# hIL6/hIL6R

通过将hIL6和hIL6R小鼠交配获得该IL6和IL6R双人源化小鼠模型。双重人源化小鼠模型可用于评估潜在免疫治疗药物组合的功效。

| | |
|---|---|
| **品系全名** | C57BL/6Smoc-*Il6*$^{em1(hIL6)}$*Il6ra*$^{em1(hIL6R)Smoc}$ |
| **目录号** | NM-HU-190025 |
| **品系状态** | 活体 |

## 基因信息

## 品系描述

通过将hIL6和hIL6R小鼠交配获得该IL6和IL6R双人源化小鼠模型。双重人源化小鼠模型可用于评估潜在免疫治疗药物组合的功效。

**应用领域**：免疫治疗；肿瘤研究；药物筛选

*使用本品系发表的文献需注明: hIL6/hIL6R mice (Cat. NO. NM-HU-190025) were purchased from Shanghai Model Organisms Center, Inc..

## 验证数据

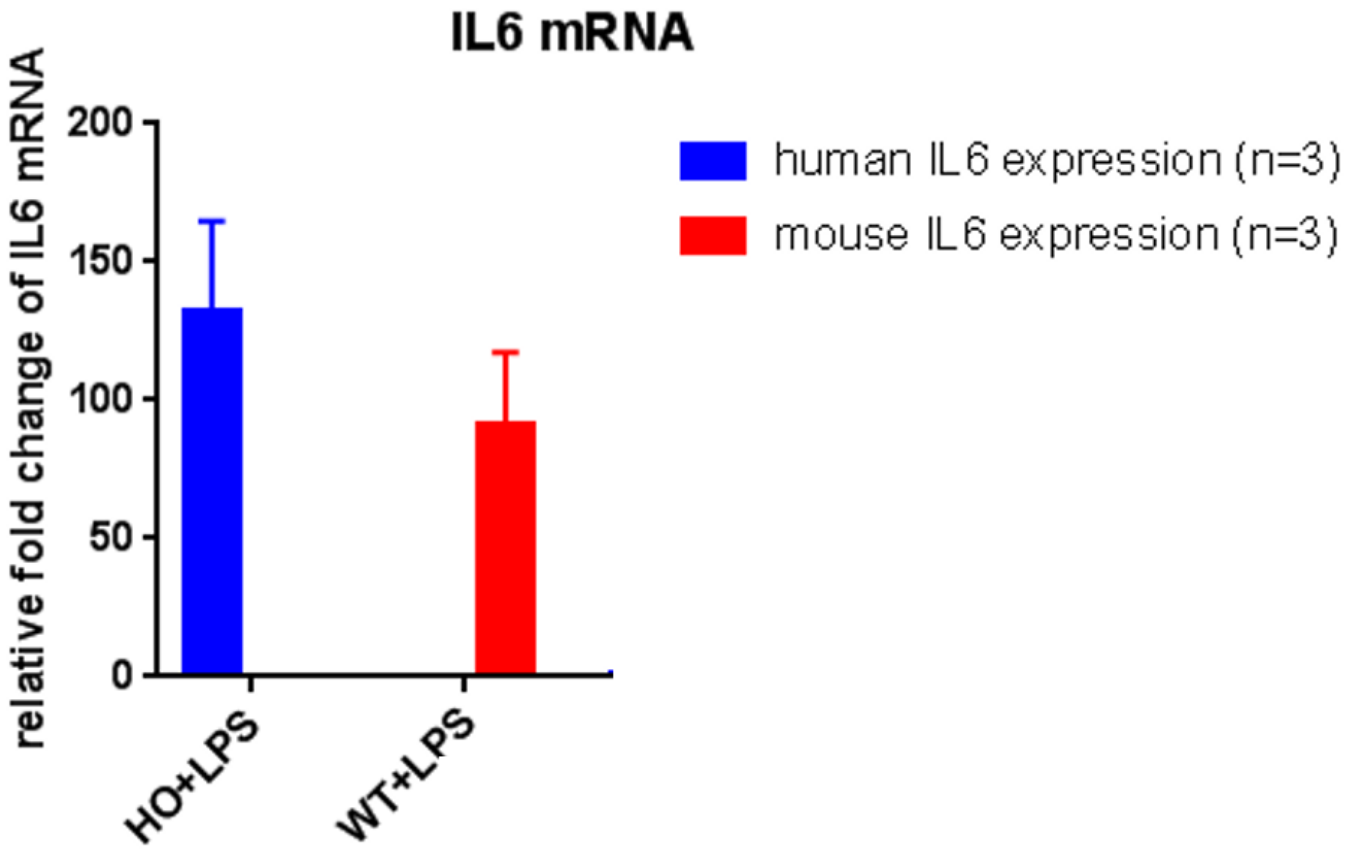


Fig1. The expression of human IL6 in liver tissue of humanized IL6/IL6R mice was measured by qPCR. The results showed that the active expression of humanized IL6 can be detected in liver tissue of homozygous humanized IL6/IL6R mice after LPS Activation.

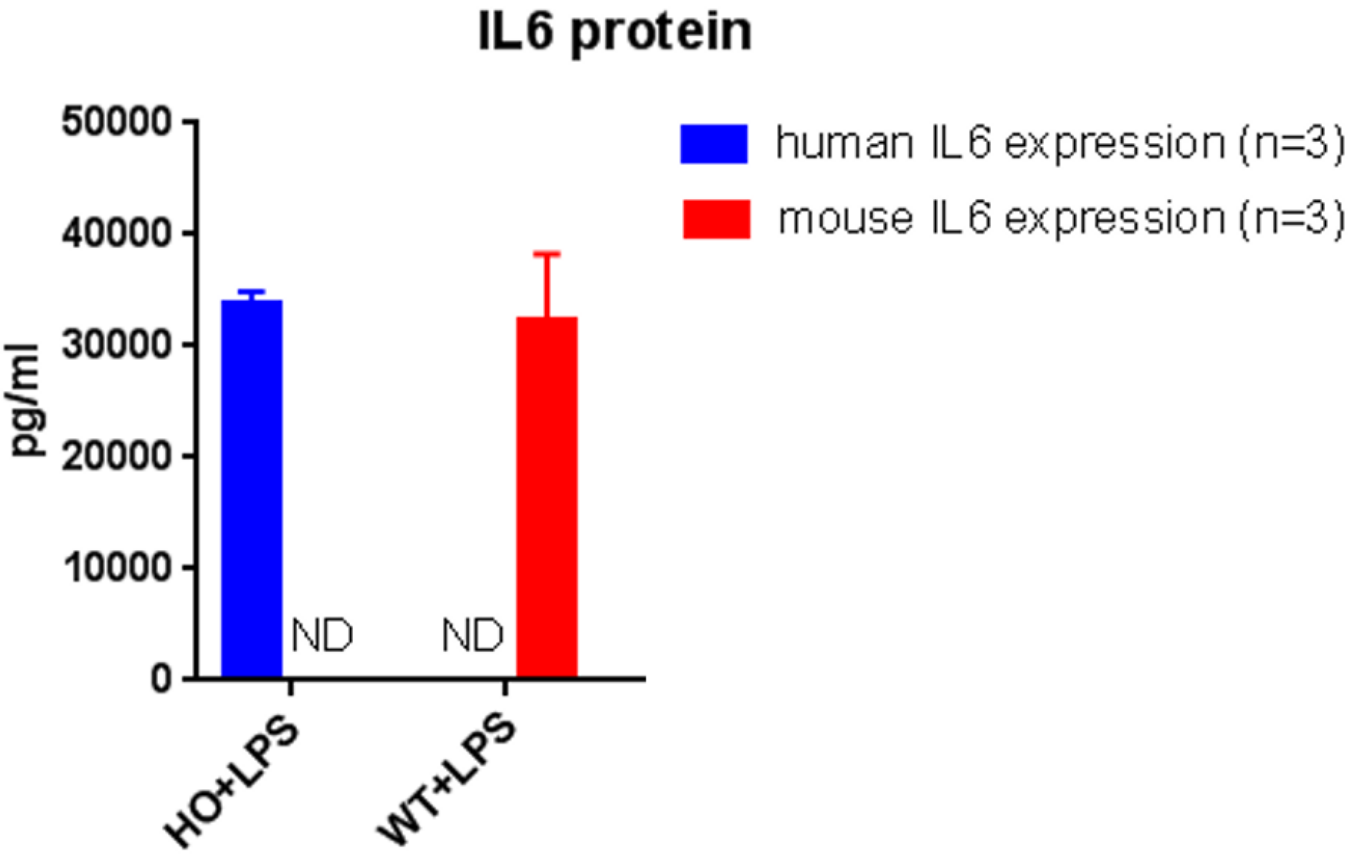

Fig2. Expression of human IL6 in the serum of humanized IL6/IL6R homozygous mice is detected by Elisa. The results showed that the expression of human IL6 can be detected in the serum collected from homozygous mice after LPS Activation.

