



GENETICALLY
ENGINEERED
MODELS
(GEM)



MICE
Mutant inbred

NATURAL
IMMUNO-
DEFICIENT

NRG Ckit Mouse

WILD TYPE

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

Type: Mutant inbred mouse, GMO

Origin: Janvier Labs, 2023

NATURAL
MUTANTS

Colour and related genotype:
Albino mouse



Presentation of the model

The NRG-Ckit strain is a model with severe immunodeficiency, based on a NOD background and incorporating three mutations. Two of these mutations are Knock Out (KO) mutations affecting the *Il2rg* gene (interleukin-2 receptor subunit gamma) and the *Rag2* gene (recombination activating gene 2), along with a V831M point mutation in the *Kit* gene.

The *Rag2^{tm1}* mutation is a KO mutation in the gene responsible for encoding the recombination activating protein 2, a crucial player in the generation of receptors in T and B lymphocytes. The absence of this protein hinders the development of T and B lymphocytes, resulting in immune deficiency.

The *Il2rg^{tm1}* mutation is a KO mutation in the gene that encodes the cytokine receptor common subunit gamma, associated with several interleukins (IL-2, IL-4, IL-7, IL-9, and IL-15). This gene is essential for the differentiation and function of numerous hematopoietic cells, significantly impacting Natural Killer (NK) cell development.

The V831M point mutation in the *Kit* gene results 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.

Lastly, the polymorphic *Sirpa* gene in the NRG-Ckit strain encodes a variant of the SIRPα receptor that cross-reacts with the human CD47 ligand. Consequently, human cells transplanted into NRG-Ckit mice can engage the CD47/SIRPα "don't eat me" signal, protecting them from phagocytosis by mouse macrophages.

In summary, the NRG-Ckit strain stands out as one of the most severe immunodeficient models, exhibiting a complete absence of T, B, and NK lymphocyte compartments, an enhanced phagocytic tolerance, and enabling humanization without myeloablation.

The animals are bred to maintain both the genetic background and the mutations of interest in their homozygous forms. The NRG strain is bred in inbreeding mode and the phenotype is controlled according to the JANVIER LABS GENETIC POLICY®.



Main application and research fields

ONCOLOGY

INFECTIOUS DISEASE

GRAFT VS. HOST DISEASE

DIABETES

IMMUNOTHERAPY

IMMUNOLOGY

HUMANIZATION

HUMAN ORGAN TRANSPLANTATION

REGENERATIVE MEDICINE

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