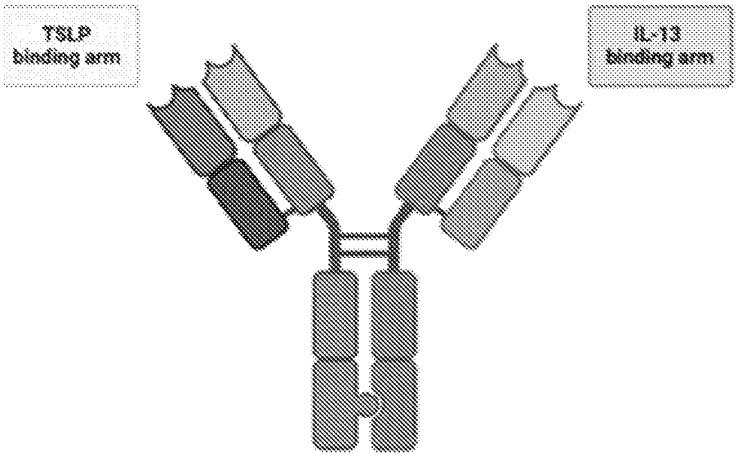


TSLP/IL-13 BsAb

FIG. 1A

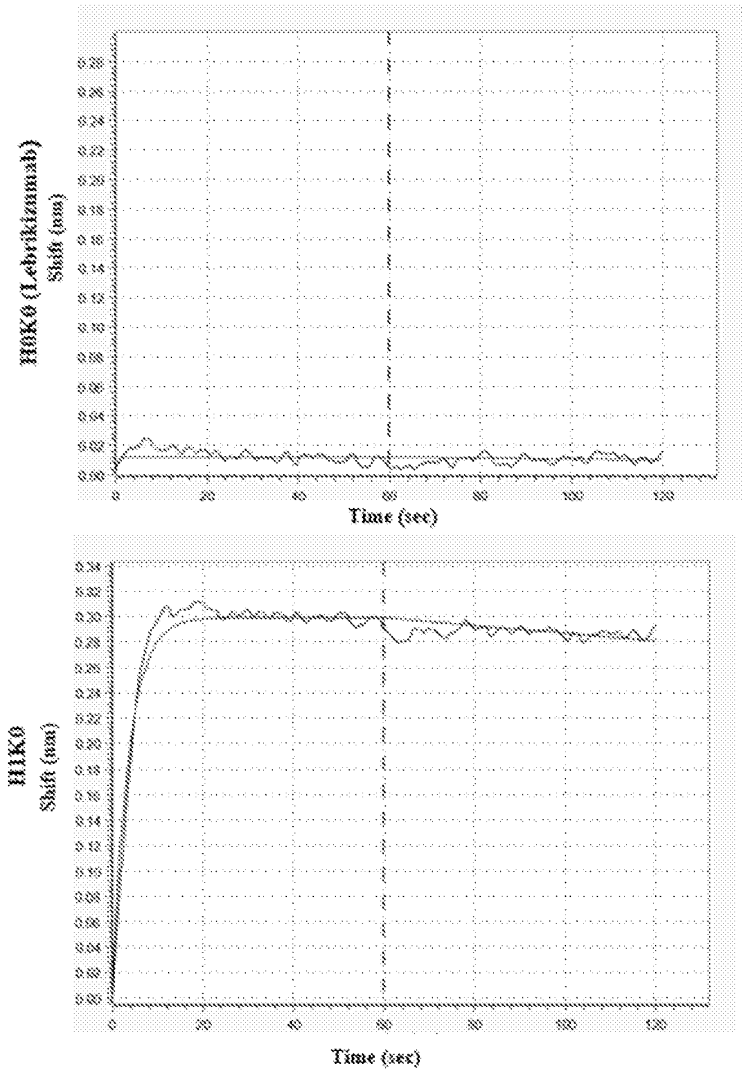


FIG. 1B

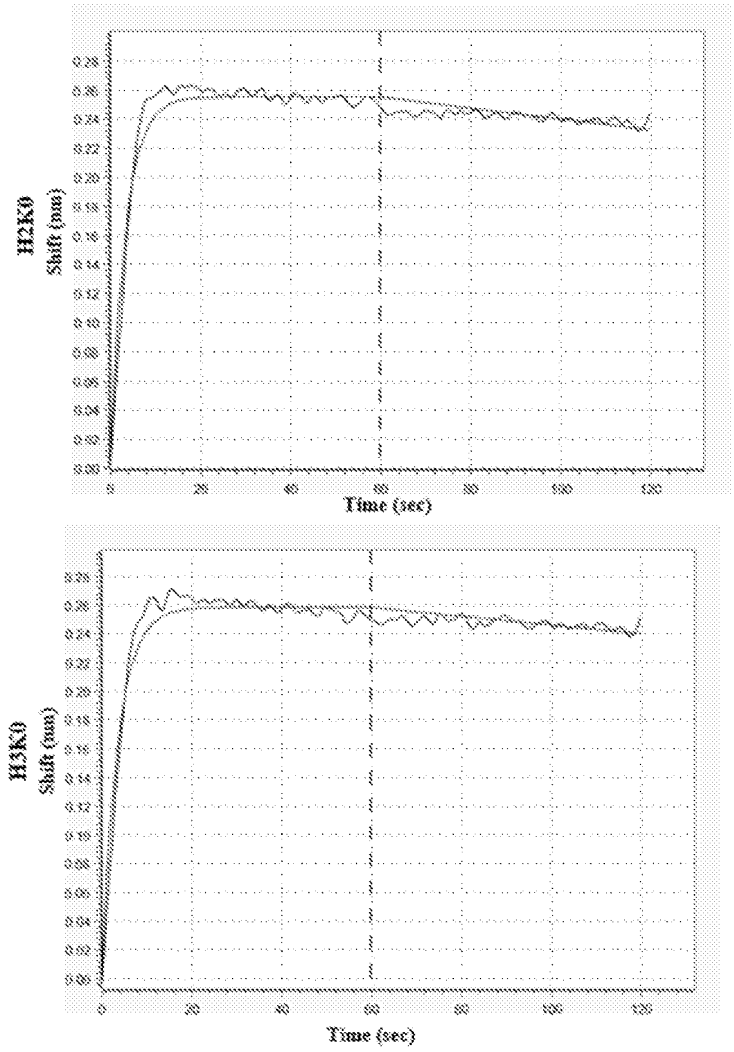


FIG. 1C

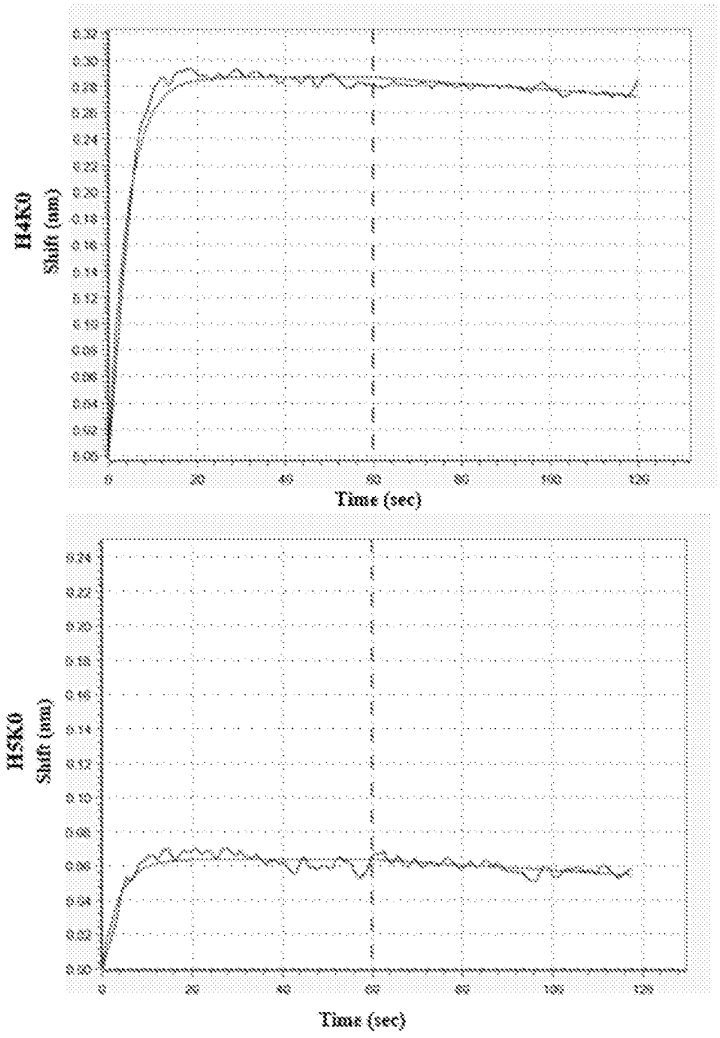


FIG. 1D

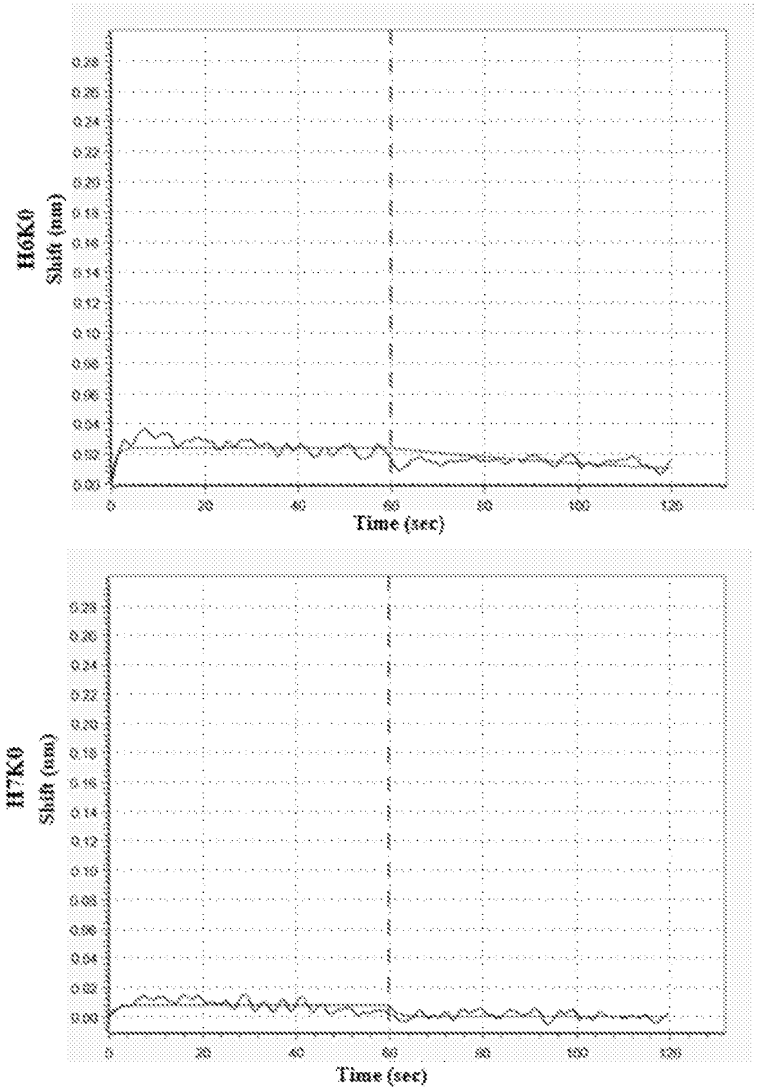


FIG. 1E

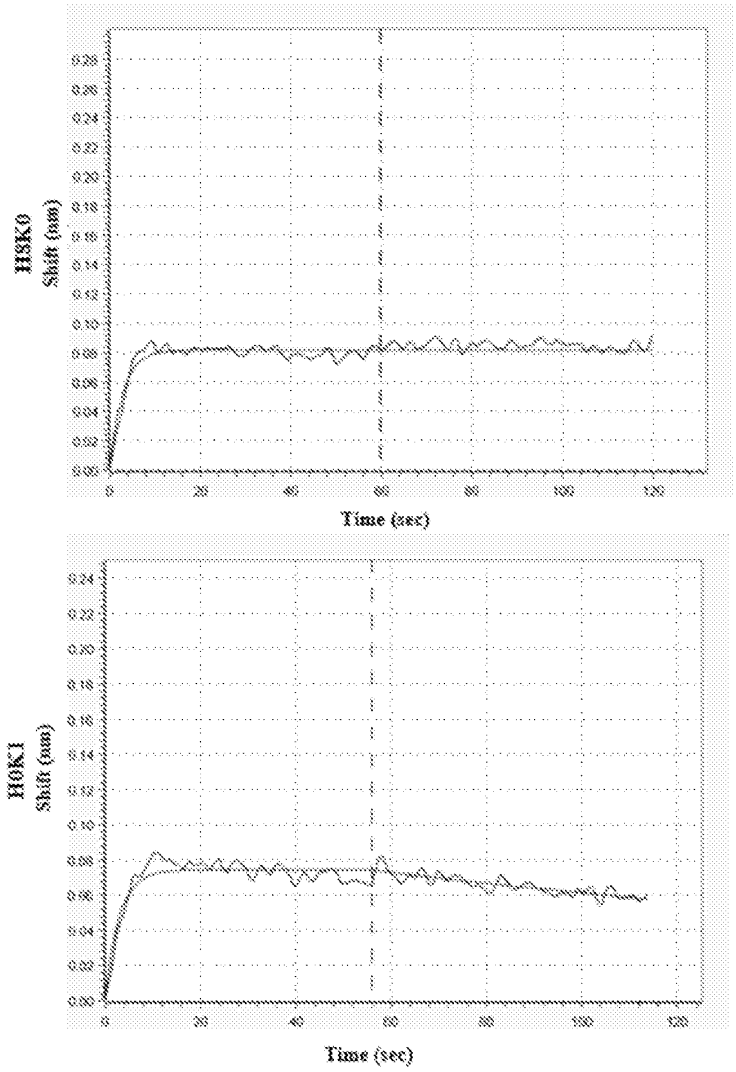


FIG. 1F

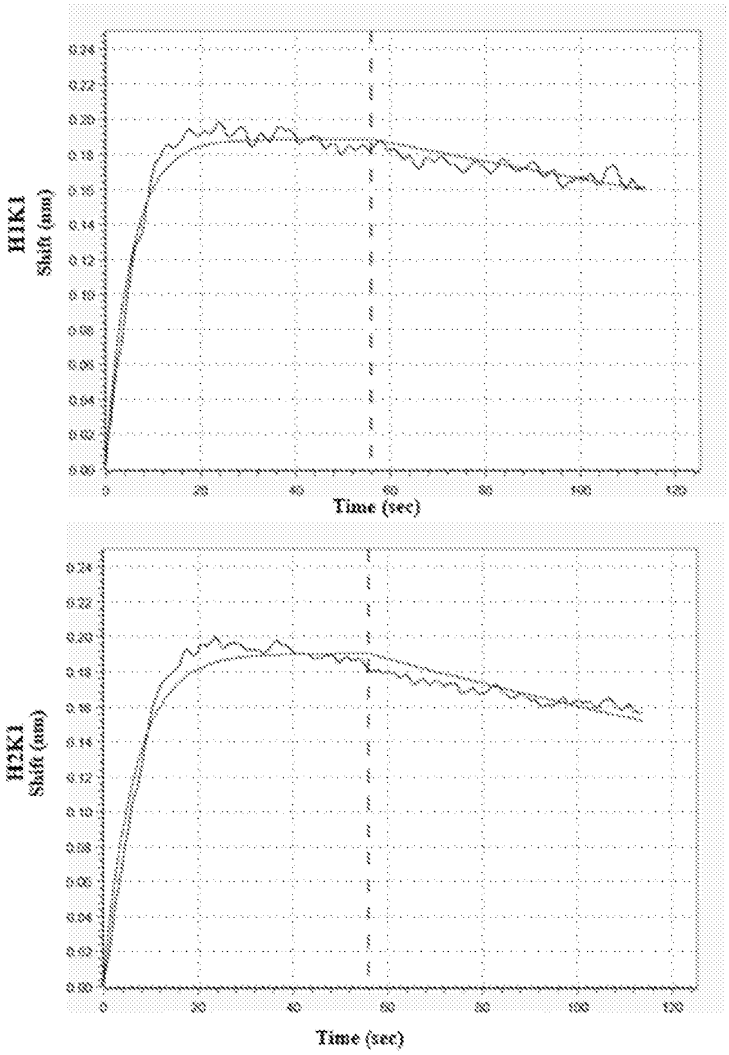


FIG. 1G

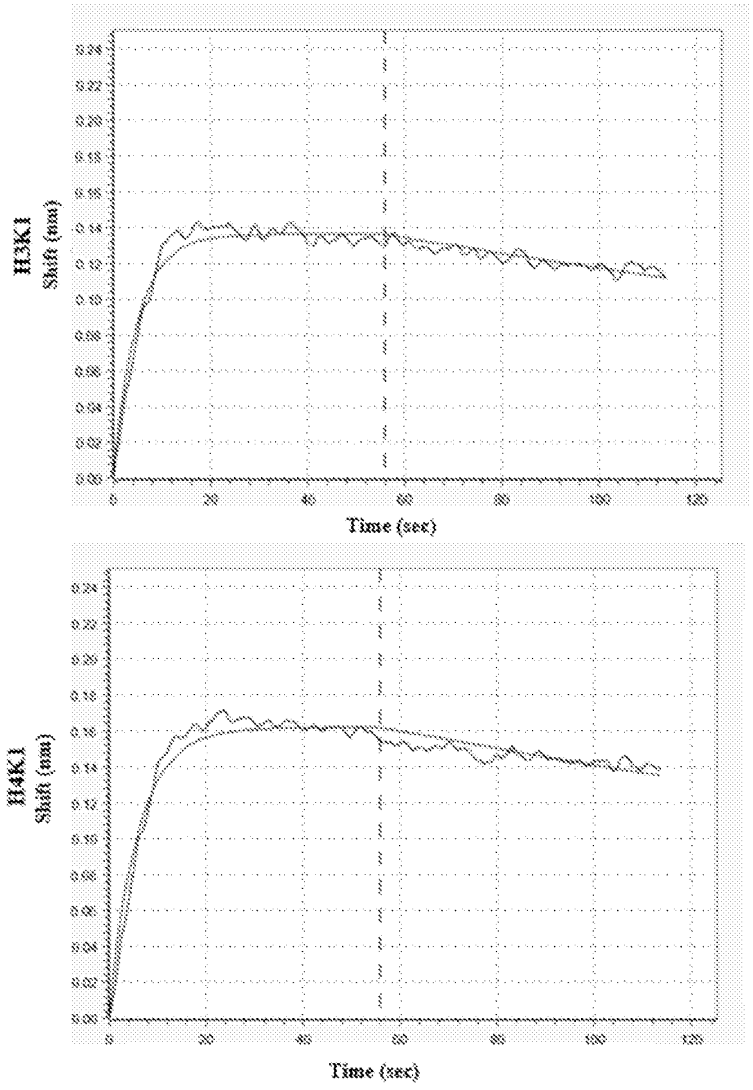


FIG. 1H

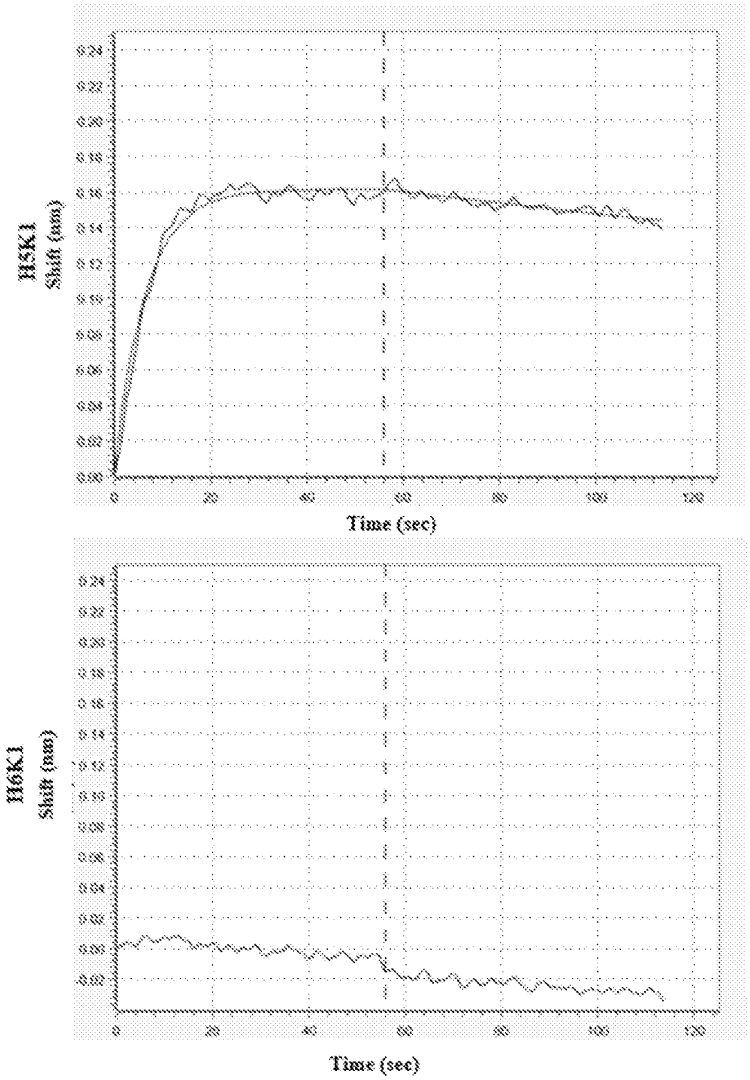


