

HUMANIZED MICE:

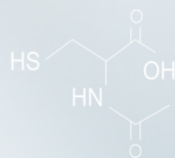
NEXT GENERATION OF *IN VIVO* MODELS

2025



PULSE 82

SBD 125



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Research models and associated services

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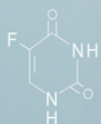


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COMMITTED TO RESEARCH FOR MORE THAN 6 DECADES

Founded in 1960, Janvier Labs is an independent company specialised in breeding of laboratory rodents and associated services.

As an international player in the field of biomedical research, Janvier Labs provides scientists (biotech and pharmaceutical companies, academics) with a comprehensive range of rodent research models from model creation, reproductive sciences, customized breeding to laboratory services.

Janvier Labs offers solutions adapted to your needs in order to ensure the success of your research programmes.

JANVIER LABS HAS THE LARGEST AND MOST ADVANCED BREEDING SITE IN EUROPE

 1 unique production site in Europe 22,000 sqm of facilities on more than 8 hectares	 Breeding capacity 3,000,000 rodents a year	 45,000 km a week travelled by our integrated transport department	 3,500 customers worldwide 412 international employees
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Janvier Labs provides scientists with models that fulfill the highest standards. With a unique state-of-the-art site based in Europe, Janvier Labs ensures rigorous breeding conditions. Our experts bring broad expertise to guarantee the success of your research.

CONTROLLED MICROBIOTA

All our models have the same microbiota that is analyzed, monitored and stable over time

03

GENETIC STABILITY

JANVIER LABS GENETIC POLICY® allows to ensure the genetic homogeneity of all the strains

04

SOPF HEALTH QUALITY

Our robust health policy ensures the highest health standards for your models

02

SCIENTIFIC SUPPORT

A team of experts to assist you in the choice of the relevant models and to advise all along your research projects

05

IMMUNO-PHENOTYPING BY JC DISCOVERY

We work with recognized experts in immunology for a comprehensive characterization of our models

01

TRANSPORT

Our 100% in-house transport department ensures the welfare of your models and a delivery flexibility

06



OUR IMMUNODEFICIENT MODELS

Janvier Labs has an extensive array of immunodeficient models featuring diverse characteristics and genetic backgrounds. These models can accommodate all your xenograft requirements, including tumors, immune cells, organs, and beyond.

	Background	Breeding	Coat	T Lymphocytes	B Lymphocytes	Leakiness	NK cells	Dendritic cells	Macrophages	Complement	Irradiation tolerance	Humoral immunity	Phagocytic Tolerance	Mutations of interest
	NOD	Inbred	Albino	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Very low	High	Absent	High	<i>Sirpa</i> ^{NOD} <i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1} <i>Kit</i> ^{em1}
NXG-β2m	NOD	Inbred	Albino	Absent	Absent	Very low	Absent	Dysfunc.	Dysfunc.	Very low	Low	Absent	High	<i>Sirpa</i> ^{NOD} <i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1} <i>B2m</i> ^{em1}
NXG	NOD	Inbred	Albino	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Very low	Low	Absent	High	<i>Sirpa</i> ^{NOD} <i>Prkd</i> ^{csid} <i>Il2rg</i> ^{tm1}
NRG	NOD	Inbred	Albino	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Very low	High	Absent	High	<i>Sirpa</i> ^{NOD} <i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1}
NRG Nude	NOD	Inbred	Albino	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Very low	High	Absent	High	<i>Sirpa</i> ^{NOD} <i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1} <i>Foxn1</i> ^{nu}
BRGS A2DR2	BALB/c	Inbred	Albino	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Low	High	Absent	High	<i>Sirpa</i> ^{NOD} <i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1}
BRGS TSLP	BALB/c	Inbred	Albino	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Low	High	Absent	High	<i>Sirpa</i> ^{NOD} <i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1}
B6RGS Nude	C57BL/6NRj	Inbred	Nude	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Low	High	Absent	High	<i>Sirpa</i> ^{NOD} <i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1} <i>Foxn1</i> ^{nu}
B6RGS	C57BL/6NRj	Inbred	Black	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Low	High	Absent	High	<i>Sirpa</i> ^{NO} <i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1}
B6RG	C57BL/6NRj	Inbred	Black	Absent	Absent	Low	Absent	Dysfun.	Dysfun.	Normal	High	Absent	Low	<i>Rag2</i> ^{tm1} <i>Il2rg</i> ^{tm1}
NOD Scid	NOD	Inbred	Albino	Absent	Absent	Medium	Normal	Normal	Normal	Low	Low	Absent	High	<i>Sirpa</i> ^{NOD} <i>Prkd</i> ^{csid}
B6R Nude	C57BL/6NRj	Inbred	Nude	Absent	Absent	Medium	Normal	Normal	Normal	Normal	High	Absent	Low	<i>Rag2</i> ^{tm1} <i>Foxn1</i> ^{nu}
CB17 Scid Nude	CB17	Inbred	Nude	Absent	Absent	Medium	Normal	Normal	Normal	Normal	Low	Absent	Low	<i>Prkd</i> ^{csid} <i>Foxn1</i> ^{nu}
B6R	C57BL/6NRj	Inbred	Black	Absent	Absent	Medium	Normal	Normal	Normal	Normal	High	Absent	Low	<i>Rag2</i> ^{tm1}
B6G	C57BL/6NRj	Inbred	Black	Low	Low	High	Absent	Dysfun.	Dysfun.	Normal	High	Absent	Low	<i>Il2rg</i> ^{tm1}
CB17 Scid	CB17	Inbred	Albino	Absent	Absent	High	Normal	Normal	Normal	Normal	Low	Absent	Low	<i>Prkd</i> ^{csid}
B6 Nude	C57BL/6NRj	Inbred	Nude	Absent	Normal	High	Normal	Normal	Normal	Normal	High	Normal	Low	<i>Foxn1</i> ^{nu}
BALBc/ Nude	BALB/c	Inbred	Nude	Absent	Normal	High	Normal	Normal	Normal	Normal	High	Normal	Low	<i>Foxn1</i> ^{nu}
NMRI Nude	NMRI	Outbred	Nude	Absent	Normal	High	Normal	Normal	Normal	Normal	High	Normal	Low	<i>Foxn1</i> ^{nu}
ATHYMIC Nude	BALB/c	Outbred	Nude	Absent	Normal	High	Normal	Normal	Normal	Normal	High	Normal	Low	<i>Foxn1</i> ^{nu}

OUR HUMANIZED IMMUNE SYSTEM MICE

WHAT ARE HIS MICE?

