GENETICALLY ENGINEERED MODELS (GEM)

NATURAL IMMUNO-DEFICIENT

WILD TYPE

NATURAL MUTANTS

MICE
Mutant inbred

B6RGS Mouse

Strain name:
C57BL/6N-Rag2^{tm1}-IL2rg^{tm1}-Sirpa^{NOD}/Rj

Type: Mutant inbred mouse, GMO

Origin: CIPHE, Marseille France, in 2019, JANVIER Labs 2021

Colour and related genotype:
Black mouse, a (a/a) non agouti

Presentation of the model

The B6RGS mouse is a severely immunodeficient mouse with two Knock Out (KO) genetic mutations: the γc KO gene (Interleukin 2 receptor gamma chain, IL2rg^{tm1}) and the Rag2 KO (Rag2^{tm1} mutation) gene.
The Rag2tm1 mutation commonly called Rag2 is a KO mutation of the gene coding for the 2 recombinase enzyme that plays a key role in producing T and B cell receptors. This lack leads to an immune deficiency. Homozygous mice for this mutation appear with a total lack of peripheral T and B lymphocyte cells.

The IL2rg^{tm1} mutant called γc is a KO mutation of the gene coding for the γc gamma chain that is common (in particular) to interleukins (IL-2, IL-4, IL-7, IL-9 and IL-15). This gene is necessary for the differentiation and the function of numerous hematopoietic cells with a full impact on the development of Natural Killer cells (NK).
The combination of both mutations Rag2^{tm1}-IL2rg^{tm1} on a B6 background leads to a severe immunodeficiency with no T, B and NK cells.

The B6RGS mouse carries the sirpa gene from the NOD genetic background. Expression of the sirpa protein (NOD alleles) on the surface of bone marrow macrophages allows high affinity binding with the CD47 markers of human hematopoietic cells.
This binding induces a “don’t eat me” signal blocking murine macrophages and preventing phagocytosis of transplanted human cells. This is a notable feature of the NOD genetic background which gives it an advantage in human transplantation and xenografting in general. JANVIER LABS obtained the B6 Rag2γc (C57BL/6N-Rag2^{tm1}-IL2rg^{tm1}/Rj) through a homologous recombination (ES cells from B6N mice), developed at the Center of Immunophenomics (Ciphe, Marseille, France) in 2019.
The sirpa gene has been identified by PCR and extracted from the NOD fund by crossing on B6 funds. The B6RGS have been backrossed (>10 generations) in 2021 to the B6 background. The B6 Rag2 strain is bred in an inbred manner and the phenotype is controlled according to the JANVIER LABS GENETIC POLICY®.

Main application and research fields

ONCOLOGY
- Tumor implantation on studies
- Studies on gene therapy
- Studies of cancer therapies

IMPLANTATION OF HUMAN CELLS IN A MURINE MODEL
This is a step in the humanization on process

THE B6RGS STRAIN
is useful for tumor implantation studies using an invasive radiotherapy treatment; it generally resists to such a phase

IMMUNOLOGY AND IMMUNOTHERAPY

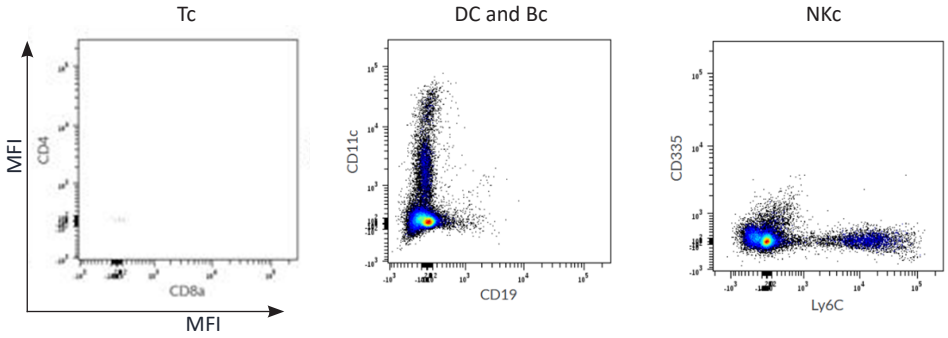
TRANSPLANTS AND GRAFTS

Our added value

- The «JANVIER LABS Genetic Policy», specific programme, guarantees homozygosity of autosomal pairs
- Animals with the SPF or SOPF standards
- A gentling policy for docile and easy-to-handle animals
- Optimal stability conditions of our models during shipments, thanks to our dedicated and internal transport service
- A scientific support with a team of Veterinarians and PhD

JANVIER LABS

Flow cytometry analysis, spleen



Representative flow cytometry analysis confirming the absence of positive B cells (CD19), positive T cells (CD4 and CD8) and NK cells (CD335) in the peripheral blood of B6RGS mice.

Fluorescence intensities (MFI) represent specific expressions of clusters of differentiations.

Clouds of points are obtained, each point representing a cell.

We can then determine the negative/single and positive/double positive cells in each population (defined by « Cluster of Differentiation »), fixing or not the two antibodies carrying the fluorochromes.

Characterisation phenotypic

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

Background	Breeding	Coat	T Lymphocytes	B Lymphocytes	Leakiness	NK cells	Dendritic cells
C57BL/ 6NRj	Inbred	Black	Absent	Absent	-	Absent	Dysfonctional
Macrophages	**Complement**	**Irradiation tolerance**	**Life span**	**Humoral immunity**	**Lymphoma outcome**	**Genes of interest**	
Normal	Normal	High	89 Wk.	Absente	Indefinite	RAG2 IL2rg	

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