FIG. 1I

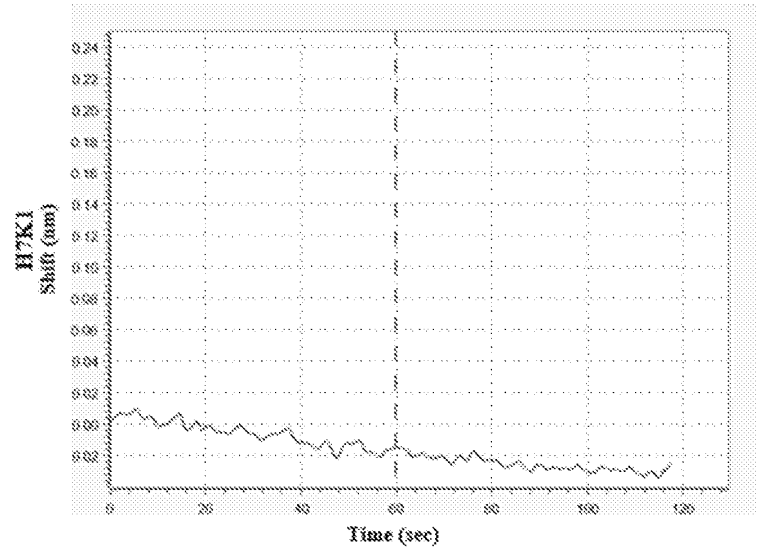


FIG. 1J

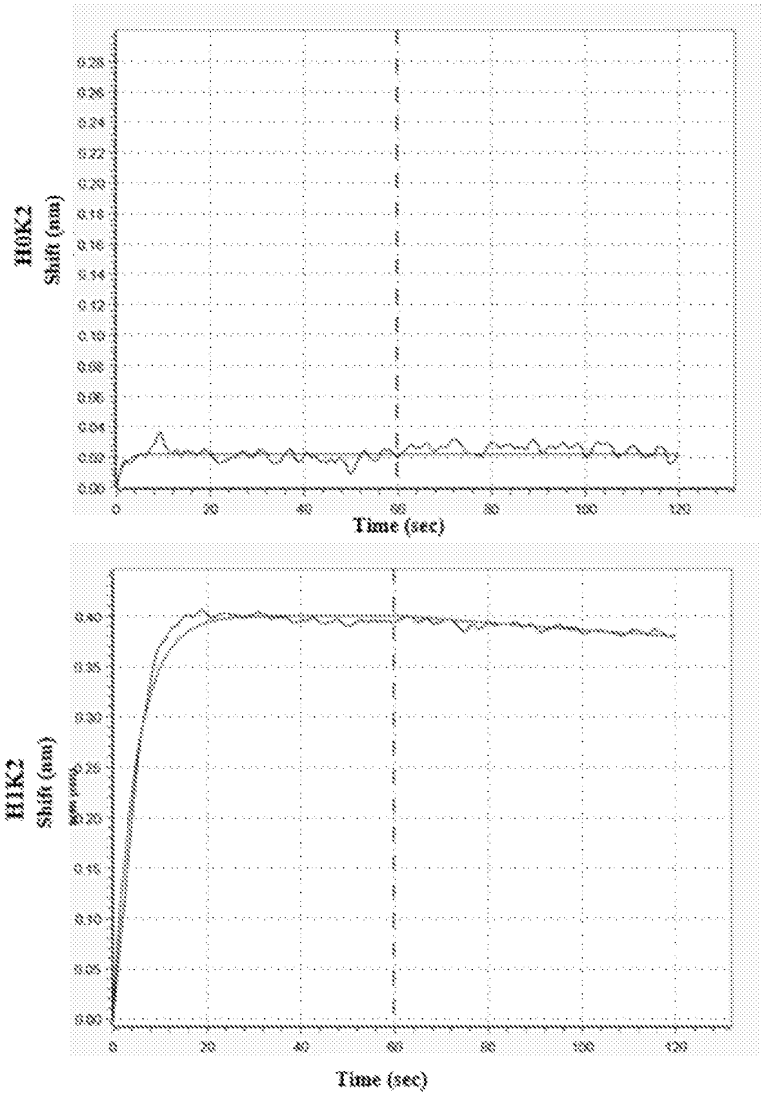


FIG. 1K

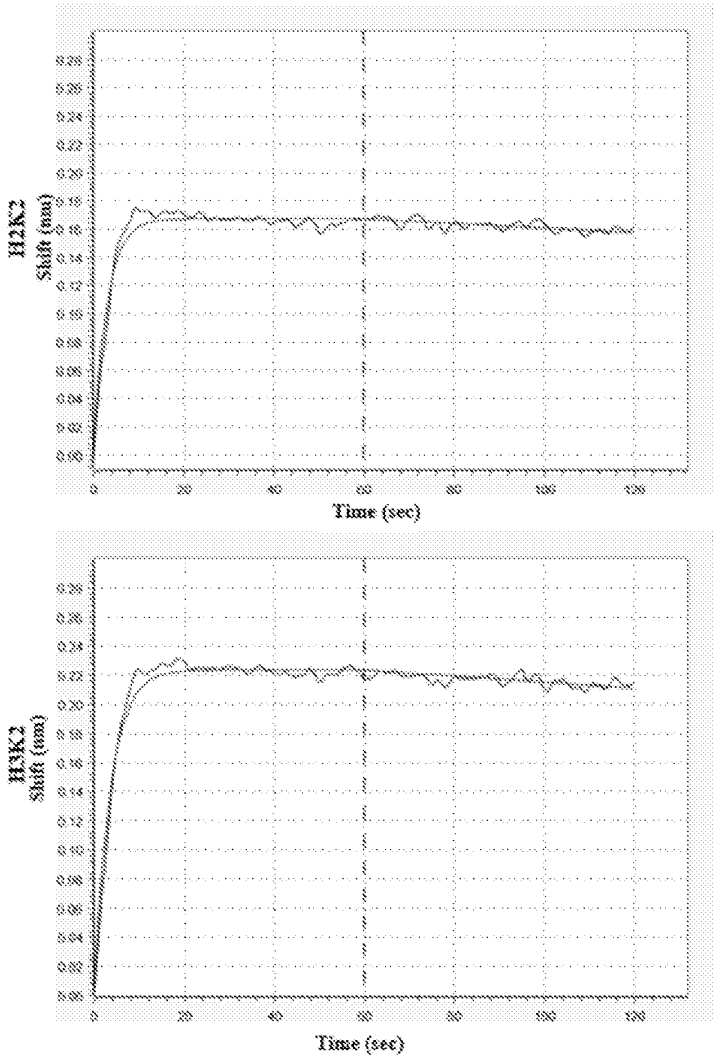


FIG. 1L

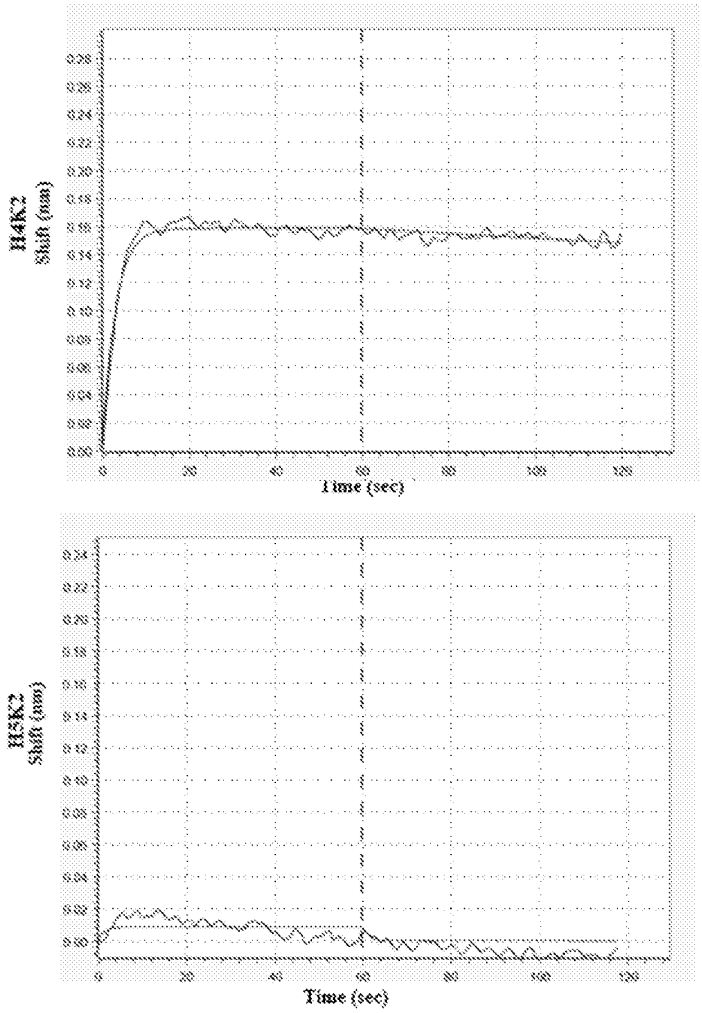


FIG. 1M

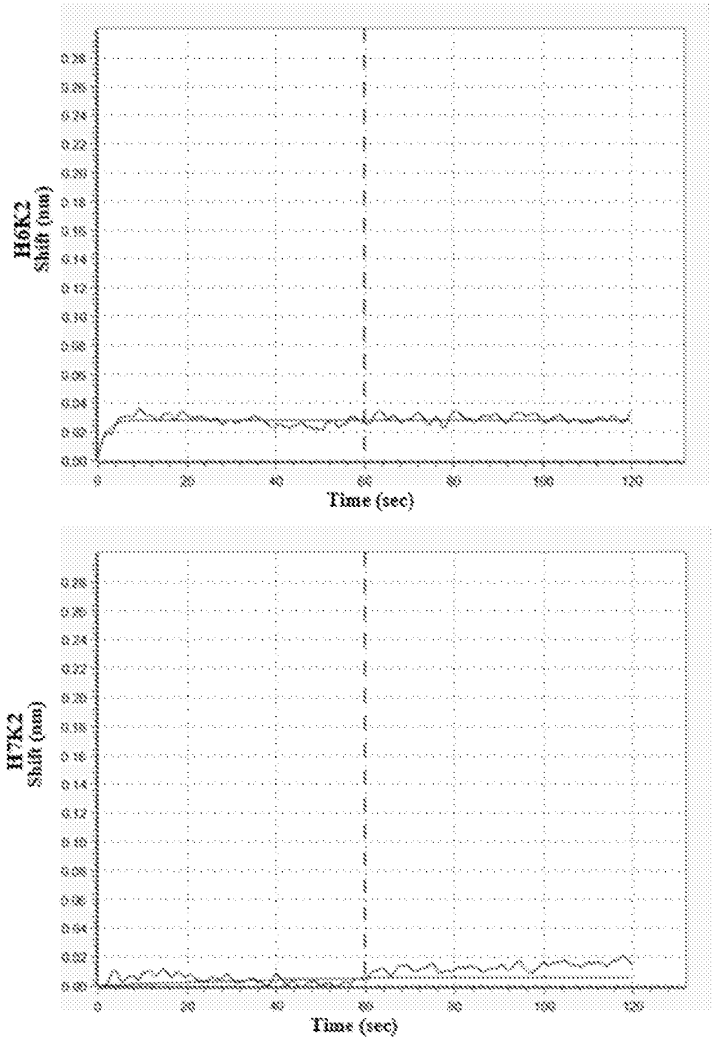


FIG. 1N

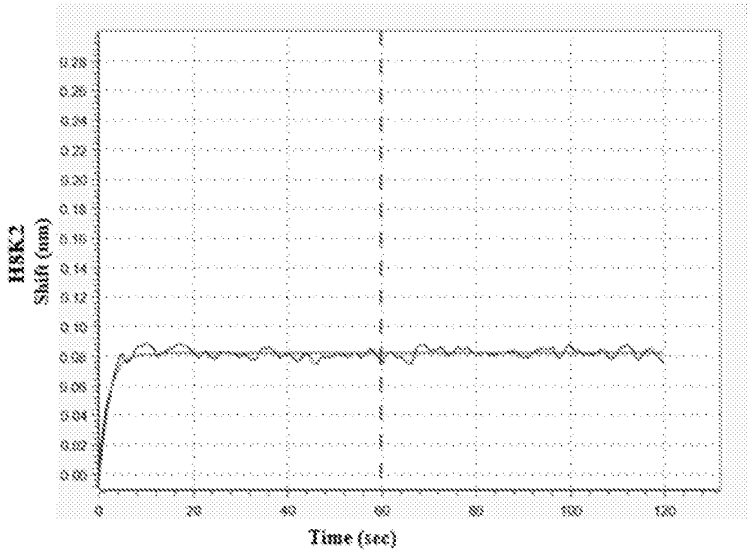
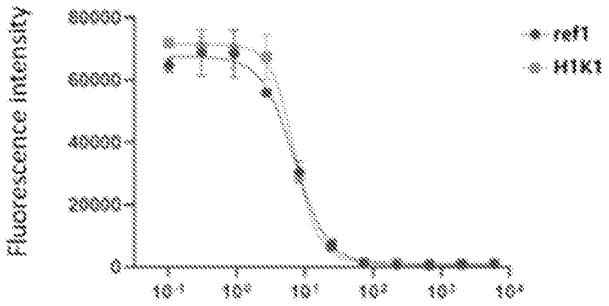
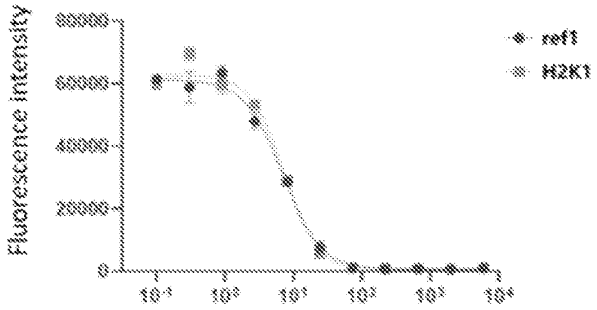


FIG. 10



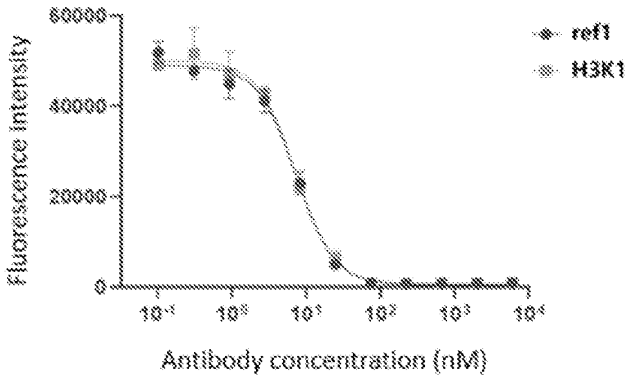
	ref1	H1K1