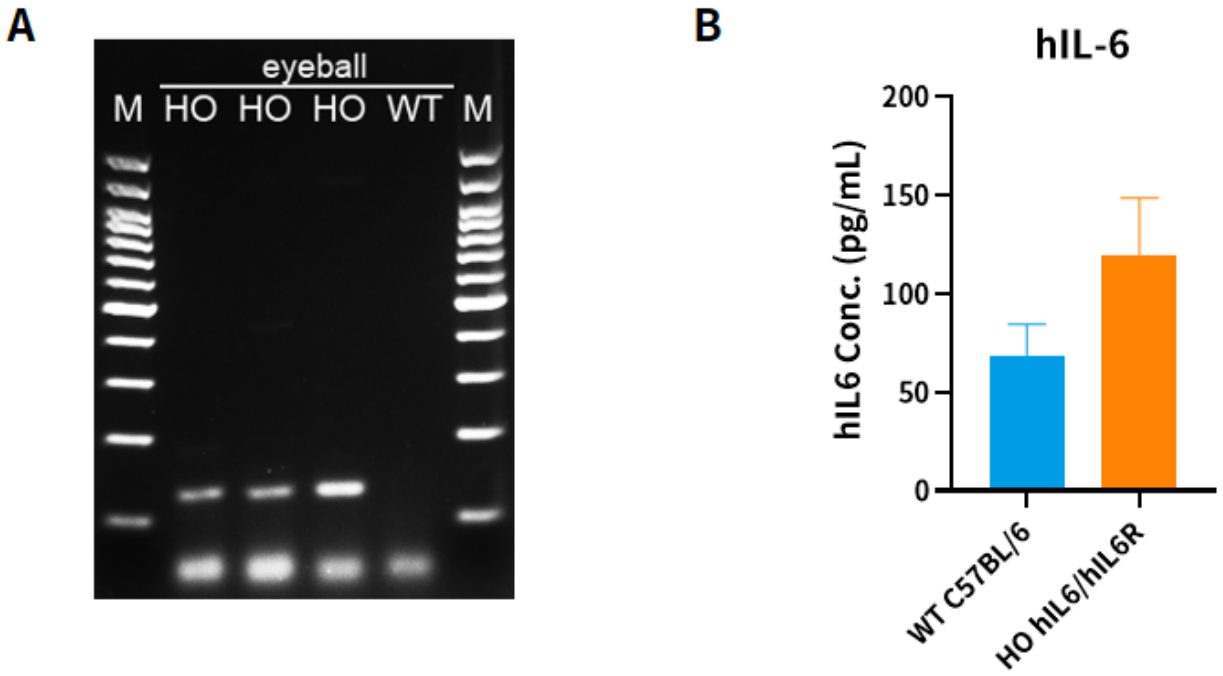


Fig3. Validation of human IL6 mRNA and protein expression by RT-PCR and ELISA in eyeball.

LPS was dissolved in endotoxin-free water and administered as a local eye drop at a concentration of 10 μg/μL (5 μL per eye). To ensure uniform distribution of the eye drop, the mouse was restrained for 1 minute. Four hours later, the whole eyeball was collected and homogenized to extract RNA and protein to detect hIL6 and hIL6R expression. (HO: humanized IL6/IL6R homozygous mice; WT:  wild type C57BL/6 mice)

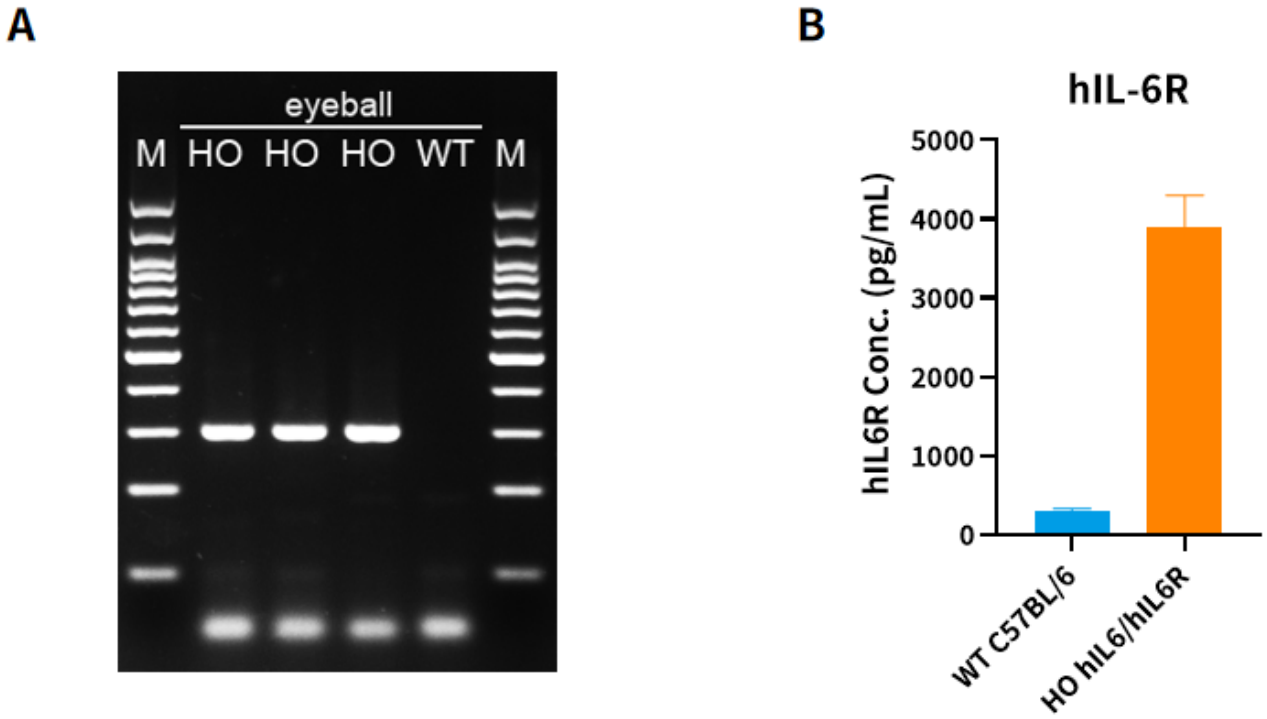


Fig4. Detection of hIL-6R expression in eyeball by RT-PCR and ELISA(n=3). Humanized mice express human IL-6R.

Abbr. HO, homozygous; WT, wild type.

