GENETICALLY ENGINEERED MODELS (GEM)

NATURAL IMMUNO-DEFICIENT

WILD TYPE

NATURAL MUTANTS

MICE
Mutant inbred

NRG Mouse

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

Type:
Inbred mutant mouse, GMO

Origin:
Janvier Labs, Laval, France, in 2021

Colour and related genotype:
Albino mouse

Presentation of the model

The NRG or NOD Rag2 γc 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 *Rag2*^{tm1} mutation is a knockout of one of the two genes controlling the expression of recombinase activity for VDJ genes, crucial for the formation of B and T cell receptors. This absence hinders the development of these cells, resulting in a total lack of T and B lymphocytes.

The *Il2rg*^{tm1} mutation is a knockout of the gene encoding the gamma c chain, shared by several interleukins (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, Rag2^{tm1} and Il2rg^{tm1}, induces severe immunodeficiency, characterized by the absence of T, B, and NK cells. The NRG strain also expresses the NOD variant of the polymorphic *Sirpa* gene. This expression of the SIRPA protein on murine bone marrow macrophages allows cross-recognition with CD47 ligands on human cells, reducing phagocytosis of transplanted human cells.

Compared to the NXG strain (NOD-*Prkdc*^{scid}-*Il2rg*^{tm1}/Rj), the NRG strain differs by replacing the *Prkdc*^{scid} 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. Janvier Labs obtained the B6 Rag2γc strain (C57BL/6N-*Rag2*^{tm1}- *IL2rg*^{tm1}/Rj) through homologous recombination (B6N mouse ES cells) from the Centre d'immunophénomique (Ciphe, Marseille, France) in 2019. The congenic NRG model was subsequently created by speed backcrossing (N=6) onto the NOD background in 2021.

Animals are bred while maintaining both the genetic background and the mutations of interest in their homozygous forms. The phenotype of the NRG strain is monitored in accordance with Janvier Labs® Genetic Policy.

Main application and research fields

- ONCOLOGY
- IMMUNOLOGY
- AUTO-IMMUNE DISEASES
- INFECTIOUS DISEASES
- RADIOTHERAPY & CHEMOTHERAPY
- PHYSIOLOGY
- TOXICOLOGY

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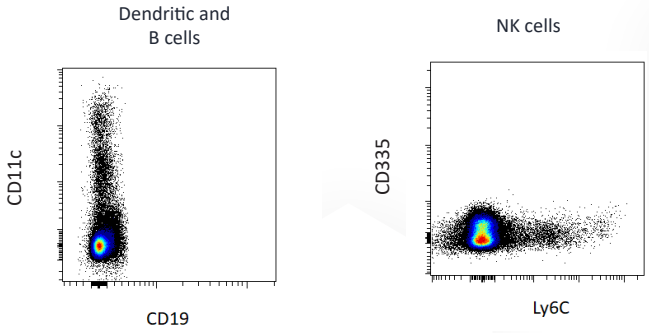
Characterisation phenotypic

This model has been entirely characterized. The immunological and hematological parameters were characterized by Center of Immunophenomics (Ciphe, Marseille, France).

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	*Sirpa*^{NOD} *Rag2*^{tm1} *Il2rg*^{tm1}	

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.

contact@janvier-labs.com
Tel +33 (0)2 43 02 11 91
www.janvier-labs.com