

Our **IMMUNO-ONCOLOGY** offer



# IMMUNO-ONCOLOGY

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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

 <b>1 unique production site</b> in Europe <b>22,000 sqm of facilities</b> on more than 8 hectares	 Breeding capacity <b>3,000,000 rodents a year</b>	 <b>45,000 km a week travelled</b> by our integrated transport department	 <b>3,500 customers</b> worldwide <b>412 international employees</b>
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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 CENTRE OF IMMUNOPHENOMICS (CIPHE)

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



# I. OUR

# IMMUNODEFICIENT

# MOUSE MODELS

Janvier Labs supports your research projects by offering an expanded range of immunodeficient models

## FIELDS OF APPLICATION

Janvier Labs research models show different immunodeficiency levels and are available under different genetic backgrounds, so that each of your studies benefits from a model with its own immune characteristics. They cover numerous study areas such as:

- ✕ The understanding of immune system and of its mechanisms
- ✕ The development of new vaccines and immunotherapy products
- ✕ Tissue grafts including tumors
- ✕ The development and the optimization of anti-cancer immunotherapies
- ✕ The development of new imaging methods
- ✕ Inflammation processes

### CYTOKINE-HUMANIZED STRAINS

NEW



NXG-hIL15



NXG-EXL (hIL3, hGM-CSF)



NXG-hIL2



NXG-hIL6/hIL6R

### TRIPLE IMMUNODEFICIENT STRAINS



NXG



NXG B2M-KO



NRG



NRG Nude



NRG-cKit



BRGS TSLP



B6RGS



B6RGS Nude



Corresponding humanized model available

### MHC-HUMANIZED STRAINS



NXG-HLA-A2\*01



BRGS A2DR2

### T- AND B-CELLS DEFICIENT STRAINS

Ranked in descending order of severity



NOD Scid



B6R



CB17 Scid Nude



CB17 Scid



BALB/c Nude



NMRI Nude

# TECHNICAL DATA

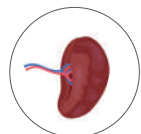
	Background	Breeding	Coat	T Lymphocytes	B Lymphocytes	Leakiness	NK cells	Dendritic cells	Macrophages	Complement	Irradiation tolerance	Humoral immunity	Phagocytic Tolerance	Mutations of interest
<b>NRG-cKIT</b>	NOD	Inbred	Albino	Absent	Absent	Very low	Absent	Dysfun.	Dysfun.	Very low	High	Absent	High	<i>Sirpa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

# 01 HAEMATOLOGICAL PARAMETERS

Designation	Unit
Red blood cell absolute count	(x1E6/uL)
Platelet absolute count	(x1E3/uL)
Reticulocyte absolute count	(x1E3/uL)
White blood cell count	(x1E3/uL)
Reticulocytes percentage	(%)
Hematocrite	(%)
Mean corpuscular hemoglobin	(pg)
Hemoglobin	(g/dL)

Designation	Unit
Mean corpuscular hemoglobin concentration	(g/dL)
Mean corpuscular volume	(f1-)
Platelet larger cell ratio	(0/0)
Plateletcrit	(%)
Low fluorescence ratio reticulocyte	(%)
Medium fluorescence ratio reticulocyte	(%)
High fluorescence ratio reticulocyte	(%)
Immature reticulocyte fraction	(%)

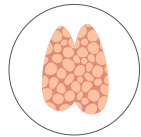
# 02 IMMUNOLOGICAL PARAMETERS



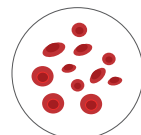
Spleen



Bone marrow



Thymus



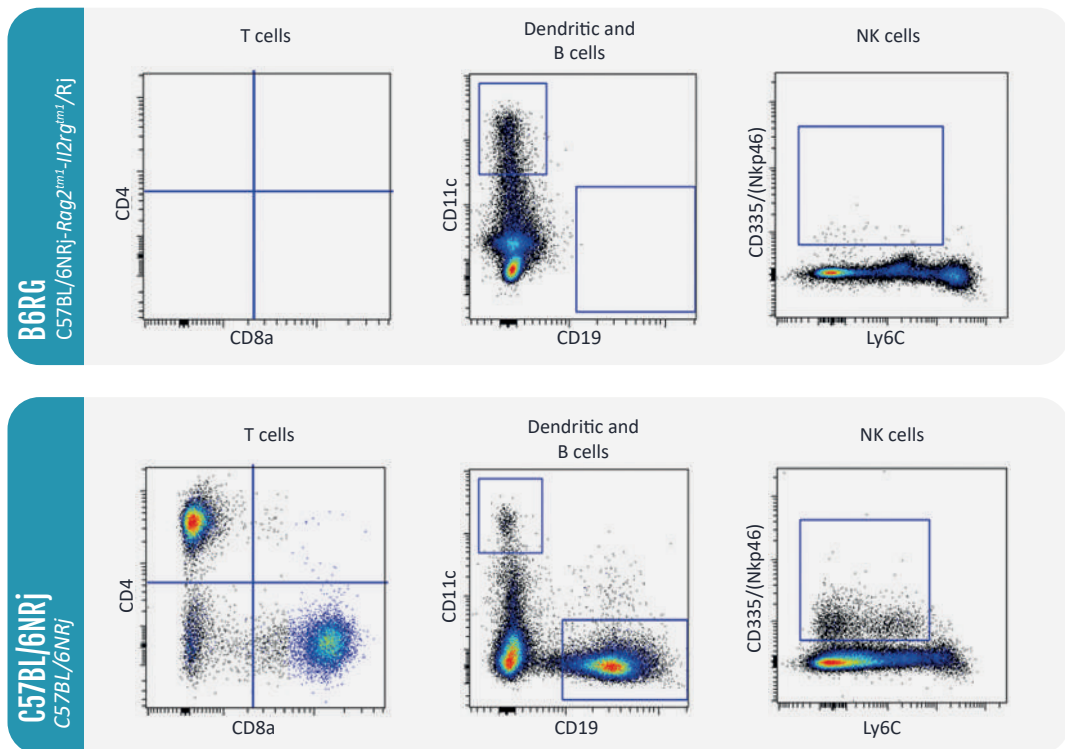
Peripheral blood



All our immunodeficient models were immunophenotyped.

Example of a cytometric analysis of the spleen of our B6RG and C57BL/6NRj (Wild Type) models.

Contact us



The cell composition of all lymphoid organs of our models was analyzed and divided into 12 different cell populations.