IC_{50} (nM)	7.14	7.16

FIG. 2A



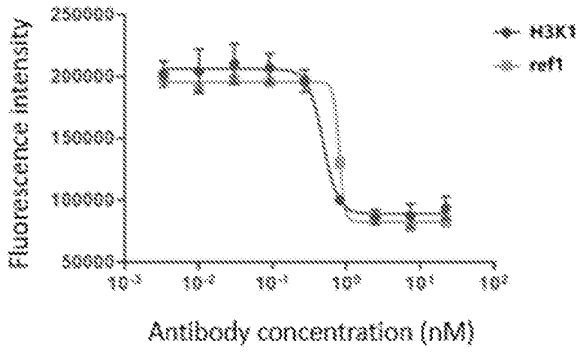
	ref1	H2K1
IC_{50} (nM)	7.10	7.32

FIG. 2B



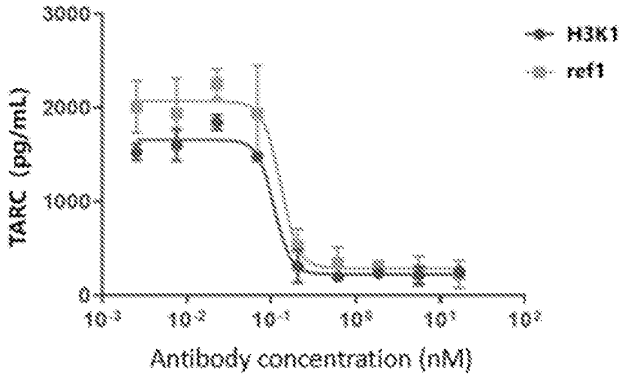
	ref1	H3K1
IC_{50} (nM)	7.29	7.13

FIG. 2C



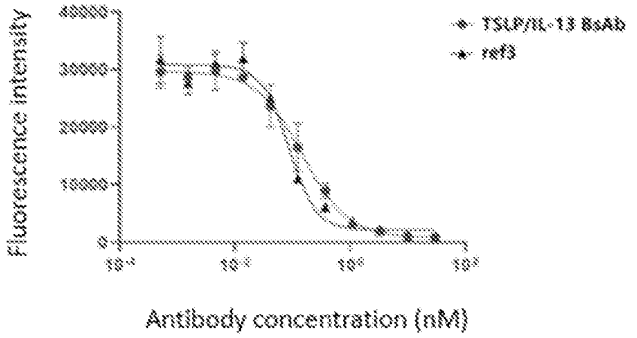
	ref1	H3K1
IC_{50} (nM)	0.80	0.48

FIG. 3



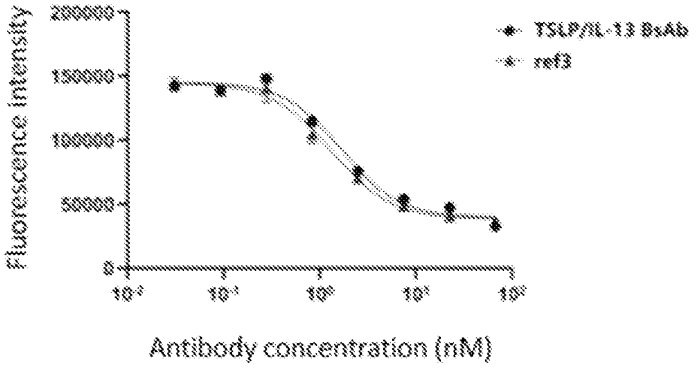
	ref1	H3K1
IC_{50} (nM)	0.13	0.11

FIG. 4



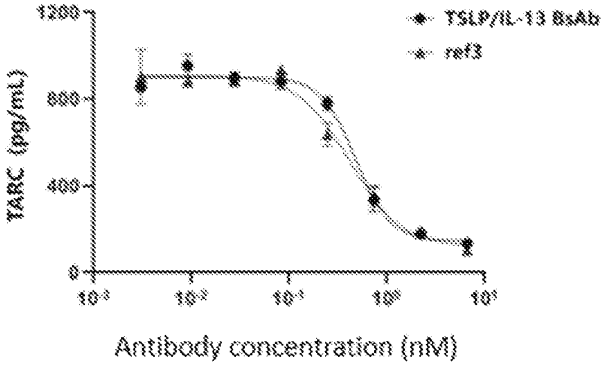
	TSLP/IL-13 BsAb	ref3
IC_{50} (nM)	0.15	0.06

