

hPD-1

The endogenous mouse *Pdcd1* gene was replaced by human PDCD1(PD-1) gene .

Nomenclature	C57BL/6Smoc- <i>Pdcd1</i> ^{em1(hPDCD1)} /Smoc
Cat. NO.	NM-HU-00015
Strain State	Repository Live

Gene Summary

Gene Symbol Pdcd1	Synonyms	PD-1; Pdc1; Ly101
	NCBI ID	18566
	MGI ID	104879
	Ensembl ID	ENSMUSG00000026285
	Human Ortholog	PDCD1

Model Description

The endogenous mouse *Pdcd1* gene was replaced by human PDCD1(PD-1) gene .

Research Application: Immunotherapy,cancer research,drug screening

*Literature published using this strain should indicate: hPD-1 mice (Cat. NO. NM-HU-00015) were purchased from Shanghai Model Organisms Center, Inc..

Validation Data

- Data from flow cytometry (FACS) analysis

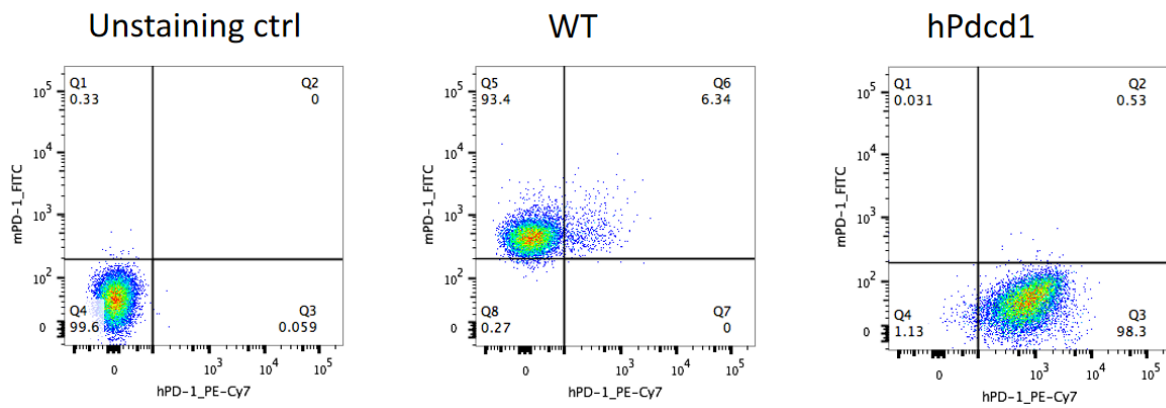


Fig1 . Expression of PD-1 in the activated spleen lymphocytes of humanized PD-1 Homozygous mice is detected by FACS.