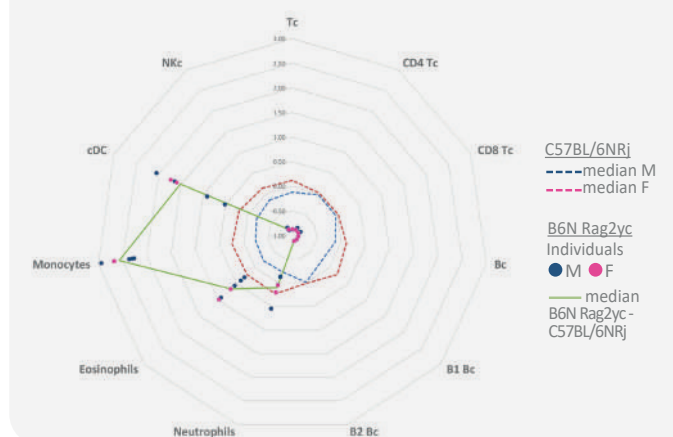
Contact us

## 12 CELL POPULATIONS



We also offer an immunophenotyping service for the immunodeficient models at each stage of your research protocols.

## COMPARISON RADAR CHART B6N RAG2YC VS C57BL/6NRJ



# SPOTLIGHT ON: THE NXG STRAIN



## Denomination

NOD-Prkdc<sup>scid</sup>-Il2rg<sup>tm1</sup>/Rj

## Type

Inbred mutant mouse, GMO

## Origin

Janvier Labs, 2019

## Presentation of the model

The **NXG mouse** is an inbred strain model with two knockout key mutations, similar to its counterpart models NSG, NCG, and NOG (NOD SCID Gamma).

- The **Prkdc<sup>scid</sup>** (SCID) mutation inhibits the development of T and B cells, resulting in their complete absence.
- The **Il2rg<sup>tm1</sup>** mutation is a knockout (KO) of the gene encoding the interleukin-2 receptor subunit gamma, which is shared by several interleukin receptors (IL-2, IL-4, IL-7, IL-9, and IL-15). This gene is essential for the differentiation and proper functioning of many immune system cells, including natural killer (NK) cells.

The combination of these two mutations on a NOD background induces severe immunodeficiency, leading to the absence of **T, B, and NK lymphocytes**, as well as a **lack of circulating complement**.

The expression of the **NOD variant** of the polymorphic Sirpa gene on murine macrophages enables cross-recognition with **human CD47** on human cells, which is essential for the «don't eat me» signal. This feature greatly facilitates the engraftment of transplanted human cells.

## Phenotypic characterisation

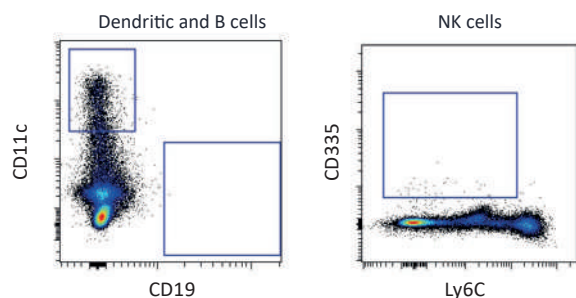
Background	Breeding	Coat	T Lymphocytes	B Lymphocytes	Leakiness	NK cells	Dendritic cells
NOD	Inbred	Albino	Absent	Absent	-	Absent	Dysfunctional
Macrophages	Complement	Irradiation tolerance	Life span	Humoral immunity	Phagocytic tolerance	Mutations of interest	
Dysfunctional	-	Low	89 Wk.	Absent	High	Sirpa <sup>NOD</sup> Prkdc <sup>scid</sup> Il2rg <sup>tm1</sup>	

## Applications

The **NXG model** is a robust platform for the establishment of cancer-derived xenografts and patient-derived xenografts. The model features an important versatility. It allows to study cancer biology such as the inflammation processes and tumour microenvironment. In parallel, it enables the screening of candidate compounds, and the assessment of their efficacy as mono or combined therapies.

*Janvier Labs provides access to NXG mice reconstituted with peripheral blood mononuclear cells or hematopoietic stem and progenitor cells. For more information, please refer to our dedicated booklet or contact us.*

## Flow cytometry analysis, spleen

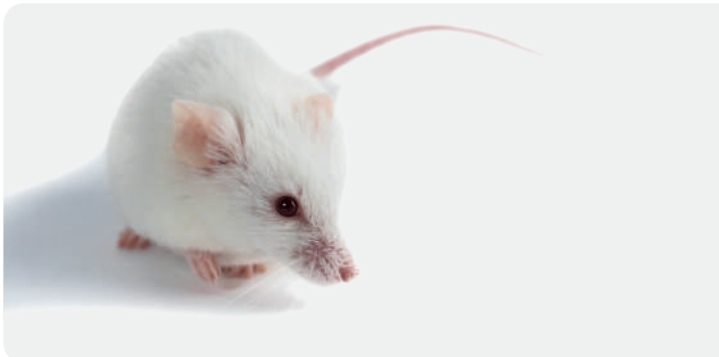


Flow cytometry analysis of the spleen of our NXG shows a complete absence of T, B or NK lymphocytes, confirming the severe immunodeficiency.

## Selected references

- Ascic E, et al. In vivo dendritic cell reprogramming for cancer immunotherapy. *Science*. 2024;386(6719)
- Baldwin JG, et al. Intercellular nanotube-mediated mitochondrial transfer enhances T cell metabolic fitness and antitumor efficacy. *Cell*. 2024;187(23)
- Bhin J, et al. MYC is a clinically significant driver of mTOR inhibitor resistance in breast cancer. *J Exp Med*. 2023;220(11)

# SPOTLIGHT ON: THE NRG STRAIN



## Denomination

NOD-*Rag2-Il2rg<sup>tm1</sup>*/Rj

## Type

Inbred mutant mouse, GMO

## Origin

Janvier Labs, 2021

## Presentation of the model

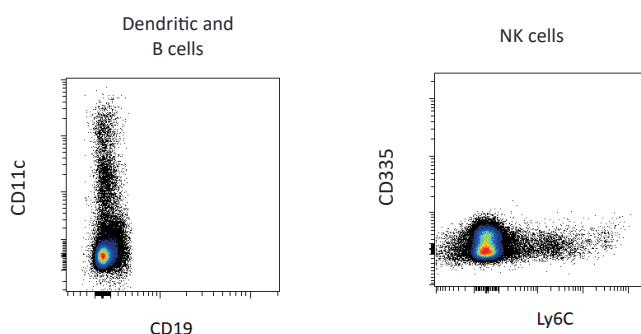
The NRG or NOD *Rag2*  $\gamma$ c strain is a highly immunodeficient inbred model with two knockout mutations in the *Il2rg* (interleukin-2 receptor subunit gamma) and *Rag2* (recombination activating gene 2) genes. The NRG mouse exhibit an absence of T, B and NK cells and a lack of circulating complement. The model is suitable for the engraftment of human tissues, similarly to the NXG model (NOD-*Prkdc<sup>scid</sup>-Il2rg<sup>tm1</sup>*/Rj).