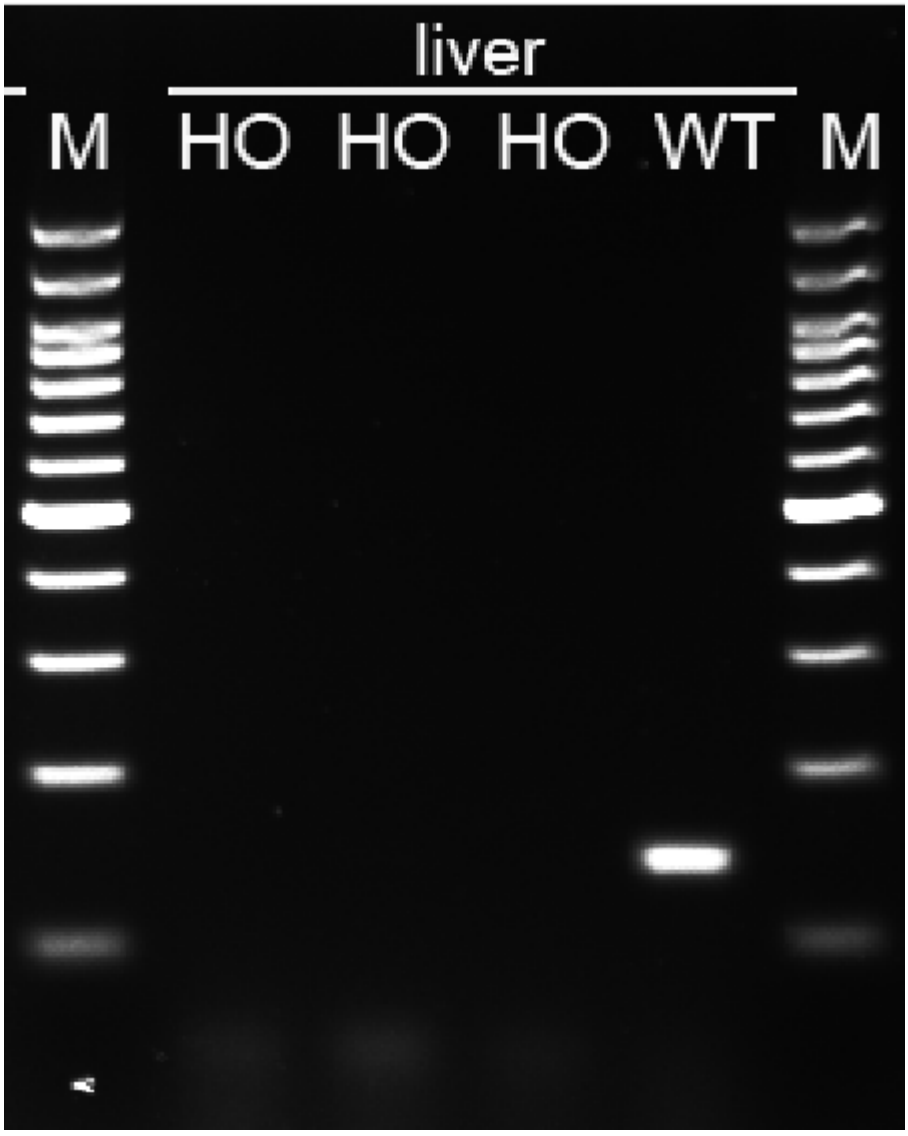


Fig5. Detection of mIL-6R expression in liver by RT-PCR. Humanized mice do not express mouse IL-6R.

Abbr. HO, homozygous; WT, wild type.

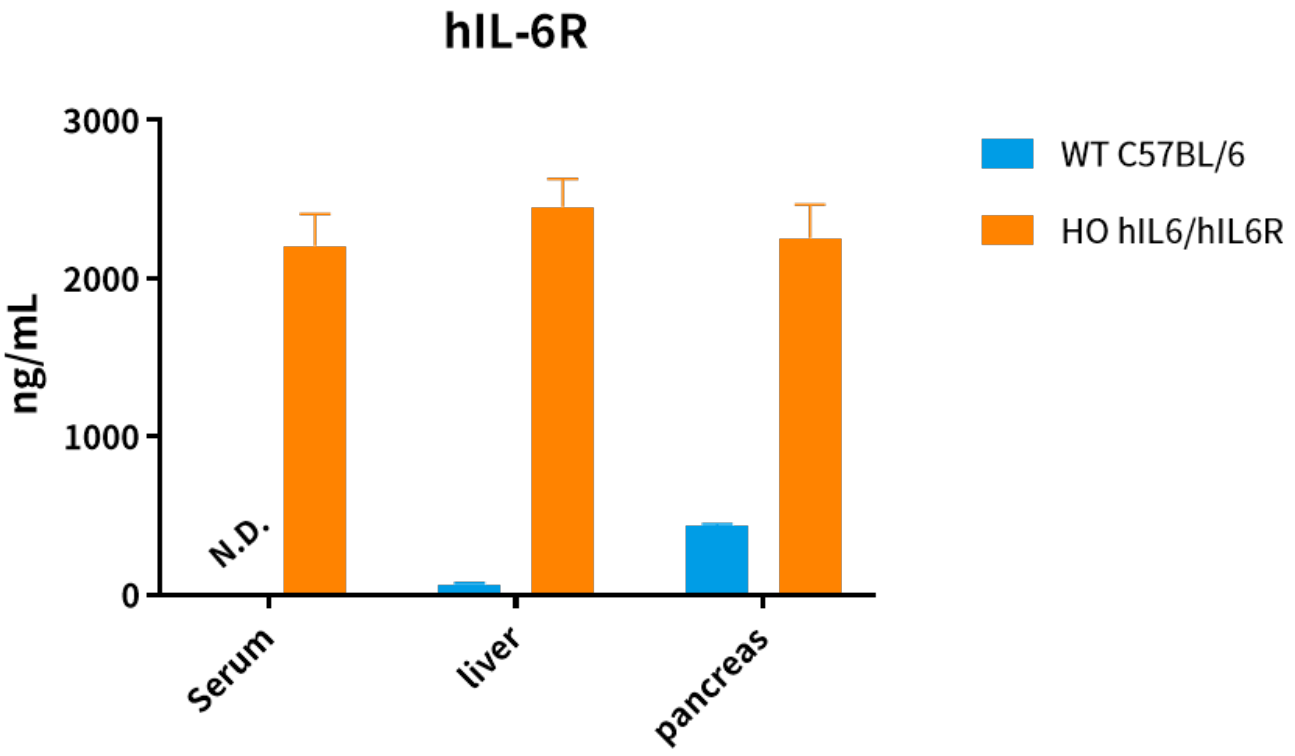


Fig6. Expression of human IL6R in the serum, liver and pancreas of HO hIL6/IL6R mice is detected by Elisa.

The results showed that the expression of human IL6R can be detected in the serum, liver and pancreas collected from homozygous mice.

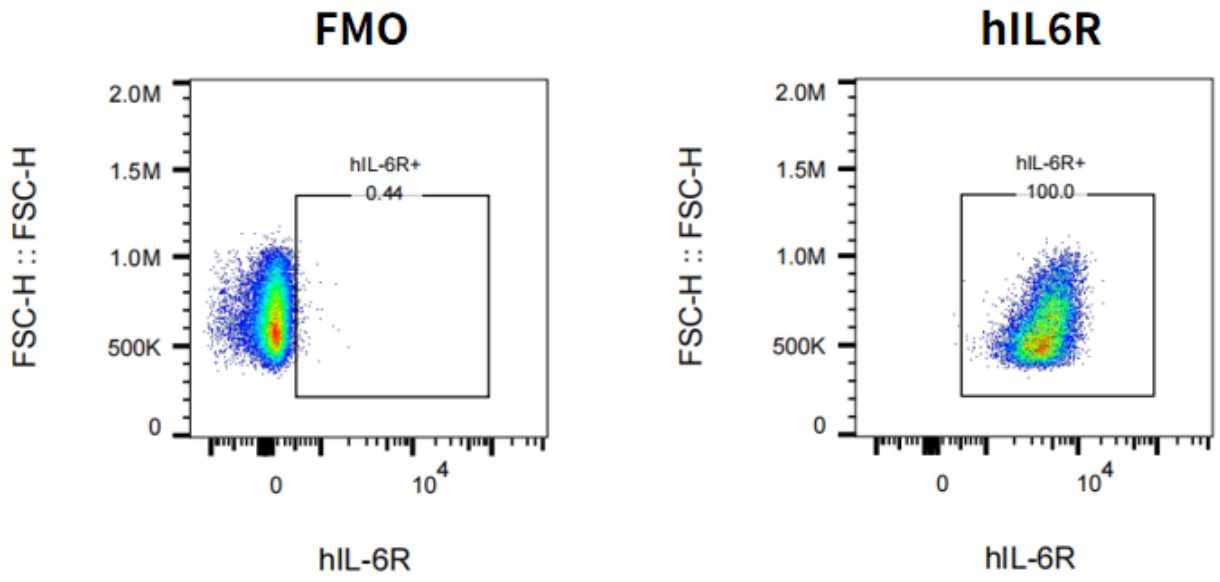


Fig7. Detection of hIL-6R expression in MM.1S cells.

