GENETICALLY ENGINEERED MODELS (GEM)

NATURAL IMMUNO-DEFICIENT

WILD TYPE

NATURAL MUTANTS

MICE
Mutant inbred

B6 CTLA-4 Mouse

Strain name:
C57BL/6Smoc-Ctla$^{em1(CTLA4)}$/SmocRj

Type: Mutant inbred mouse, GMO

Origin: Shanghai Model Organism Center

Colour and related genotype:
Black mouse

Presentation of the model

The B6 hCTLA-4 mouse model is a genetically engineered knock-in strain where the murine *Ctla4* gene has been replaced by its human counterpart, *CTLA4*. CTLA-4 (Cytotoxic T-Lymphocyte Antigen 4) is a critical immune checkpoint receptor expressed on T cells. It functions as a negative regulator of immune activation by outcompeting the costimulatory molecule CD28 for binding to the ligands CD80 and CD86 on antigen-presenting cells. This mechanism plays a key role in maintaining immune homeostasis and preventing autoimmunity.
This strain is a valuable tool for studying the regulation of immune responses and the mechanisms of immune tolerance. It facilitates the evaluation of human-specific monoclonal antibodies or other biologics targeting *CTLA-4* for immuno-oncology applications. Additionally, the model can be used to explore the combination of *CTLA-4* blockade with other immunotherapies, such as PD-1 inhibitors or cancer vaccines. Beyond oncology, this strain is relevant for research into autoimmune diseases and transplant rejection, where modulation of *CTLA-4* signaling is a therapeutic goal.

The B6 hCTLA-4 model serves as an essential bridge between murine studies and clinical applications, offering insights into the safety, efficacy, and mechanisms of emerging immunotherapies targeting CTLA-4.

This strain originates from the Shanghai Model Organism Center and was licensed to Janvier Labs in 2024.

The animals are bred to maintain both the genetic background and the mutations of interest in their homozygous forms. The B6 hCTLA-4 strain is bred in inbreeding mode and the phenotype is controlled according to the JANVIER LABS GENETIC POLICY®.

Main application and research fields

- ONCOLOGY
- IMMUNOLOGY AND IMMUNOTHERAPY
- TRANSPLANTATION
- AUTO-IMMUNE DISEASES

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

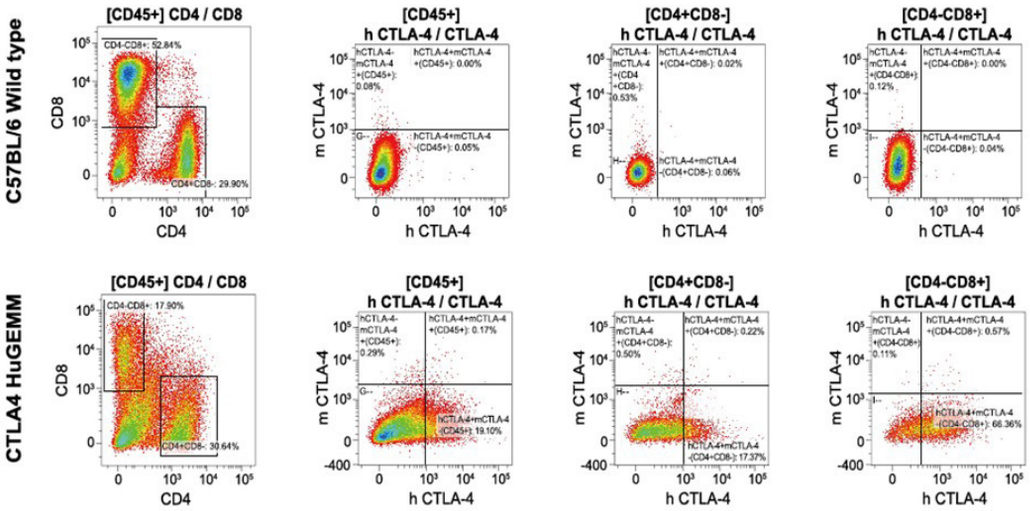

Figure 1. Expression of CTLA4 in the activated spleen lymphocytes of humanized CTLA4 mice is detected by FACS.

Splenic lymphocytes from homozygous humanized CTLA4 mice were activated using anti-CD3 and anti-CD28 antibodies for 72 hours before being harvested for analysis.
Flow cytometry (FACS) was used to detect the expression of humanized CTLA4. The results demonstrated that active expression of humanized CTLA4 was present in both activated CD4+ and CD8+ T lymphocytes derived from the homozygous humanized CTLA4 mice.

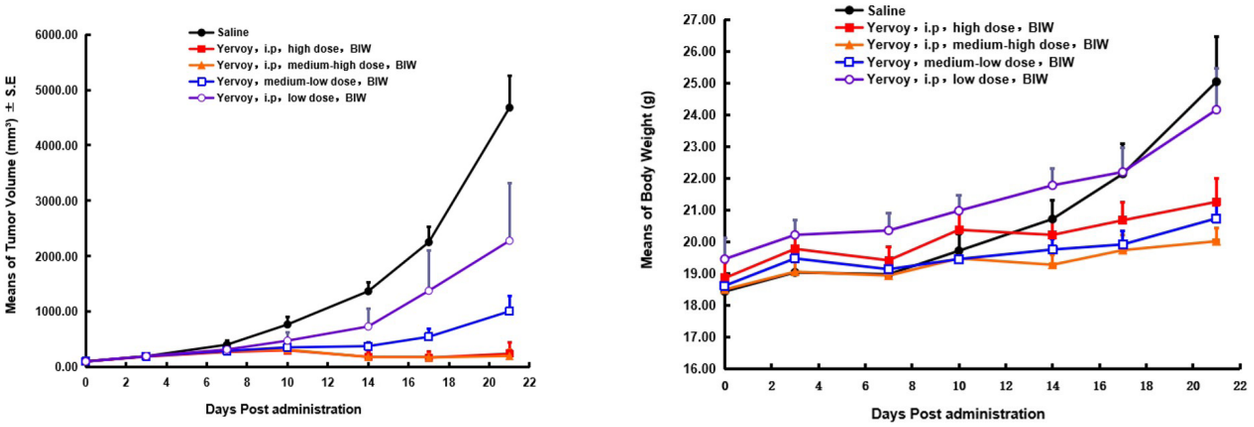

Figure 2. In vivo anti-tumor effect of Ipilimumab, a humanized anti-CTLA4 antibody, in a humanized mouse model of CTLA4.

In vivo evaluation of the anti-tumor efficacy of Yervoy was performed using a MC38 tumor-bearing model in homozygous humanized CTLA4 mice. These mice were inoculated with MC38 colon cancer cells, and treatment with Yervoy, a therapeutic antibody targeting human CTLA4, resulted in a highly significant anti-tumor effect ($p<0.001$). These findings confirm that the humanized CTLA4 mouse model is a robust in vivo platform for validating the efficacy of therapeutic antibodies targeting human CTLA4.

contact@janvier-labs.com
Tel +33 (0)2 43 02 11 91
www.janvier-labs.com