GENETICALLY ENGINEERED MODELS (GEM)

NATURAL IMMUNO-DEFICIENT

WILD TYPE

NATURAL MUTANTS

MOUSE
Mutant inbred

hIL-15 NXG Mouse

Strain name :
NOD-*Prkdc*^{scid}-*IL2rg*^{tm1}-*Il15*$^{em1(IL15)}$/Rj

Type :
Inbred mutated mouse

Origin :
JANVIER Labs, en 2019

Colour and related genotype :
Albino mouse

Presentation of the model

The hIL-15 NXG model was developed by replacing the murine *Il15* gene with the human *IL15* gene in the NXG strain.

Key Mutations:
• *Prkdc*^{scid}: This mutation disrupts the development of T and B cells, resulting in their complete absence.
• *I2rg*^{tm1}: A knockout of the gene encoding the IL-2 receptor subunit gamma, which is essential for several interleukins (IL-2, IL-4, IL-7, IL-9, IL-15). This mutation results in the absence of NK cells.

These combined mutations lead to severe immunodeficiency with the absence of T, B, and NK cells. Additionally, the hIL-15 NXG strain expresses the NOD variant of the *Sirpa* gene, enhancing cross-recognition between murine macrophages and human cells, thereby reducing the phagocytosis of transplanted human cells.

•*Il15*$^{em1(IL15)}$: The murine *Il15* gene was replaced with the human *IL15* gene. IL-15 is a cytokine crucial for the development, survival, and activation of NK cells and memory T cells, playing a vital role in immune response regulation.

hIL-15 Feature: This model exhibits physiological hIL-15 expression, with a resting serum level of approximately 80 pg/mL, rising to 400 pg/mL in response to inflammation and immune activation. This response closely mirrors human physiological conditions compared to other strains.

Model Development:
• The NXG strain (NOD-*Prkdc*^{scid}-*IL2rg*^{tm1}/Rj) was generated through homologous recombination of the *IL2rg*^{tm1} mutation using B6N mouse embryonic stem cells.
• In 2019, Janvier Labs developed the congenic NXG model through speed backcrossing (N=5) onto the NOD background.
• The IL15 gene was inserted into the murine *Il15* loci using CRISPR technology in 2023.

Breeding and Maintenance: Animals are bred to retain both the genetic background and key mutations in their homozygous state. The phenotype of the hIL-15 NXG strain is continually monitored in line with Janvier Labs' Genetic Policy to ensure stability and consistency.

Main application and research fiels

- ONCOLOGY
- NATURAL KILLER CELLS
- IMMUNOLOGY AND IMMUNOTHERAPY
- HUMAN IMMUNE SYSTEM ENGRAFTMENT
- INFECTIOUS DISEASES
- REGENERATIVE MEDICINE

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