

hCD40

Nomenclature	C57BL/6Smoc- <i>Cd40</i> ^{em1(hCD40) Smoc}
Cat. NO.	NM-HU-00076
Strain State	Repository Live

Gene Summary

Gene Symbol CD40	Synonyms	IGM; p50; Bp50; GP39; IMD3; TRAP; HIGM1; T-BAM; Tnfrsf5; AI326936
	NCBI ID	21939
	MGI ID	88336
	Ensembl ID	ENSMUSG00000017652
	Human Ortholog	CD40

Model Description

The endogenous extracellular mouse Cd40 gene was replaced by the extracellular region of human CD40 gene.

Research Application: cancer research, Immunotherapy, drug screening

*Literature published using this strain should indicate: hCD40 mice (Cat. NO. NM-HU-00076) were purchased from Shanghai Model Organisms Center, Inc..

Validation Data

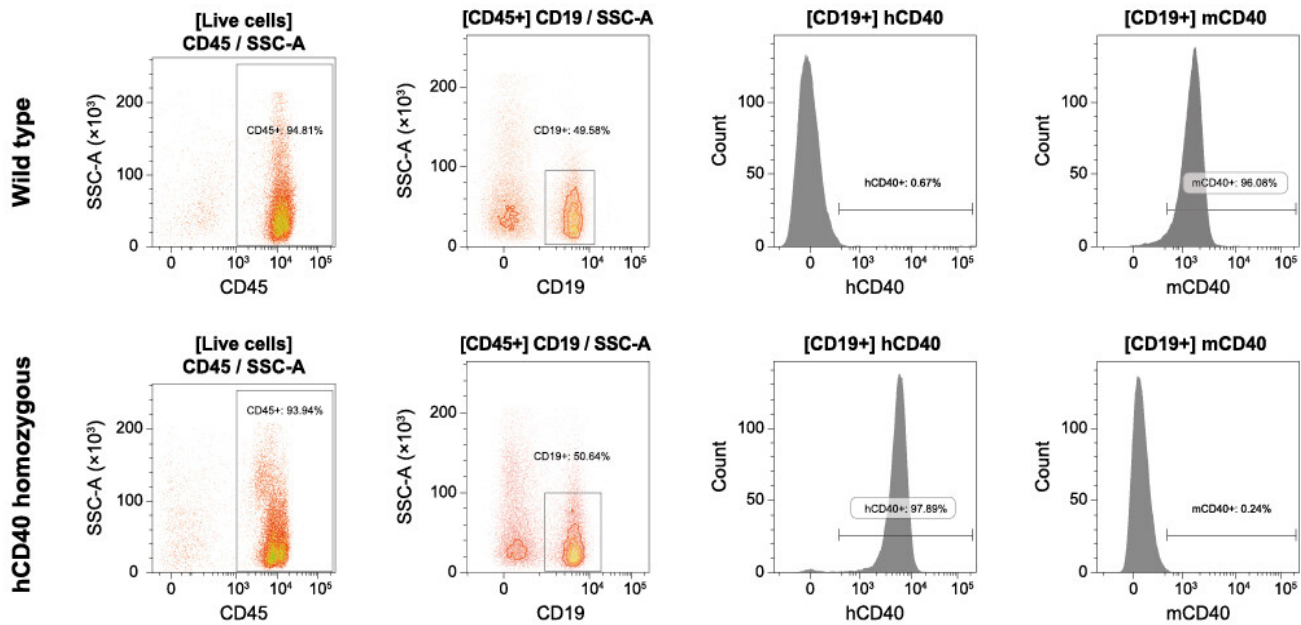


Figure 1. Detection of CD40 expression in peripheral blood cells of humanized CD40 mice. The FACS results of peripheral blood cells collected from homozygous humanized CD40 mice and wild-type mice showed that the active expression of humanized CD40 was detected in CD19 positive cells collected from homozygous humanized CD40 mice, and its expression level was similar to that of murine Cd40 expression in wild-type mice. (Completed in collaboration with CrownBio).