As the demand for advanced therapies to address unmet medical needs like cancer and autoimmune diseases continues to rise, there is an increasing necessity for enhanced preclinical models with greater predictive capability. While *in vitro* studies utilizing human cells or organoids are valuable, animal models offer a more comprehensive understanding of complex biological processes in mammals.

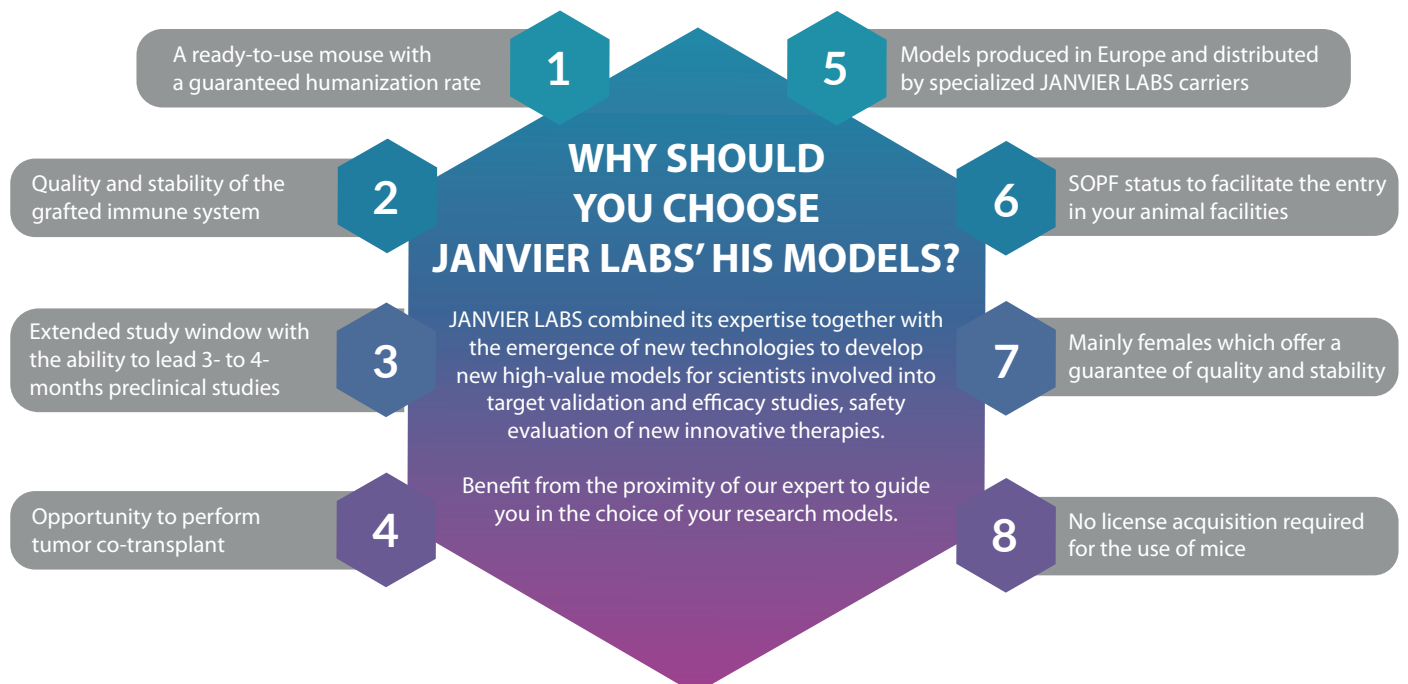
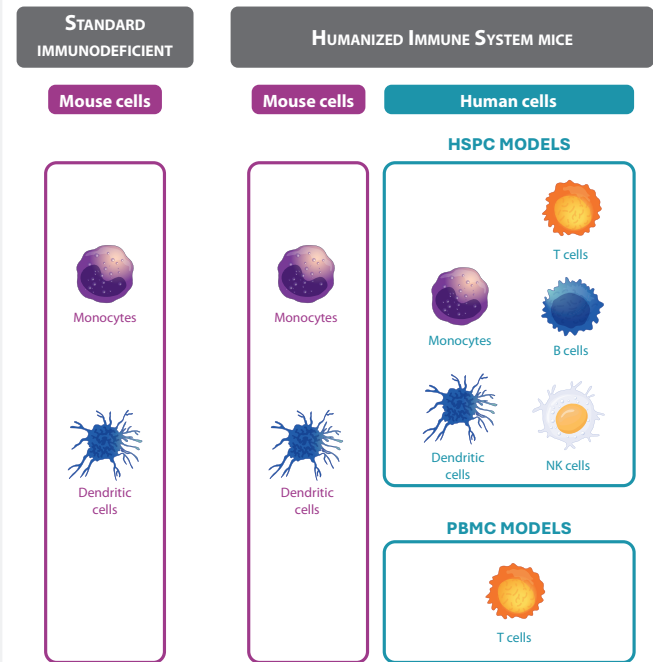
Humanized immune system (HIS) mice involve the engraftment of human immune cells into immunodeficient mice, resulting in various types of humanized immune systems depending on the engrafted cell type.

Janvier Labs offers diverse HIS models generated by engrafting either CD34+ hematopoietic stem and progenitor cells (HSPC) or peripheral mononuclear cells (PBMC).

Humanized mice represent the pinnacle of mouse models as surrogate systems for human research. Their applications span across immunology, oncology, infectious diseases, safety studies and beyond. This innovative approach serves to bridge the gap between *in vitro* experimentation and clinical trials, furnishing a platform for more precise and translational investigations.

Compared lymphoid and myeloid cells presence in:

- standard immunodeficient models
- immunodeficient models engrafted with either HSPC or PBMC



OUR HSPC PLATFORM

Janvier Labs prides itself in having one of the most robust HSPC mice production platforms available on the market.



THE HUMANIZATION PROCESS:

The process of humanization involves injecting cord blood-derived human CD34+ cells into mice after inducing myeloablation (irradiation or chemoablation). 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.



THE QUALITY CONTROL:

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 HSPC is tested and analyzed before sending and use. HSPC mice are produced with SOPF status. Each batch provided is supplied with a list showing the animal repartition according to the different CD34+ donors. Quality control is typically performed 14-15 weeks post engraftment and allows to measure the relative humanization rate of humanized mice in the peripheral blood.



THE MODELS:

Janvier Labs offers 6 different models of HIS mice to its customers with different areas of application, perfect to accommodate your needs along your research process.

