



DUAL HUMANIZED IMMUNE MODEL

# Dual Humanized IL4 / IL4R Mouse

hIL4/hIL4R · IT-HU-2000106

A dual humanized mouse model engineered for studying IL-4/IL-13 signaling pathways and developing targeted therapeutics for allergic diseases and asthma – with the authentic human ligand–receptor pairing antibody programs require.



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**PHONE** +1 (631) 468-8534  
**EMAIL** [inquiry@genetargeting.com](mailto:inquiry@genetargeting.com)  
**ADDRESS** 761-80 Coates Avenue, Holbrook, NY 11741

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BACKGROUND

C57BL/6

HUMANIZED GENES

IL4, IL4R

ZYGOSITY

Homozygous

STRAIN STATE

Repository Live



## 01 THE MODEL

# Dual Humanized **IL4 / IL4R** Mouse

The **hIL4/hIL4R** dual humanized mouse model is a critical tool for studying IL-4/IL-13 signaling pathways and developing targeted therapeutics for allergic diseases and asthma.

<b>MODEL NAME</b> hIL4/hIL4R	<b>CATALOG NUMBER</b> IT-HU-2000106
<b>GENETIC BACKGROUND</b> C57BL/6	<b>HUMANIZED GENES</b> IL4, IL4R
<b>ZYGOSITY</b> Homozygous	<b>STRAIN STATE</b> Repository Live <b>READY TO SHIP</b>
<b>RESEARCH APPLICATION</b> Immunotherapy, cancer research, drug screening	

## 02 RATIONALE

# Why Dual **IL4/IL4R** Humanization?

IL-4 signaling through the type I receptor complex (IL4 + IL4R $\alpha$  +  $\gamma$ c) drives Th2 immune responses. Human therapeutics targeting IL4 or IL4R require **both** the human ligand and the human receptor for proper binding and signaling.

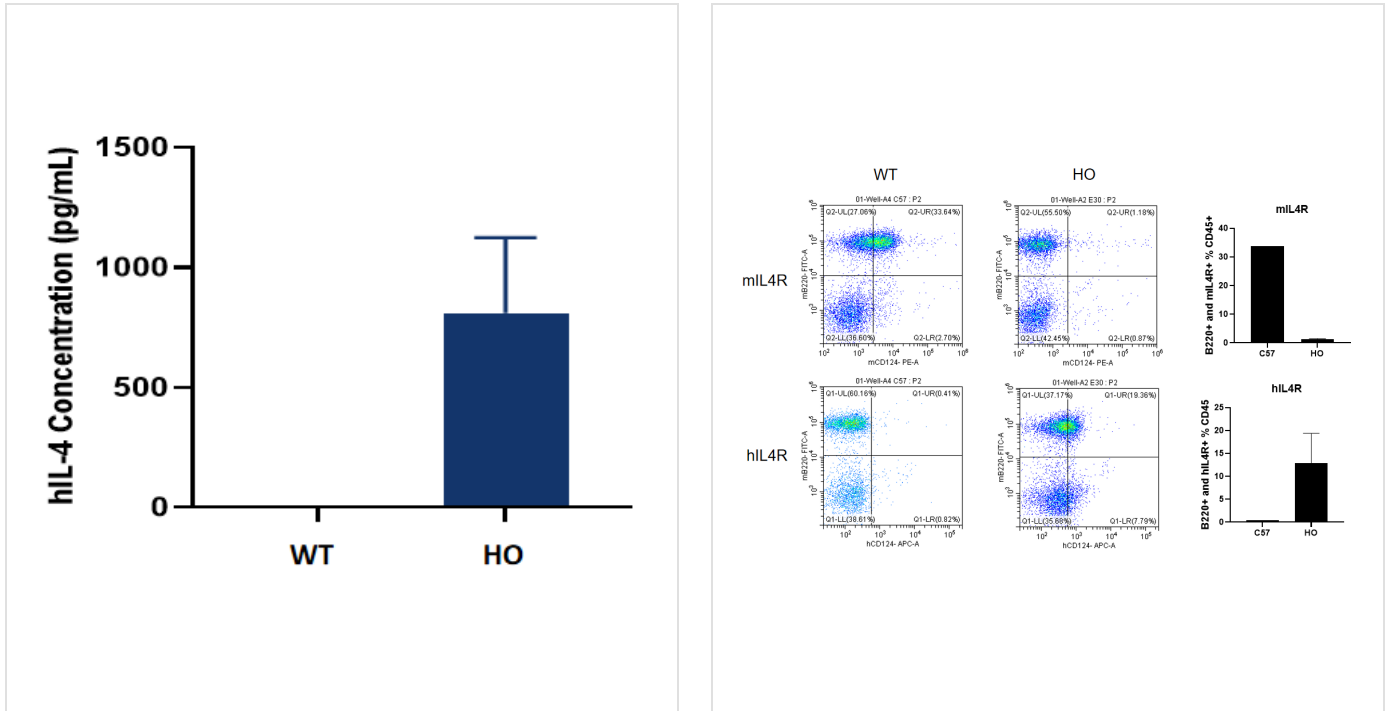
The hIL4/hIL4R model humanizes both genes so antibody and protein therapeutics engage their native human targets within an intact mouse immune system.

### Dual humanization provides

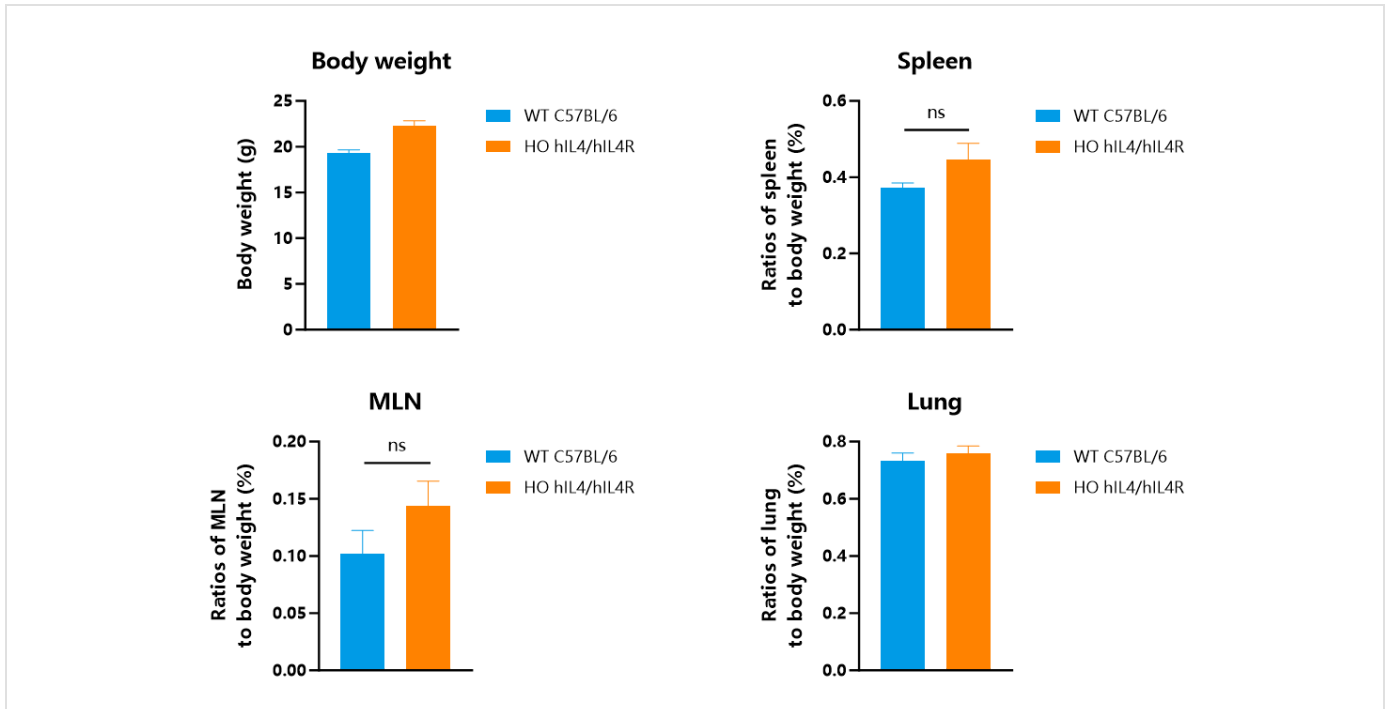
- Human IL4 ligand binding to human IL4R receptor
- Authentic type I receptor complex formation
- Proper downstream signaling through humanized pathway
- Normal mouse immune system architecture

This dual humanization enables testing of **anti-IL4/IL4R therapeutics** with their native human targets in a fully immunocompetent model.