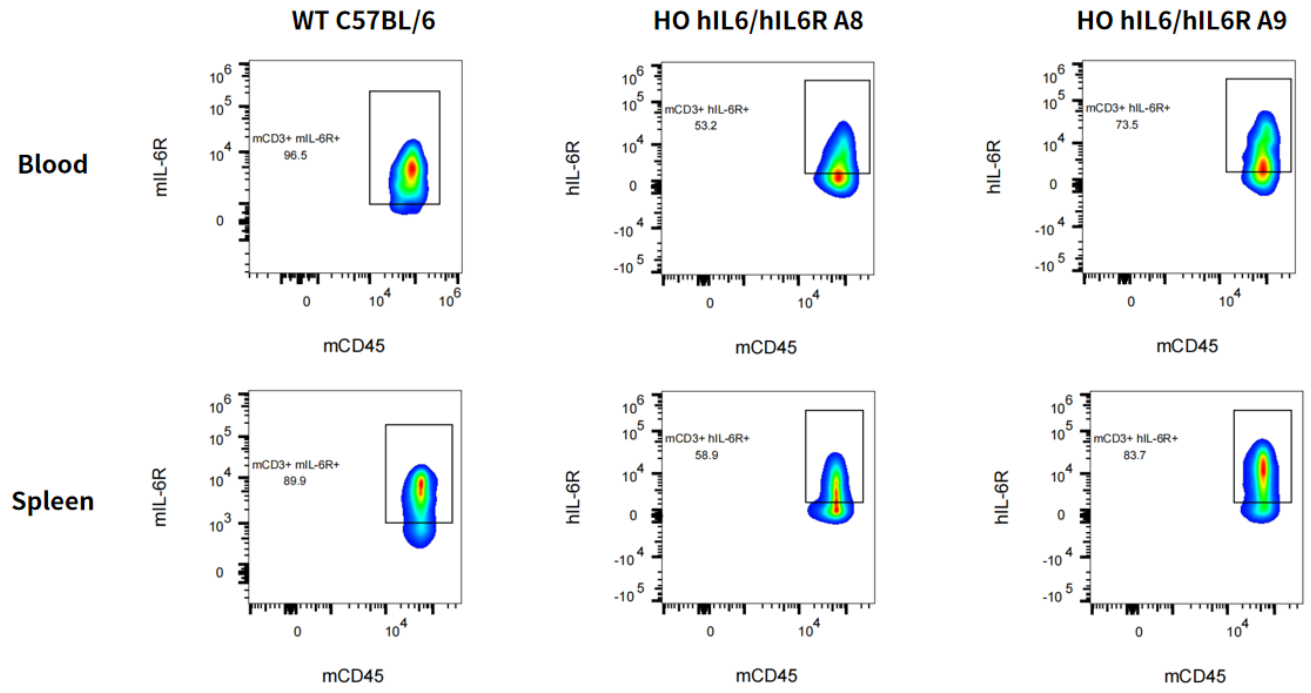


Fig8. Detection of hIL-6R expression in T cells in WT C57BL/6 and HO hIL6/hIL6R mice.

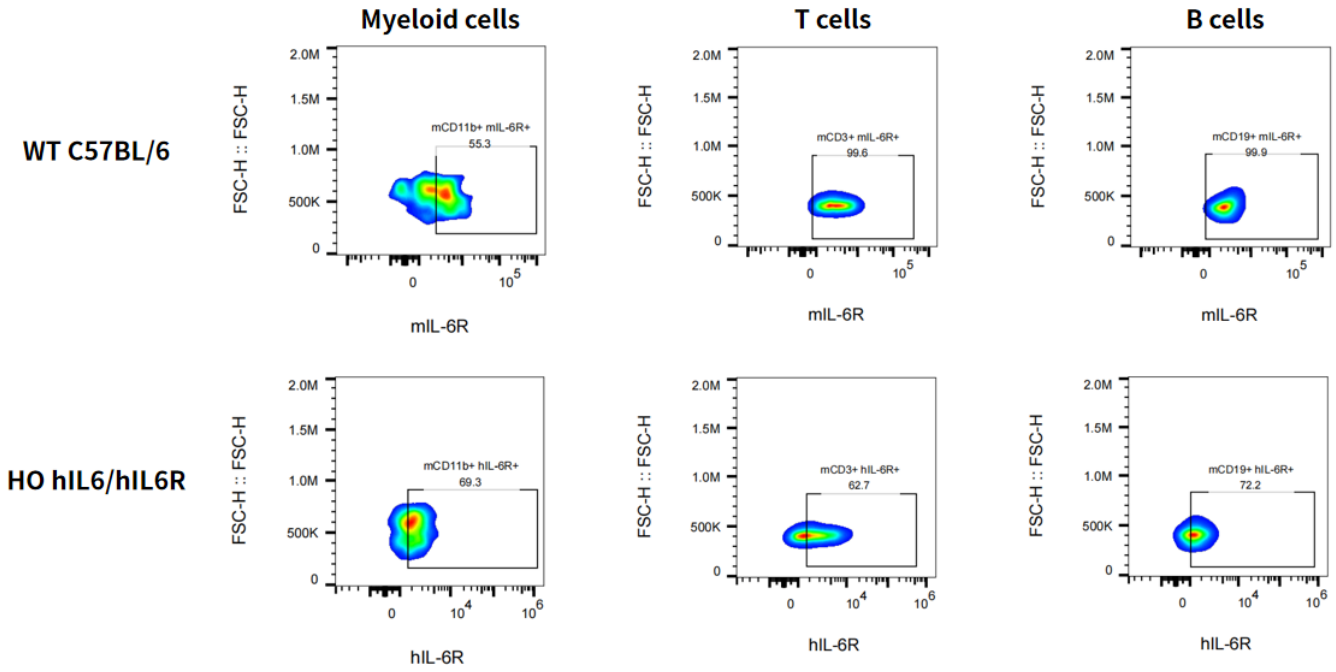


Fig9. Detection of hIL-6R expression in Myeloid cells, T cells and activated B cells in hIL6/hIL6R mice.

Note. Splenocytes from C57BL/6 and homozygous IL-6/hIL-6R mice were stimulated with LPS *in vitro*.