FIG. 5A



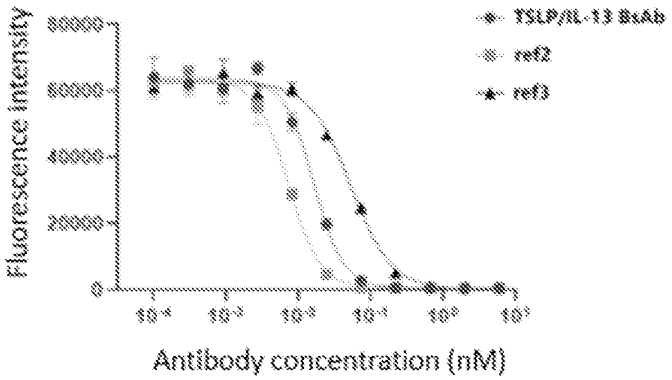
	TSLP/IL-13 BsAb	ref3
IC_{50} (nM)	1.67	1.31

FIG. 5B



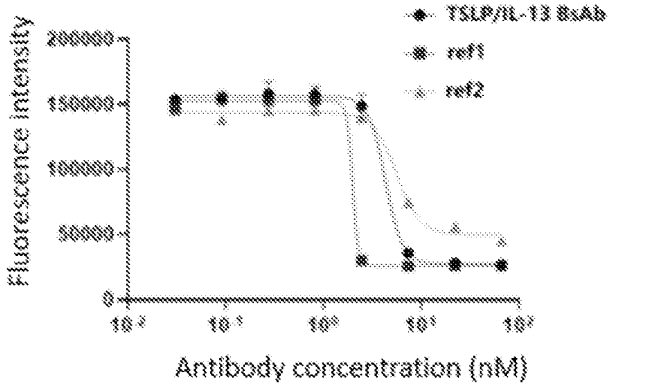
	TSLP/IL-13 BsAb	ref3
IC_{50} (nM)	0.479	0.416

FIG. 5C



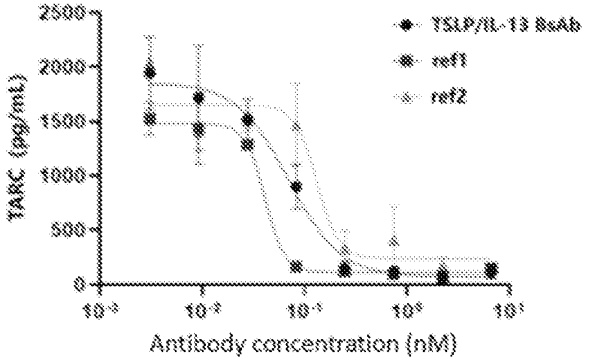
	TSLP/IL-13 BsAb	ref1	ref2
IC_{50} (nM)	0.016	0.007	0.053

FIG. 6A



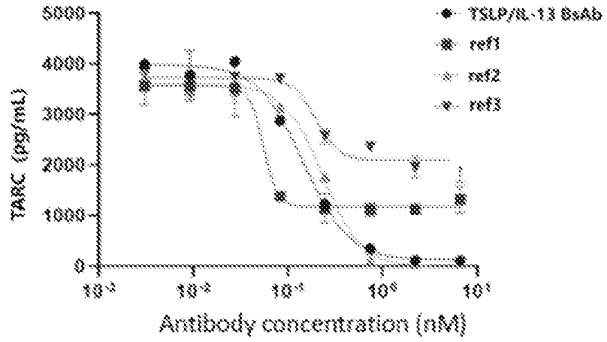
	TSLP/IL-13 BsAb	ref1	ref2
IC_{50} (nM)	4.31	1.99	5.60

FIG. 6B



	TSLP/IL-13 BsAb	ref1	ref2
IC_{50} (nM)	0.069	0.041	0.131

FIG. 6C



	TSLP/IL-13 BsAb	ref2
IC_{50} (nM)	0.145	0.233

FIG. 7

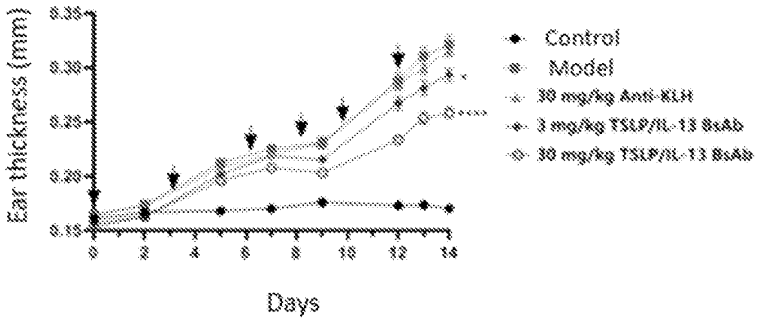

Ear thickness (mm)
0.15
0.20
0.25
0.30
0.35
0
2
4
6
8
10
12
14
Days
Control
Model
30 mg/kg Anti-KLH
3 mg/kg TSLP/IL-13 BsAb
30 mg/kg TSLP/IL-13 BsAb

FIG. 8A

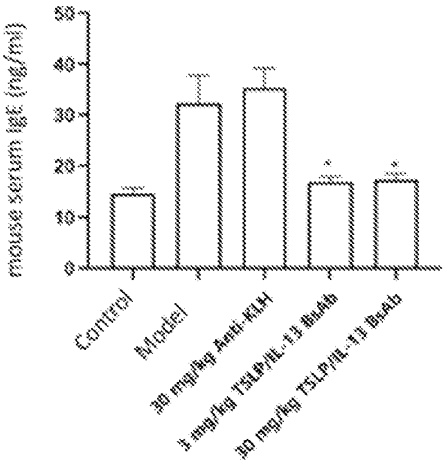

mouse serum IgE (ng/ml)
0
10
20
30
40
50
Control
Model
30 mg/kg Anti-KLH
3 mg/kg TSLP/IL-13 BsAb
30 mg/kg TSLP/IL-13 BsAb

FIG. 8B

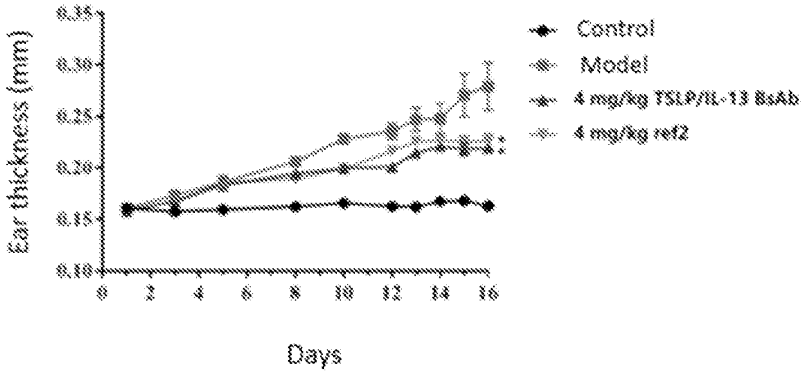

Ear thickness (mm)
0.35
0.30
0.25
0.20
0.15
0.10
0
2
4
6
8
10
12
14
16
Days
Control
Model
4 mg/kg TSLP/IL-13 BsAb
4 mg/kg ref2

FIG. 8C

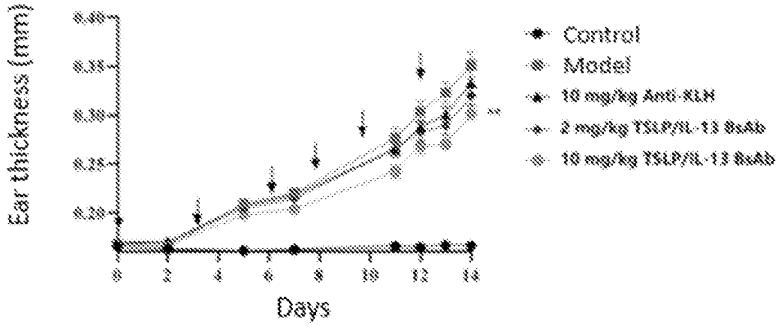

Ear thickness (mm)
Days
Control
Model
10 mg/kg Anti-KLH
2 mg/kg TSLP/IL-13 BsAb
10 mg/kg TSLP/IL-13 BsAb

FIG. 9A

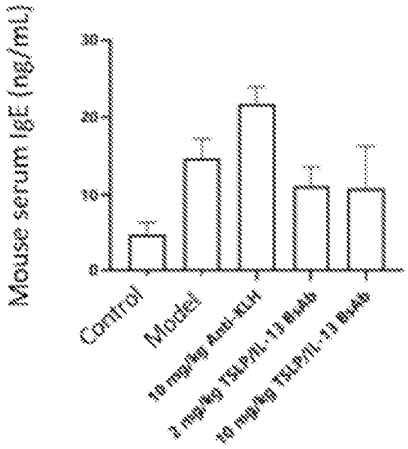

Mouse serum IgE (ng/mL)
Control
Model
10 mg/kg Anti-KLH
2 mg/kg TSLP/IL-13 BsAb
10 mg/kg TSLP/IL-13 BsAb

FIG. 9B

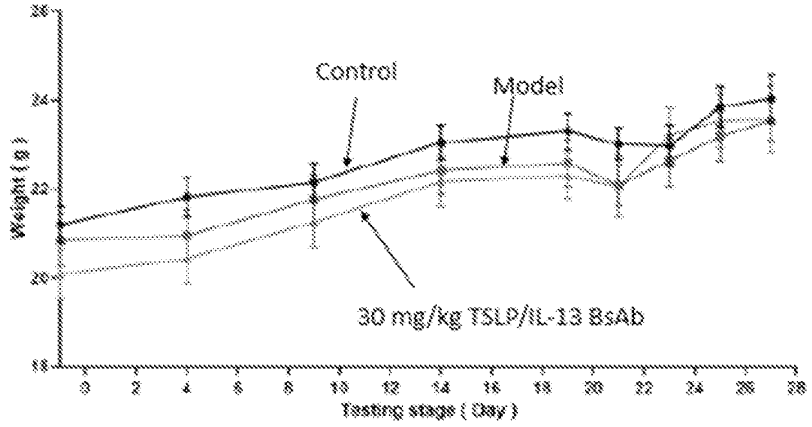

Control
Model
30 mg/kg TSLP/IL-13 BsAb
Weight (g)
Testing stage (day)

FIG. 10

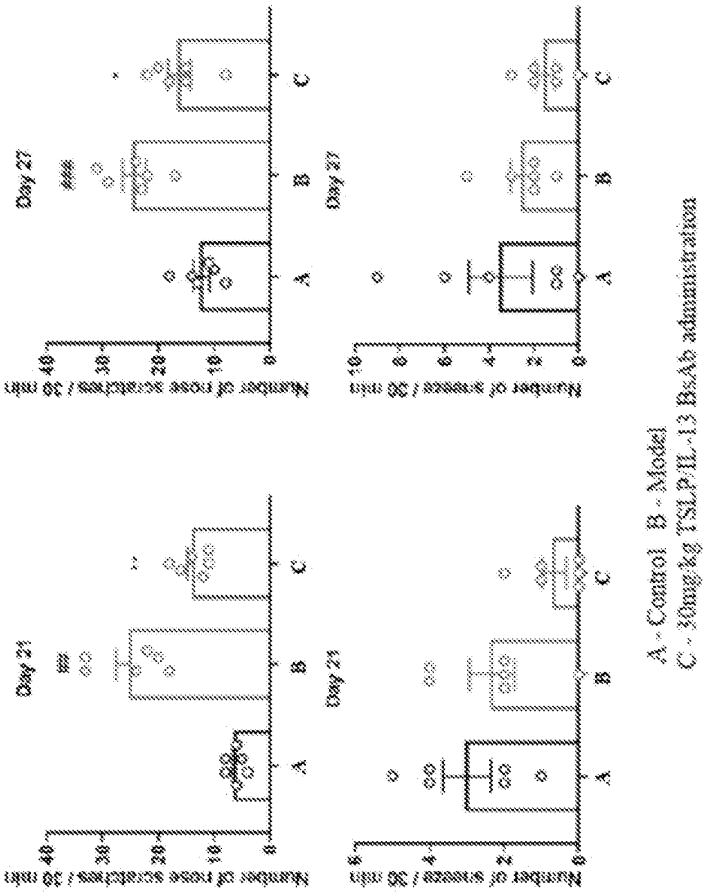

Day 21
Day 27
Number of nose scratchings / 30 min
Number of sneeze / 30 min
A
B
C
A - Control B - Model
C - 30mg/kg TSLP/IL-13 BsAb administration