# Humanized Expression & Phenotype

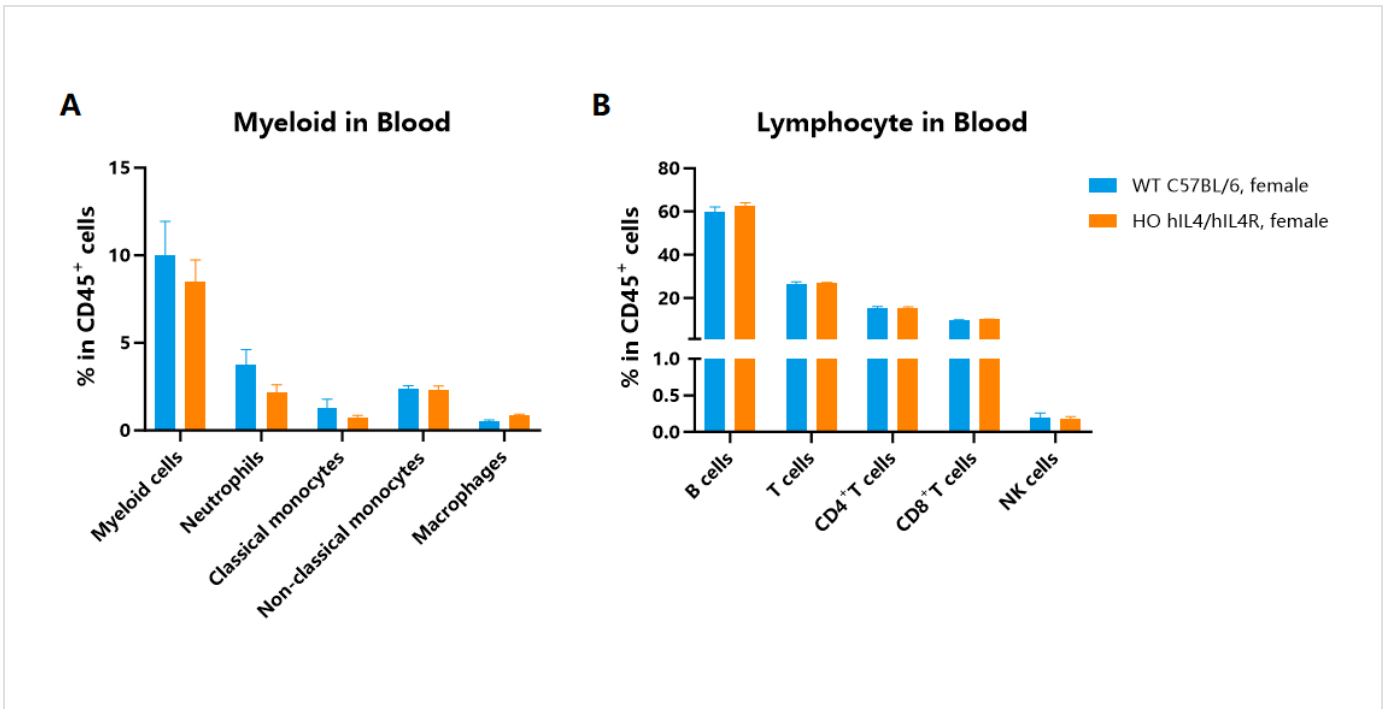


**Fig. 1-2** (1) hIL4 expression in serum by ELISA – homozygous KI mice express hIL4 after concanavalin A treatment. (2) hIL4R expression in spleen by FACS – KI mice express hIL4R; WT express only mIL4R.

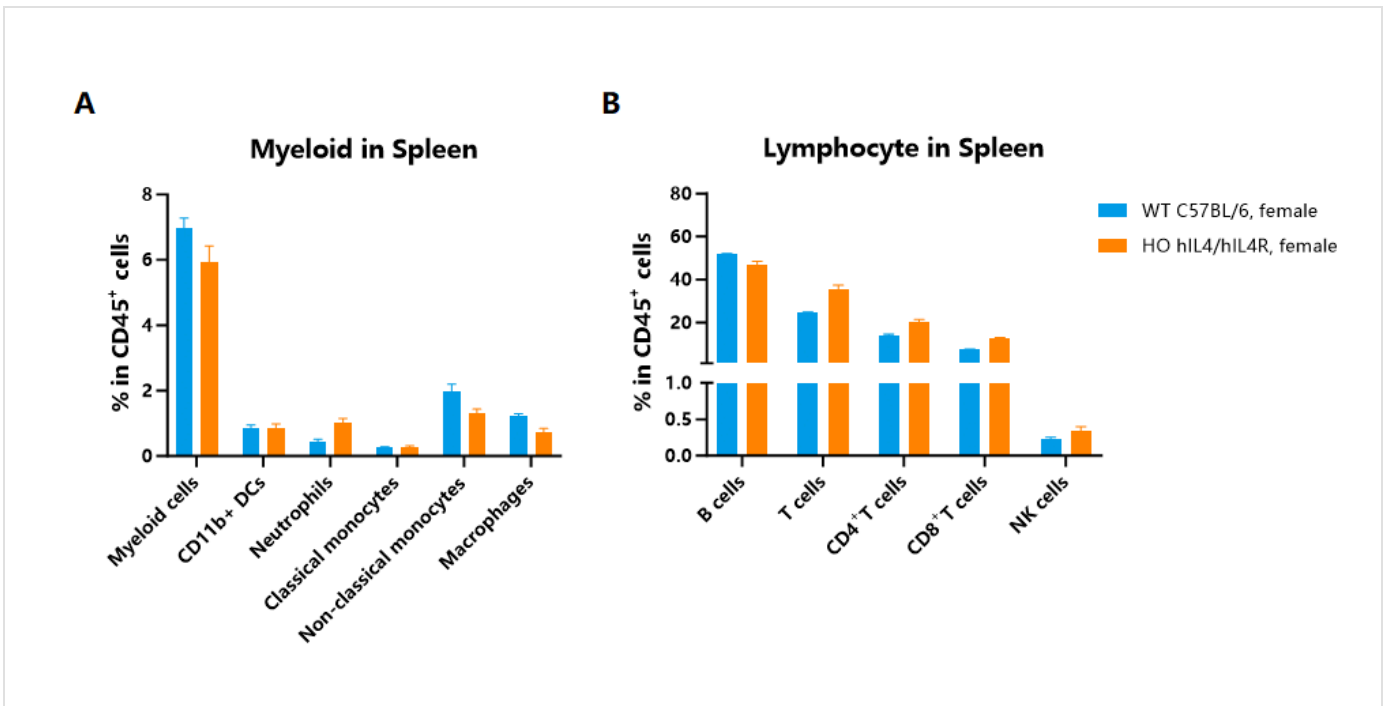


**Fig. 3** Body weight and ratios of spleen, MLN, and lung to body weight of WT and hIL4/hIL4R knockin mice (n=5–6, female, 8–10 weeks old, Mean ± SEM).  
 Abbr. HO, homozygous; WT, wild type; MLN, mesenteric lymph nodes.