The model however differs from the NXG model, by replacement of the *Prkdc<sup>scid</sup>* mutation (commonly known as «SCID») with the *Rag2* knockout. This makes it more resistant to irradiation, genotoxic products, and stress, thereby improving its durability and stability for xenograft purposes.

## Phenotypic characterisation

Background	Breeding	Coat	T Lymphocytes	B Lymphocytes	Leakiness	NK cells	Dendritic cells
NOD	Inbred	Albino	Absent	Absent	-	Absent	Dysfunctional
Macrophages	Complement	Irradiation tolerance	Life span	Humoral immunity	Phagocytic tolerance	Mutations of interest	
Normal	-	High	89 Wk.	Absent	High	<i>Sirpa<sup>NOD</sup> Rag2<sup>tm1</sup> Il2rg<sup>tm1</sup></i>	

## Flow cytometry analysis, spleen



Flow cytometry analysis of the spleen of our NRG shows a complete absence of T, B or NK lymphocytes, confirming the severe immunodeficiency.

## Selected references

- Gaballa A, et al. PAF1c links S-phase progression to immune evasion and MYC function in pancreatic carcinoma. *Nat Commun.* 2024;15(1)
- Almeida A, et al. Antitumor Effect by Either FLASH or Conventional Dose Rate Irradiation Involves Equivalent Immune Responses. *Int J Radiat Oncol Biol Phys.* 2024;118(4)
- Krenz B, et al. MYC- and MIZ1-Dependent Vesicular Transport of Double-Strand RNA Controls Immune Evasion in Pancreatic Ductal Adenocarcinoma. *Cancer Res.* 2021;81(16)

# SPOTLIGHT ON: THE NRG cKit STRAIN



## Denomination

NOD-Rag2<sup>tm1</sup>-Il2rg<sup>tm1</sup>-Kit<sup>em1</sup>/Rj

## Type

Inbred mutant mouse, GMO

## Origin

Janvier Labs, 2023

## Presentation of the model

The NRG cKIT mouse features an additional V831M point mutation in the *Kit* gene, resulting in a disruption of its endogenous functionality. The absence of the KIT protein's kinase function hampers mouse hematopoietic stem cells, facilitating the engraftment of human hematopoietic stem cells without the need for irradiation. Moreover, it fosters enhanced hematopoietic chimerism in peripheral blood and an increased count of circulating human red blood cells.

*Janvier Labs provides access to NRG cKit mice reconstituted with hematopoietic stem and progenitor cells. For more information, please refer to our dedicated booklet or contact us.*

# CYTOKINE-HUMANIZED IMMUNODEFICIENT STRAINS

## hIL-15 NXG



## Denomination

NOD-Prkdc<sup>scid</sup>-IL2rg<sup>tm1</sup>-Il15<sup>em1(hIL15)</sup>/Rj

## Type

Inbred mutant mouse, GMO

## Origin

Janvier Labs, 2023

## Presentation of the model

The hIL-15 NXG model was developed by replacing the murine Il15 gene with the human IL-15 gene in the NXG strain. This model exhibits physiological hIL-15 expression, closely mirrors human physiological conditions.

	Serum hIL-15 levels
Resting conditions	approximately 80 pg/mL
Inflammation and immune activation	Up to 400 pg/mL

## Applications

IL-15 is crucial for NK cell survival and expansion. Humanized IL-15 mice better support human NK cell engraftment, function, and persistence, making them ideal for studying NK biology, NK cell-based therapies, IL-15- and NK-targeting compounds.

*Janvier Labs provides access to hIL15 NXG mice reconstituted with hematopoietic stem and progenitor cells. For more information, please refer to our dedicated booklet or contact us.*

Coming in 2025: NXG EXL (hIL-3:hGM-CSF) | NXG hIL6/hIL-6R | NXG hIL-2

# GENETICALLY ENGINEERED MODELS (GEM)

## BRGS A2DR2

C-*Rag2*<sup>tm1</sup>-*Il2rg*<sup>tm1</sup>-*Sirpa*<sup>NOD</sup>-Tg(HLA-A\*02-HHD)-Tg(HLA-DR2)/Rj



**Origin** Institut Pasteur, Lille, France, in 2022

The BRGS A2DR2 model is an immunodeficient Balb/c mouse with two knockout mutations of the *Il2rg* and *Rag2* genes. This strain also expresses the NOD variant of the *Sirpa* gene, promoting phagocytic tolerance. Additionally, it expresses two human transgenes: HLA-A\*02 and HLA-DR2. Besides severe immunodeficiency resulting in the total absence of murine T, B, and NK cells, the expression of class I and II HLA enhances the differentiation, maturation, and specificity of human T cells after transplantation.

## BRGS TSLP

C-*Rag2*<sup>tm1</sup>-*Il2rg*<sup>tm1</sup>-*Sirpa*<sup>NOD</sup>-Tg(*Tslp*)/Rj



**Origin** Institut Pasteur, Lille, France, in 2022

The BRGS TSLP model is an immunodeficient Balb/c mouse with two knockout mutations in the *Il2rg* and *Rag2* genes. This strain also expresses the NOD variant of the *Sirpa* gene, promoting phagocytic tolerance. Additionally, it has been modified to overexpress the *Tslp* (thymic-stromal-cell-derived lymphopoietin) gene. Besides severe immunodeficiency resulting in the total absence of murine T, B, and NK cells, TSLP expression leads to the complete development of lymph nodes, an enlarged thymus, and an enhanced antigen-specific response. When transplanted with human hematopoietic stem cells, this model develops atopic dermatitis, making it an ideal model for studying inflammatory diseases.

# IMMUNODEFICIENT RAT MODELS

Oncology has become a major area of research. The Janvier Labs' immunodeficient rats have been developed to meet your needs of models to advance your research and development programs in oncology, immunology, inflammation and all related immune-based therapeutics.