- *In vivo* validation in a MC38 tumor-bearing model of humanized PD-1 mice

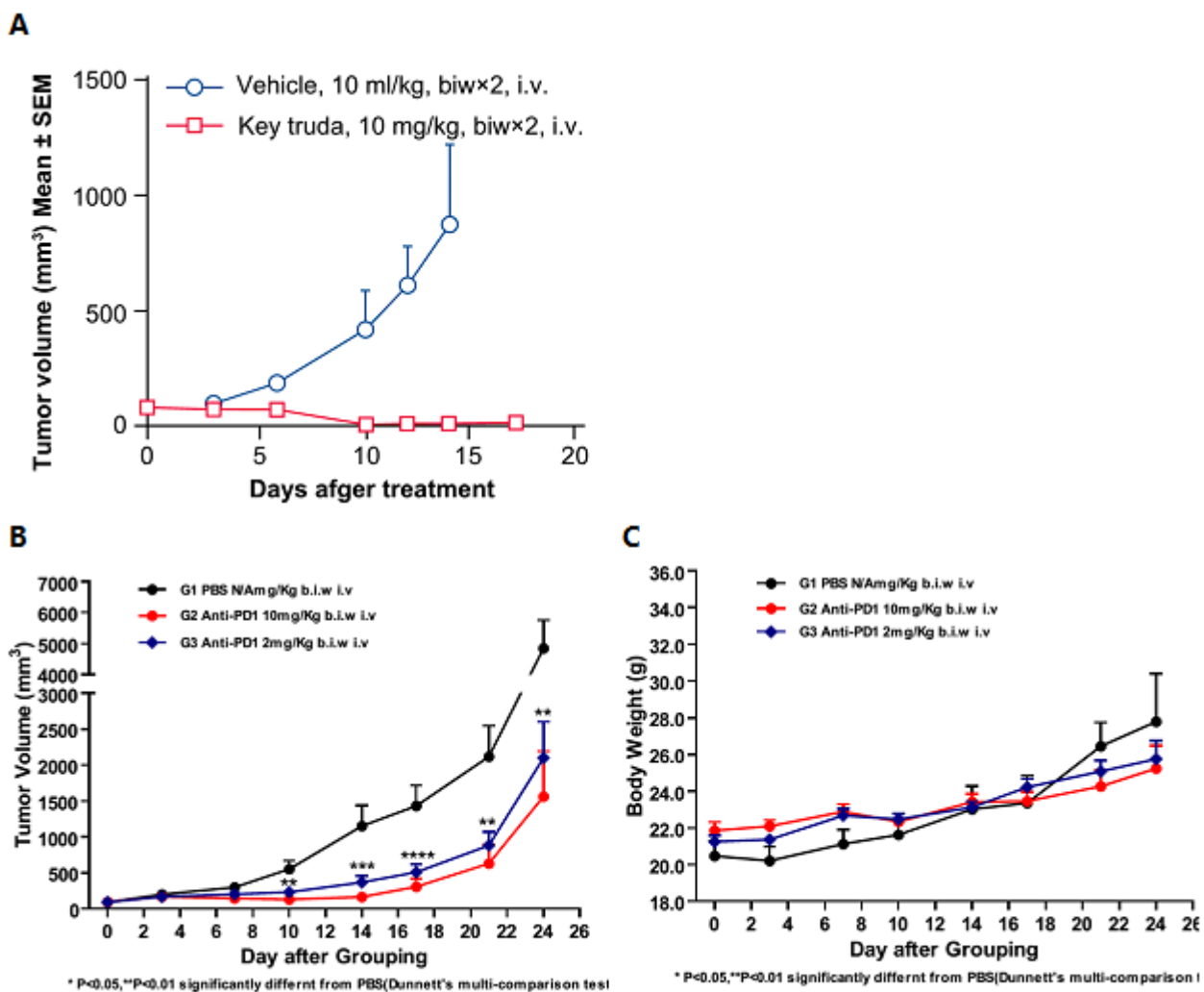


Fig2 . *In vivo* anti-tumor effect of an anti-human PD-1 antibody in a humanized mouse model of PD-1. Anti-human-PD-1 drugs significantly inhibited the growth of MC38 tumors in PD-1 mice,

demonstrating that the humanized PD-1 mice can be used to assess the anti-human PD-1 antibody.

A. Mean volume \pm SEM of tumor tissues (completed in cooperation with Genscript).

In vivo validation of anti-tumor efficacy in a MC38 tumor-bearing model of humanized PD-1 mice. Homozygous humanized PD-1 mice were inoculated with MC38 colon cancer cells. After the tumors grew to 100 mm³, the animals were randomly assigned into a control group and a treatment group (n=8). The drug was given twice a week for a total of 4 administrations. The results showed that Keytruda, a drug targeting human PD-1, exerted a very significant anti-tumor effect ($p < 0.001$), demonstrating that the humanized PD-1 mice are a good *in vivo* model for validating the efficacy of antibodies targeting human PD-1.

B. Mean volume \pm SEM of tumor tissues. C. Mean body weight \pm SEM of mice (data were obtained in cooperation with PharmaLegacy).

In vivo dose validation of anti-tumor efficacy in a MC38 tumor-bearing model of humanized PD-1 mice. Homozygous humanized PD-1 mice were inoculated with MC38 colon cancer cells. After the tumors grew to about 90 mm³, the animals were randomly assigned into a control group and a treatment group (n=9). The results showed that the antibodies targeting human PD-1 showed a very significant antitumor effect ($p < 0.001$), and such antitumor effect is dose-dependent.