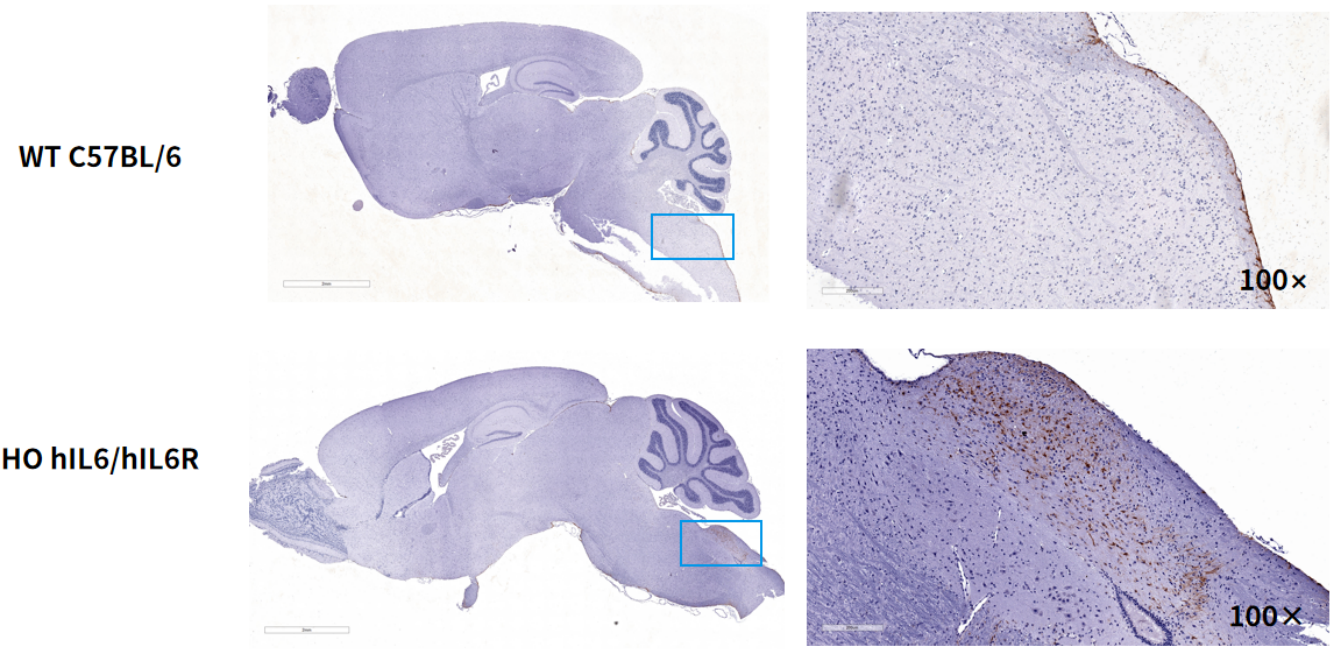


Fig10. Detection of hIL-6R expression in brainstem in WT C57BL/6 and HO hIL6/hIL6R mice by IHC.

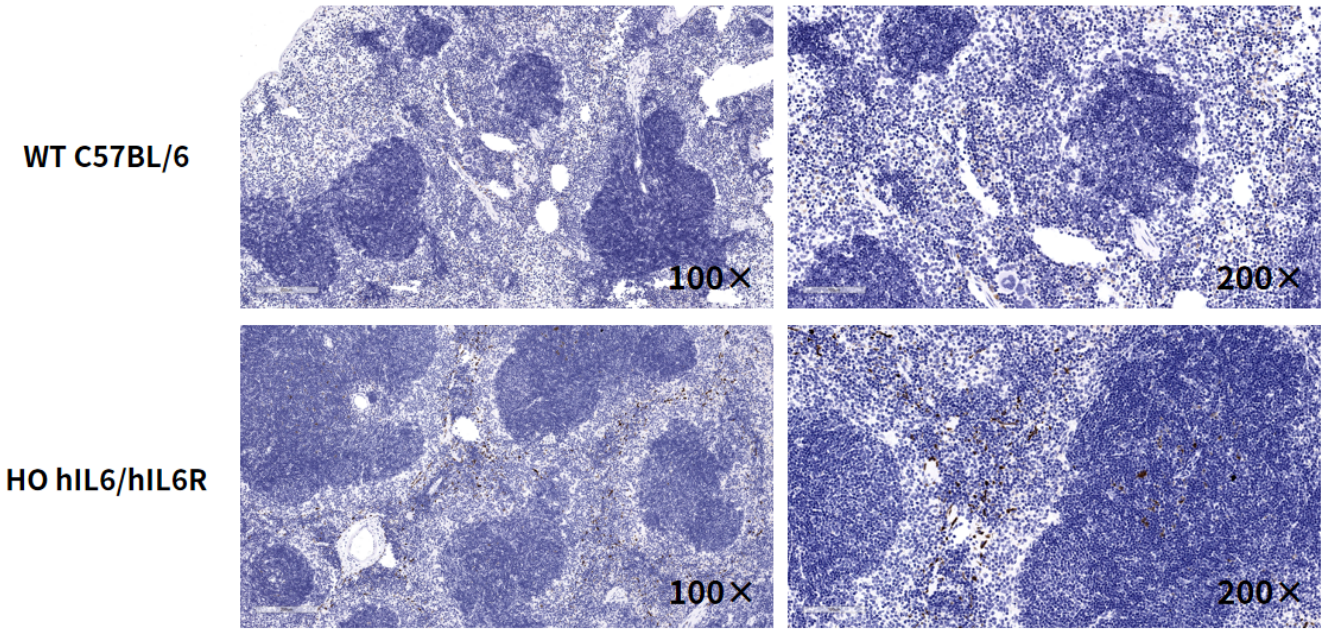


Fig11. Detection of hIL-6R expression in spleen in WT C57BL/6 and HO hIL6/hIL6R mice by IHC.

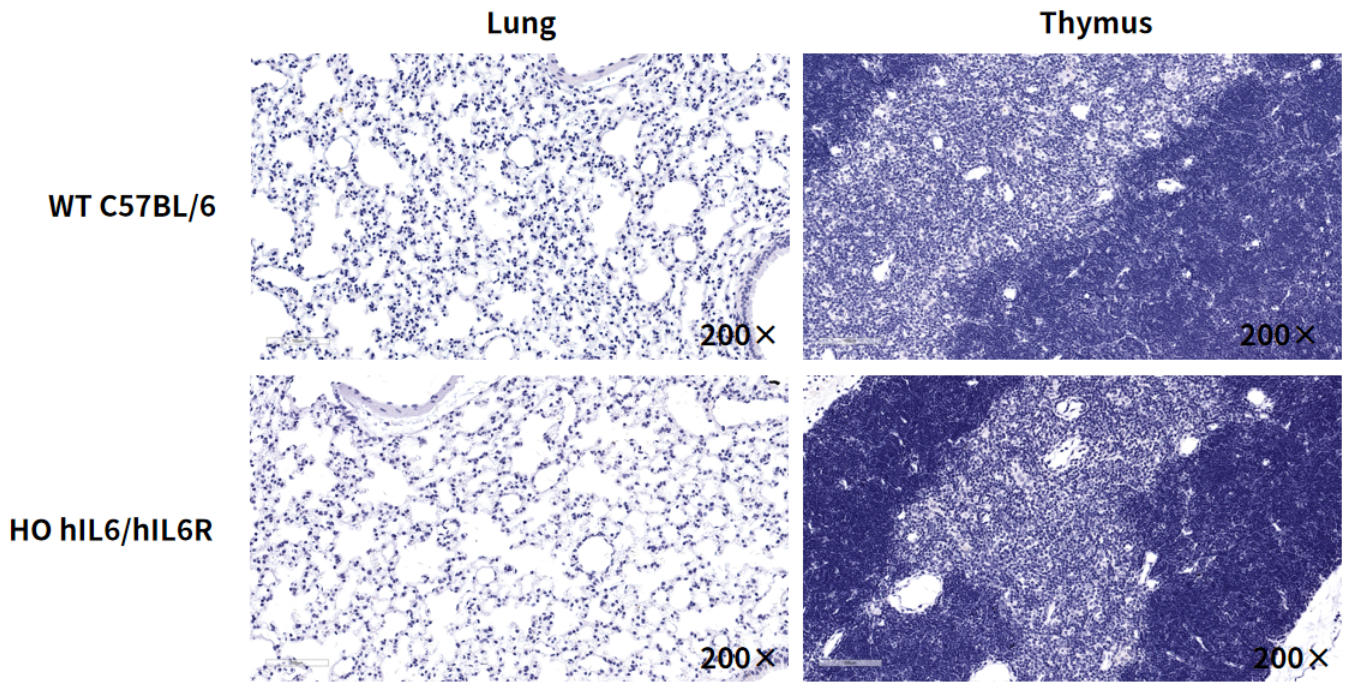


Fig12. Detection of hIL-6R expression in lung and thymus in WT C57BL/6 and HO hIL6 /hIL6R mice by IHC.