Our team can help you identify the best immunodeficient rat model for your research, advising on the levels of immunodeficiency and phenotypic characteristics you need.

## ATHYMIC Nude rat

Rj:ATHYM-*Foxn1*<sup>tmu</sup>



**Origin** Janvier Labs, Laval, France, in 2018

The ATHYMIC Nude rat is a model carrying a genetic mutation called «nude» on an outbred LOU-FISCHER genetic background. The ATHYMIC Nude model is characterized by the lack of fur and reduced immunity, including the absence of T cells and diminished functionality of B cells.

## LOU Nude

LOU-*Foxn1*<sup>tmu</sup>/Rj



**Origin** Institut Pasteur, Lille, France, in 2008

The LOU Nude rat is a model carrying a genetic mutation called «nude» on an inbred LOU genetic background. The LOU Nude model is characterized by the lack of fur and reduced immunity, including the absence of T cells and diminished functionality of B cells.

## FISCHER Nude

F344-*Foxn1*<sup>tmu</sup>/Rj



**Origin** Janvier Labs, Laval, France, in 2018

The FISCHER Nude rat is a model carrying a genetic mutation called «nude» on an inbred FISCHER genetic background. The FISCHER Nude model is characterized by the lack of fur and reduced immunity, including the absence of T cells and diminished functionality of B cells.

# WATCH OUR WEBINARS ON IMMUNODEFICIENT MODELS



## BRIDGING THE GAP: HARNESSING HUMANIZED MOUSE MODELS FOR IMMUNOLOGY AND LIVER STUDIES

Our two experts, Pierre Dillard, Head of R&D at Janvier Labs, and Devorah Goldman, Head of R&D at Yecuris, discuss:

- Understanding the Humanized Immune System mice: Hu-PBL, Hu-SRC, BLT: what they are, how to select them, how to make the most of them in your research
- FRG Liver-Humanized Mice: overview, applications, selected examples of pre-clinical studies
- Future directions



## HUMANIZED MODELS IN ONCOLOGY AND IMMUNOLOGY: THE FUTURE OF RODENT ANIMAL RESEARCH

Make your immuno-oncology drug development efficient with the most translatable ready-to-use models: NXG and its humanized equivalent, the NXG-HIS mouse model. Get access to information on engraftment, humanization process, characterization and benefits of NXG and NXG-HIS strains.

The new NXG-HIS humanized platform at Janvier Labs designs and generates humanized mice with human biological functions to ensure high-quality translational data during your early and preclinical drug evaluation.



## IMMUNODEFICIENT MICE FOR YOUR PRECLINICAL TESTING: UPDATES AND NEWS

Make your drug development efficient with the most translatable ready-to-use models and immunoprofiling services.

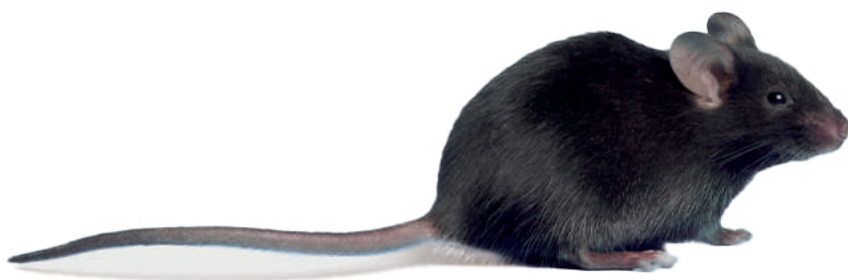
The following topics have been covered during this webinar:

- Genetic background impact, immunodeficiencies and genes, immunodeficient models and applications, handling features
- Use of NXG models in preclinical oncology trials, with examples of grafting tumors and associated chemotherapies and immunotherapies
- Humanized mouse models: Engraftment process, quality-control of CD34 and humanization level of canonical hematopoietic cell lineages
- Ongoing comparative analysis of engraftment level depending on myeloablative conditioning method, route of CD34 injection and genetical background of recipient animals.



## II. OUR KNOCK-IN HUMANIZED MOUSE MODELS

Knock-in humanized mouse models are fully immunocompetent mice in which one or more mouse genes have been replaced by their human orthologs. This enables the assessment of compounds that specifically target human proteins. These models are also suitable for transplanting tumor cells of mouse origin to generate syngeneic tumor models.

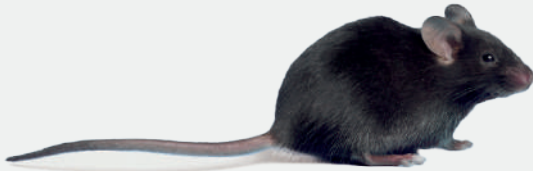


Janvier Labs is granting the exclusive access in Europe to genetically engineered mice developed by the Shanghai Model Organisms Center, Inc. (SMOC).

A selection of preclinical immunology mouse models available at Janvier Labs is introduced in the next pages.

For additional models, please contact our team.

# B6 hPD-1



## Denomination

C57BL/6Smoc-*Pdcd1*<sup>em1(PDCD1)</sup>/SmocRj

## Type

Inbred mutant mouse, GMO

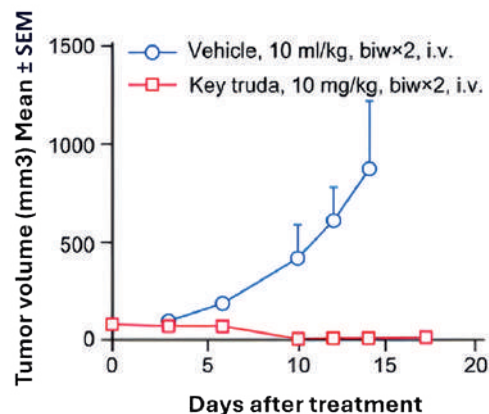
## Origin

SMOC, 2024

## Presentation of the model

The B6 hPD-1 mouse features replacement of the mouse *Pdcd1* gene with its human ortholog. The humanized PD-1 protein retains its ability to interact with mouse PD-L1 due to cross-reactivity and maintains its intracellular signaling properties [1].

Validation data show that human-specific anti-PD-1 antibodies, such as Pembrolizumab and Nivolumab, effectively inhibit tumor growth in syngeneic tumor models.



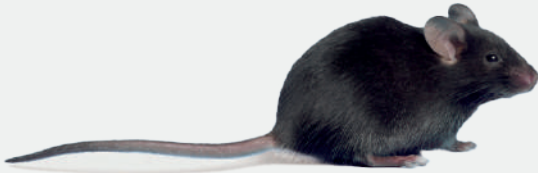
### *In vivo* response of MC38 tumor-bearing humanized PD-1 mice to Keytruda.