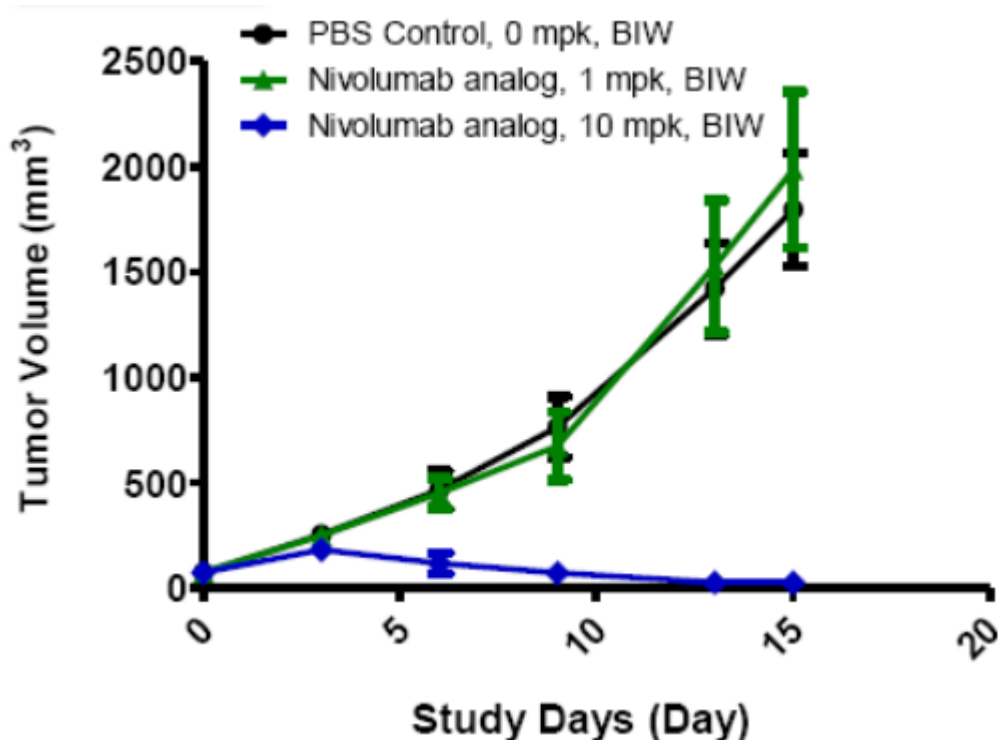


Fig3 . *In vivo* dose validation in a MC38 tumor-bearing model of humanized PD-1 mice. Homozygous humanized PD-1 mice were inoculated with MC38 colon cancer cells. After the tumors grew to 100 mm³, the animals were randomly assigned into a control group and a treatment group (n=8). The drug was given twice a week for a total of 4 administrations.

Case Study

As one of the first five anti-PD-1 drugs with BLAs accepted by CFDA, Sintilimab has shown potent T cell stimulating activity and significant anti-tumor efficacy. ([read more](#))