| Parameter | WT C57BL/6 ♀ 10 weeks; n=5 | WT C57BL/6 ♂ 10 weeks; n=5 | HO hIL6/hIL6R ♀ 10 weeks; n=5 | HO hIL6/hIL6R ♂ 10 weeks; n=5 | Parameter | WT C57BL/6 ♀ 10 weeks; n=5 | WT C57BL/6 ♂ 10 weeks; n=5 | HO hIL6/hIL6R ♀ 10 weeks; n=5 | HO hIL6/hIL6R ♂ 10 weeks; n=5 |
|---|---|---|---|---|---|---|---|---|---|
| WBC(10^3/uL) | 1.63±0.57 | 3.88±1.54 | 2.26±0.89 | 3.46±0.89 | BASO#(10^3/uL) | 0±0 | 0±0 | 0±0 | 0±0 |
| RBC(10^6/uL) | 10.43±0.47 | 9.96±0.38 | 8.74±0.41 | 9.98±0.89 | | | | | |
| HGB(g/dL) | 15.5±0.7 | 15.12±0.51 | 13.04±0.8 | 14.5±1.38 | NEUT%(%) | 9.78±2.39 | 7.56±1.11 | 10.6±3.07 | 29.72±5.77 |
| HCT(%) | 50.16±2.04 | 49.96±1.34 | 42.38±2.09 | 47.28±4.15 | LYMPH%(%) | 88.52±2.98 | 89.22±1.42 | 87.08±4.37 | 67.34±5.06 |
| MCV(fL) | 48.08±0.49 | 50.16±1.15 | 48.48±0.28 | 47.36±0.43 | MONO%(%) | 0.62±0.44 | 1.72±0.7 | 1.68±1.27 | 2.28±0.67 |
| MCH(pg) | 14.86±0.23 | 15.18±0.37 | 14.9±0.29 | 14.5±0.35 | EO%(%) | 1.08±0.51 | 1.5±0.71 | 0.64±0.63 | 0.66±0.57 |
| | | | | | BASO%(%) | 0±0 | 0±0 | 0±0 | 0±0 |
| MCHC(g/dL) | 30.9±0.41 | 30.26±0.25 | 30.74±0.48 | 30.66±0.59 | RET%(%) | 3.63±0.56 | 4.62±0.76 | 5.1±0.34 | 4.47±0.47 |
| | | | | | RET#(10^6/uL) | 0.38±0.07 | 0.46±0.07 | 0.44±0.02 | 0.44±0.03 |
| RDW-SD(fL) | 23.54±0.5 | 28.38±2.32 | 25.46±1.41 | 25.06±1.57 | IRF(%) | 61.1±1.97 | 61.62±3.11 | 63.3±3.16 | 60.24±2.71 |
| RDW-CV(%) | 16.84±0.38 | 17.6±1.29 | 16.18±1.16 | 17.22±1.43 | LFR(%) | 38.9±1.97 | 38.38±3.11 | 36.7±3.16 | 39.76±2.71 |
| PDW(fL) | 6.18±0.13 | 6.36±0.27 | 6.34±0.19 | 6.16±0.24 | | | | | |
| MPV(fL) | 6.28±0.08 | 6.42±0.19 | 6.6±0.12 | 6.32±0.13 | MFR(%) | 21.54±1.01 | 18.46±0.52 | 24.54±1.95 | 18.98±1.19 |
| P-LCR(%) | 2.32±0.68 | 3.02±0.62 | 3.22±0.57 | 2.48±0.66 | | | | | |
| PCT(%) | 0.82±0.07 | 1.08±0.11 | 0.93±0.09 | 0.92±0.13 | HFR(%) | 39.56±2.34 | 43.16±3.23 | 38.76±4.57 | 41.26±2.26 |
| NRBC#(10^3/uL) | 0.02±0.01 | 0.03±0.01 | 0.02±0.01 | 0.02±0 | RET-He(pg) | 17.2±0.26 | 16.78±0.16 | 17.02±0.36 | 16.9±0.38 |
| NRBC%(%) | 1.1±0.23 | 0.84±0.25 | 0.82±0.13 | 0.68±0.28 | IPF(%) | 0.08±0.04 | 0.1±0 | 0.2±0.07 | 0.12±0.04 |
| | | | | | PLT-O(10^3/uL) | 1103.2±63.69 | 1341±54.47 | 1089.8±135.93 | 1194±206.06 |
| NEUT#(10^3/uL) | 0.15±0.05 | 0.29±0.1 | 0.23±0.08 | 1.04±0.41 | | | | | |
| | | | | | PLT-F(10^3/uL) | 1123±70.87 | 1346.2±27.23 | 1154±143.09 | 1230.2±197.95 |
| LYMPH#(10^3/uL) | 1.45±0.53 | 3.47±1.39 | 1.98±0.82 | 2.32±0.55 | | | | | |
| | | | | | RBC-O(10^6/uL) | 9.72±0.41 | 9.3±0.48 | 8.15±0.44 | 9.26±0.79 |
| MONO#(10^3/uL) | 0.01±0.01 | 0.07±0.05 | 0.04±0.02 | 0.08±0.03 | | | | | |
| | | | | | PLT-I(10^3/uL) | 1304.4±105.49 | 1676.4±126.44 | 1416±141.07 | 1454.4±206.34 |
| EO#(10^3/uL) | 0.02±0.01 | 0.05±0.02 | 0.01±0.01 | 0.02±0.01 | | | | | |

Table 1 Blood routine test results of HO hIL6/hIL6R mice (Data are presented as mean and ± SEM).

| Parameter | Units | WT C57BL/6 ♀ 10 weeks; n=5 | WT C57BL/6 ♂ 10 weeks; n=5 | HO hIL6/hIL6R ♀ 10 weeks; n=5 | HO hIL6/hIL6R ♂ 10 weeks; n=5 |
|---|---|---|---|---|---|
| ALT | (U/L) | 31.7±6.59 | 29.64±7.34 | 35.03±16.57 | 27.31±14.56 |
| AST | (U/L) | 119.13±15.24 | 110.96±22.98 | 117.19±42.32 | 124.64±19.4 |
| UREA | (mmol/L) | 8.18±1.04 | 9.03±0.77 | 7.72±0.49 | 7.62±0.64 |
| CREA | (μmol/L) | 27.52±5.05 | 28.7±3.95 | 29.29±3.99 | 24.89±7.98 |

Table 2 Biochemistry examinations results of HO hIL6/hIL6R mice (Data are presented as mean and ± SEM)