Homozygous humanized PD-1 mice (n=16) were inoculated with MC38 colon cancer cells. Randomization and treatment initiation were performed once the tumors grew to 100 mm<sup>3</sup>. Keytruda exerted a very significant anti-tumor effect (p<0.001). (Data from SMOC/Genscript)

## References

- [1] Masubuchi et al., *Sci. Immunol.* 10, eads6295 (202)
- [2] Ju F et al. *J Immunother Cancer.* 12(1):e004762corr1.
- [2] Xu X et al. *Cancers (Basel).*16(17):3052.

# B6 hPD-L1



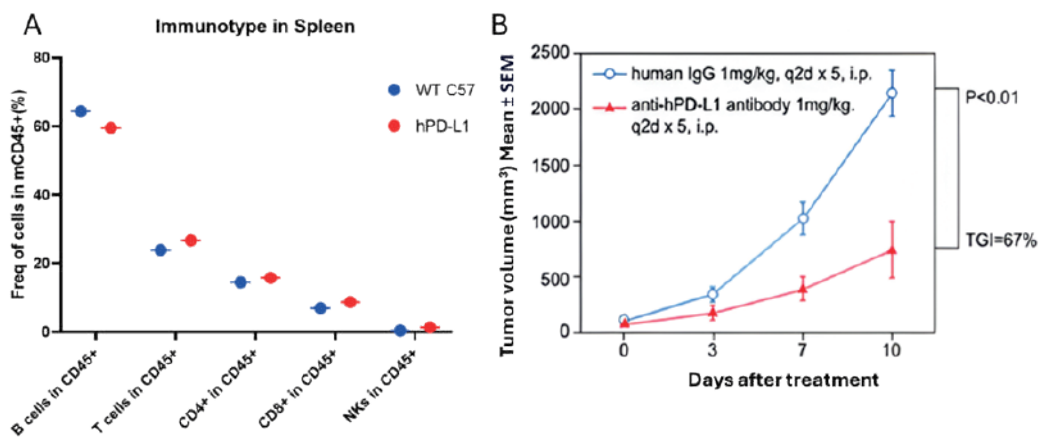
**Denomination**  
C57BL/6Smoc-*Cd274*<sup>em1(CD274)</sup>/SmocRj

**Type**  
Inbred mutant mouse, GMO

**Origin**  
SMOC, 2024

## Presentation of the model

The B6 hPD-L1 mouse features the replacement of the mouse *B7-H1* gene with its human ortholog. This model has been shown to effectively predict the anti-tumor effects of candidate anti-hPD-L1 blocking antibodies.



A. Immunophenotyping comparison of the spleens of homozygous hPD-L1 and WT mice.

B. *In vivo* response of MC38 tumor-bearing humanized PD-L1 mice to anti-hPD-L1.

Homozygous hPD-L1 mice (n=10) were inoculated with MC38 colon cancer cells. Randomization and treatment initiation were performed once the tumors grew to 100 mm<sup>3</sup>. Candidate compounds induced a significant tumor growth inhibition ( $p < 0.001$ ).

## References

- [1] Zhang X et al. *Cell Mol Immunol.* 2019;16(4):392-400
- [2] Huang A, et al. *Sci Rep.* 2017;7:42687.

# B6 hPD-1/hPD-L1



## Denomination

C57BL/6Smoc-Pdcd1<sup>em1(PDCD1)</sup>-Cd274<sup>em1(PD-L1)</sup>/SmocRj

## Type

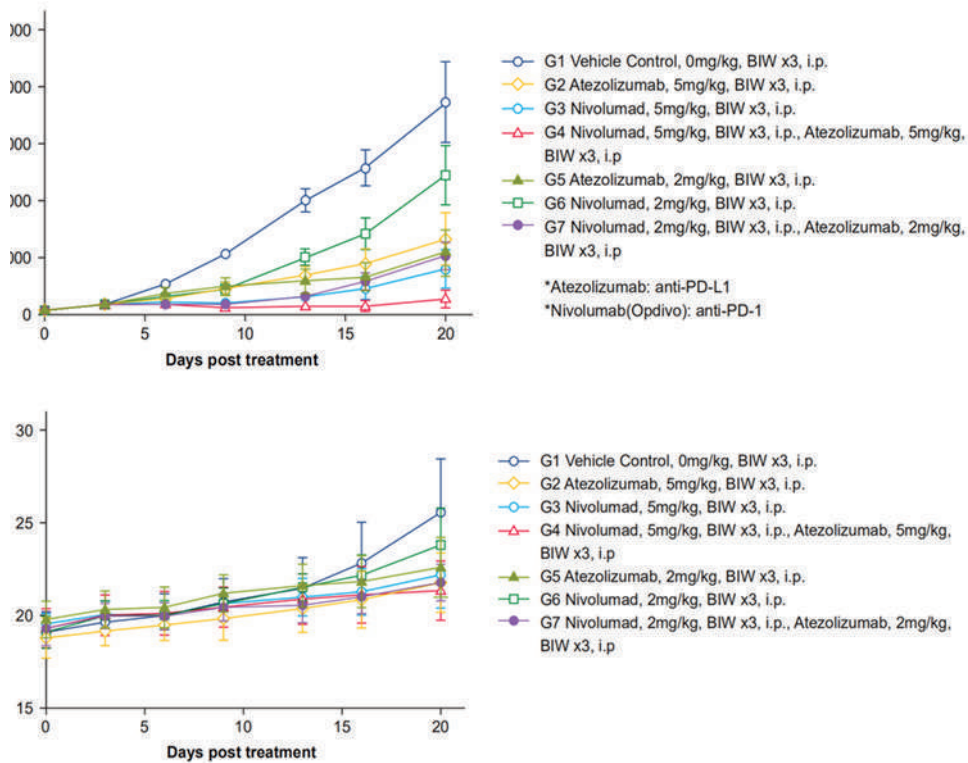
Inbred mutant mouse, GMO

## Origin

SMOC, 2024

## Presentation of the model

The double humanized B6 hPD-1/hPD-L1 mouse was created by crossbreeding the B6 hPD-1 and B6 hPD-L1 mice.