MODELS	KEY FEATURES	AVAILABILITY	DELIVERY
NXG-HSPC	- Most versatile model - Highest degree of hu CD45+ cells engraftment - Sensitive to irradiation	Off-the-shelf	- Starting 2 weeks post-engraftment without FACS QC - 17 weeks post-engraftment with FACS QC
NXG HIL-15-HSPC	- Supports development and persistence of human NK cells - Useful for studying NK cell biology, immuno-oncology, and adoptive NK therapies		
NRG-HSPC	- Similar to the NXG-HSPC model - Very resistant to genotoxic agents	On-demand	
NRG CKIT-HSPC	- Efficient human HSPC engraftment without preconditioning - Supports higher levels of human myeloid and erythroid lineage cells		
BRGS A2DR2-HSPC	- Expresses HLA class I and II - Enhances T-cell population development - Human-like TCR repertoire		
BRGS TSLP-HSPC	- Overexpressed mouse TSLP - Full development of secondary lymphoid tissues - Model of atopic dermatitis		



THE SERVICES:

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



GENETICALLY
ENGINEERED
MODELS
(GEM)



MICE
Mutant inbred

NATURAL
IMMUNO-
DEFICIENT

NXG-HSPC Mouse

WILD TYPE

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

NATURAL
MUTANTS



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.



Main application and research fields

ONCOLOGY

IMMUNOTHERAPY

REGENERATIVE MEDICINE

IMMUNOLOGY

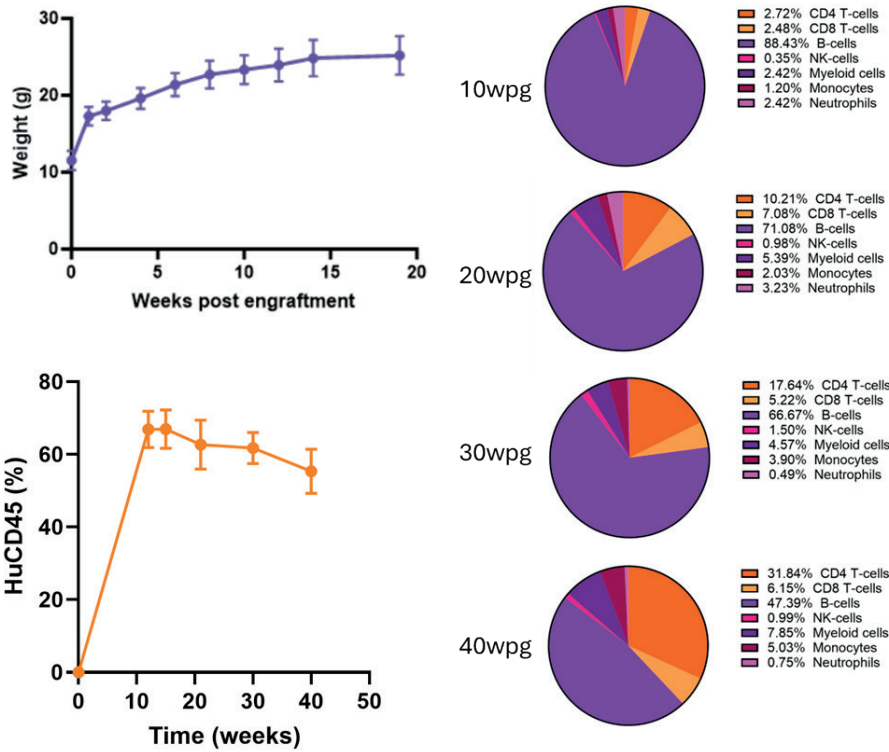
AUTO-IMMUNE DISEASES

INFECTIOUS DISEASES

HUMAN ORGAN TRANSPLANTATION

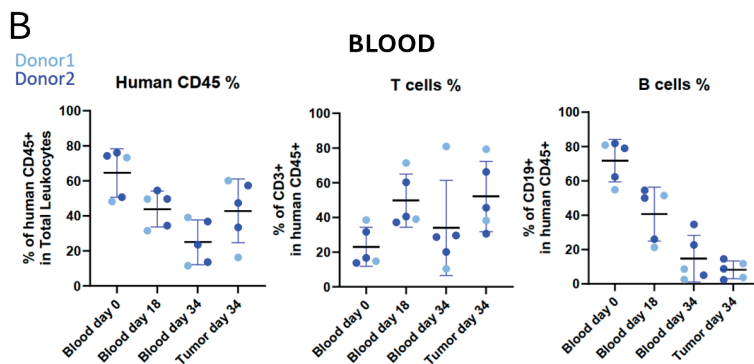
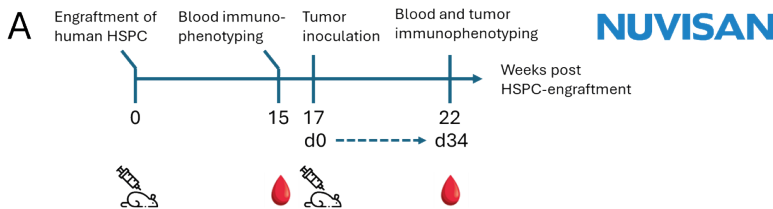


Peripheral blood and weight



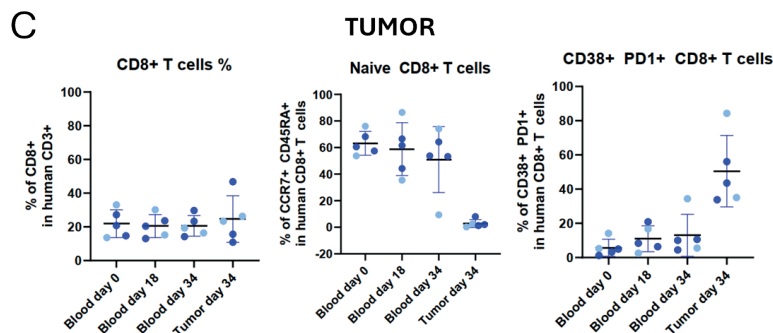
NXG-HSPC mouse model features. (A) weight evolution upon engraftment with HSPC cells (B) frequency of hCD45+ cells in the peripheral blood, among total number of CD45+ cells. (C) Evolution of immune cell distribution in the peripheral blood of NXG-HSPC. HSPC = hematopoietic stem and progenitor cells,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

Analysis of the tumor microenvironment in NXG-HSPC mice inoculated with MDA-MB-231 breast cancer cells. Janvier Labs would like to thank Dr. Carlo Stresemann and Dr. Ulrike Litzenburg from Nuvisan for kindly providing the data.