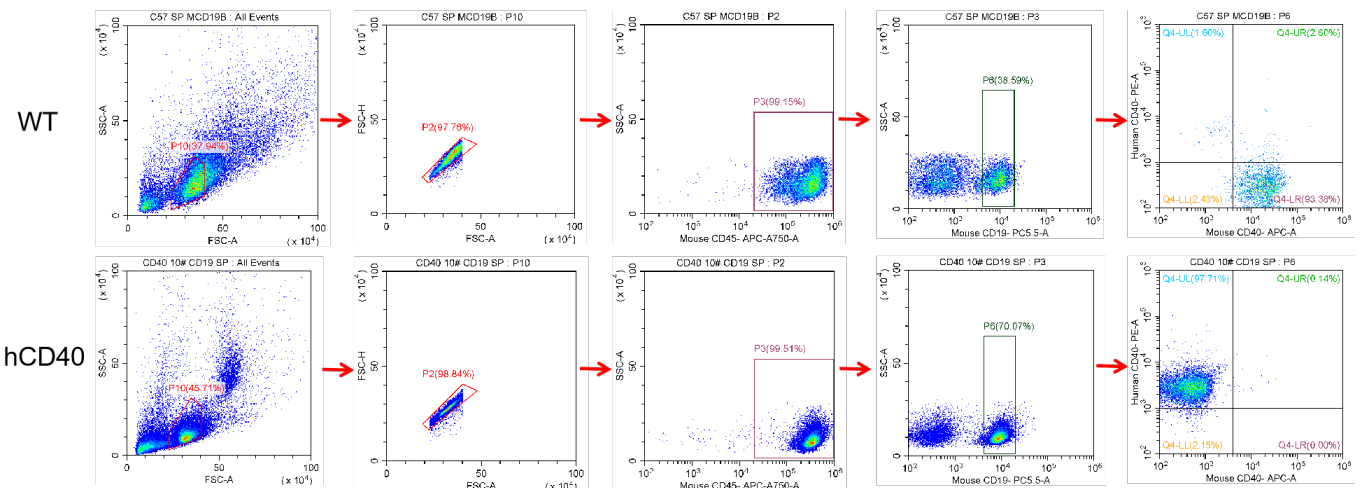


Fig2. Analysis of human CD40 expression in the spleen by FACS. The homozygous KI animal expresses human CD40 on the CD19+ B cells.

Application

Case study 1: In vivo validation in a MC38 tumor-bearing model of humanized CD40 mouse