***In vivo* efficacy of Sirukumab in Collagen induced Rheumatoid Arthritis (CIA) model in hIL6/hIL6R mice.**

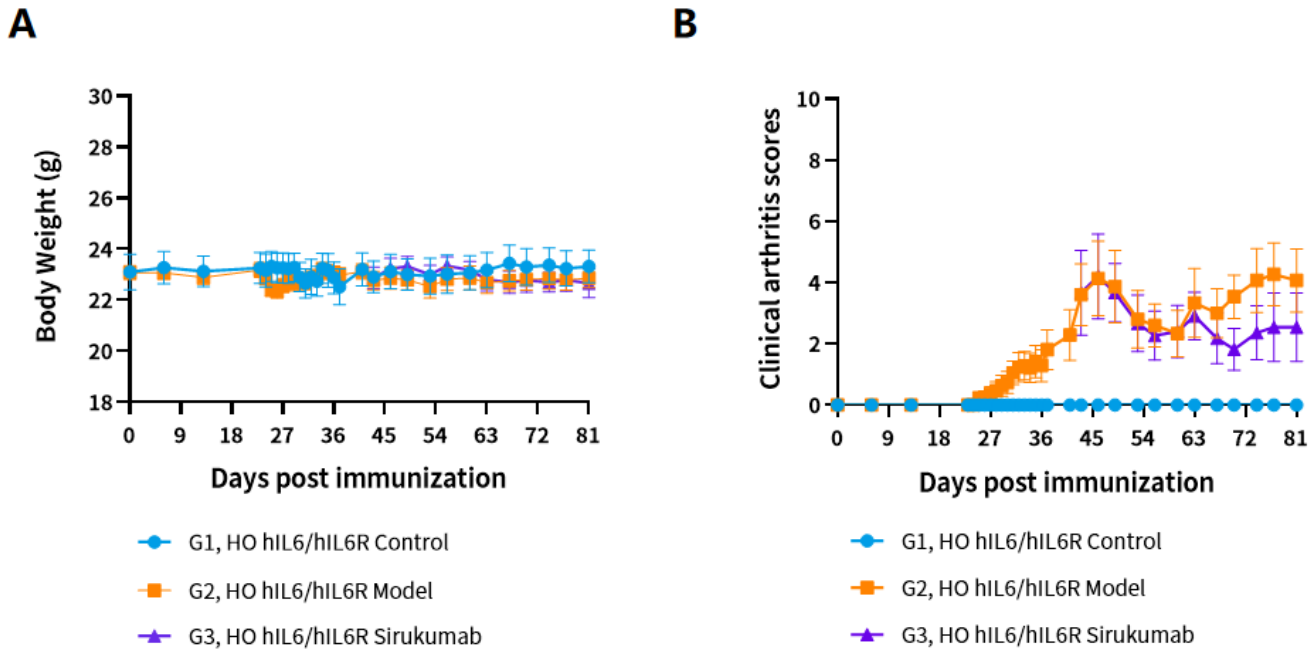


**Fig.1 Efficacy of Sirukumab in hIL6/hIL6R mice in collagen-induced arthritis (CIA) model.**

Group 1 received no immunization. Group 2 were immunized to induce CIA. Group 3 were immunized to induce CIA and treated with Sirukumab. Body weight was monitored throughout the study and remained stable across all groups (A). After CIA induction, clinical score increase, indicating successful model establishment. Mice treated with Sirukumab exhibited reduction in arthritis severity as evidenced by decreased clinical scores (B). Data are presented as mean ± SEM (n=10-15).

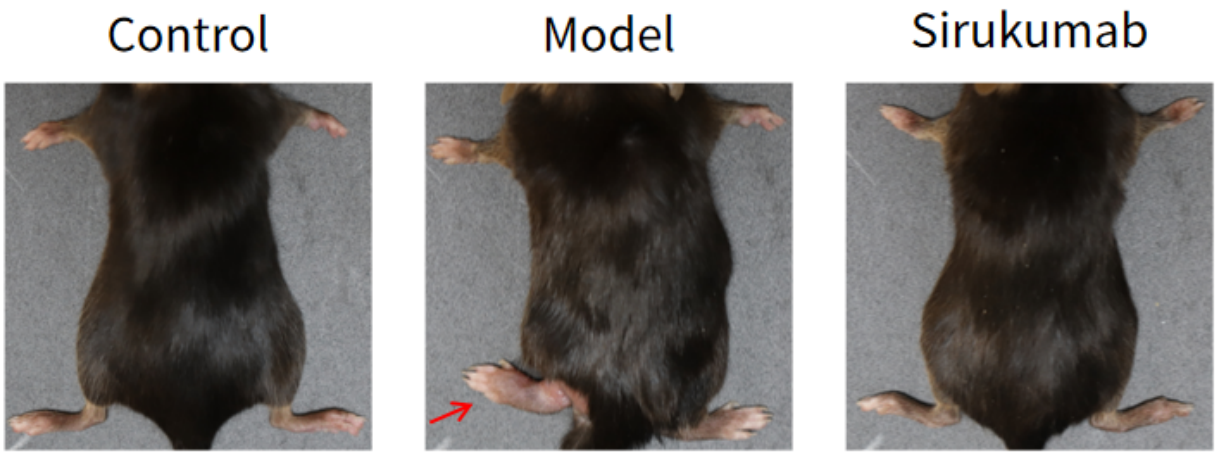


**Fig.2 Efficacy of Sirukumab in hIL6/hIL6R mice in collagen-induced arthritis (CIA) model.**

Group 1 received no immunization. Group 2 were immunized to induce CIA. Group 3 were immunized to induce CIA and treated with Sirukumab. Representative diagram of hind limb joints of mice in each group at the end of the study.

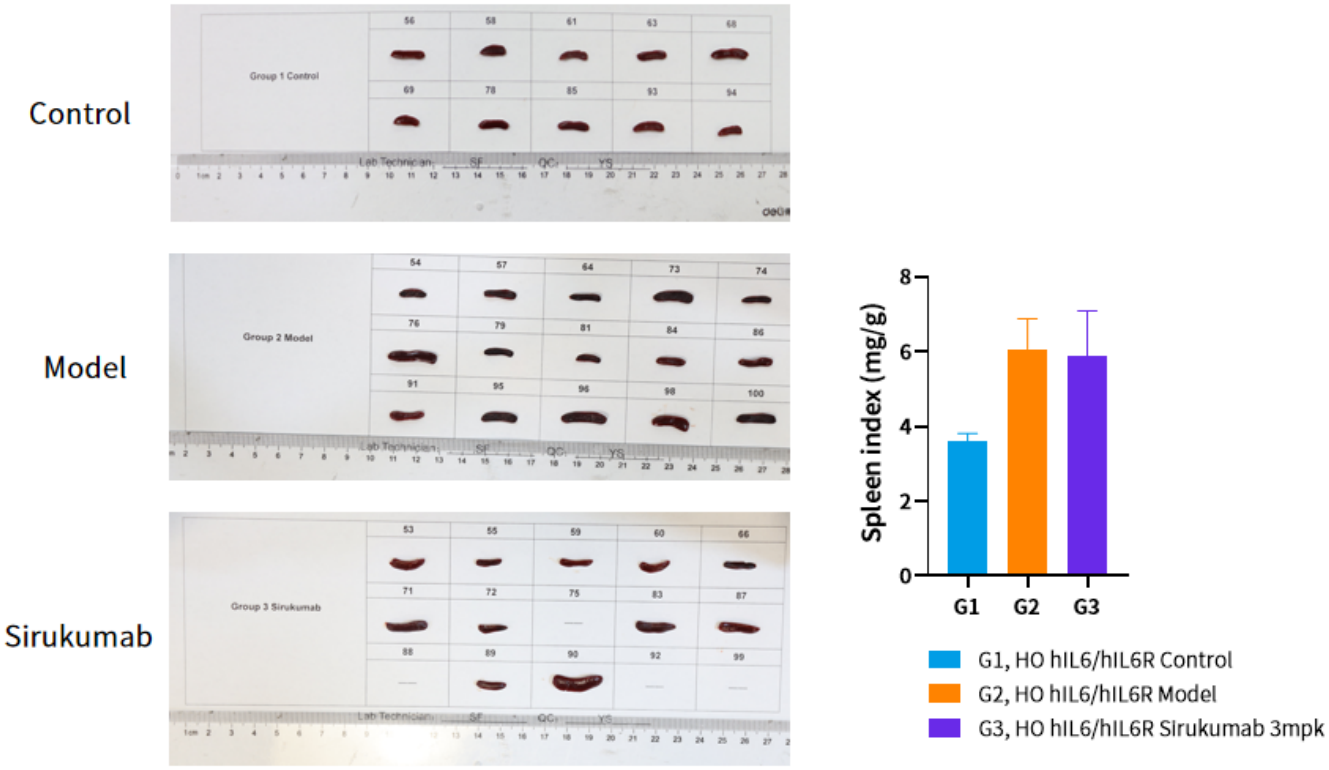


**Fig.3 Gross pathology and relative weight of spleen each group in collagen-induced arthritis (CIA) model in hIL6/hIL6R mice.**

Group 1 received no immunization. Group 2 were immunized to induce CIA. Group 3 were immunized to induce CIA and treated with Sirukumab. Data are presented as mean ± SEM (n=10-15).