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

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



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

Selected references

- Carretero-Iglesia, Laura et al. "ISB 2001 trispesific 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



GENETICALLY
ENGINEERED
MODELS
(GEM)



MICE
Mutant inbred

NATURAL
IMMUNO-
DEFICIENT

NRG-HSPC 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

Grafted human cells:
CD34 from blood cord

NATURAL
MUTANTS

Treatment: Irradiation



Presentation of the model

Humanized CD34+ mice are the reference model among murine models used as substitutes 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-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 NRG mouse model

The NRG or NOD *Rag2* yc 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 engraft purposes.

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



Main application and research fields

ONCOLOGY

IMMUNOTHERAPY

REGENERATIVE MEDICINE

IMMUNOLOGY

AUTO-IMMUNE DISEASES

RADIOTHERAPY

INFECTIOUS DISEASES

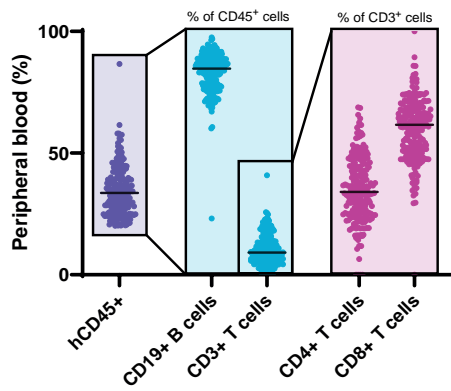
HUMAN ORGAN TRANSPLANTATION

CHEMOTHERAPY



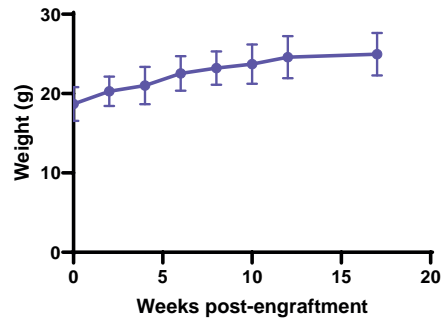
Peripheral blood and weight

Flow cytometry analysis of human cells 14 weeks after engraftment



Relative percentage of human CD45+ cells, T-cells and B-cells

Growth curve





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

NATURAL
MUTANTS

Colour and related genotype:
Albino mouse



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.



Main application and research fields

ONCOLOGY

IMMUNOLOGY

DIABETES

INFECTIOUS DISEASE

HUMANIZATION

IMMUNOTHERAPY

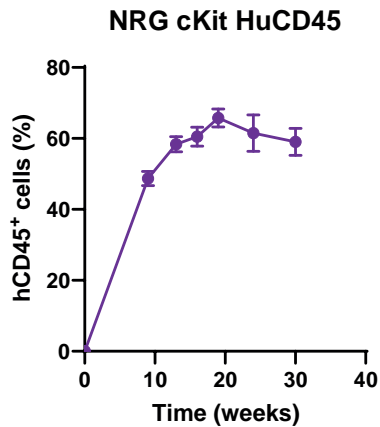
GRAFT VS. HOST DISEASE

REGENERATIVE MEDICINE

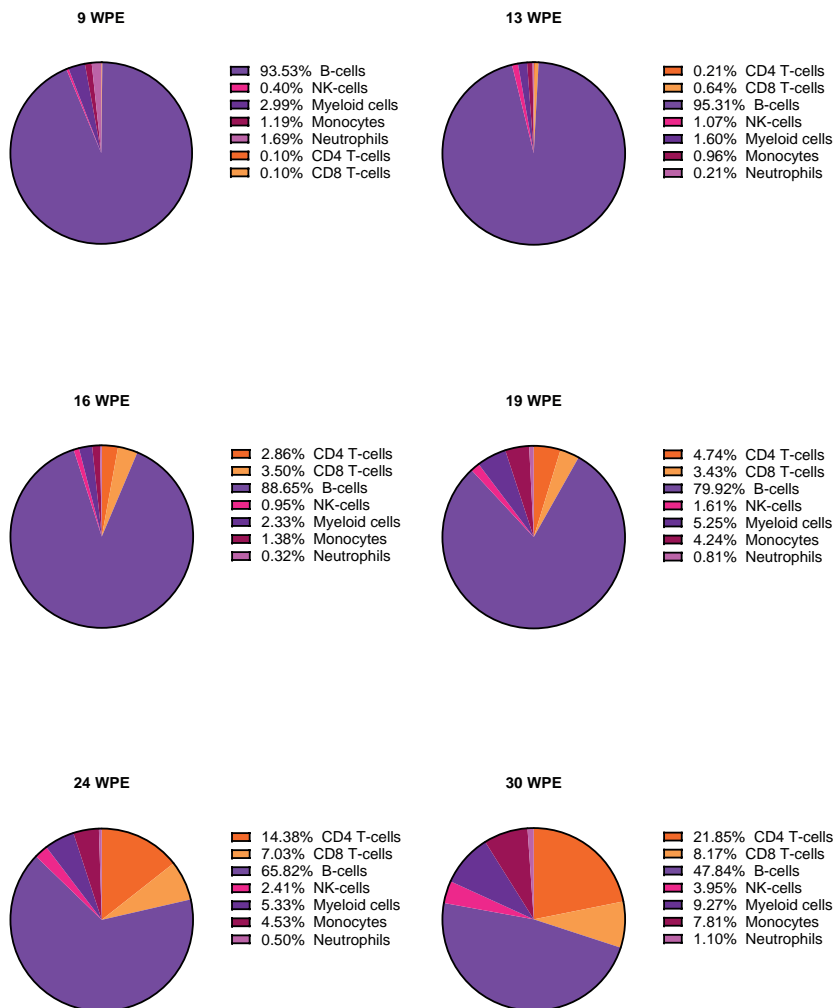
HUMAN ORGAN TRANSPLANTATION



Flow cytometry analysis, spleen



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.



GENETICALLY
ENGINEERED
MODELS
(GEM)



MICE
Mutant inbred

NATURAL
IMMUNO-
DEFICIENT

BRGS A2DR2 HSPC Mouse

Strain name: *C-Rag2^{tm1}-Il2rg^{tm1}-Sirpa^{NOD}-Tg(HLA-A*02-HHD)-Tg(HLA-DR2)/Rj*

Type: Inbred transgenic mouse, GEMM

Origin: Pasteur institute, 2022

Colour and related genotype:
Albino mouse

Grafted human cells:
CD34 from blood cord

Treatment: Irradiation

WILD TYPE

NATURAL
MUTANTS



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, BRGS A2DR2 HSPC mice go one step further in comparison to other humanized models by providing accelerated thymopoiesis as well as improved T-cell responses

The BRGS A2DR2 mouse model

The BRGS A2DR2 strain is a highly immunodeficient inbred model characterized by knockout mutations in the *Il2rg* and *Rag2* genes, with a NOD background gene. The *Rag2* knockout inhibits the formation of B and T cell receptors, leading to the absence of T and B lymphocytes. The *Il2rg* knockout affects the gamma c chain crucial for immune cell differentiation, resulting in the absence of T, B, and NK cells. The combination of these mutations induces severe immunodeficiency. Additionally, the strain carries the NOD variant of the *Sirpa* gene, reducing phagocytosis of transplanted human cells. Finally, this strain expresses human HLA-A*02 and HLA-DR2 transgenes.