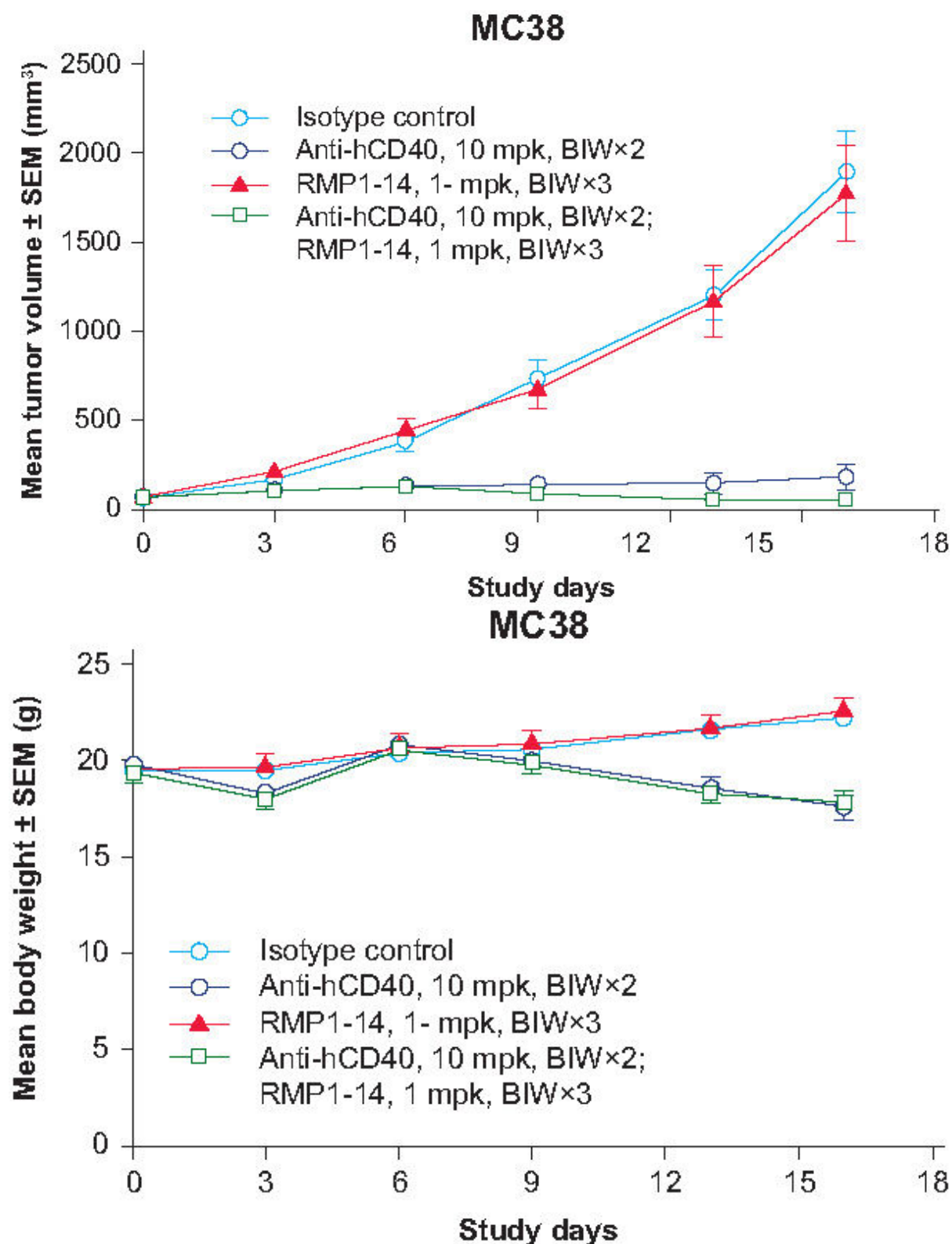


Figure 2. In vivo validation of anti-tumor efficacy in a MC38 tumor-bearing model of humanized CD40 mice. Humanized CD40 mice were inoculated with MC38 colon cancer cells. After the tumors grew to 100 mm³, the animals were randomly assigned into different group (n=8). The results indicated that the antibodies targeting human CD40 showed a very significant antitumor effect (p<0.001). Combination of anti-CD40 and anti-PD-1 is shown more significant anti-Tumor effect. (Cooperation with CrownBio)

Case study 2: In vivo efficacy and safety evaluation of anti-human CD40 antibody using hCD40 mice