# Immune Cell Profiling



**Fig. 4** Detection of myeloid (A) and lymphocyte (B) populations in the blood of hIL4/hIL4R knockin mice by FACS (n=3 in all groups, 8–10 weeks old).  
Abbr. WT, wild type; HO, homozygous.



**Fig. 5** Detection of myeloid (A) and lymphocyte (B) populations in the spleen of hIL4/hIL4R knockin mice by FACS (n=3 in all groups, 8–10 weeks old).  
Abbr. WT, wild type; HO, homozygous.

# Hematology & Clinical Chemistry

Parameter	Full Name	WT C57BL/6 ♂ 8-10 weeks; n=5	WT C57BL/6 ♀ 8-10 weeks; n=5	hIL4/hIL4R ♂ 8-10 weeks; n=5	hIL4/hIL4R ♀ 8-10 weeks; n=5	Parameter	Full Name	WT C57BL/6 ♂ 8-10 weeks; n=5	WT C57BL/6 ♀ 8-10 weeks; n=5	hIL4/hIL4R ♂ 8-10 weeks; n=5	hIL4/hIL4R ♀ 8-10 weeks; n=5
WBC(10 <sup>3</sup> /μL)	白细胞计数	8.30±0.53	6.05±0.37	9.18±0.81	7.70±0.46	EO#(10 <sup>3</sup> /μL)	嗜酸性粒细胞数	0.22±0.01	0.15±0.03	0.20±0.03	0.16±0.02
RBC(10 <sup>6</sup> /μL)	红细胞计数	10.52±0.18	10.73±0.18	11.03±0.27	9.87±0.37	BASO#(10 <sup>3</sup> /μL)	嗜碱性粒细胞数	0.01±0.00	0.01±0.00	0.01±0.00	0.01±0.00
HGB(g/dL)	血红蛋白量	15.60±0.24	16.16±0.22	15.98±0.40	14.84±0.47	NEUT%(%)	中性粒细胞百分率	16.24±3.24	8.12±1.46	6.48±0.72	8.78±3.43
HCT(%)	红细胞比积	49.50±0.82	50.60±0.67	51.16±0.98	47.04±1.19	LYMPH%(%)	淋巴细胞百分率	76.28±3.48	86.70±1.82	89.58±1.11	87.30±3.65
MCV(fL)	平均红细胞体积	47.04±0.35	47.18±0.27	46.40±0.28	47.76±0.73	MONO%(%)	单核细胞百分率	4.64±0.48	2.58±0.38	1.68±0.25	1.76±0.31
MCH(pg)	平均红细胞血红蛋白量	14.84±0.12	15.08±0.12	14.48±0.02	15.04±0.12	EO%(%)	嗜酸性细胞百分率	2.72±0.19	2.46±0.43	2.20±0.29	2.08±0.28
MCHC(g/dL)	平均红细胞血红蛋白浓度	31.52±0.18	31.94±0.16	31.24±0.22	31.54±0.39	BASO%(%)	嗜碱性细胞百分率	0.12±0.04	0.14±0.04	0.06±0.02	0.08±0.02
RDW-SD(fL)	红细胞分布宽度-标准差	25.98±0.94	23.44±0.81	20.96±0.48	23.66±1.12	RET%(%)	网织红细胞百分率	3.35±0.32	4.26±0.39	5.10±1.14	9.05±2.29
RDW-CV(%)	红细胞分布宽度-变异系数	18.40±0.21	17.26±0.19	16.76±0.08	16.74±0.17	RET#(10 <sup>6</sup> /μL)	网织红细胞数	0.35±0.03	0.46±0.04	0.55±0.11	0.87±0.19
PDW(fL)	血小板分布宽度	6.54±0.10	6.60±0.06	6.44±0.04	6.50±0.08	IRF(%)	未成熟网织红细胞分数	58.16±2.40	53.38±0.77	54.18±3.44	60.28±3.98
MPV(fL)	平均血小板体积	6.54±0.07	6.48±0.04	6.44±0.05	6.58±0.09	LF(%)	低荧光网织红细胞比率	41.84±2.40	46.62±0.77	45.82±3.44	39.72±3.98
P-LCR(%)	大血小板比率	3.30±0.25	2.90±0.43	3.02±0.30	2.90±0.29	MFR(%)	中荧光网织红细胞比率	12.36±0.43	16.86±0.41	16.10±0.38	15.72±0.75
PCT(%)	血小板比积	1.03±0.09	0.94±0.05	1.25±0.04	1.12±0.08	HFR(%)	高荧光网织红细胞比率	45.80±2.71	36.52±0.48	38.08±3.44	44.56±4.54
NRBC(10 <sup>3</sup> /μL)	有核红细胞数	0.03±0.01	0.02±0.00	0.03±0.00	0.05±0.01	RET-He(pg)	网织红细胞血红蛋白含量	17.66±0.11	17.76±0.13	16.96±0.09	17.06±0.15
NRBC%(%)	有核红细胞百分率	0.32±0.07	0.40±0.09	0.36±0.07	0.60±0.09	IPF(%)	未成熟血小板比例	0.16±0.02	0.10±0.00	0.10±0.00	0.10±0.00
NEUT%(%)	中性粒细胞数	1.39±0.31	0.50±0.10	0.58±0.06	0.68±0.27	PLT-F(10 <sup>3</sup> /μL)	血小板计数-光学法	1173.40±63.64	1096.40±52.65	1420.60±42.17	1291.40±47.61
LYMPH%(%)	淋巴细胞数	6.29±0.37	5.24±0.34	8.23±0.79	6.72±0.51	EO#(10 <sup>3</sup> /μL)	嗜酸性粒细胞数	0.22±0.01	0.15±0.03	0.20±0.03	0.16±0.02
MONO%(%)	单核细胞数	0.39±0.05	0.16±0.02	0.15±0.02	0.13±0.02	BASO#(10 <sup>3</sup> /μL)	嗜碱性粒细胞数	0.01±0.00	0.01±0.00	0.01±0.00	0.01±0.00

