GENETICALLY ENGINEERED MODELS (GEM)

NATURAL IMMUNO-DEFICIENT

WILD TYPE

NATURAL MUTANTS

MICE
Mutant inbred

NRG Nude Mouse

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

Type:
Inbred mutant mouse

Origin:
Janvier Labs, 2023

Colour and related genotype:
Albino mouse
Homozygote nu/nu, a A/A, Tyrc/Tyrc
MHC: Haplotype H2g7

Presentation of the model

The NRG Nude model, or NOD Rag2 γc "nude", is a severely immunodeficient inbred strain (NOD background) that carries two knockout (KO) genetic mutations and one natural mutation: a γc KO gene (*Interleukin 2 receptor gamma chain, Il2rg*^{tm1}), a Rag2 KO gene (*Recombination Activating Gene 2*), and a natural Nude mutation (*Foxn1*$^{nu/nu}$).
The Rag2tm1 mutation, commonly referred to as Rag2, is a knockout of the gene encoding the recombinase 2 enzyme, which plays a key role in generating T and B lymphocyte receptors. This mutation blocks the development of T and B cells and results in immunodeficiency. Mice homozygous for this mutation exhibit a complete absence of peripheral T and B lymphocytes.
The *Il2rg*^{tm1} mutation, known as *γc*, is a knockout of the gene encoding the common gamma chain shared by several interleukins (IL-2, IL-4, IL-7, IL-9, and IL-15). This gene is essential for the differentiation and function of multiple hematopoietic cell types and has a direct impact on the development of natural killer (NK) cells.

The combination of the Rag2^{tm1} and Il2rg^{tm1} mutations results in severe immunodeficiency, with the absence of T, B, and NK cell compartments.

The Nude mutation (*Foxn1*$^{nu/nu}$), is an autosomal recessive mutation in the *Foxn1* (Forkhead box N1) gene located on chromosome 11. It was first identified in a colony of outbred mice. This mutation causes total or partial thymic aplasia, leading to T and B cell immunodeficiency. It also affects keratinization in hair follicles and the epidermis, leading to the appearance of transient fuzz, which eventually disappears, resulting in near-complete hairlessness.

The NRG Nude strain has also been screened for the Sirpα gene polymorphism. Expression of the Sirpα protein (NOD background alleles) on the surface of bone marrow macrophages allows high-affinity binding to human hematopoietic cell CD47 markers. This interaction delivers a "don't eat me" signal that inhibits murine macrophage phagocytosis of human grafted cells. This feature is a notable advantage of the NOD background, making it particularly suited for human transplantation and xenograft models.

Comparison with the NXG model

The NRG Nude strain differs from the NXG strain (NOD-*Prkdc*^{scid}-*Il2rg*^{tm1}/Rj) by the absence of the Prkdcscid mutation, commonly referred to as "SCID" (Severe Combined Immunodeficiency). As a result, NRG Nude mice are more resistant to irradiation, genotoxic agents, and stress. This makes them a more stable and durable platform for xenograft experiments. Their hairless phenotype is especially advantageous for precise subcutaneous tumor transplantation.

Development of the model

JANVIER LABS obtained the B6 Rag2γc strain (C57BL/6N-*Rag2*^{tm1}-*Il2rg*^{tm1}-*Sirpα*^{NOD}/Rj) through homologous recombination (using B6N mouse ES cells), developed at the Centre d'Immunophénomique (Ciphe, Marseille, France) in 2019.
The NRG congenic model was then generated by high-speed backcrossing (N=6) onto the NOD background in 2021.
The Nude gene (*Foxn1*$^{nu/nu}$) was subsequently backcrossed into the NRG model in 2022.
Animals are bred to maintain both the genetic background and the relevant mutations in homozygous form.
The NRG strain is bred as an inbred line, and phenotypes are validated in accordance with the JANVIER LABS GENETIC POLICY®.

Main application and research fields

- ONCOLOGY
- IMMUNOLOGY
- PRECLINICAL
- INFECTIOUS DESEASES
- PHYSIOLOGY-PHYSIOPATHOLOGY

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