and *Rag2* genes, and a V831M point mutation in the *kit* gene. The *Rag2* KO mutation disrupts T and B lymphocyte development, causing immune deficiency, while the *Il2rg* KO mutation impairs cytokine signaling, affecting Natural Killer (NK) cell development and other hematopoietic cells. The V831M mutation in the *kit* gene reduces endogenous KIT protein expression, enhancing engraftment of human hematopoietic stem cells without irradiation and promoting human red blood cell production. Additionally, the strain's polymorphic *Sirpa* gene allows human cells to evade mouse macrophage phagocytosis via the CD47

The humanization process:

The humanization process involves injecting human CD34+ cells derived from cord blood into mice. The mutation in the *Kit* gene eliminates the need for myeloablation, which is typically required to enhance CD34+ cell engraftment in other HSPC models. This approach enables the development of a functional,

multi-lineage human immune system within the murine host. Cord blood serves as an advantageous source of hematopoietic stem cells due to its accessibility, ethical benefits, and potential to generate diverse immune cell populations.

Following injection, the humanization process produces a diverse population of multi-lineage immune cells, with a notable proportion of T-cells. The engraftment remains stable over an extended period (>40 weeks), and the strain benefits from a long-life expectancy (>80 weeks).

Proper engraftment of the immune system engraftment is assessed between weeks 12-14 by ensuring that over 25% of human CD45+ cells are present in the peripheral blood.

Services:

The scientific team at Janvier Labs is always available to assist you in optimizing the utilization of our NRG-HSPC 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 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-HSPC mice to your research needs, we can selectively choose animals that best suit your requirements.



Main application and research fields

ONCOLOGY

IMMUNOLOGY

DIABETES

INFECTIOUS DISEASE

HUMANIZATION

IMMUNOTHERAPY

GRAFT VS. HOST DISEASE

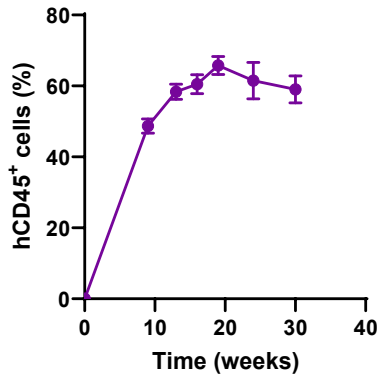
REGENERATIVE MEDICINE

HUMAN ORGAN TRANSPLANTATION

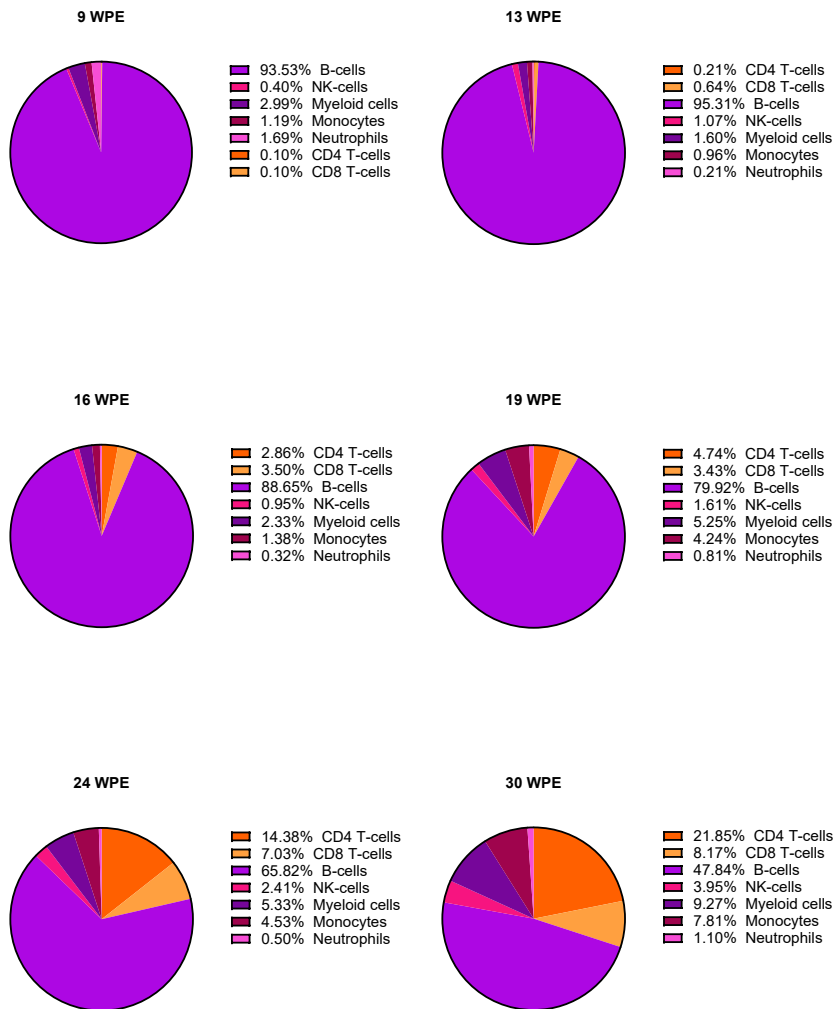


Flow cytometry analysis, spleen

NRG cKit HuCD45



Percentage of human CD45+ cells in the blood of NRG cKit mice (whole blood) over time upon CD34+ cells injection. Each point represents average +/- SEM.



Human immune cells repartition in the blood of NRG cKit mice after CD34+ cells injection (WPE) over time.

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