FIG. 11

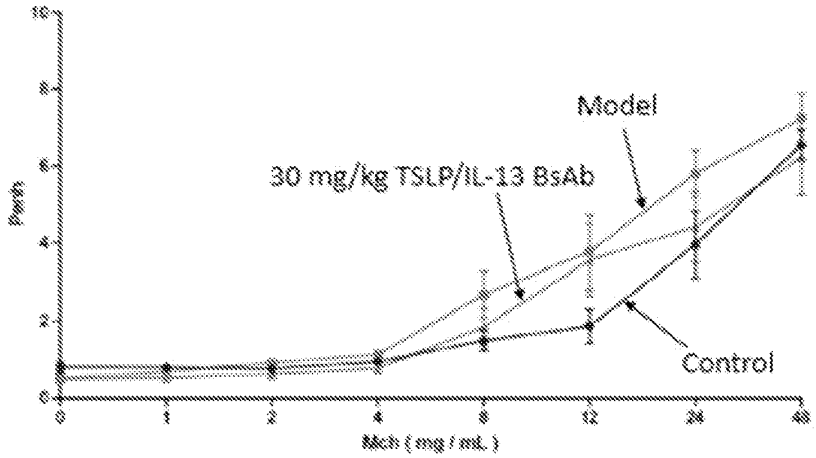


FIG. 12A

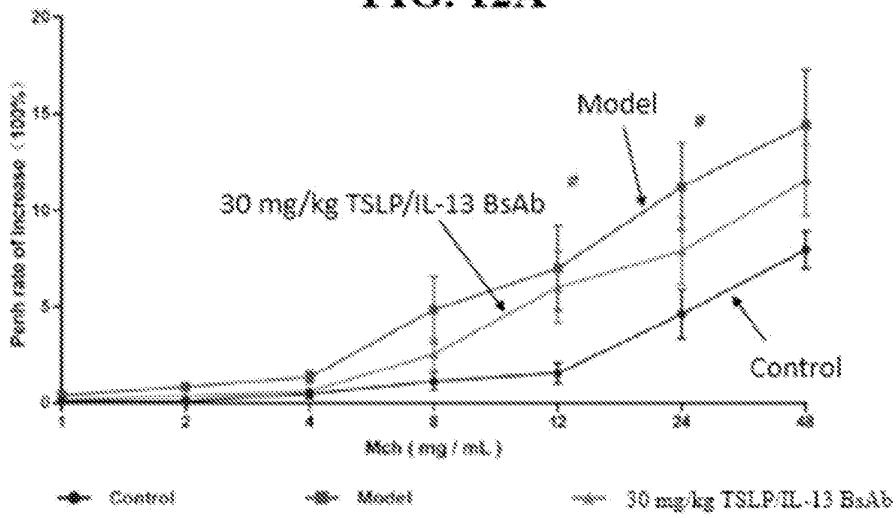


FIG. 12B

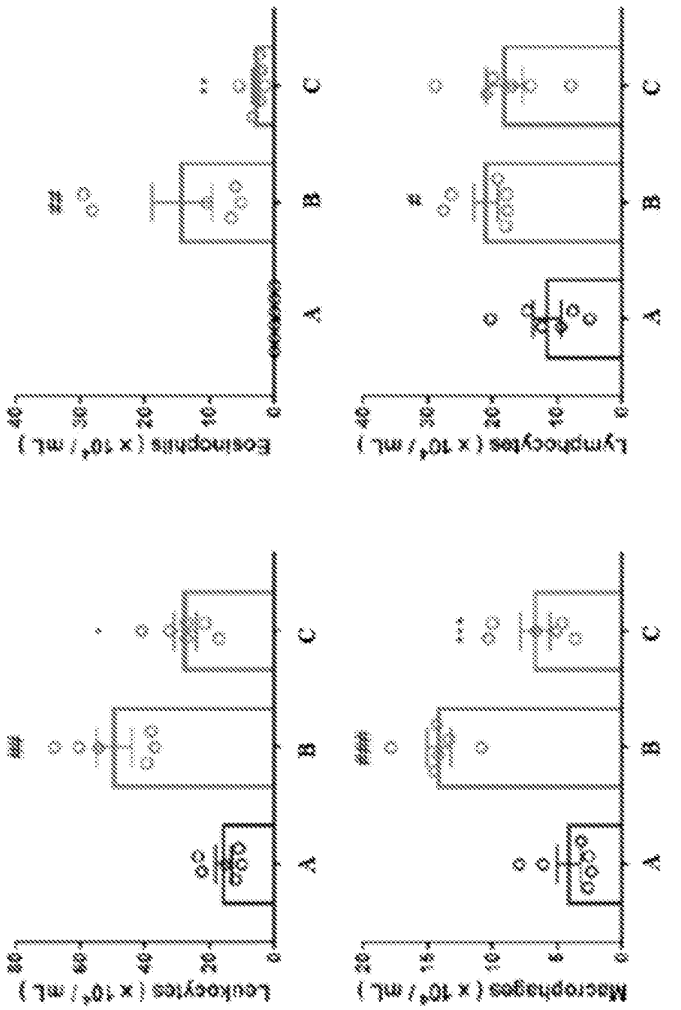
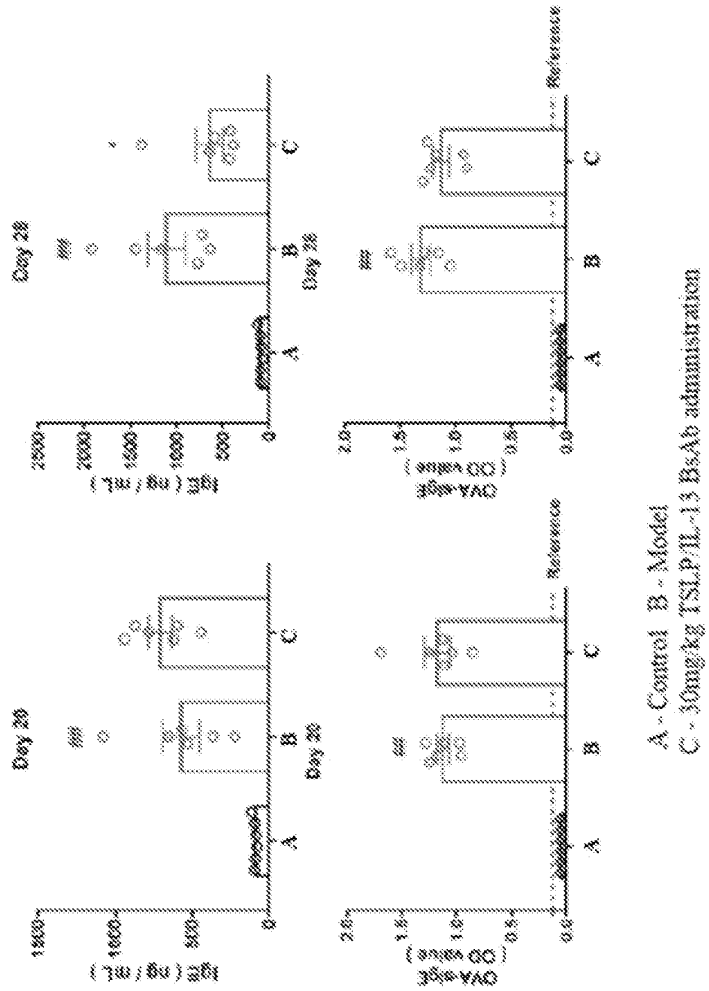

Eosinophils (× 10⁶ / mL)
Lymphocytes (× 10⁶ / mL)
Leukocytes (× 10⁶ / mL)
Macrophages (× 10⁶ / mL)
A
B
C
A - Control B - Model
C – 30 mg/kg TSLP/IL-13 BsAb administration

FIG. 13



A - Control B - Model
C - 30mg/kg TSLP/IL-13 BsAb administration

FIG. 14

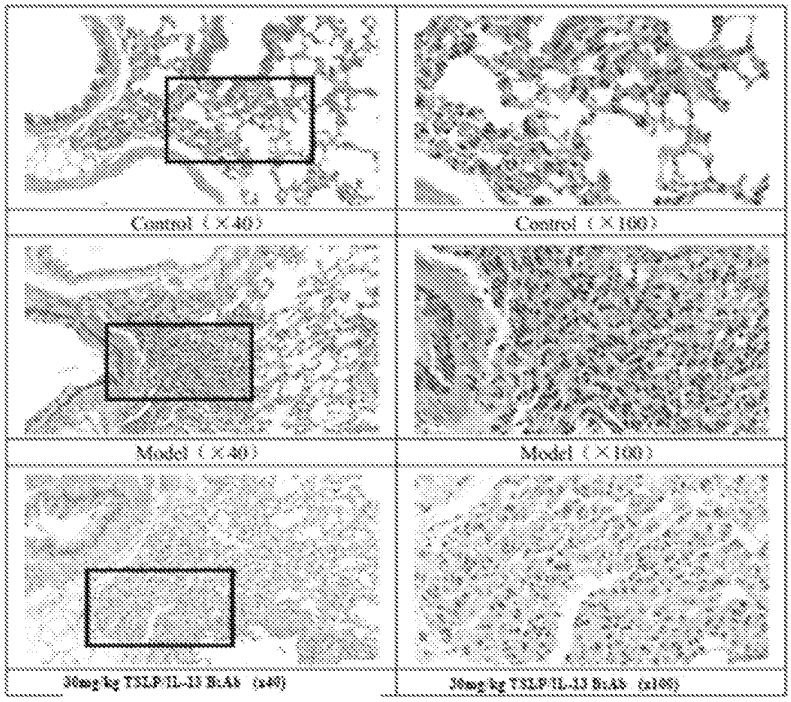

Control（×40）
Control（×100）
Model（×40）
Model（×100）
30mg/kg TSLP/IL-13 BsAb (x40)
30mg/kg TSLP/IL-13 BsAb (x100)

FIG. 15

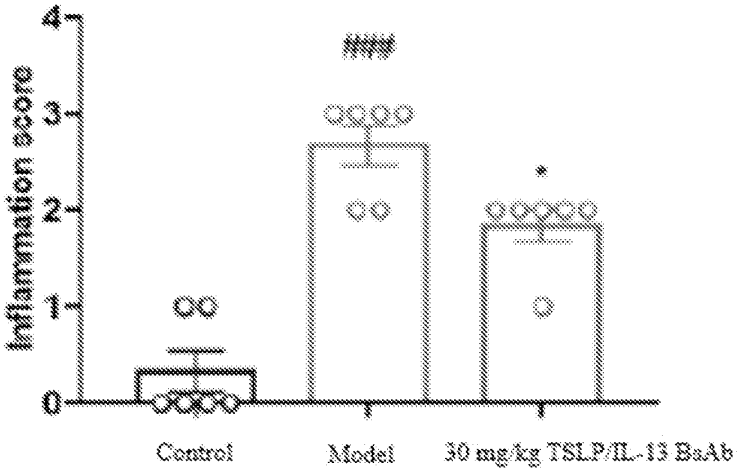

Inflammation score
4
3
2
1
0
####
*
Control
Model
30 mg/kg TSLP/IL-13 BsAb

FIG. 16

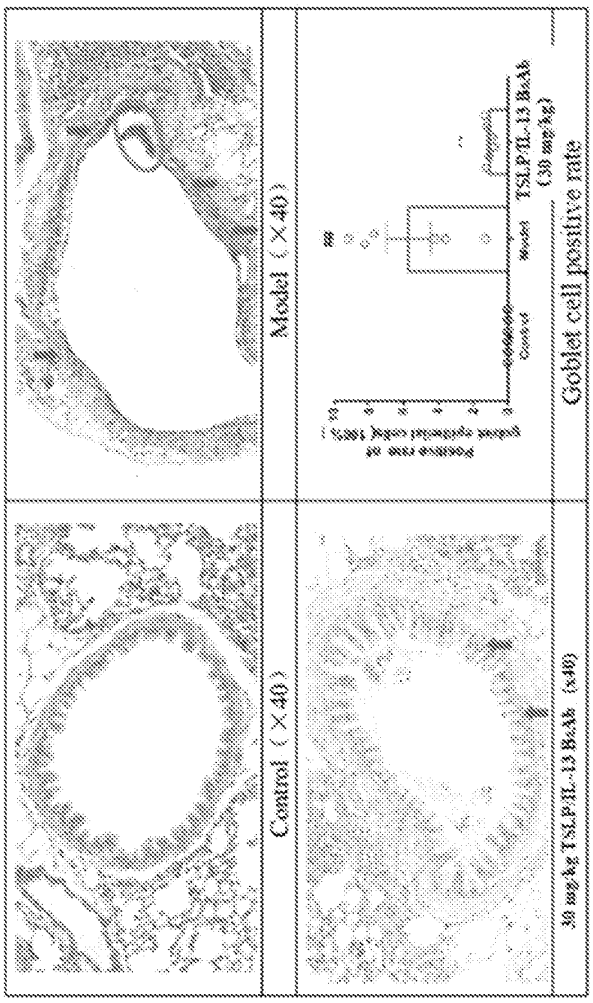

Control (×40)
Model (×40)
30 mg/kg TSLP/IL-13 BsAb (x40)
Goblet cell positive rate
Control
TSLP/IL-13 BsAb (30 mg/kg)