### *In vivo* response of MC38 tumor-bearing humanized hPD-1/hPD-L1 mice to combo-therapy.

Homozygous hPD-1/hPD-L1 mice (n=8 per group) were inoculated with MC38 colon cancer cells. Randomization and treatment initiation were performed once the tumors grew to 100 mm<sup>3</sup>. Both Atezolizumab and Nivolumab induced a significant tumor growth inhibition, with combo-therapy featuring improved response without affecting the body weight.

# B6 hCTLA-4



## Denomination

C57BL/6Smoc-*Ctla4*<sup>em1(CTLA4)</sup>/SmocRj

## Type

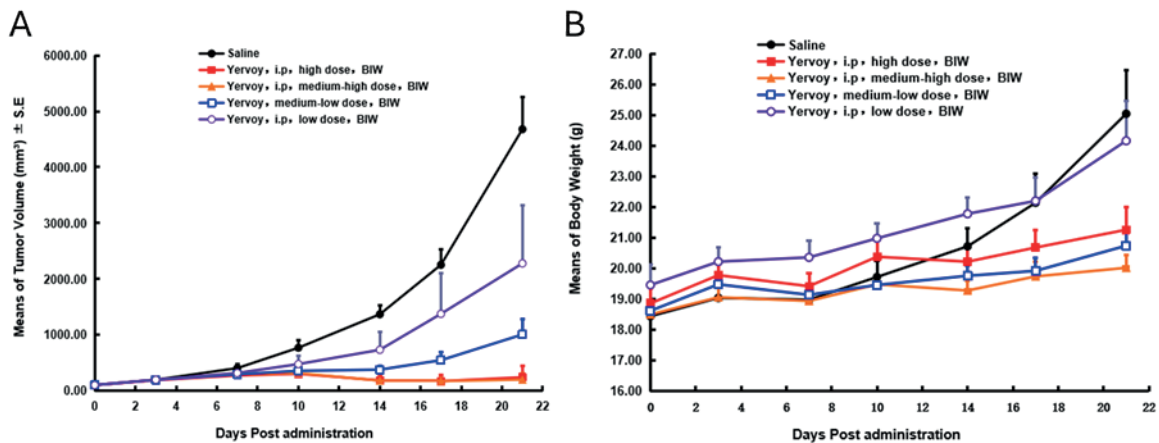
Inbred mutant mouse, GMO

## Origin

SMOC, 2024

## Presentation of the model

The B6 hCTLA-4 mouse features the replacement of the mouse *Ctla4* gene with its human ortholog.

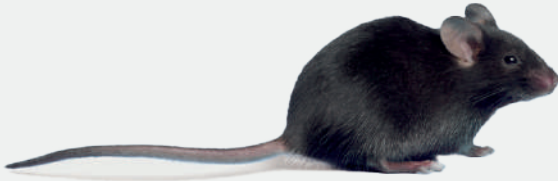


Tumor growth inhibition (A) and body weight evolution (B) in MC38 tumor-bearing humanized hCTLA-4 mice treated with indicated doses of ipilimumab.

## Reference

[1] Guan J et al.. *MAbs*. 2023;15(1):2153409.

# B6 hPD-1/hCTLA-4



## Denomination

C57BL/6Smoc-*Pdcd1*<sup>em1(PDCD1)</sup>-*Ctla4*<sup>em1(CTLA4)</sup>/SmocRj

## Type

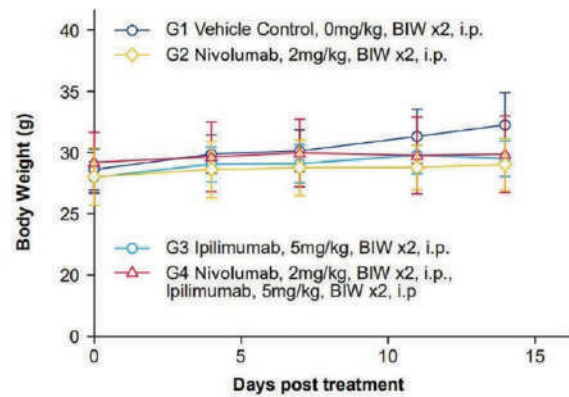
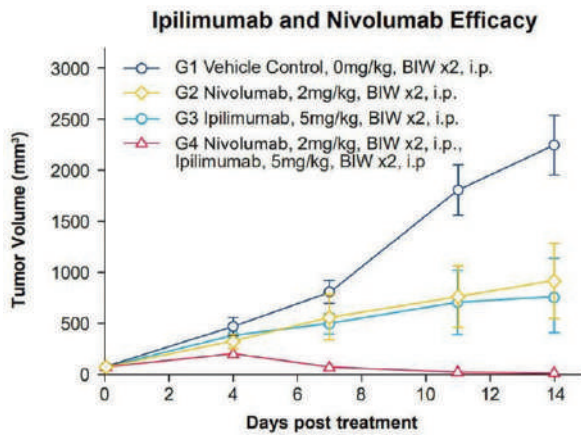
Inbred mutant mouse, GMO

## Origin

SMOC, 2024

## Presentation of the model

The double humanized B6 hPD-1/hCTLA-4 mouse was created by crossbreeding the B6 hPD-1 and B6 hCTLA-4 mice.



### *In vivo* response of MC38 tumor-bearing humanized hPD-1/hCTLA-4 mice to combo-therapy.

Homozygous hPD-1/hCTLA-4 mice (n=8 per group) were inoculated with MC38 colon cancer cells. Randomization and treatment initiation were performed once the tumors grew to 100 mm<sup>3</sup>. Combo-therapy with anti-hCTLA-4 Ipilimumab and anti-hPD-1 Nivolumab induced efficient tumor growth inhibition without affecting the animal body weight

# B6 hPD-L1/hCTLA-4



## Denomination

C57BL/6Smoc-*Ctla4*<sup>em1(CTLA4)</sup>-*Cd274*<sup>em1(CD274)</sup>/SmocRj

## Type

Inbred mutant mouse, GMO

## Origin

SMOC, 2024

## Presentation of the model

The double humanized B6 hPD-L1/hCTLA-4 mouse was created by crossbreeding the B6 hPD-L1 and B6 hCTLA-4 mice. This model has been shown to effectively predict the anti-tumor effects of both single and combination therapies targeting hPD-L1 and hCTLA-4. Memory immunity was confirmed through a re-challenge experiment.