I. In vivo anti-tumor effect of an anti-human CD40 antibody in hCD40 mice.

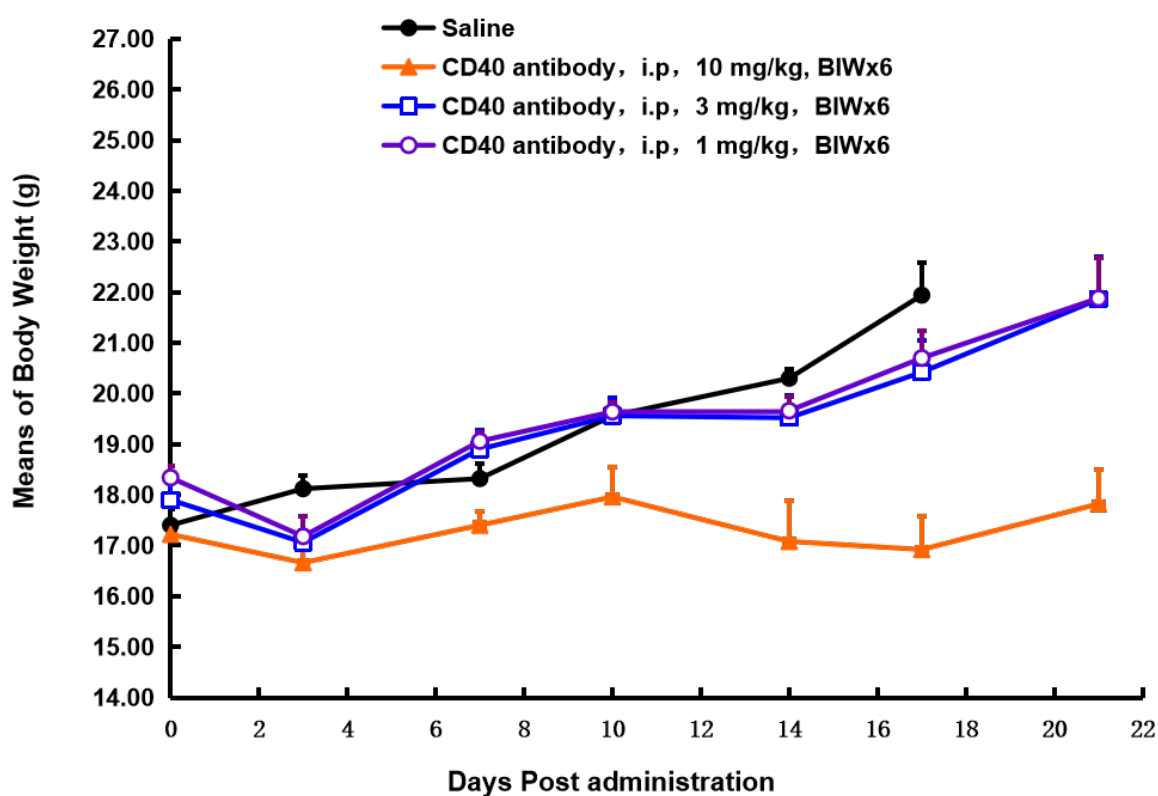