**Table 1** Blood routine test results of homozygous hIL4/hIL4R mice (data presented as mean ± SEM).

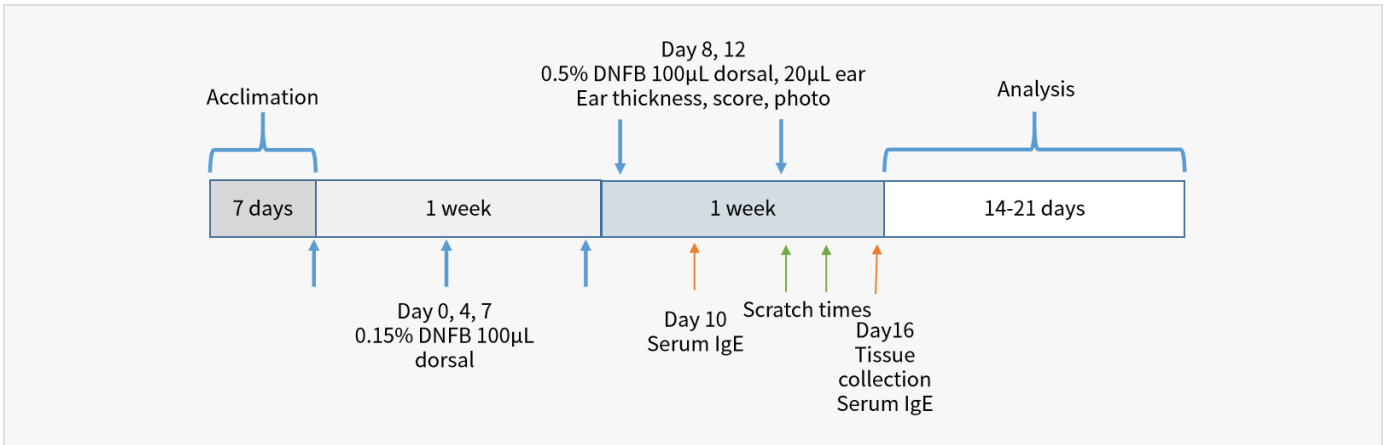
Parameter	WT C57BL/6 ♂ 8-10 weeks; n=5	WT C57BL/6 ♀ 8-10 weeks; n=5	hIL4/hIL4R ♂ 8-10 weeks; n=5	hIL4/hIL4R ♀ 8-10 weeks; n=5
ALT(U/L)	27.23±2.18	28.66±2.77	25.17±3.96	27.62±1.54
ALP(U/L)	242.04±7.40	182.50±4.75	198.20±17.45	168.12±7.38
TP(g/L)	61.21±1.83	57.19±1.04	59.03±1.10	61.44±0.38
ALB(g/L)	32.29±1.16	26.59±0.65	30.60±0.62	29.23±0.25
CHE(U/L)	7018.65±332.28	4887.72±167.34	6208.64±121.30	5427.08±165.97
TBIL(μmol/L)	2.25±0.45	2.07±0.38	1.95±0.49	2.20±0.33
UREA(mmol/L)	8.78±0.92	8.08±0.48	8.35±0.47	9.40±0.63
CREA(μmol/L)	26.43±2.79	24.18±0.52	24.72±1.00	23.94±0.59
TG(mmol/L)	1.51±0.17	1.97±0.20	1.55±0.20	3.07±0.28
T-CHO(mmol/L)	2.36±0.13	2.72±0.15	2.40±0.12	2.92±0.09
HDL-C(mmol/L)	1.22±0.11	1.42±0.10	1.14±0.06	1.43±0.06
CK(U/L)	1003.23±194.11	1213.88±94.72	1263.04±226.76	1901.17±296.52
LDH(U/L)	438.15±46.50	482.12±24.22	442.61±107.41	457.26±17.60
P(mmol/L)	2.34±0.04	2.64±0.11	2.94±0.12	3.11±0.08
Fe(μmol/L)	40.73±2.83	23.91±0.78	31.76±2.05	27.63±1.59
GLU(mmol/L)	8.55±0.29	10.13±0.86	8.72±0.62	9.06±0.28

**Table 2** Biochemistry examination results of homozygous hIL4/hIL4R mice (data presented as mean ± SEM).

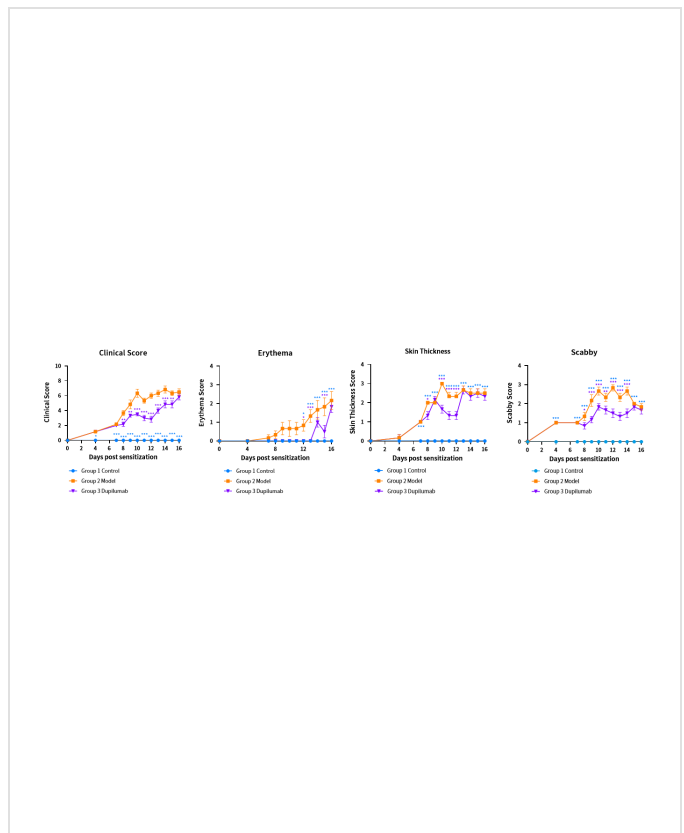
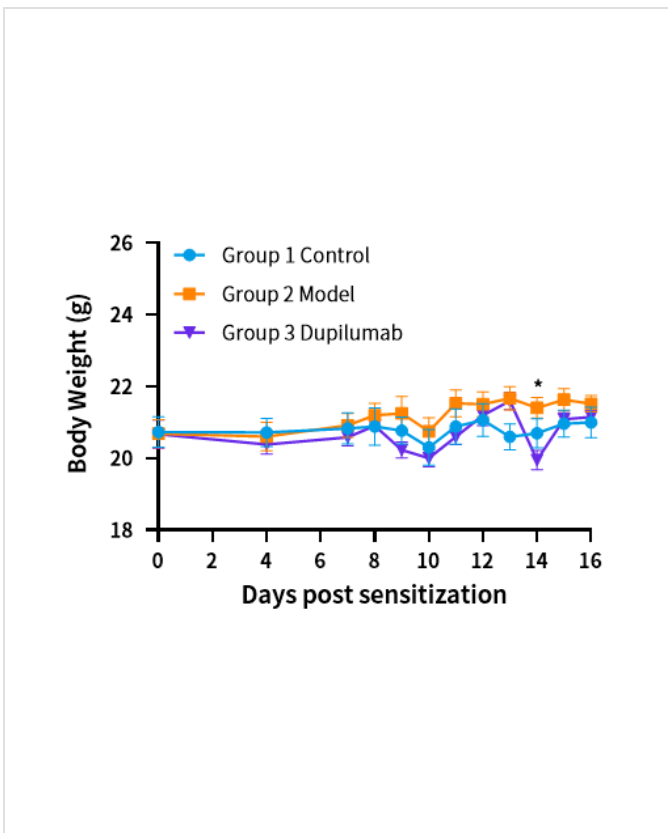
# Anti-IL4RA mAb in a DNFB Atopic Dermatitis Model

In vivo efficacy of an anti-human IL4RA monoclonal antibody (dupilumab) in the DNFB-induced atopic dermatitis model built on hIL4/hIL4R mice.