FIG. 17

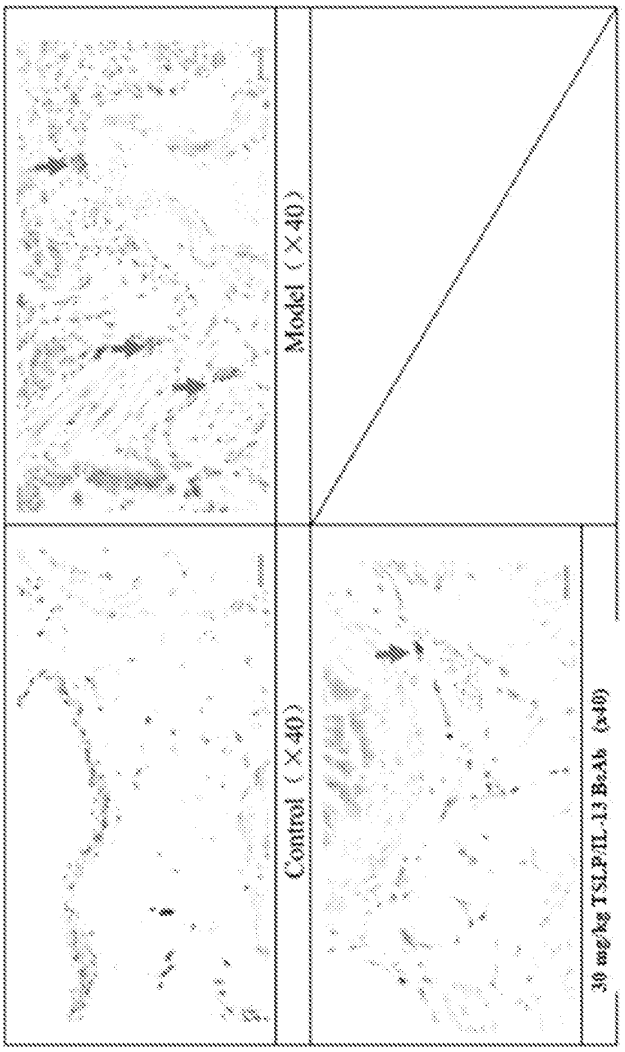


FIG. 18

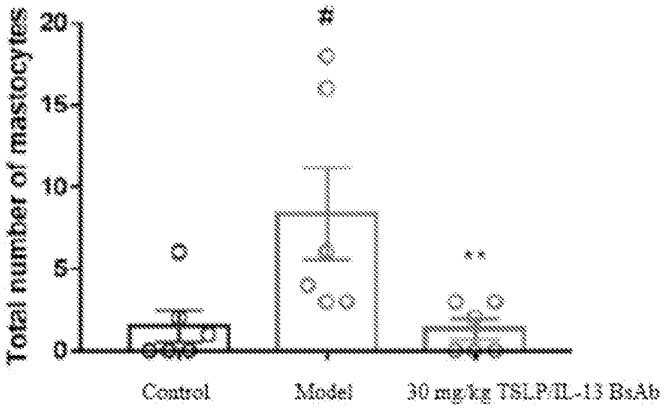


FIG. 19A

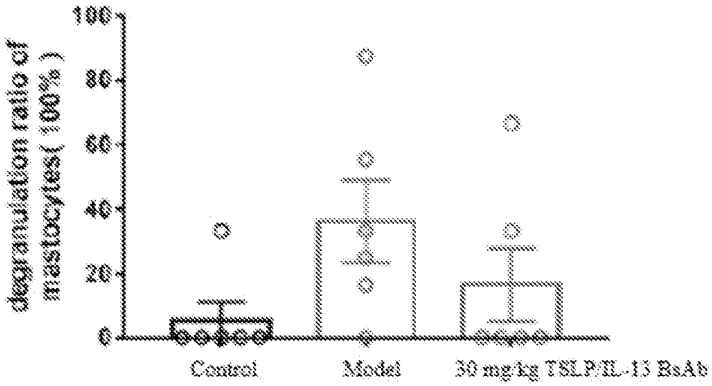


FIG. 19B

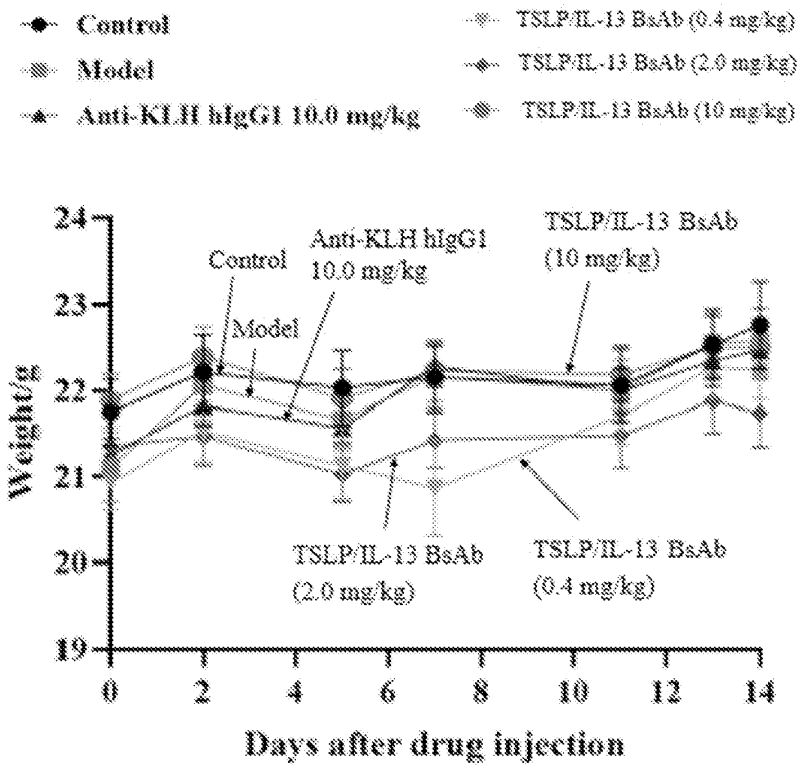

Control
Model
Anti-KLH hIgG1 10.0 mg/kg
TSLP/IL-13 BsAb (0.4 mg/kg)
TSLP/IL-13 BsAb (2.0 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
Weight/g
24
23
22
21
20
19
0
2
4
6
8
10
12
14
Days after drug injection
Control
Model
Anti-KLH hIgG1
10.0 mg/kg
TSLP/IL-13 BsAb
(10 mg/kg)
TSLP/IL-13 BsAb
(2.0 mg/kg)
TSLP/IL-13 BsAb
(0.4 mg/kg)

FIG. 20A

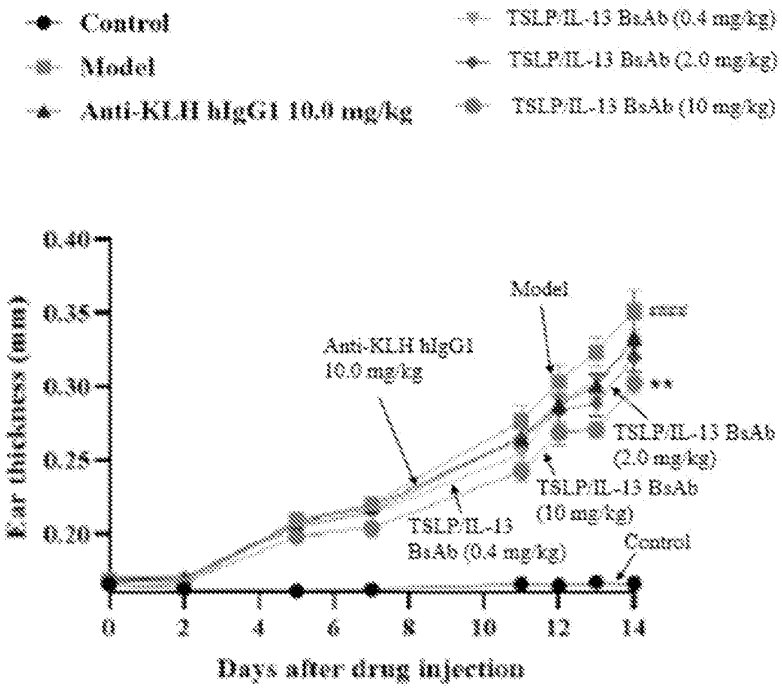

Control
Model
Anti-KLH hIgG1 10.0 mg/kg
TSLP/IL-13 BsAb (0.4 mg/kg)
TSLP/IL-13 BsAb (2.0 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
Ear thickness (mm)
0.40
0.35
0.30
0.25
0.20
0
2
4
6
8
10
12
14
Days after drug injection
Model
Anti-KLH hIgG1
10.0 mg/kg
TSLP/IL-13
BsAb (0.4 mg/kg)
TSLP/IL-13 BsAb
(2.0 mg/kg)
TSLP/IL-13 BsAb
(10 mg/kg)
Control
**

FIG. 20B

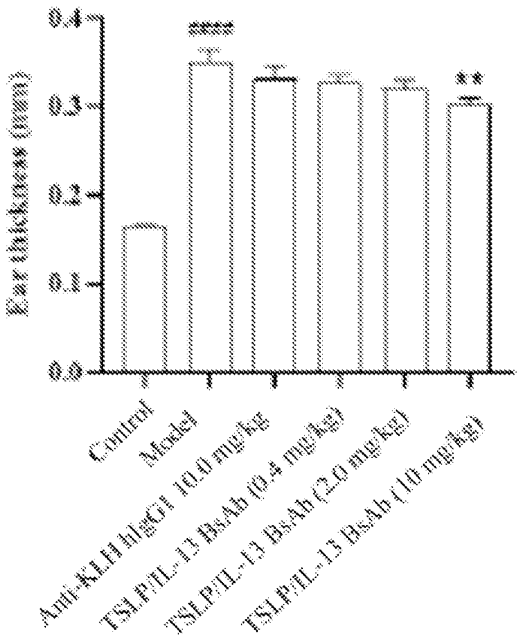

Ear thickness (mm)
0.4
0.3
0.2
0.1
0.0
****
**
Control
Model
Anti-KLH hIgG1 10.0 mg/kg
TSLP/IL-13 BsAb (0.4 mg/kg)
TSLP/IL-13 BsAb (2.0 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)

FIG. 20C

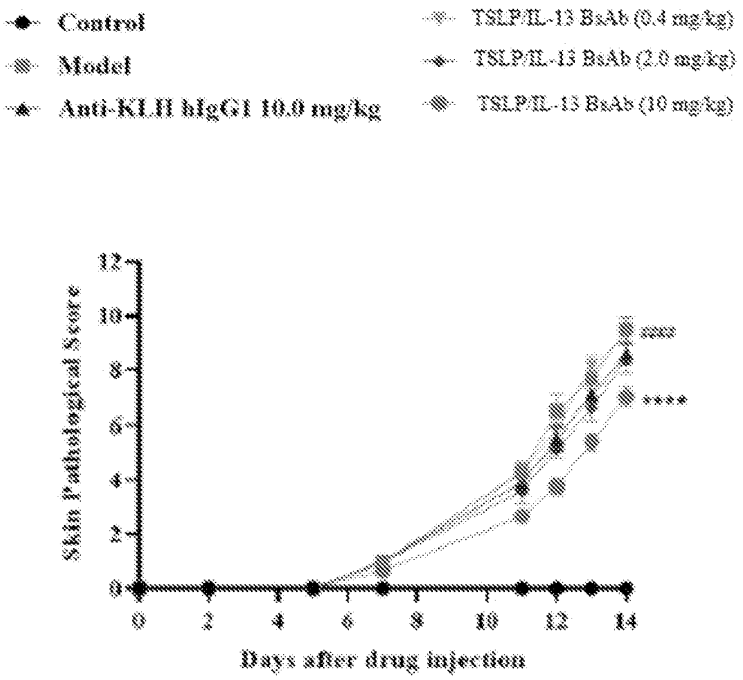

Control
Model
Anti-KLH hIgG1 10.0 mg/kg
TSLP/IL-13 BsAb (0.4 mg/kg)
TSLP/IL-13 BsAb (2.0 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
Skin Pathological Score
Days after drug injection
0
2
4
6
8
10
12
14
****
****

FIG. 21A

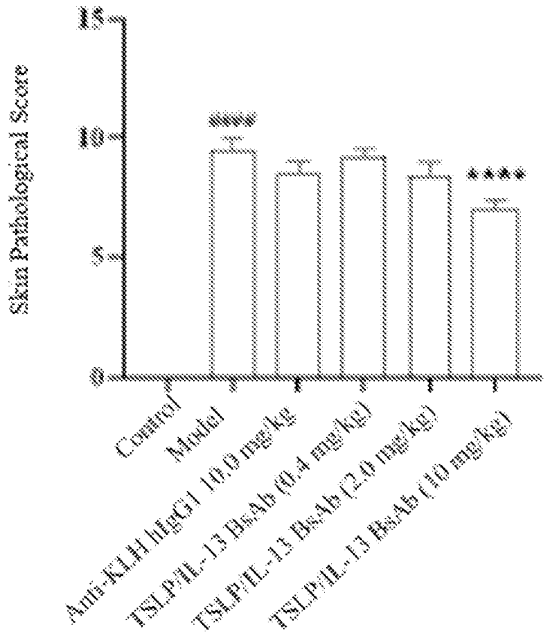

Skin Pathological Score
15
10
5
0
****
****
Control
Model
Anti-KLH hIgG1 10.0 mg/kg
TSLP/IL-13 BsAb (0.4 mg/kg)
TSLP/IL-13 BsAb (2.0 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)