Main application and research fields

XENOGRAFT

- Tumor xenograft (syngeneic, CDX, PDX...)
- Human CD34+ hematopoietic stem cells
- Human PBMCs
- Organs (pancreas...)

PRE-CLINICAL DEVELOPMENT

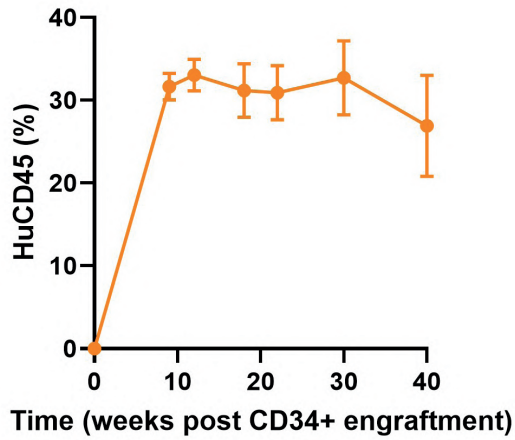
- Therapeutic antibodies
- Cell therapy (TCR-redirectioned T-cells, CAR...)
- Vaccines (DNA, mRNA, peptides...)
- Surgery
- Chemotherapy
- Radiotherapy

THERAPEUTIC AREAS

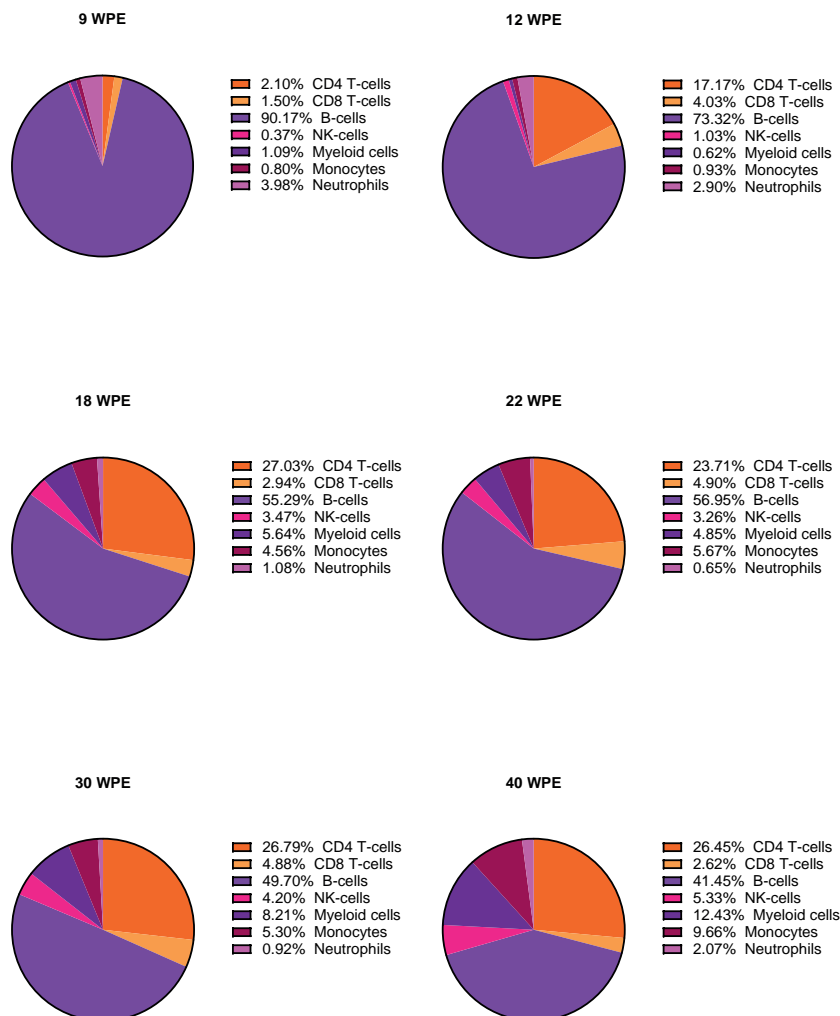
- Oncology
- Infectious diseases (HIV, EBV, malaria, dengue...)
- Auto-immune diseases (type I diabetes...)



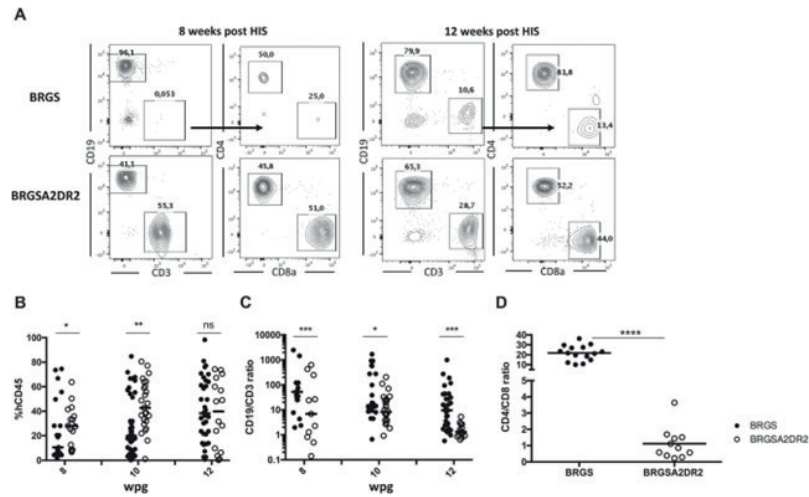
Flow cytometry analysis, spleen



Percentage of human CD45+ cells in the blood of BRGS A2DR2 mice over time upon CD34+ cells injection. Each point represents average +/- SEM.



Human immune cells repartition in the blood of BRGS A2DR2 mice after CD34+ cells injection (WPE) over time.