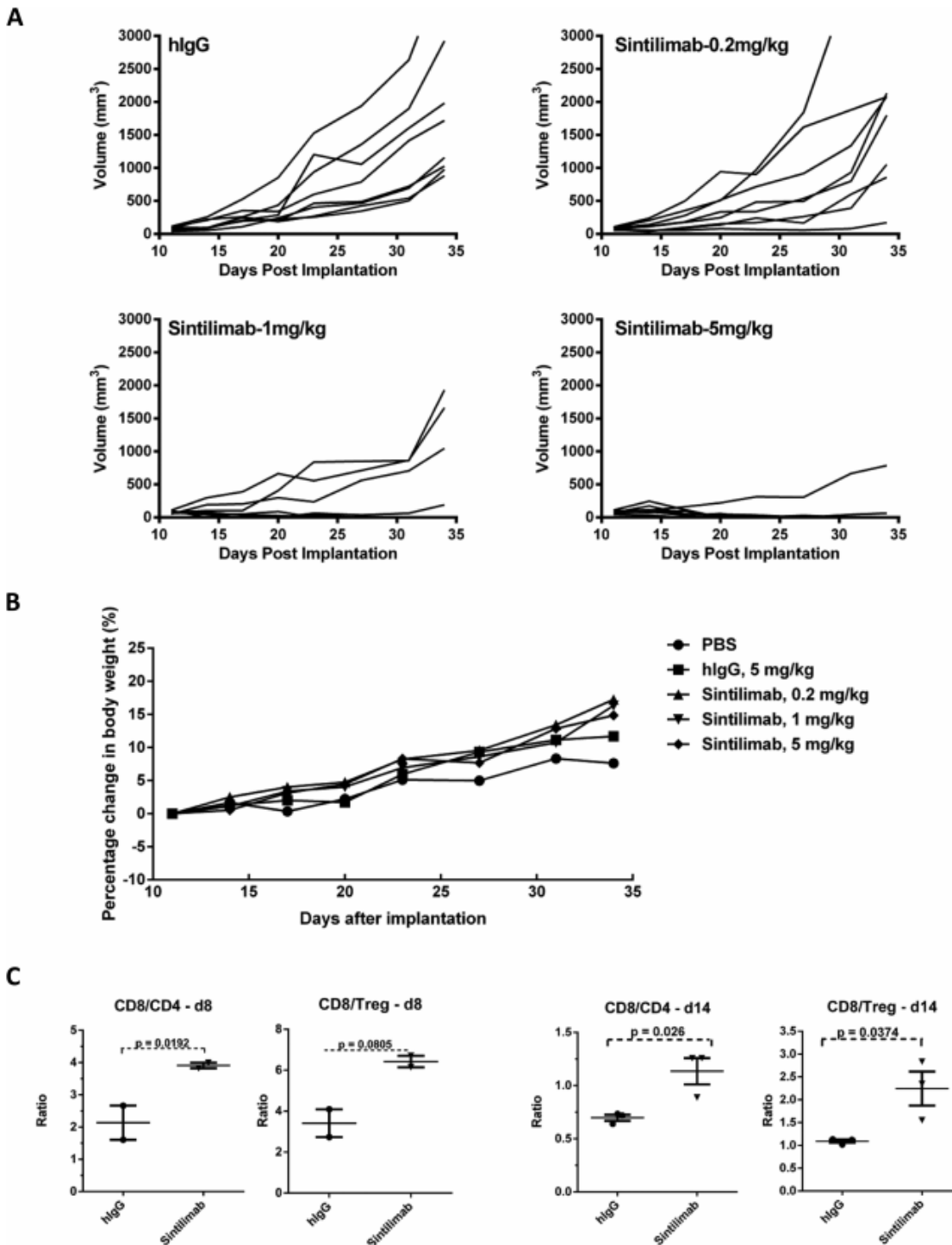


Fig4 . *In vivo* hPD-1 knock-in mouse model to test anti-tumor efficacy of Sintilimab. (A) Tumor growth inhibition (TGI) of MC38 tumors in hPD-1 knock-in mice of individual animals treated with different doses of Sintilimab. (B) Effect of Sintilimab on percentage changes in mouse body weight(mean). (C) Changes in ratios of tumor infiltrating CD4+, CD8+ and Treg cells. For d8: IgG (n

= 2); Sintilimab (n = 2). For d14, n = 3 for all groups. P values were calculated using a two-tailed t-test method.

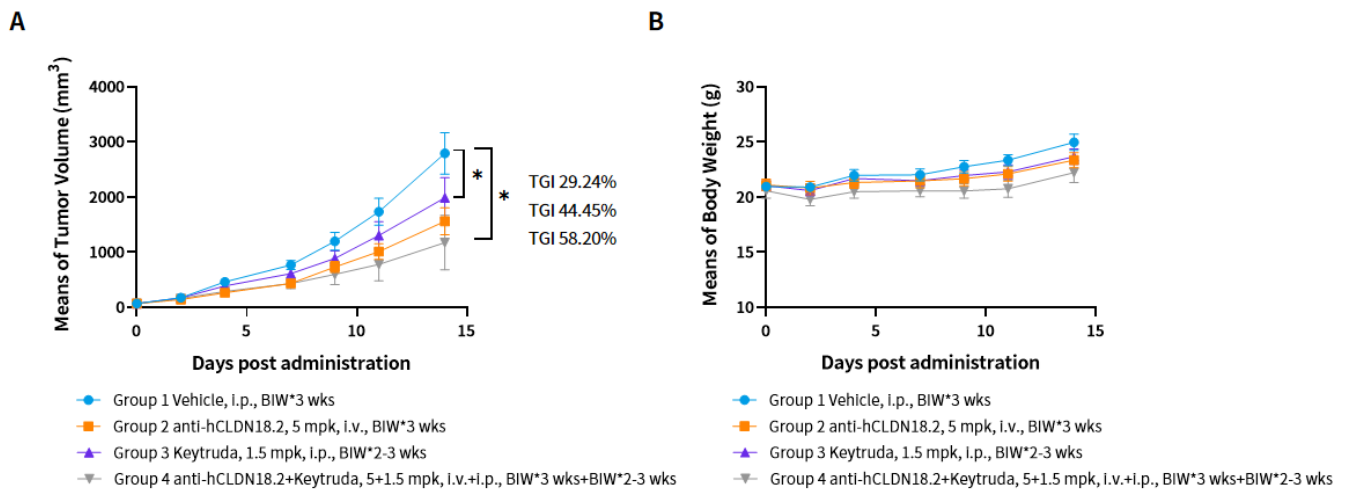


Fig5. Means of tumor volume(A) and body weight(B). PD-1 humanized mouse model implanted with MC38-hCLDN18.2 tumors to evaluate the in vivo antitumor efficacy of anti-hCLDN18.2 mAb alone and in combination with Keytruda. The anti-hCLDN18.2 mAb in combination with Keytruda significantly inhibited the growth of MC38-hCLDN18.2 tumors in PD-1 humanized mice, demonstrating that this model is suitable for evaluating the in vivo efficacy of anti-hCLDN18.2 mAb alone and in combination with PD-1/PD-L1 antibodies. n=8. Mean±SEM. t-test,*P < 0.05.

Publications

[Enhanced Therapeutic Efficacy of a Novel Oncolytic Herpes Simplex Virus Type 2 Encoding an Antibody Against Programmed Cell Death 1](#)

References: Molecular Therapy Oncolytics