# B6 hLAG-3



## Denomination

C57BL/6Smoc.129S-Cd223<sup>tm1(CD223)</sup>/SmocRj

## Type

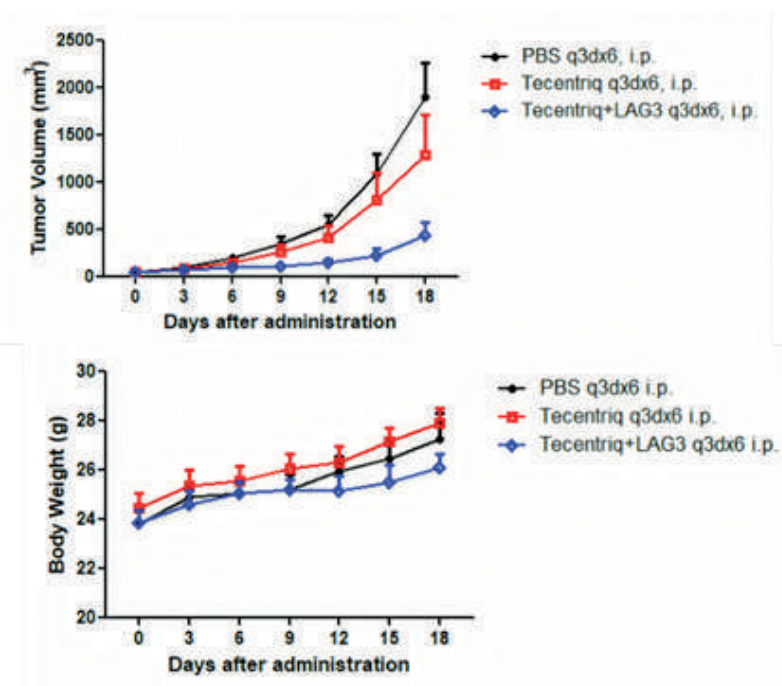
Inbred mutant mouse, GMO

## Origin

SMOC, 2024

## Presentation of the model

The replacement of the mouse *Lag3* gene with its human ortholog enables the preclinical validation of anti-hLAG-3 compounds. Combined treatment with candidate anti-hLAG-3 compounds and Atezolizumab resulted in efficient tumor growth inhibition.



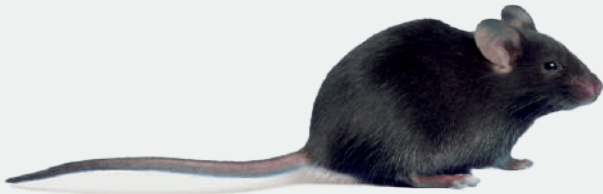
### *In vivo* response of MC38 tumor-bearing humanized hLAG3 mice to combo-therapy.

Homozygous hLAG3 mice (n=8 per group) were inoculated with MC38 colon cancer cells. Randomization and treatment initiation were performed once the tumors grew to 70-80 mm<sup>3</sup>. A significant anti-tumor effect was observed when the antibody targeting human LAG3 was administered together with Tecentriq.

## References

- [1] Shi N et al. *Front Immunol.* 2022;13:1047610.
- [2] Zhou M, et al. *J Immunother Cancer.* 2024;12(7):e009153

# B6 hTIM-3



## Denomination

C57BL/6Smoc-Havcr2<sup>em1(HAVCR2)</sup>/SmocRj

## Type

Inbred mutant mouse, GMO

## Origin

SMOC, 2024

## Presentation of the model

The replacement of the mouse *Havcr2* gene with its human ortholog gene enables the preclinical validation of compounds targeting human TIM-3. A low expression of TIM-3 was observed in naïve CD4- and CD8-positive T cells, which was successfully induced upon *ex vivo* stimulation. Expression of hTIM3 on blood and spleen myeloid cells was confirmed (*data available on demand*).

## Reference

[1] Kuang Z et al. *Antib Ther.* 2020;3(4):227-236.



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# B6 hTIGIT



## Denomination

C57BL/6Smoc-*Tigit*<sup>em1(TIGIT)</sup>/SmocRj

## Type

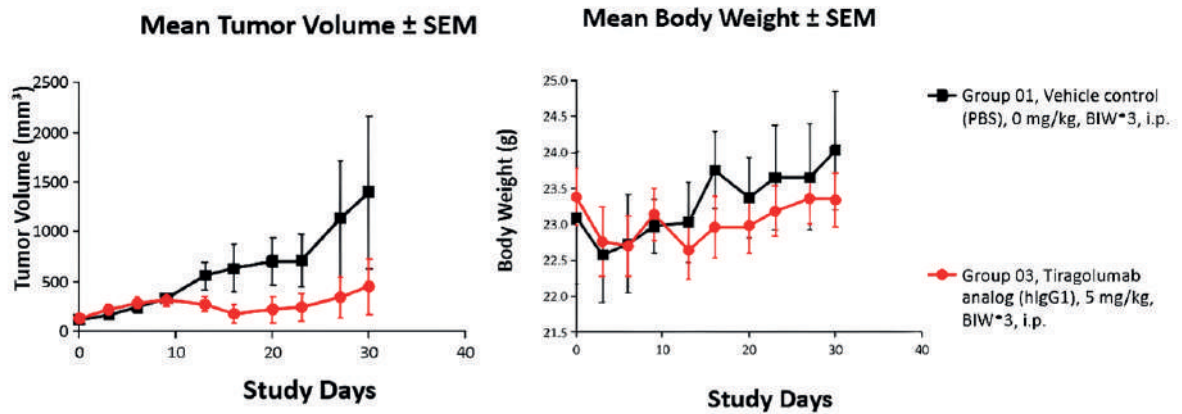
Inbred mutant mouse, GMO

## Origin

SMOC, 2024

## Presentation of the model

The replacement of the mouse *Tigit* gene with its human ortholog enables the preclinical validation of compounds targeting human TIGIT.



**B6 hTIGIT mice transplanted with Hepa1-6 liver cancer cells efficiently responded to Tiragolumab.**

Homozygous hTIGIT mice were inoculated with Hepa1-6 cells. Randomization and treatment initiation were performed once the tumors grew to 110 mm<sup>3</sup> (Data from SMOC/CrownBio)

## References

- [1] Kojima M, et al. *Commun Biol.* 2023;6(1):500.
- [2] Zeven K, et al. *Front Immunol.* 2023;14:1268900.