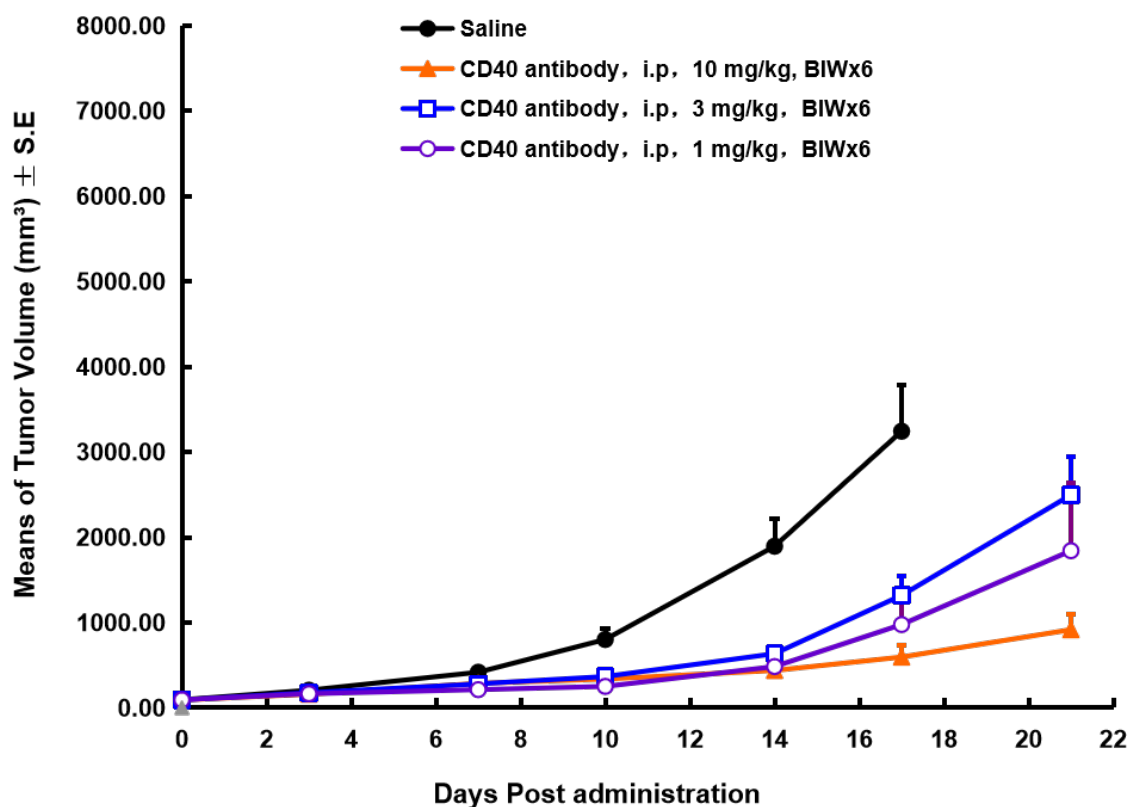
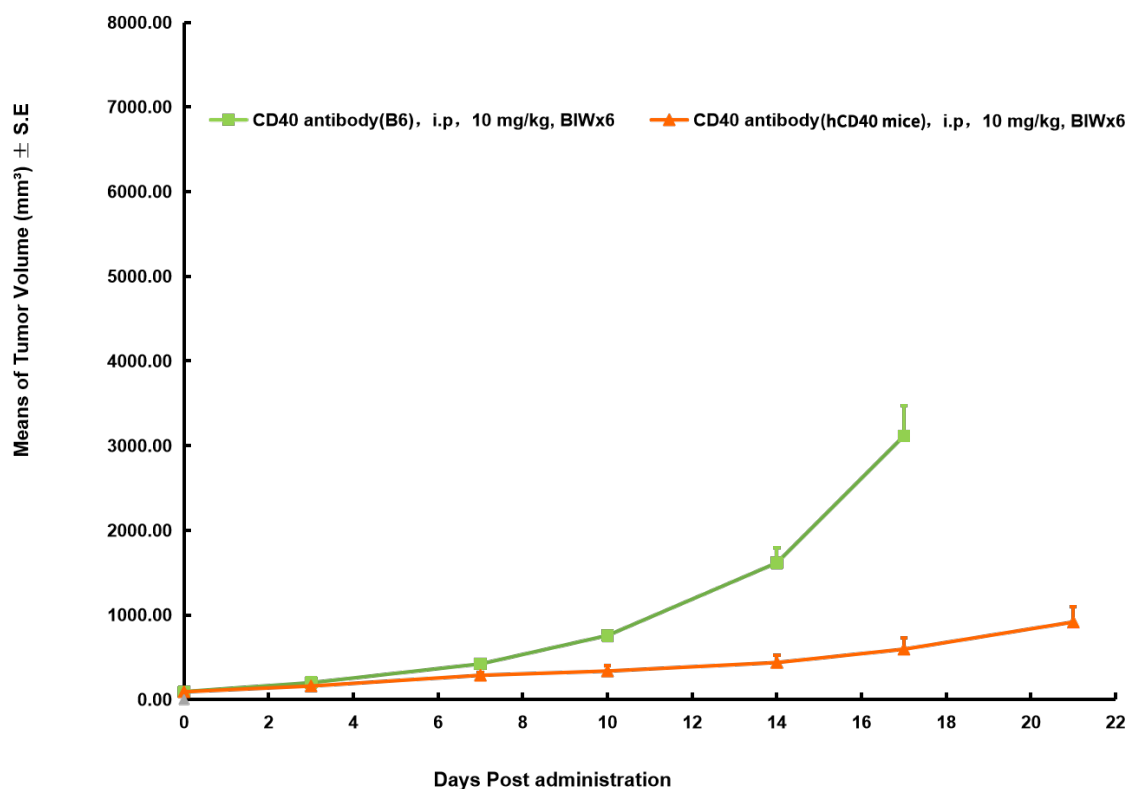