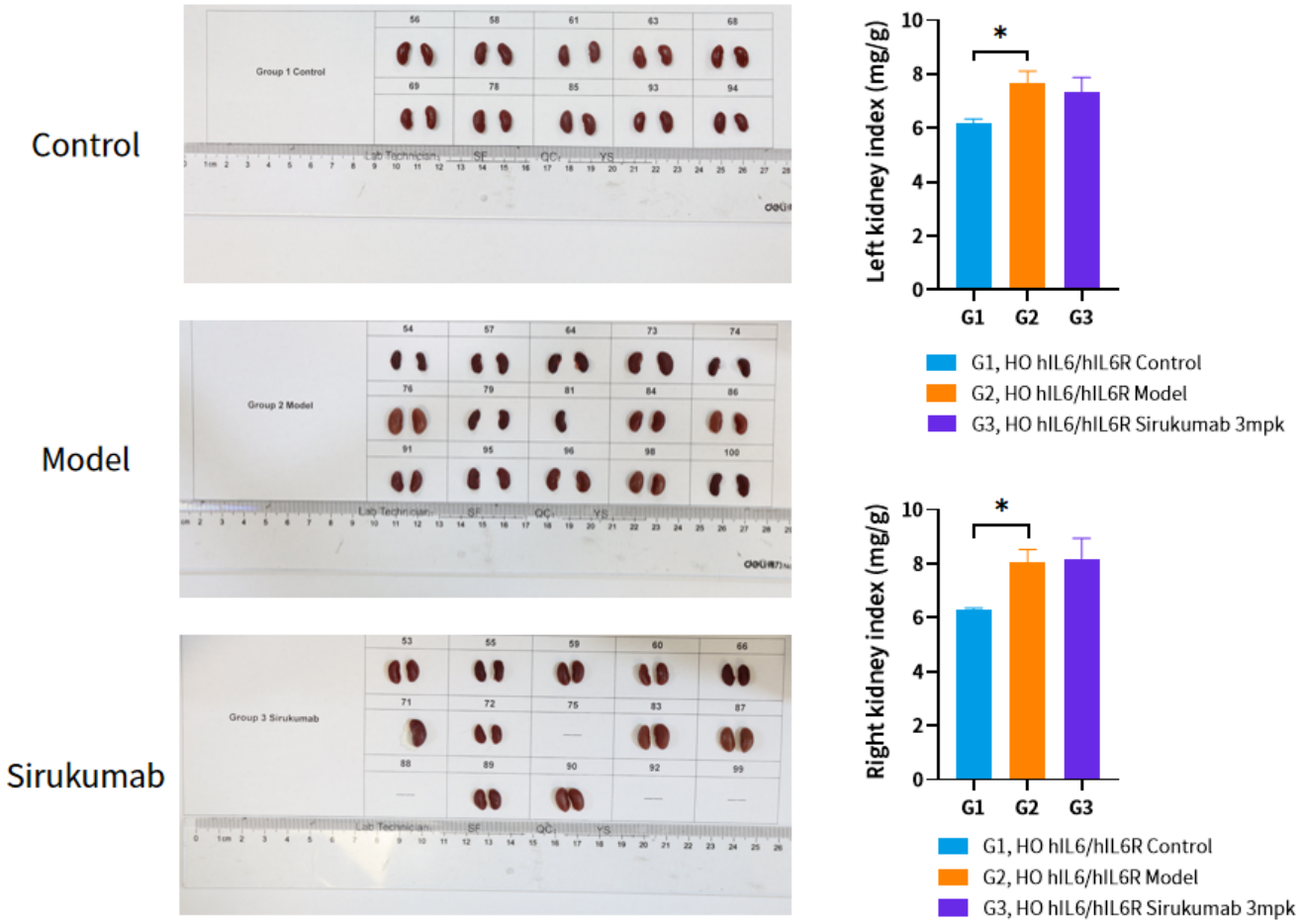


**Fig.4 Gross pathology and relative weight of kidney each group in collagen-induced arthritis (CIA) model in hIL6/hIL6R mice.**

Group 1 received no immunization. Group 2 were immunized to induce CIA. Group 3 were immunized to induce CIA and treated with Sirukumab. Data are presented as mean ± SEM (n=10-15).

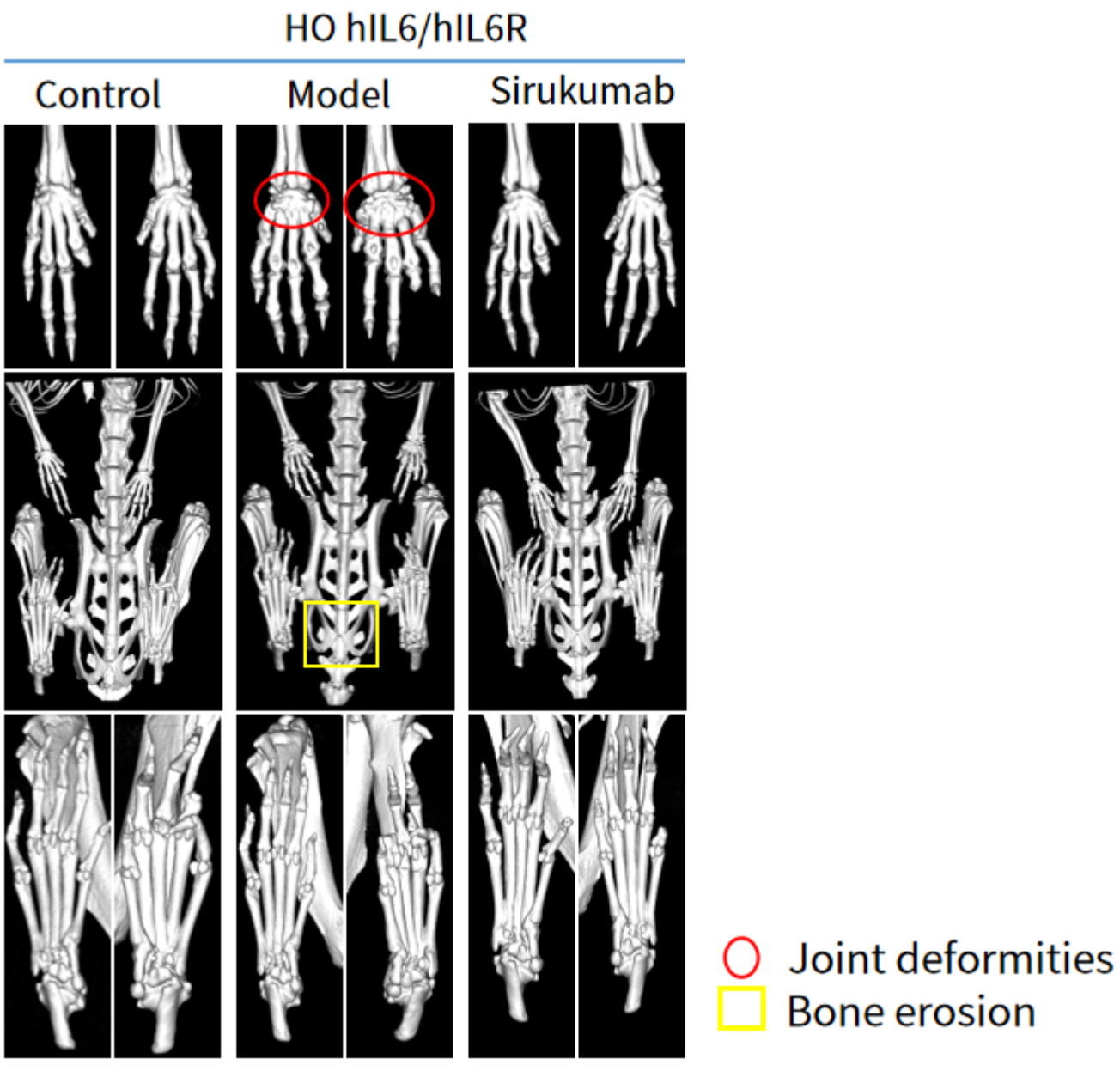


**Fig.5 Representative micro-CT images of ankle joint of each group in collagen-induced arthritis (CIA) model in hIL6/hIL6R mice.**

Group 1 received no immunization. Group 2 were immunized to induce CIA. Group 3 were immunized to induce CIA and treated with Sirukumab.