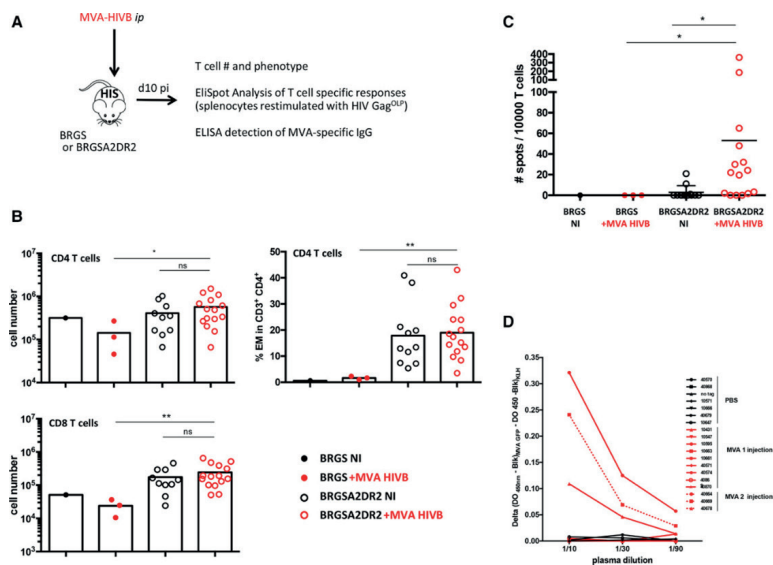


Kinetics of human cell reconstitution in the blood of BRGS versus BRGS A2DR2 HSPC mice.

(A) Representative flow cytometry immune-phenotypic analysis of hCD45⁺ blood cells at 8 weeks and 12 weeks post graft (wpg) in humanized BRGS versus BRGS HLA-A*02-HHD class I and HLA-DRB1*15 class II transgenic mice (BRGS A2DR2) reconstituted with HLA-A*02+ HLA-DRB1*15+ HSCs.

(B) Analysis of hCD45⁺ cells using the hCD45% × 100/ (hCD45% + mCD45%) formula (B) or CD19/CD3 ratio (C) over time (wpg) in BRGS (full circle) and BRGS A2DR2 (open circle).

(D) Comparison of the CD4/CD8 ratios in both models at 12 wpg. Each dot represents one mouse and data are representative from at least five independent experiments (14–34 mice in each group).



Antigen-specific HIV responses in BRGS versus BRGS A2DR2 mice.

(A) Schematic overview of the MVA-HIVB immunization of HSPC mice between 12 and 16 wpg.

(B) Splenic CD4⁺ and CD8⁺ T cells numbers in nonimmunized (black symbols) and immunized (red symbols) from BRGS (full symbols) and BRGS A2DR2 (open symbols) HSPC mice.

(C) ELISPOT IFN- γ analysis of splenocytes from BRGS (full circles) and BRGS A2DR2 (open circles) reconstituted with HLA-A*02+ HLA-DRB1*15+ HSCs 10 days after immunization with MVA-HIVGPN viral particles (red symbols).

(D) MVA vector-specific IgG response in the plasma determined by ELISA from MVA-HIVB immunized and nonimmunized BRGS A2DR2-HSPC mice. Non-immunized BRGS and BRGS A2DR2 animals were also analyzed as controls (black circles). Each dot represents one mouse. Representative data of three independent experiments with one (BRGS NI) to seven mice analyzed per group.

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 BRGS A2DR2 HSPC is tested and analyzed before sending and use. BRGS A2DR2 HSPC mice are produced with SOPF status. Each batch provided is supplied with a list showing the animal repartition according to the different CD34⁺ donors.



GENETICALLY
ENGINEERED
MODELS
(GEM)



MICE
Mutant inbred

NATURAL
IMMUNO-
DEFICIENT

WILD TYPE

NATURAL MUTANTS

BRGS TSLP-HSPC Mouse

Strain name: *C-Rag2^{tm1}-Il2rg^{tm1}-Sirpa^{NOD}-Tg(Ts/p)/Rj*

Type: Mutant inbred mouse

Origin: Institut Pasteur, France, 2022

Colour and related genotype:
Albino mouse

Use of this strain:
Is restricted to private sector users

Grafted human cells:
CD34 from blood cord

Treatment: Irradiation

Presentation of the model

BRGS TSLP-HSPC mice provides additional features in comparison to standard models by displaying a complete development of secondary lymphoid tissues (SLT) as well as consisting in the best model up to date for atopic dermatitis.

The BRGS TSLP mouse model

The BRGS TSLP strain is a highly immunodeficient inbred model characterized by two knockout mutations in the *Il2rg* and *Rag2* genes, resulting in a lack of T, B, and NK cells. The *Rag2* knockout hinders VDJ gene recombination necessary for B and T cell receptor formation, while the *Il2rg* knockout affects the gamma c chain, essential for immune cell differentiation and function. This strain also carries the NOD variant of the *Sirpa* gene, reducing phagocytosis of transplanted human cells. Compared to the NXG strain, it replaces the *Prkdc^{scid}* mutation with *Rag2* knockout, making it more resistant to various stressors and improving its stability for xenograft purposes. Additionally, it overexpresses murine thymic-stromal-cell-derived lymphopoietin (*Ts/p*).

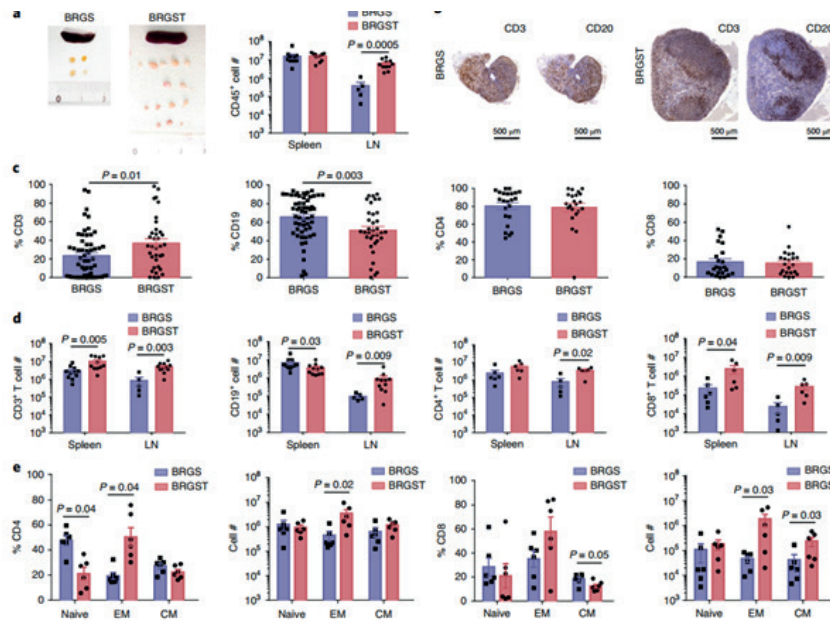
The overexpression of the *Ts/p* gene leads to the formation of a complete range of lymph nodes (LNs) containing segregated human B and T cells. In comparison to other immune system humanized mice, BRGS-TSLP mice exhibit a larger thymus, increased presence of mature B cells, and a higher number of IL-21-producing follicular helper T (T_{FH}) cells, resulting in augmented antigen-specific responses. In essence, BRGS TSLP-HSPC mice accurately represent the impact of SLT development on human immune responses and offer a valuable model for studying and manipulating immune regulation.

