

GENETICALLY  
ENGINEERED  
MODELS  
(GEM)



MICE  
Mutant inbred

NATURAL  
IMMUNO-  
DEFICIENT

## BRGS TSLP Mouse

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

**Type:** Mutant inbred mouse

**Origin:** Institut Pasteur, 2022

**Colour and related genotype:**  
Albino mouse

**Use of this strain:** Is restricted to private sector users

WILD TYPE

NATURAL  
MUTANTS



## Presentation of the model

The BRGS TSLP 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 and carrying a NOD background gene.

The *Rag2<sup>tm1</sup>* 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<sup>tm1</sup>* 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<sup>tm1</sup>* and *Il2rg<sup>tm1</sup>*, induces severe immunodeficiency, characterized by the absence of T, B, and NK cells. The BRGS TSLP strain also carries 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.

Finally, this strain overexpresses the murine thymic-stromal-cell-derived lymphopoietin gene (*Tslp*). Upon humanization with CD34+ human stem-cells, the BRGS TSLP-HIS mice develop a full array of lymph nodes with compartmentalized human B and T cells.

Compared with other humanized models, BRGS TSLP-HIS mice have a larger thymus, more mature B cells, and abundant IL-21-producing follicular helper T (T<sub>fh</sub>) cells, and show enhanced antigen-specific responses. In addition BRGS TSLP-HIS mice developed atopic dermatitis (AD) demonstrating clinical, histological, immunological and skin commensal changes resembling human AD.



## Main application and research fields

ONCOLOGY

INFECTIOUS DISEASES

INFLAMMATION

IMMUNOLOGY

AUTO-IMMUNE DISEASES

JANVIER  
LABS