FIG. 21B

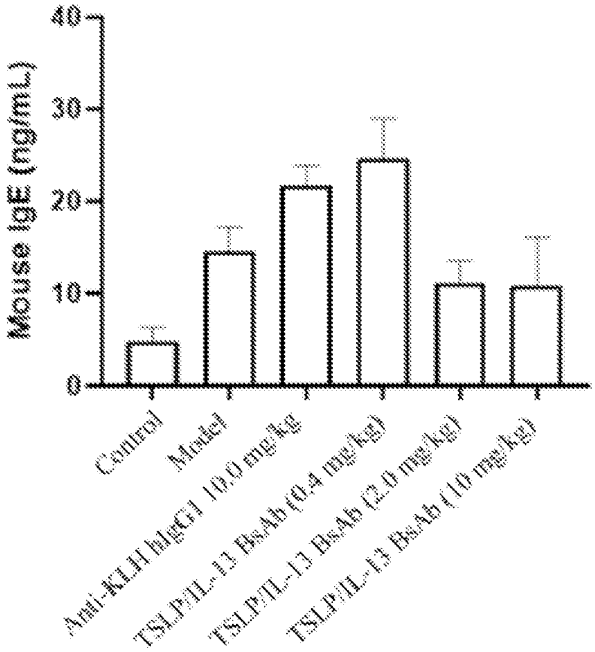

Mouse IgE (ng/mL)
40
30
20
10
0
Control
Model
Anti-KLH hIgG1 10.0 mg/kg
TSLP/IL-13 BsAb (0.4 mg/kg)
TSLP/IL-13 BsAb (2.0 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)

FIG. 22

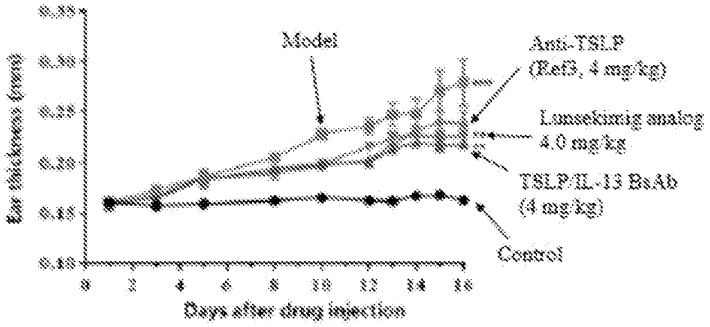


FIG. 23A

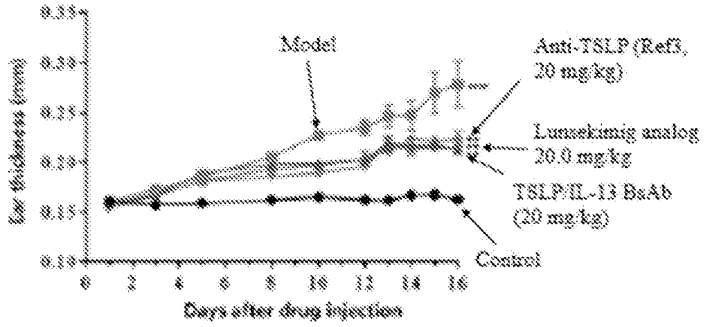


FIG. 23B

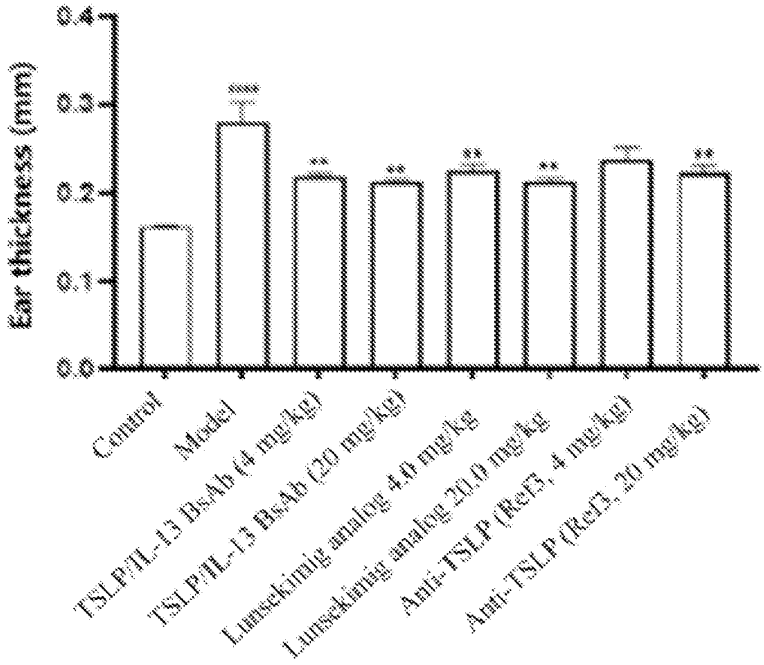
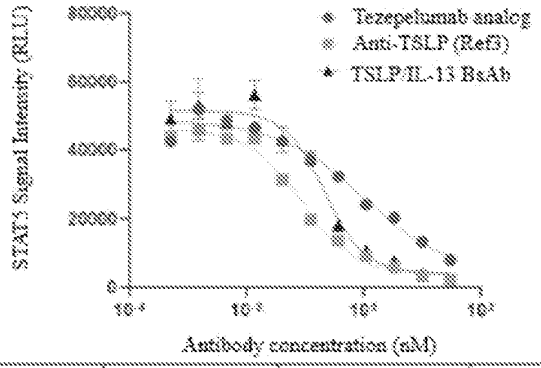
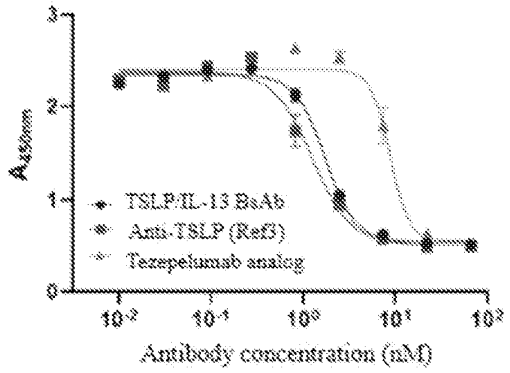

Ear thickness (mm)
0.4
0.3
0.2
0.1
0.0
Control
Model
TSLP/IL-13 BsAb (4 mg/kg)
TSLP/IL-13 BsAb (20 mg/kg)
Lunsekimig analog 4.0 mg/kg
Lunsekimig analog 20.0 mg/kg
Anti-TSLP (Ref3, 4 mg/kg)
Anti-TSLP (Ref3, 20 mg/kg)

FIG. 23C



	Tezepelumab analog	Anti-TSLP (Ref3)	TSLP/IL-13 BsAb
IC_{50} (nM)	1.02	0.09	0.22

FIG. 24



	TSLP/IL-13 BsAb	Anti-TSLP (Ref3)	Tezepelumab analog
IC_{50} (nM)	1.74	1.26	8.82

FIG. 25

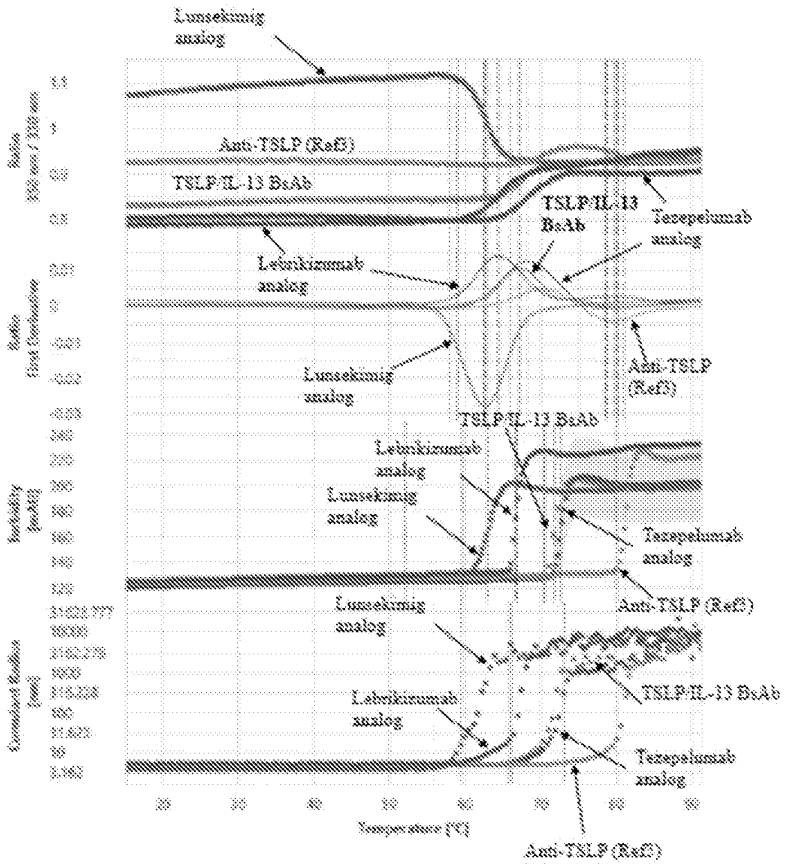
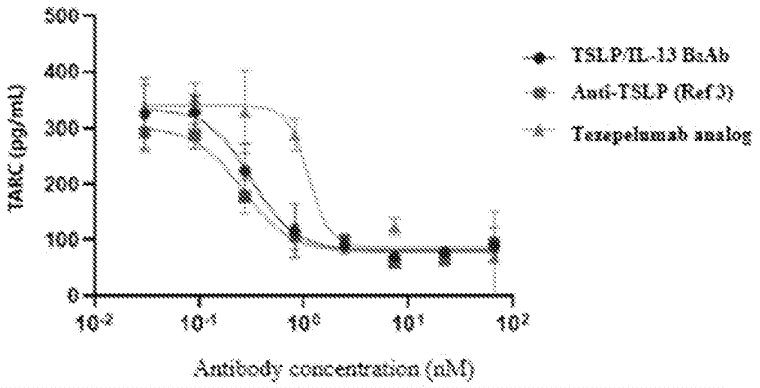
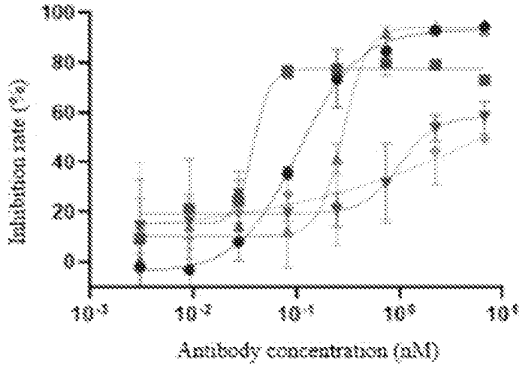

Lunsekimig analog
Anti-TSLP (Ref3)
TSLP/IL-13 BsAb
TSLP/IL-13 BsAb
Tezepelumab analog
Lebrikizumab analog
Lunsekimig analog
Anti-TSLP (Ref3)
TSLP/IL-13 BsAb
Lebrikizumab analog
Lunsekimig analog
Tezepelumab analog
Anti-TSLP (Ref3)
Lunsekimig analog
TSLP/IL-13 BsAb
Lebrikizumab analog
Tezepelumab analog
Anti-TSLP (Ref3)

FIG. 26



	TSLP/IL-13 BsAb	Anti-TSLP (Ref3)	Tezepelumab analog
IC_{50} (nM)	0.32	0.26	1.12

FIG. 27



- TSLP/IL-13 BsAb
- Anti-TSLP (Ref 3)
- Lebrikizumab analog
- Lunsekimig analog
- Tezepelumab analog

	TSLP/IL-13 BsAb	Anti-TSLP (Ref3)	Lebrikizumab analog	Lunsekimig analog	Tezepelumab analog
Maximum inhibition rate (%)	93.1	38.4	77.3	94.0	49.4

FIG. 28

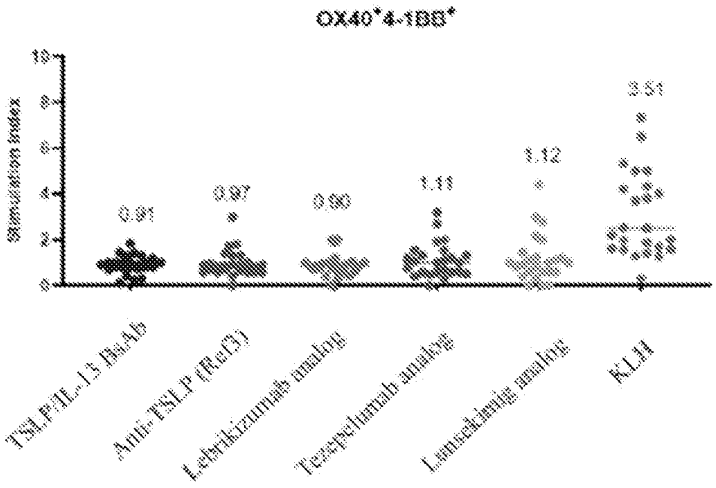

OX40+4-1BB+
Stimulation index
0
2
4
6
8
10
0.91
0.97
0.80
1.11
1.12
3.51
TSLP/IL-13 BsAb
Anti-TSLP (ReCT)
Lebrikizumab analog
Tezepelumab analog
Lunsekimig analog
KLH