A model for human atopic dermatitis

Atopic dermatitis is a chronic inflammatory skin condition characterized by dry, itchy, and inflamed patches of skin. It commonly affects individuals with a family history of allergies, asthma, or eczema, and can flare up due to triggers such as allergens, irritants, or stress. It is a prevalent condition, affecting approximately 15-20% of children and 1-3% of adults worldwide. This disease places not only heavy financial costs on patients and society, but also tremendous negative impact on the quality of life for patients and their family.

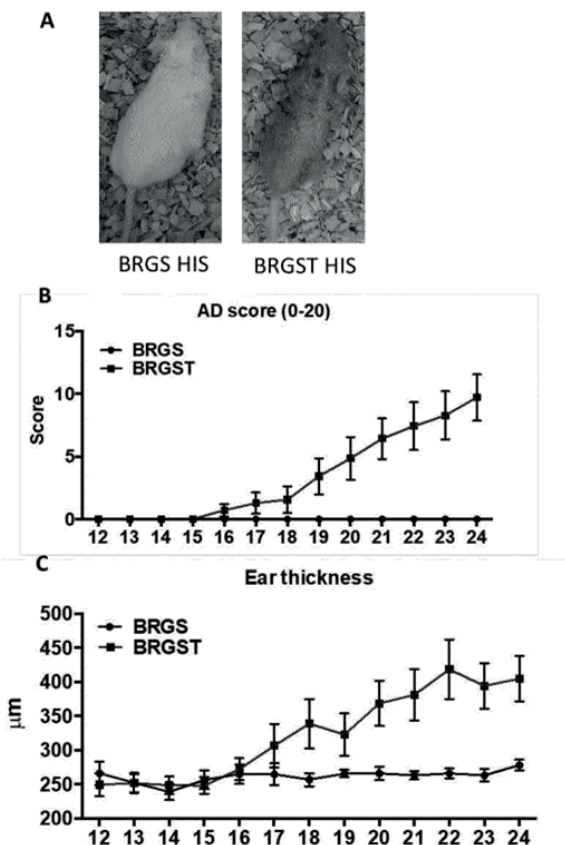
While non humanized BRGS TSLP do not show signs of AD development, BRGS TSLP-HSPC mice universally demonstrate clinical, histological, immunological and skin commensal changes resembling human AD. Multiple human hematopoietic lineages associated with human AD were identified in BRGS TSLP-HSPC mice, such as skin infiltrating Th2 and Th22 cells, IgE secreting B cells and hFcεRIα expressing mast cells and basophils. Similar to clinical findings, AD progression and skin homing chemokine receptor expression on CD4 T cells were highly correlated.

Together, BRGS TSLP-HSPC constitutes a novel humanized model, showcasing enhanced immune system development that mirrors the impact of SLT development on human immune responses. This model offers a platform for visualizing and investigating immune regulatory mechanisms. Moreover, these mice serve as the first spontaneous human AD model and represent an optimal preclinical model for evaluating novel therapeutic interventions.



Characterization of human immune cell reconstitution in BRGS TSLP-HIS mice.

a, Representative organs (left; scale bars in centimeters) and absolute numbers of human CD45+ cells (right) in the spleens and LNs of BRGS and BRGS TSLP HSPC mice (n = 11 mice per group). All visible LNs in BRGS or BRGS TSLP-HSPC mice were pooled. b, Representative immunohistochemistry images of LN sections from BRGS (left) and BRGS TSLP (right) HSPC mice. Scale bars, 500 μm. c, Percentages of human T cells and B cells (n = 60 (BRGS) or 35 (BRGS TSLP) mice) and CD4+ and CD8+ T cells (n = 23 (BRGS) or 22 (BRGS TSLP) mice) among human hematopoietic cells (hCD45+mCD45– (h, human; m, mouse)) in the blood of the indicated mice. d, Absolute numbers of human T and B cells (n = 11 mice per group) and CD4+ and CD8+ T cells (n = 6 mice per group) in the spleen and LNs of the indicated groups of mice. All visible LNs in BRGS or BRGS TSLP-HSPC mice were pooled. e, Percentages and absolute numbers of human naive and memory cell subsets, identified by expression of CCR7 and CD45RA among hCD45+CD3+CD4+ cells and hCD45+CD3+CD8+ cells in the spleen of the indicated groups (n = 6 mice per group). EM, effector memory; CM, central memory. a,c–e, Data are shown as mean ± s.e.m.; P values determined by two-tailed Mann–Whitney U test. Each black square or circle represents an individual mouse. Adapted from Li et al. 2018 under Creative Commons Attribution License



Characterization of the development of AD in BRGST TSLP-HSPC mice.

a, Representative photographs of BRGS and BRGS TSLP-HSPC mice 25 weeks post CD34+ cells engraftment. b, AD scores evolution post CD34+ cells engraftment. The scoring system based on a system scoring the hair density and coverage, the presence of erosions, crusts and scales from 4 regions of the body on a scale of 0 to 4. c, Ear thickness evolution post CD34+ cells engraftment.

Adapted from WO2020008066A1 patent under Creative Commons Attribution License.



GENETICALLY
ENGINEERED
MODELS
(GEM)



MICE
Mutant inbred

NATURAL
IMMUNO-
DEFICIENT

NXG - hPBMC Mouse

WILD TYPE

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

Type: Inbred transgenic mouse, GEMM

Origin: Janvier Labs, in 2021

Colour and related genotype:
Albino mouse

NATURAL
MUTANTS

Grafted human cells:
PBMCs



Presentation of the model

Peripheral blood mononuclear cells -engrafted mice are a benchmark for studying human immune responses in vivo. These innovative models seamlessly bridge the gap between conventional animal studies and clinical research by providing a robust platform to evaluate human immune cell dynamics.