Fig 3. In vivo validation of anti-tumor efficacy in a MC38 tumor-bearing model of humanized CD40 mice. Homozygous humanized CD40 mice were inoculated with MC38 colon cancer cells. The results showed that an anti-human CD40 antibody exerted a very significant anti-tumor effect, demonstrating that the humanized CD40 mice are a good in vivo model for validating the efficacy of antibodies targeting human CD40. Mean volume $\pm$ SEM of tumor tissues(A). Mean body weight $\pm$ SEM of mice(B).

II. Evaluation of anti-human CD40 toxicity in hCD40 mice.



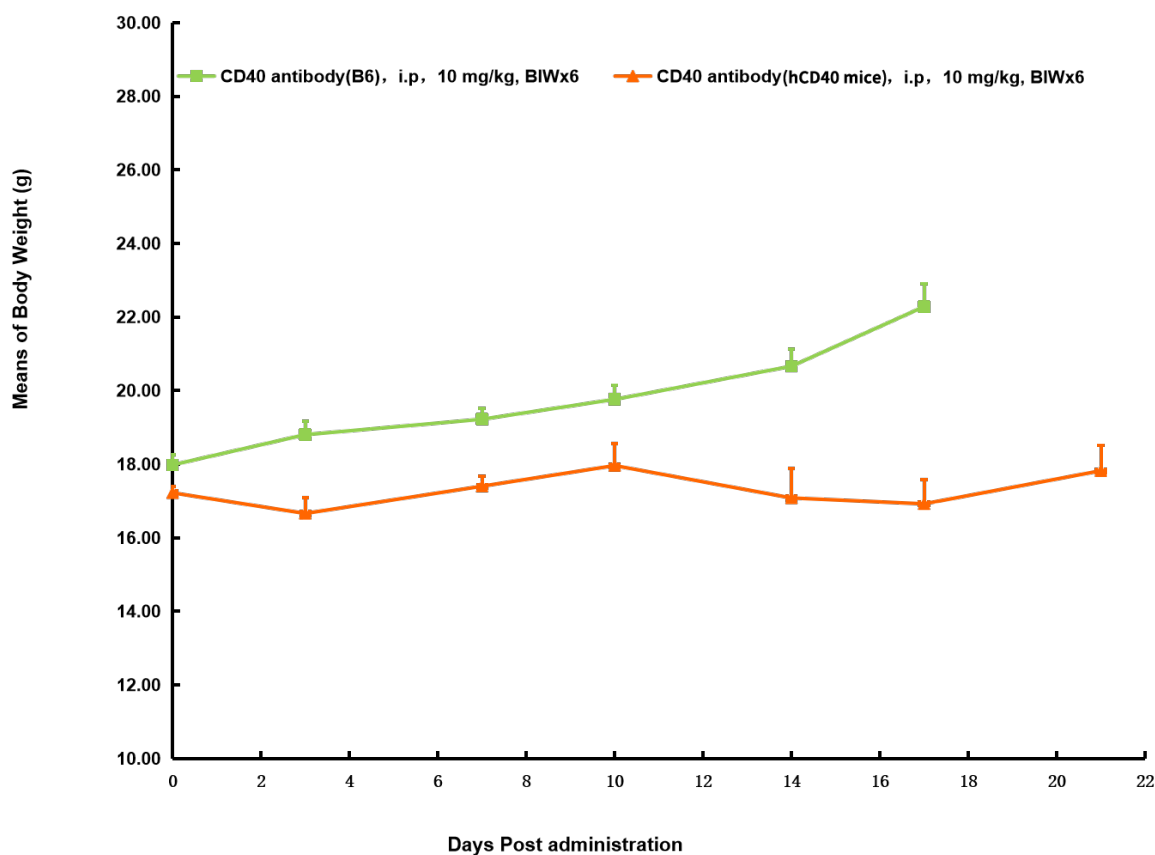
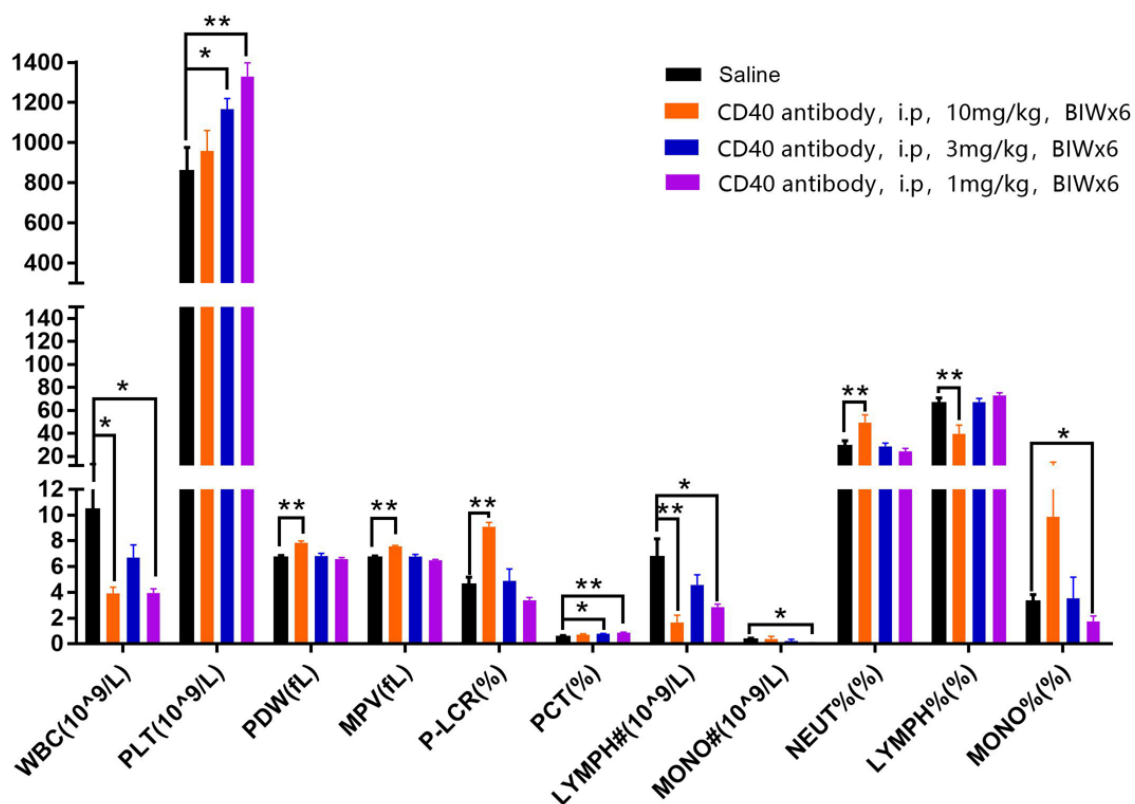
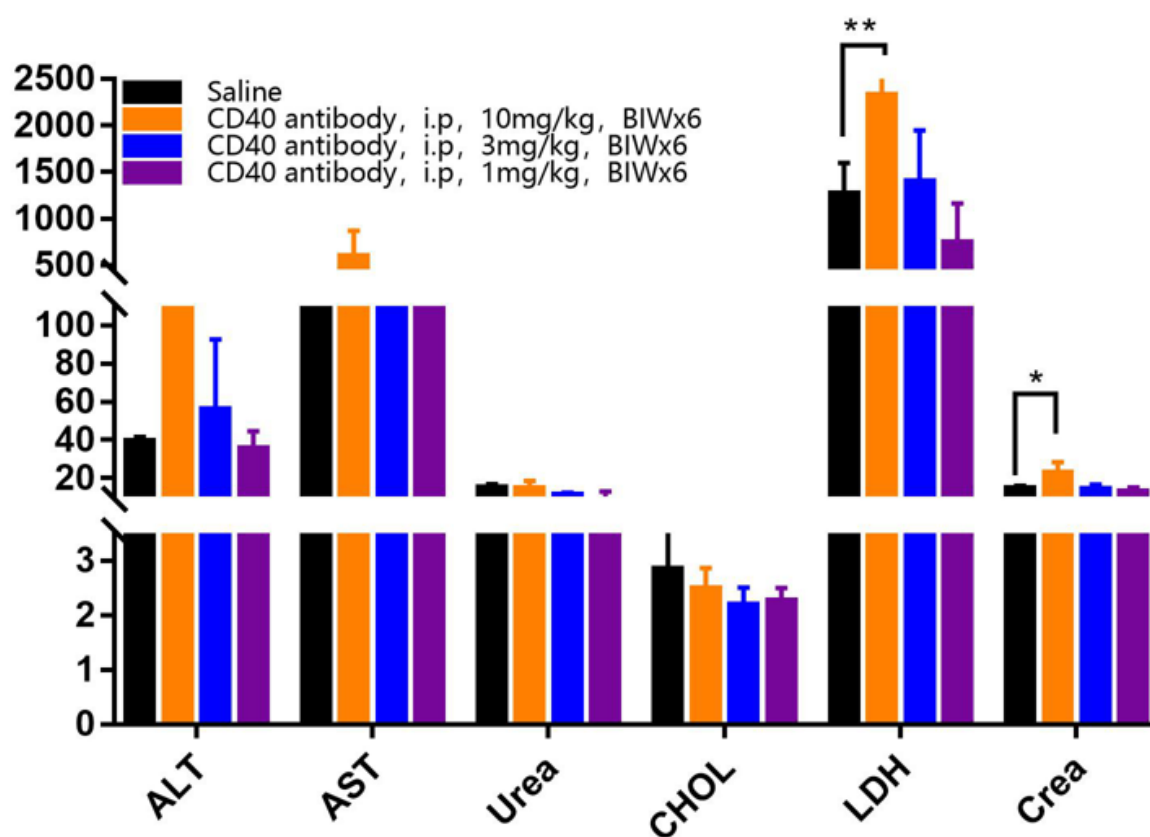