## STUDY DESIGN

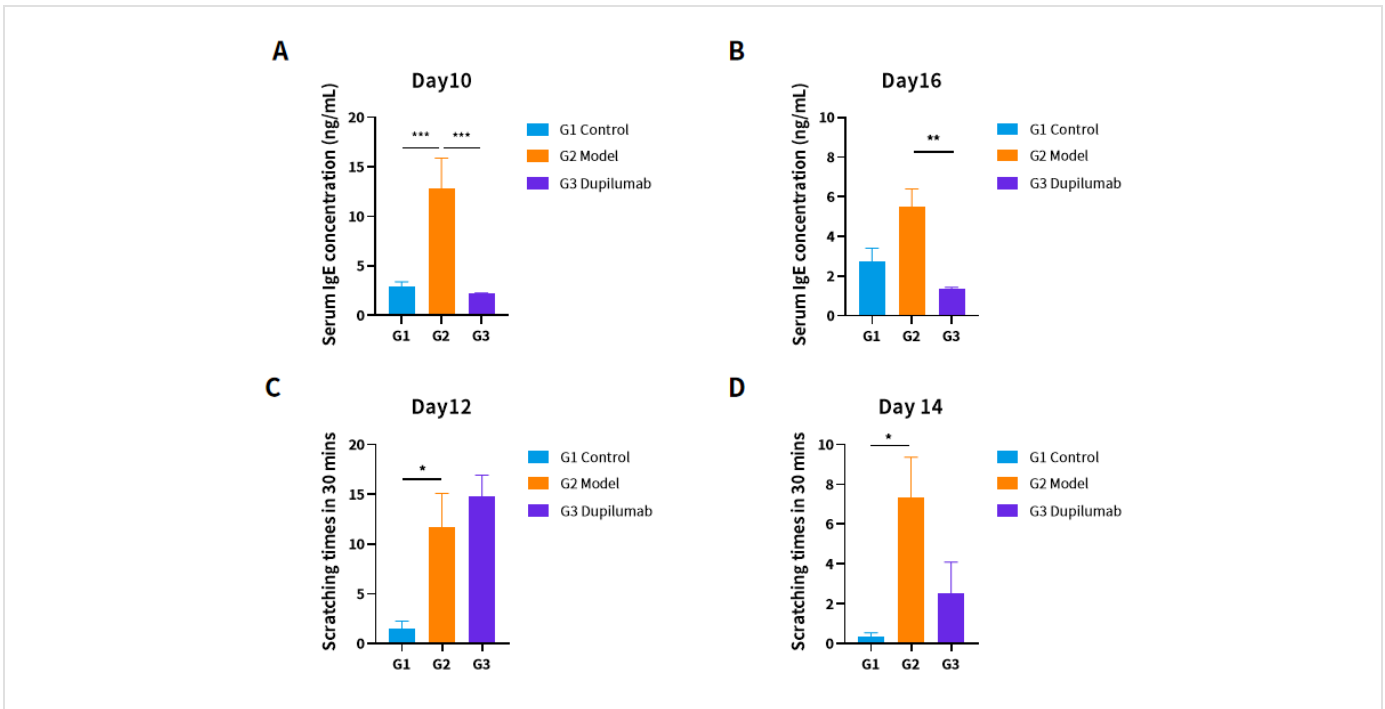


**Schema** DNFB sensitization and challenge schedule with dupilumab dosing, scoring, and tissue collection timepoints.

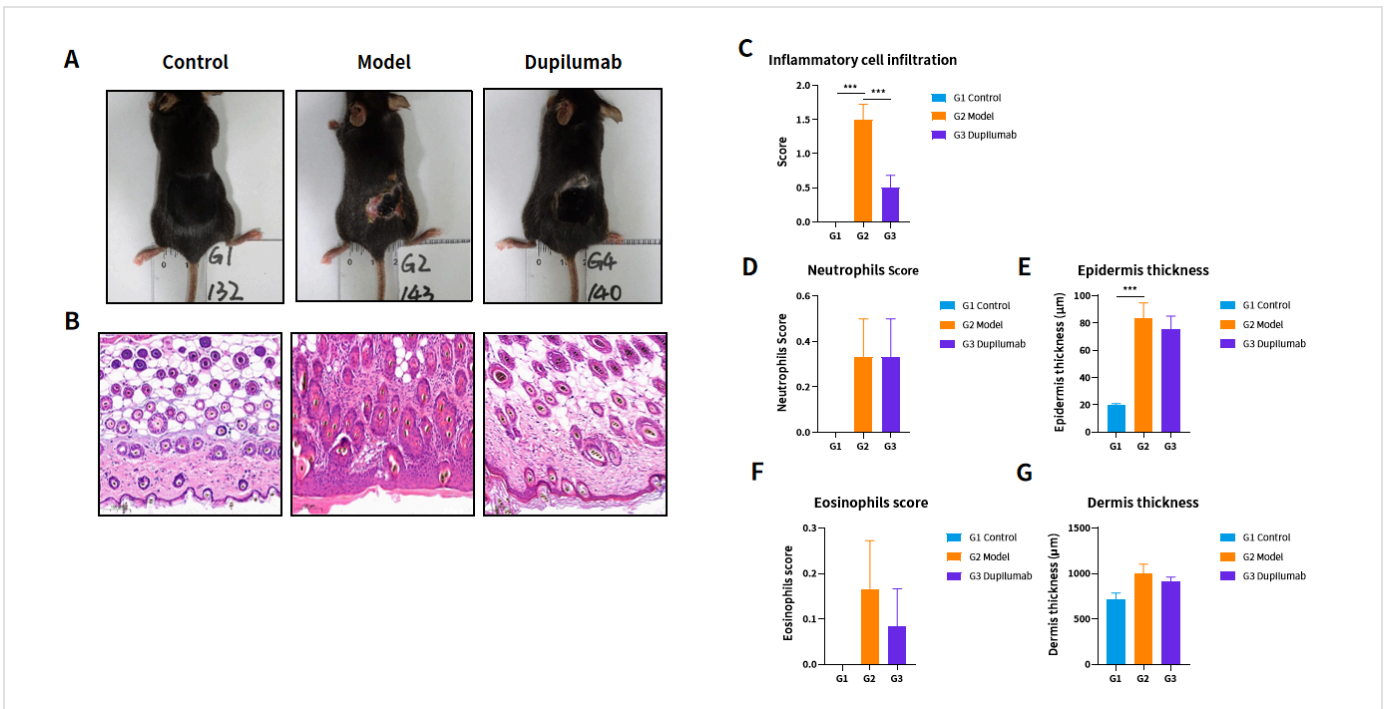


**Fig. 1-2** (1) Body weight of DNFB-induced AD model hIL4/hIL4R mice treated with dupilumab (\*P<0.05). (2) Dupilumab ameliorates overall atopic dermatitis activity (\*P<0.05, \*\*P<0.01, \*\*\*P<0.001).

# IgE, Scratching & Skin Histopathology



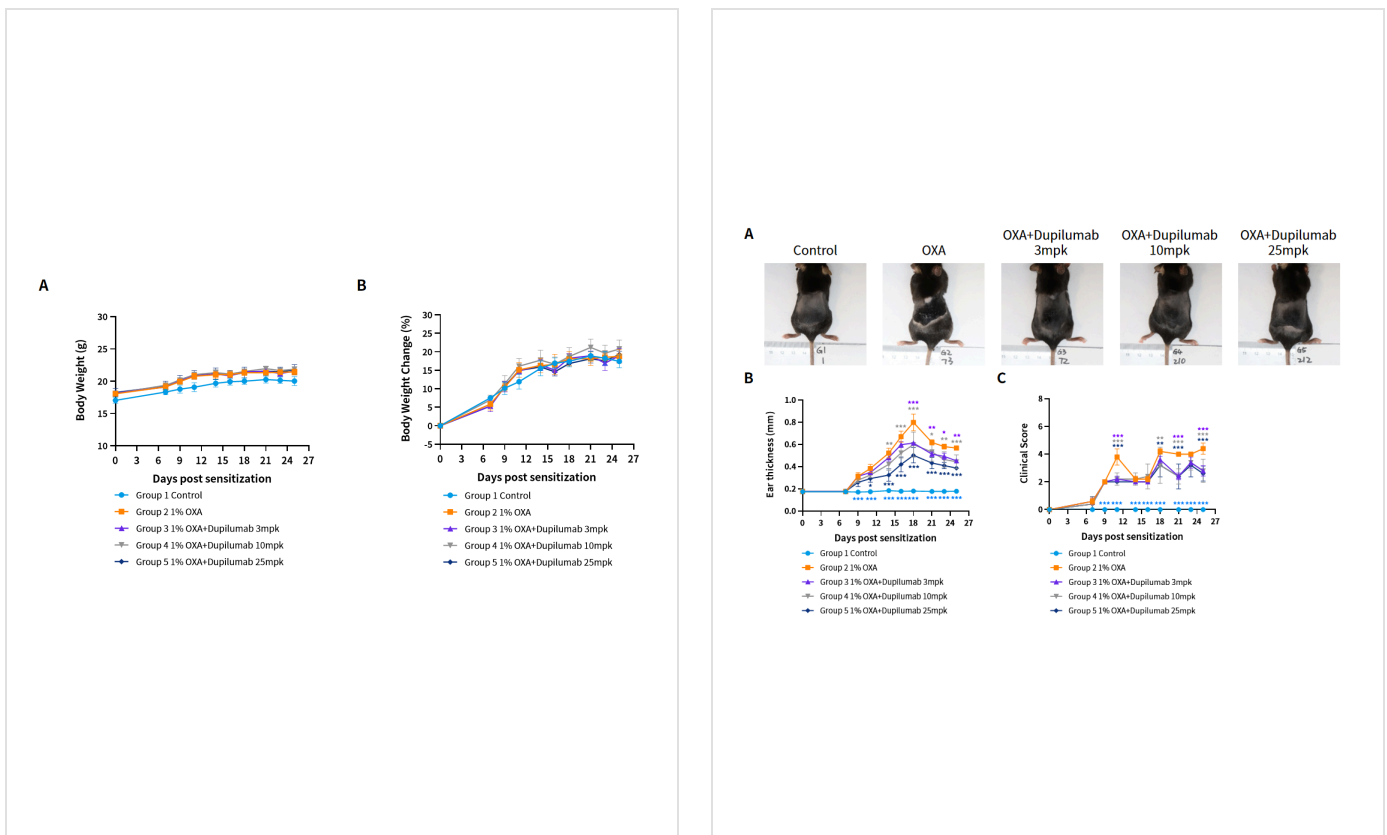
**Fig. 3** Dupilumab significantly reduced serum IgE levels and scratching frequency. (A) Day 10 serum IgE; (B) Day 16 serum IgE; (C) scratch times on Day 12; (D) scratch times on Day 14 (\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ).