# B6 hCD3EDG



## Denomination

C57BL/6Smoc-*Cd3e*<sup>tm1(CD3E)</sup>*Cd3d*<sup>tm1(hCD3D)</sup>*Cd3g*<sup>tm1(hCD3G)</sup>/SmocRj

## Type

Inbred mutant mouse, GMO

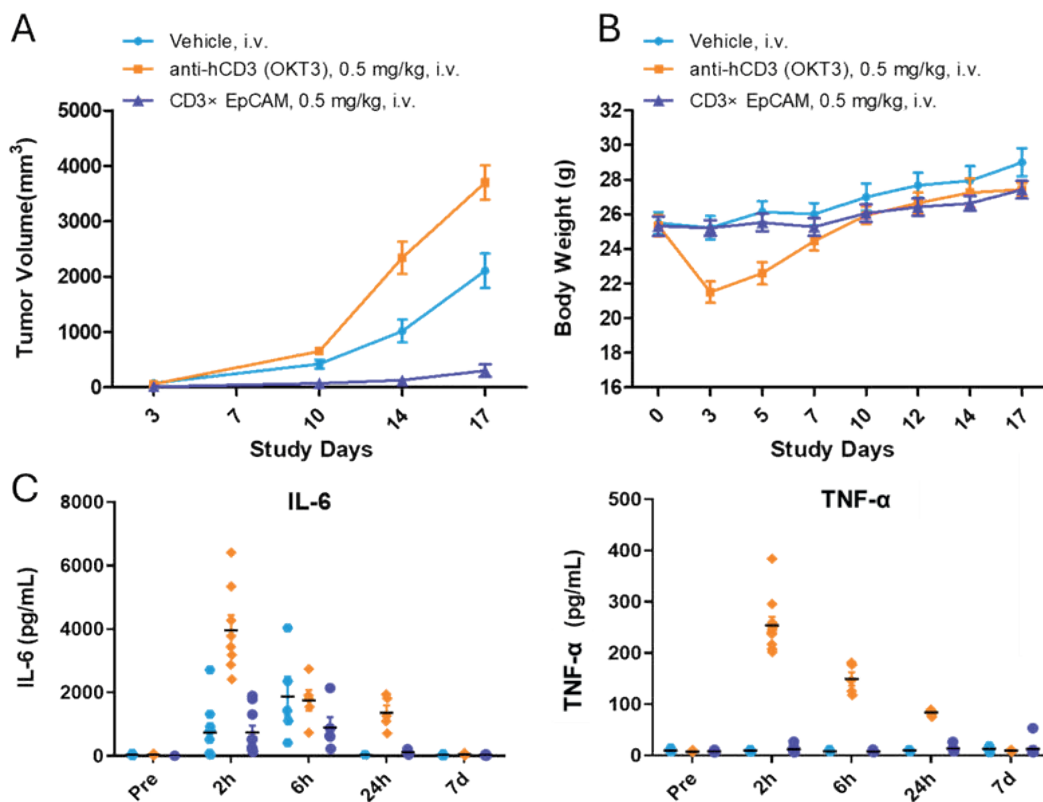
## Origin

SMOC, 2024

## Presentation of the model

The replacement of the mouse *Cd3e*/*Cd3d*/*Cd3g* genes with their human orthologs enables the preclinical validation of bispecific and multispecific T-cell engagers.

This model exhibits a similar immune cell distribution to that of the wild-type (WT) counterpart. Validation data confirm the binding of several CD3-targeting compounds, each recognizing distinct epitopes.



### Tumor growth inhibition and cytokine release induced by candidate CD3xEpCam bispecific compound.

Homozygous hCD3EDG mice were engrafted with MC38-hEpCAM and received treatment with OKT3, CD3xEpCam or vehicle. Tumor growth inhibition results are depicted in A. Body weight evolution (B) and serum cytokine levels (C) results indicate a cytokine release syndrome-like phenotype in mice receiving OKT3, but not candidate compound.

## Reference

Liu S et al. *Mol Ther Oncolytics*. 2023;30:275-285.

# B6 hCD28



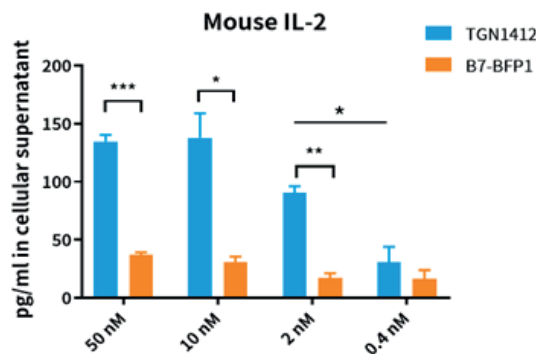
**Denomination**  
C57BL/6Smoc-*Cd28*<sup>em2(CD28)</sup>/SmocRj

**Type**  
Inbred mutant mouse, GMO

**Origin**  
SMOC, 2024

## Presentation of the model

The B6 hCD28 mouse has been modified to replace the mouse *Cd28* gene with the human ortholog. These mice show a similar distribution of immune cells as wild-type (WT) mice. Additionally, cytokine release was observed in T cells treated with TGN1412 ex vivo, demonstrating that this model is suitable for preclinical studies on efficacy and safety



Secretion of IL-2 upon stimulation of T cells with TGN1412 compound or candidate compound.

## Reference

[1] Majocchi S et al. *Cancer Immunol Res.* 2025 Jan 6:OF1-OF19

# B6 hCD3E/hCD28



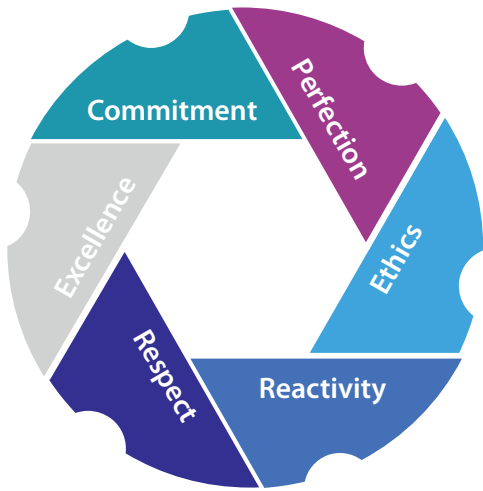
**Denomination**  
C57BL/6Smoc-*Cd3e*<sup>em1(CD3E)</sup>-*Cd28*<sup>em2(CD28)</sup>/SmocRj

**Type**  
Inbred mutant mouse, GMO

**Origin**  
SMOC, 2024

## Presentation of the model

The double humanized B6 hCD3E/hCD28 mouse was created by crossbreeding the B6 hCD3E and B6 hCD28 mice. The B6 hCD3E model features the replacement of the mouse *Cd3e* gene with its human ortholog.



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