Fig4 Tumor and weight changes over treated with anti-human CD40 antibody



Abbreviation	Stand for
WBC	White Blood Cell Count
PDW	platelet distribution width
MPV	mean platelet volume
PLCR	platelet larger cell ratio
PLT	platelet
PCT	thrombocytocrit
LYMPH#	lymphocyte count
MONO#	monocyte count
NEUT%	neutrophil count
LYMPH%	lymphocyte ratio
MONO%	monocyte ratio

Fig5. Complete blood count (CBC) of anti-human CD40-antibody treated hCD40 mice



Abbreviation Stand for

ALT	Alanine transaminase
AST	Aspartate transaminase
Urea	Urea
CHOL	Cholesterol
LDH	lactate dehydrogenase
Crea	creatinine

Fig6.Blood chemistry of anti-human CD40-antibody treated hCD40 mice

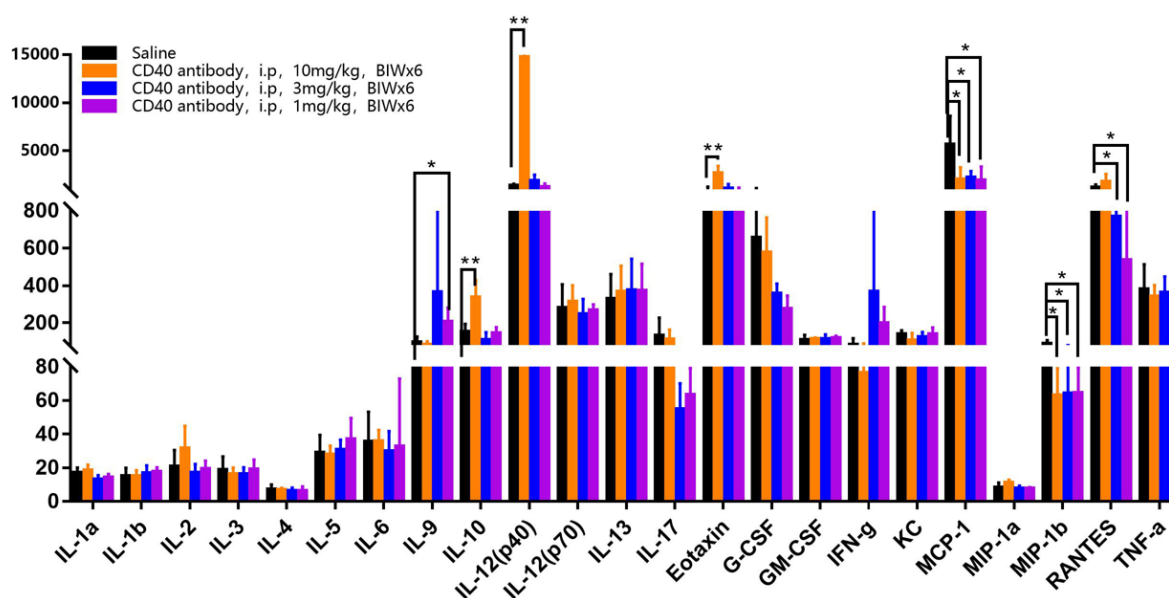


Fig7. Cytokine analysis of anti-human CD40 antibody treated hCD40 mice.

Cytokine analysis of anti-human CD40 antibody treated MC38 tumor-bearing model of humanized CD40. Anti-human CD40 antibody treatment led to significant increase several cytokines including IL-12(p40), Eotaxin, etc.