**Fig. 4** Dupilumab significantly mitigates inflammatory cell infiltration in lesioned skin on Day 14. (A) dorsal image Day 14; (B) representative pathology images; (C) inflammatory cell infiltration score; (D) neutrophil score; (E) eosinophil score; (F) epidermis thickness; (G) dermis thickness (\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ).

# Anti-IL4RA mAb in an OXA Atopic Dermatitis Model

In vivo efficacy of an anti-human IL4RA monoclonal antibody in the oxazolone (OXA)-induced atopic dermatitis model built on hIL4/hIL4R mice.



**Fig. 1-2** (1) OXA-induced AD model – (A) body weight; (B) body weight change (n=6, Mean ± SEM). (2) (A) gross observation on Day 21; (B) ear thickness; (C) clinical skin score.

# Serum IgE & Skin Pathology

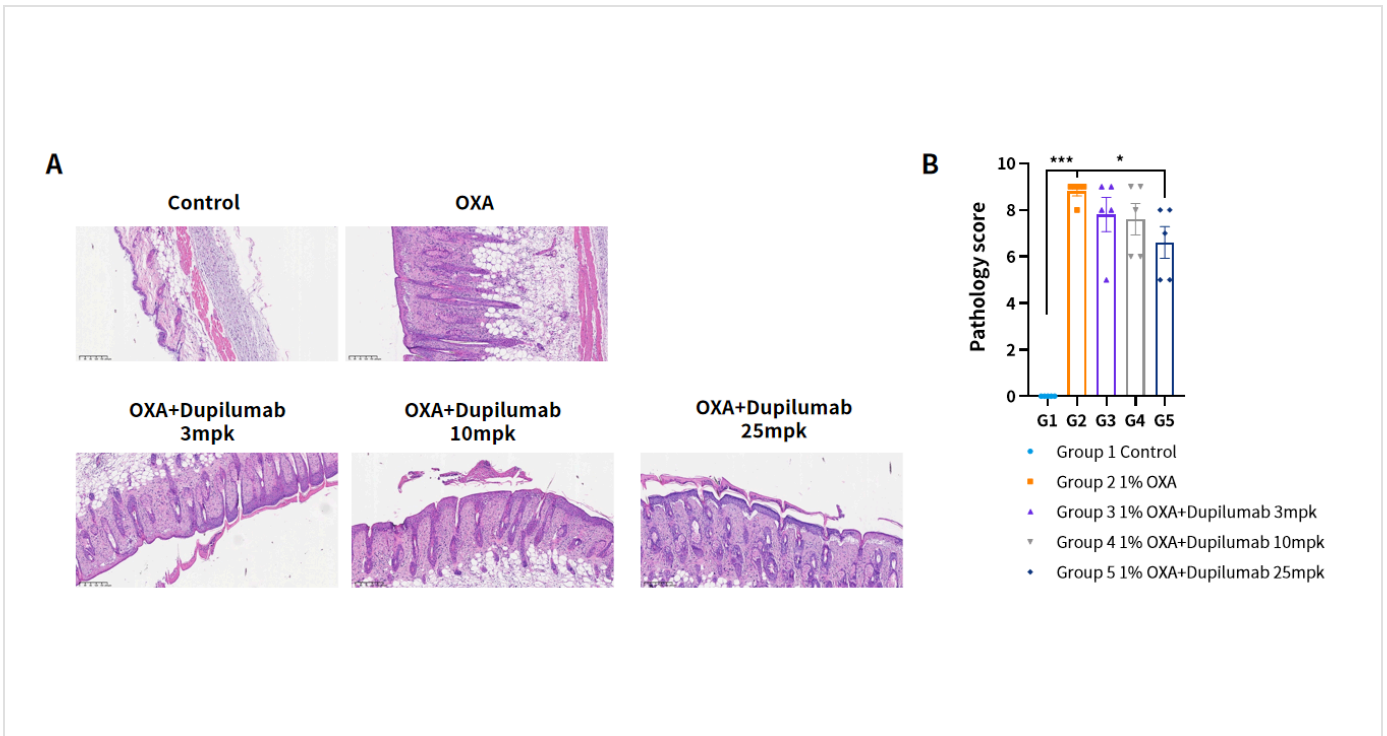


Fig. 3 OXA-induced AD model in hIL4/hIL4R mice. (A) serum IgE; (B) spleen weight.