Their applications span oncology, infectious diseases, and autoimmunity, offering unparalleled insights into tumor-immune interactions, host-pathogen mechanisms, and therapeutic responses. Leveraging cutting-edge protocols and immunodeficient strains like NXG mice, PBMC-engrafted models empower researchers with a powerful tool to decode complex immune mechanisms and accelerate the development of transformative therapies.

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.



Main application and research fields

ONCOLOGY

IMMUNOTHERAPY

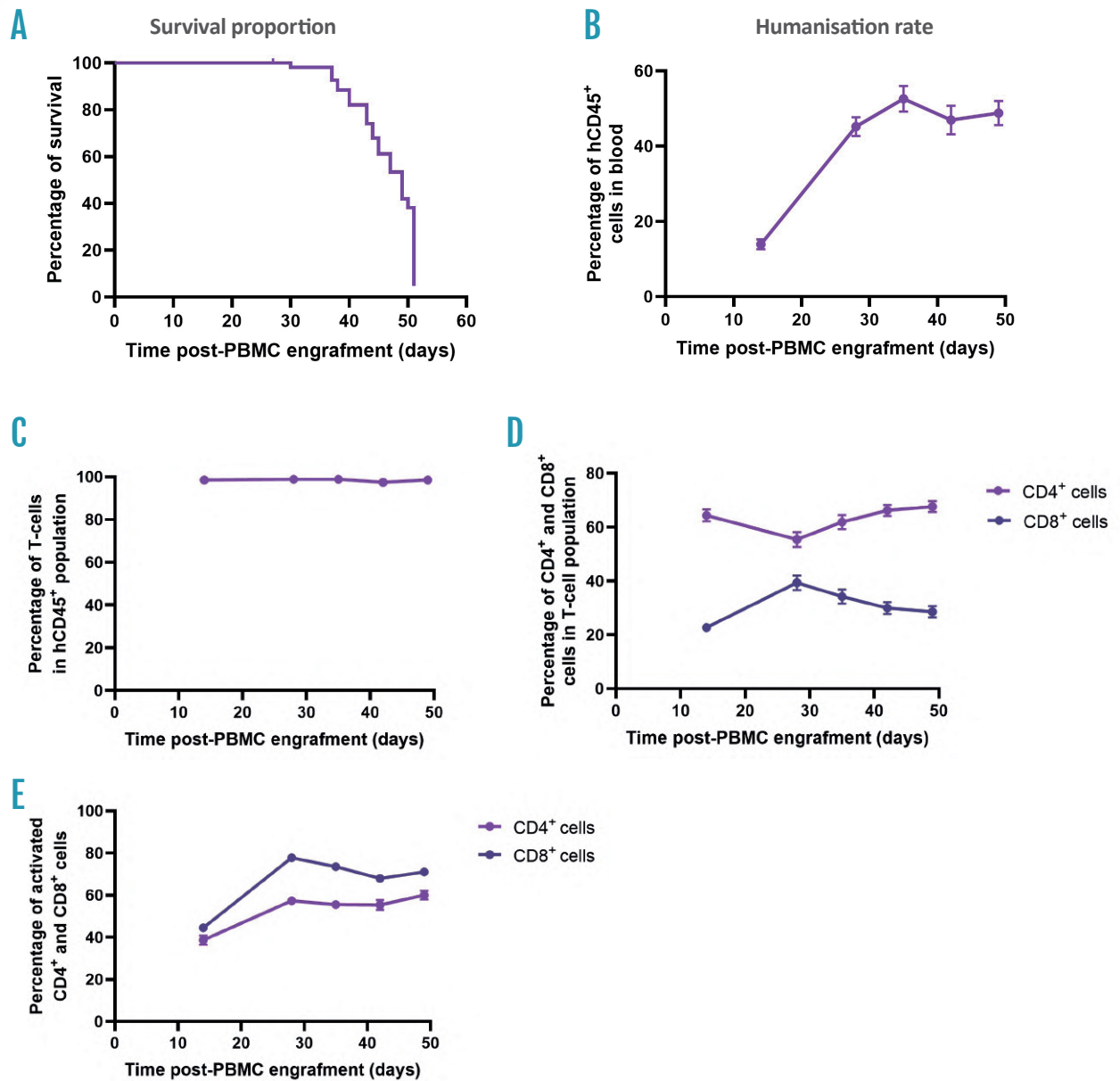
INFECTIOUS DISEASES

IMMUNOLOGY

AUTO-IMMUNE DISEASES



Peripheral blood and weight

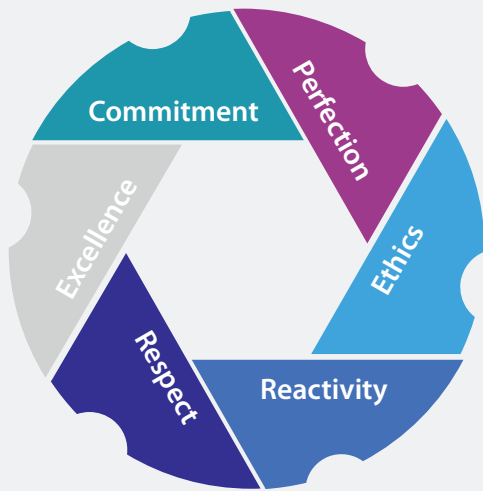


Assessment of Human Immune System Engraftment in NXG Mice Injected with Human PBMCs

Five-week-old NXG mice were injected with human PBMCs, and immune engraftment was monitored over time.

- (A) Survival curve of mice following PBMC injection, showing the proportion of mice surviving GvHD onset.
- (B) Humanization levels, represented by the percentage of hCD45⁺ cells in peripheral blood.
- (C) Percentage of human T-cells among the hCD45⁺ population.
- (D) Distribution of CD4⁺ and CD8⁺ cells within the human T-cell compartment.
- (E) Proportion of activated phenotypes (hCD4⁺ and hCD8⁺ T-cells) in peripheral blood.

Data points represent the mean values from 30 mice across two independent experiments, with error bars indicating the standard error of the mean (SEM).

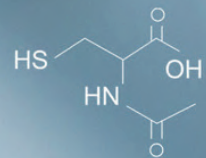


YOUR SATISFACTION: OUR PRIORITY

OUR COMMITMENTS: ADAPTABILITY AND REACTIVITY

- Flexibility in order-taking
- Tailor-made response to each of your requirements
- Personalised accompaniment for your projects
- A scientific follow-up specialised in rodents breeding
- Sales assistance on hand and ready to help
- Local sales representative for your specific needs
- Team of veterinary surgeons and experts to advise you
- An ISO 9001 certified company for all our activities

MY NOTES



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