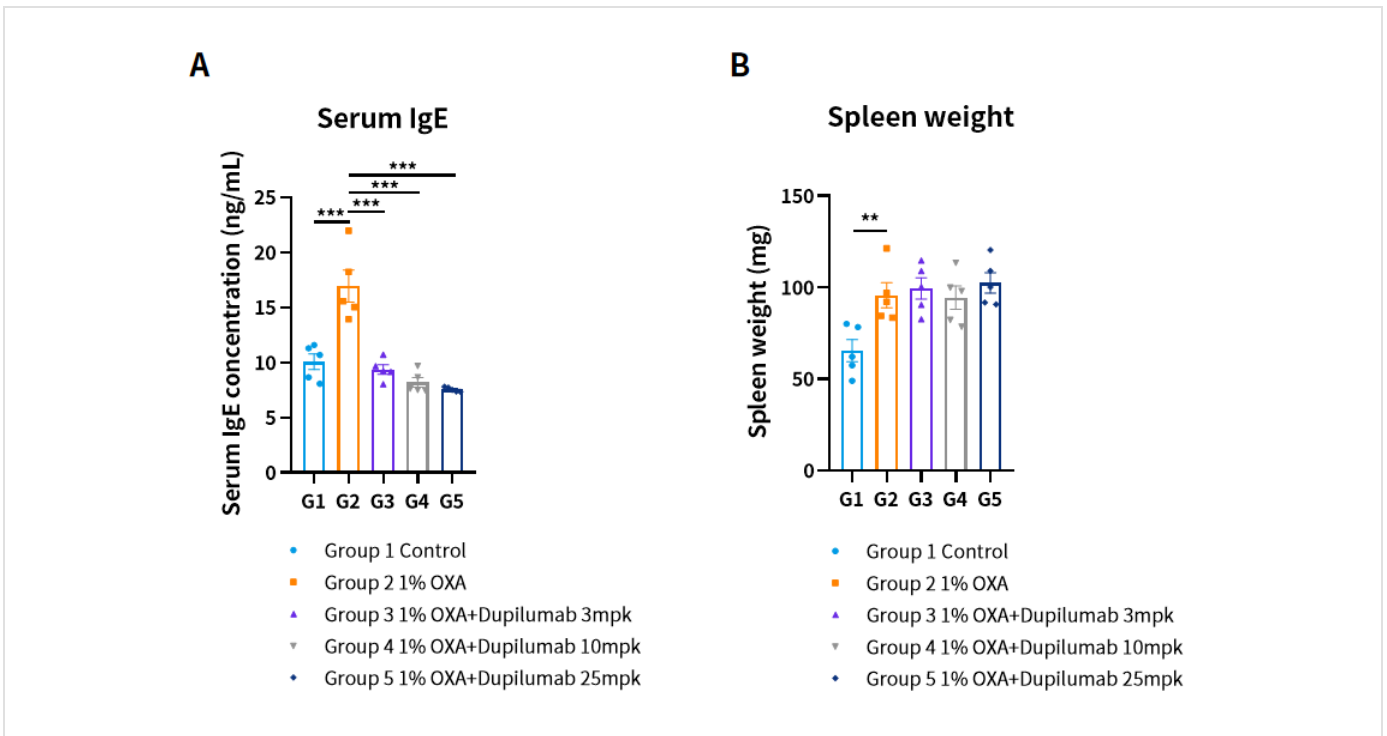
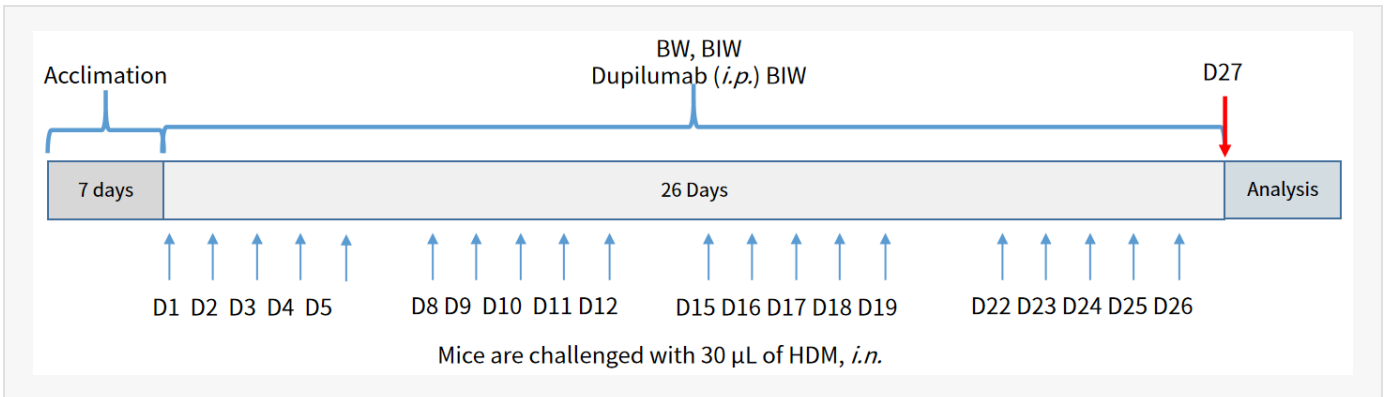


Fig. 4 OXA-induced AD model in hIL4/hIL4R mice. (A) pathology photographs; (B) pathology score.

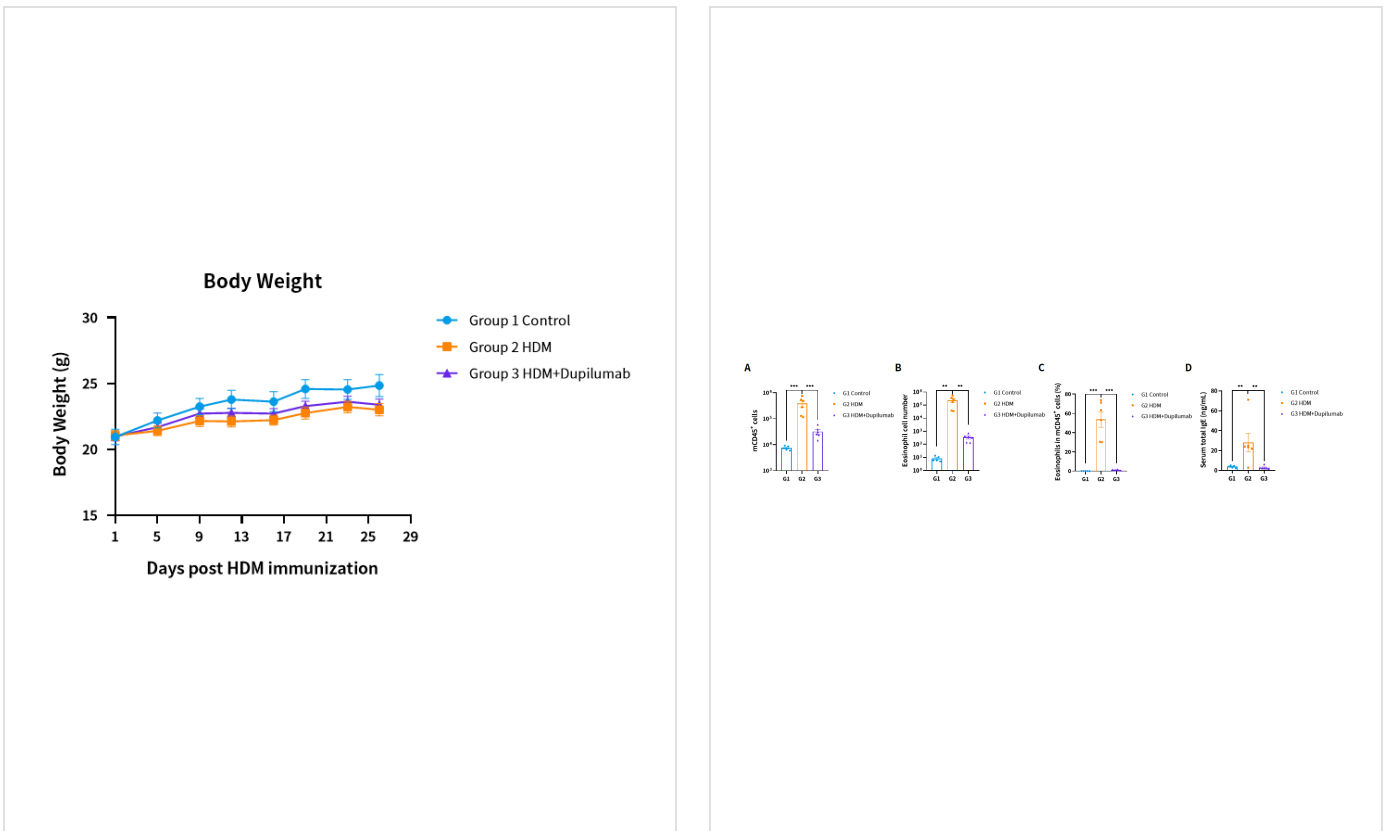
# Anti-IL4RA mAb in an HDM Asthma Model

In vivo efficacy of an anti-human IL4RA monoclonal antibody (dupilumab) in the house dust mite (HDM)-induced asthma model built on hIL4/hIL4R mice.

## STUDY DESIGN

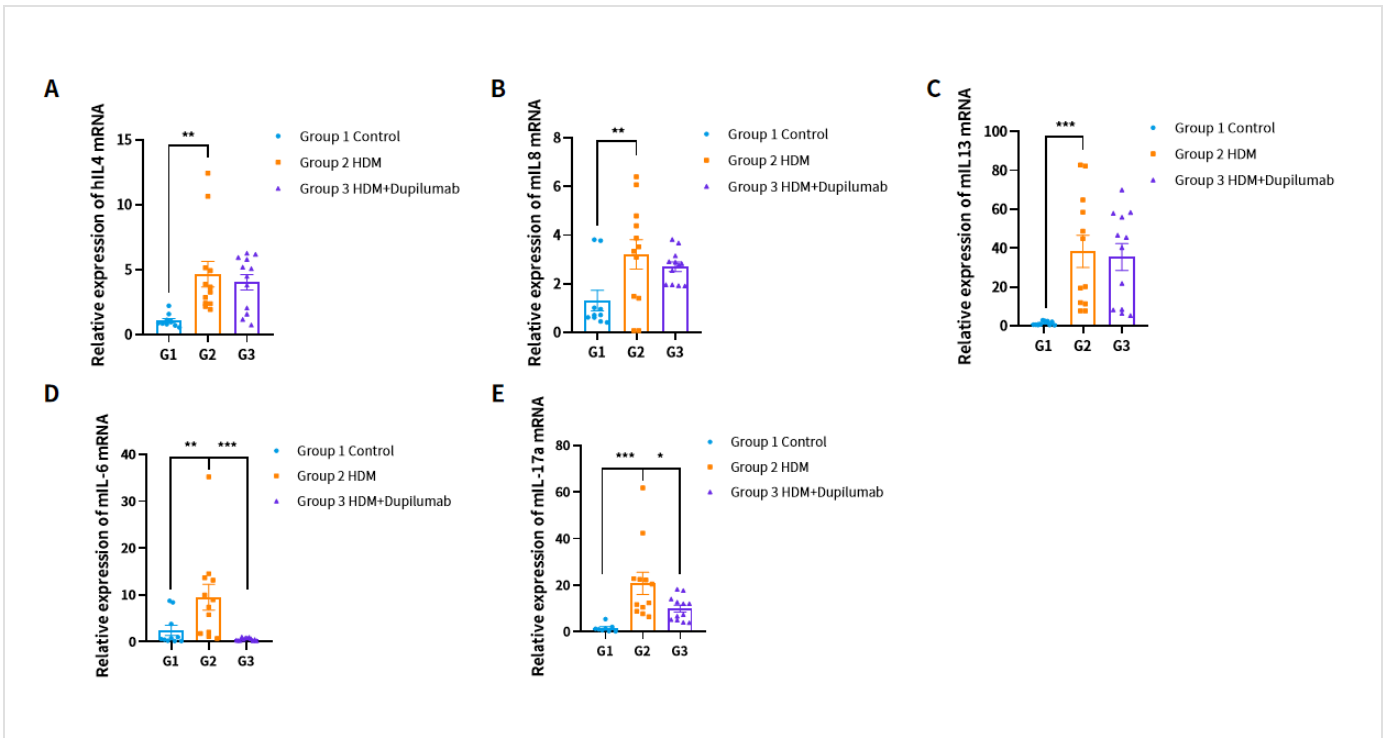


**Schema** HDM challenge and dupilumab (*i.p.*) dosing schedule across 27 days, with body-weight monitoring and Day-27 analysis.

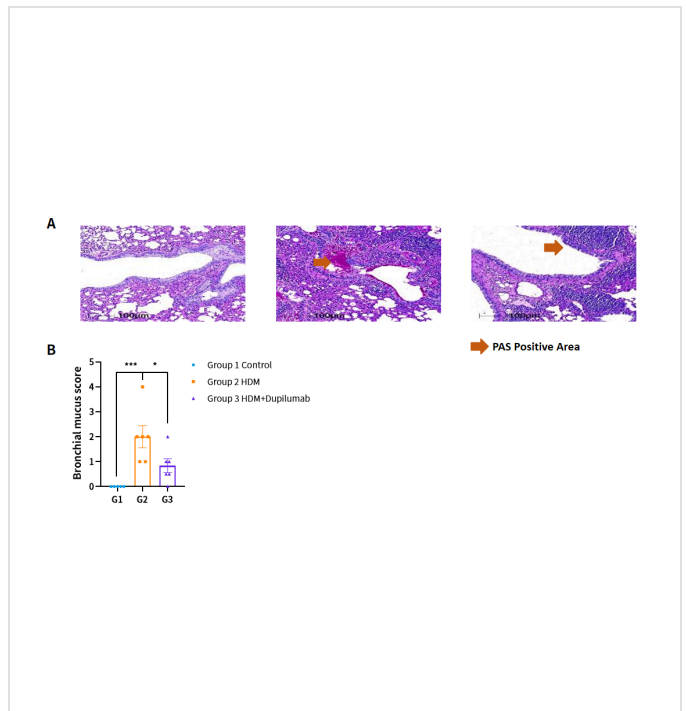
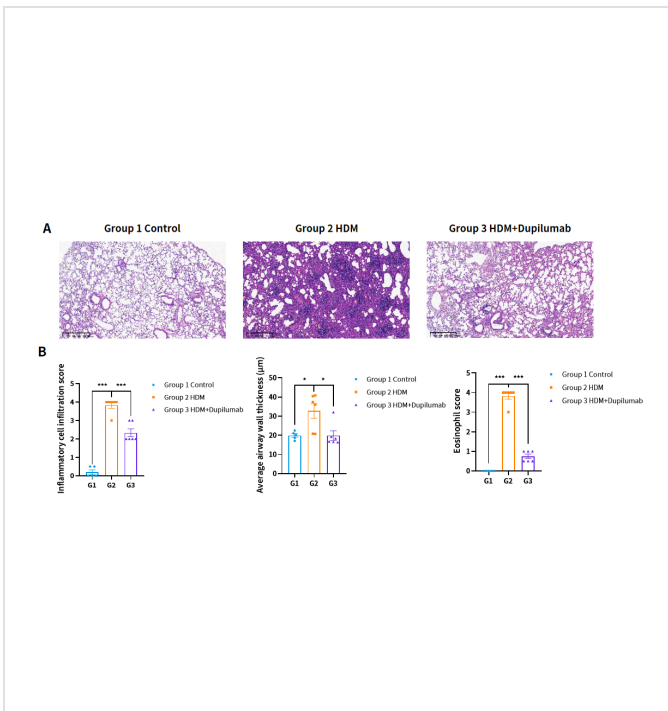


**Fig. 1-2** (1) Body weight of HDM-induced asthma model treated with dupilumab (n=6, Mean  $\pm$  SEM). (2) Dupilumab ameliorates overall asthma activity – (A) inflammatory cell number in BALF; (B) eosinophil number in BALF; (C) eosinophil percentage; (D) serum total IgE (\*\*P<0.01, \*\*\*P<0.001).

# Cytokine mRNA & Lung Histopathology



**Fig. 3** HDM-induced asthma model. mRNA expression of (A) hIL-4; (B) mIL-8; (C) mIL-13; (D) mIL-6; (E) mIL-17a (\*P<0.05, \*\*P<0.01, \*\*\*P<0.001).



**Fig. 4-5** (4) Dupilumab mitigates asthma symptoms in lung – (A) H&E staining; (B) pathology score. Magnification ×5. (5) (A) PAS staining; (B) mucus score. Magnification ×10 (\*P<0.05, \*\*P<0.01, \*\*\*P<0.001).



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# Bring the **hIL4/hIL4R** model into your program.

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IT-HU-2000106

PHONE

+1 (631) 468-8534

EMAIL

[inquiry@genetargeting.com](mailto:inquiry@genetargeting.com)

**ingenious**  
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