FIG. 29

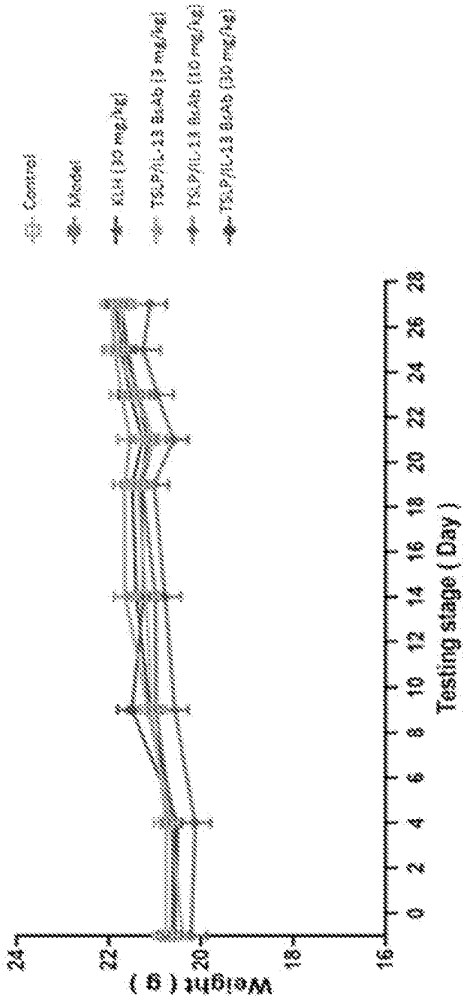

Control
Model
Ruxi (30 mg/kg)
TSLP/IL-13 BsAb (3 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
TSLP/IL-13 BsAb (30 mg/kg)
Weight (g)
24
22
20
18
16
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Testing stage (Day)

FIG. 30

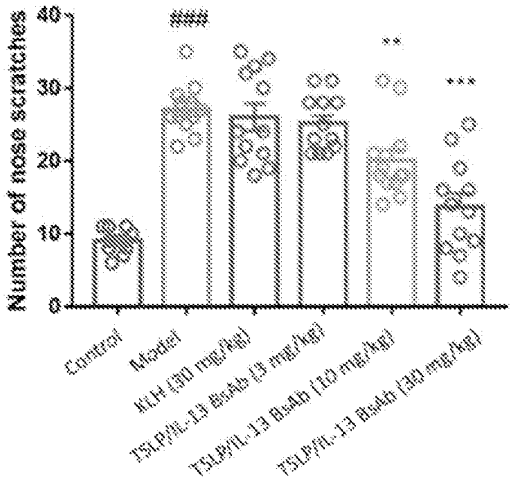


FIG. 31A

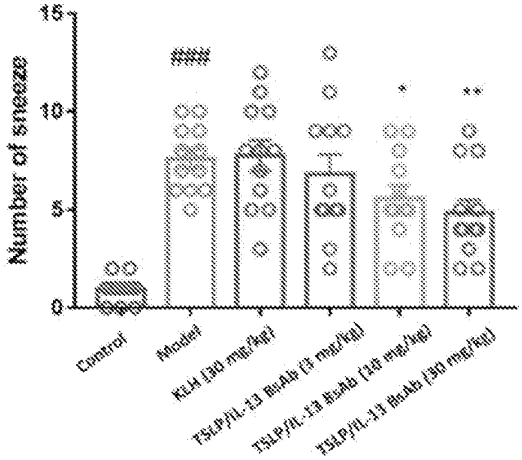


FIG. 31B

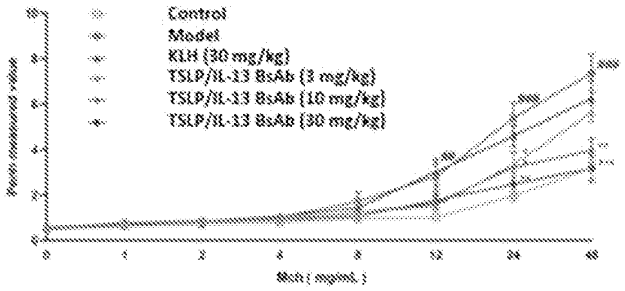


FIG. 32A

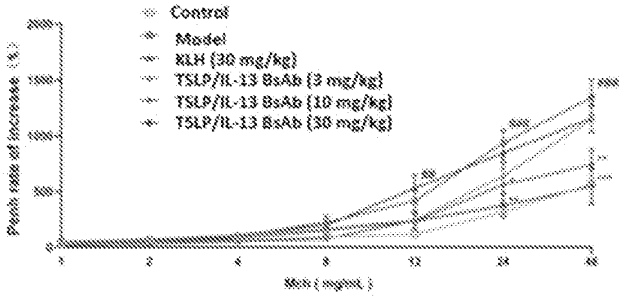


FIG. 32B

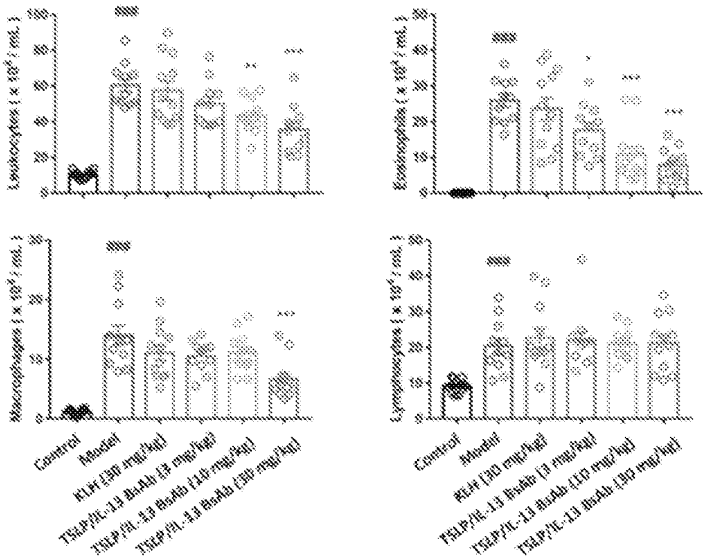

Control
Model
#LH (30 mg/kg)
TSLP/IL-13 BsAb (3 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
TSLP/IL-13 BsAb (30 mg/kg)

FIG. 33

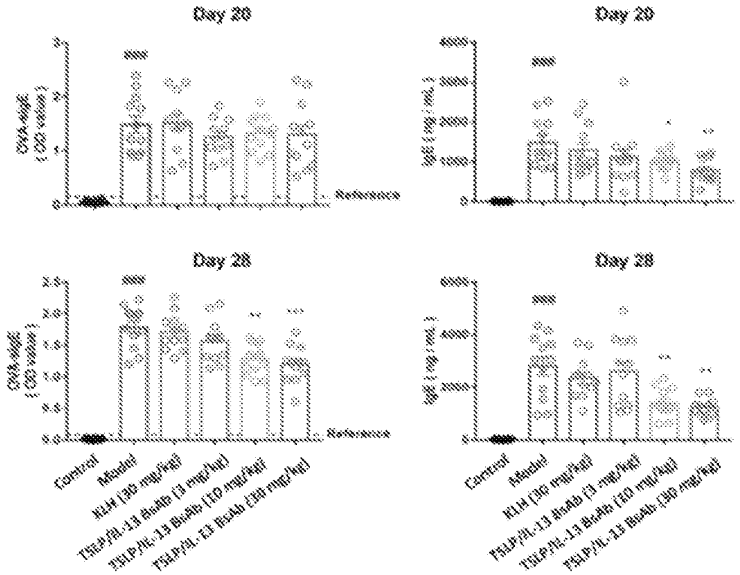

Day 20
Day 20
Day 28
Day 28
Control
Model
KLH (30 mg/kg)
TSLP/IL-13 BsAb (3 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
TSLP/IL-13 BsAb (30 mg/kg)

FIG. 34

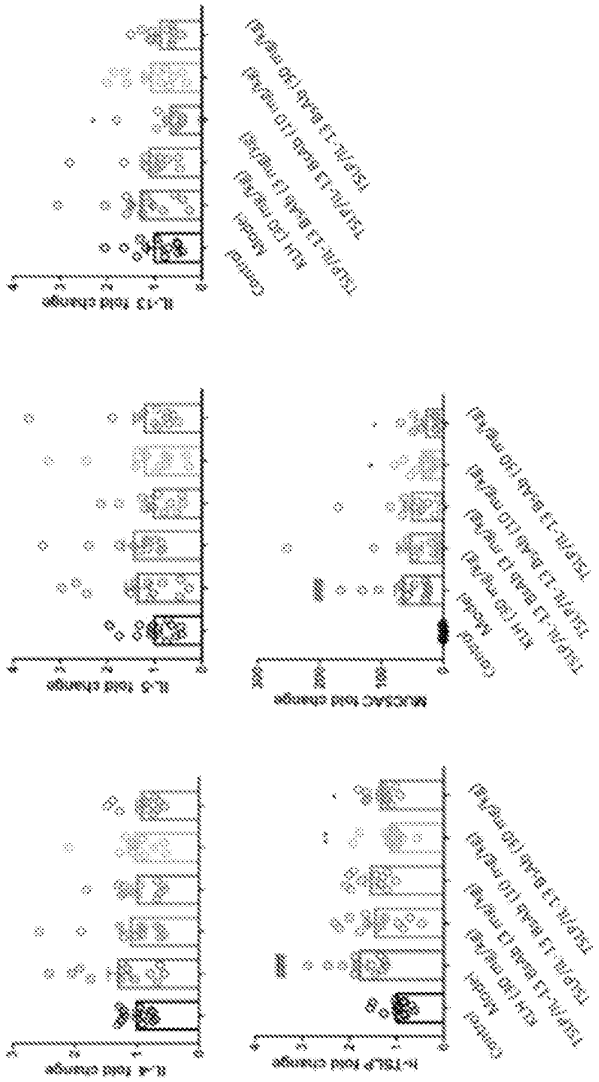


FIG. 35

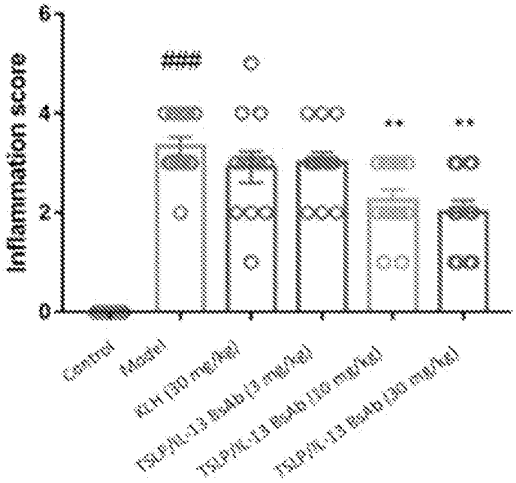

Inflammation score
6
4
2
0
####
**
**
Control
Model
4LH (30 mg/kg)
TSLP/IL-13 BsAb (3 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
TSLP/IL-13 BsAb (30 mg/kg)

FIG. 36

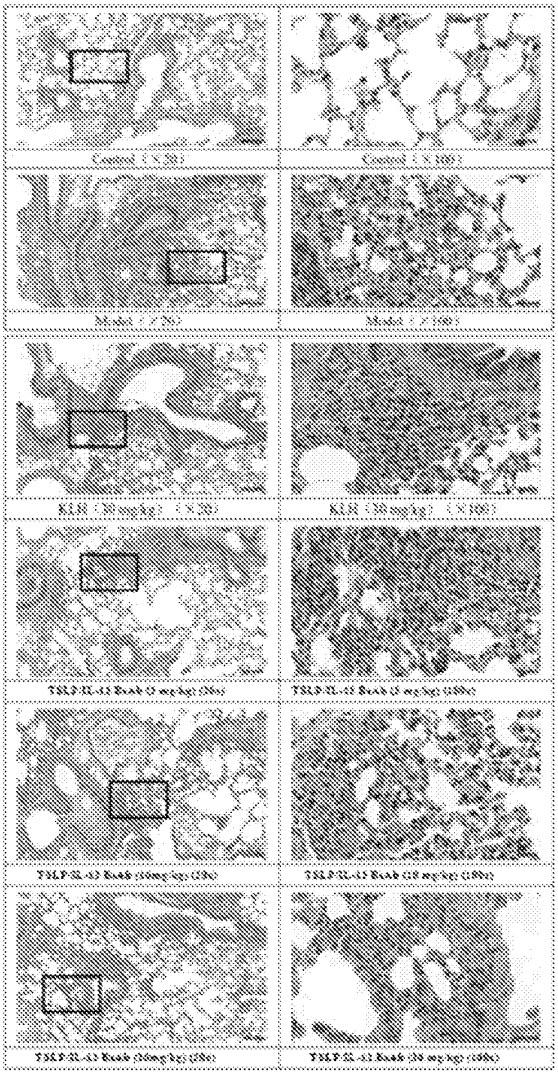


FIG. 37

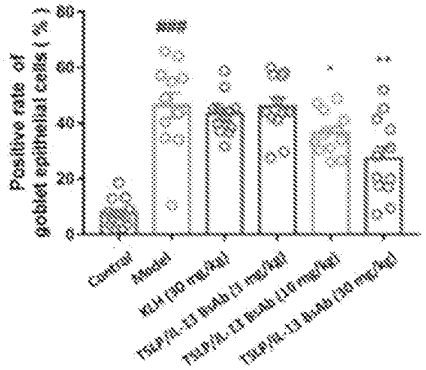

Positive rate of goblet epithelial cells (%)
0
20
40
60
80
Control
Model
KLH (30 mg/kg)
TSLP/IL-13 Bsab (3 mg/kg)
TSLP/IL-13 Bsab (10 mg/kg)
TSLP/IL-13 Bsab (30 mg/kg)

FIG. 38

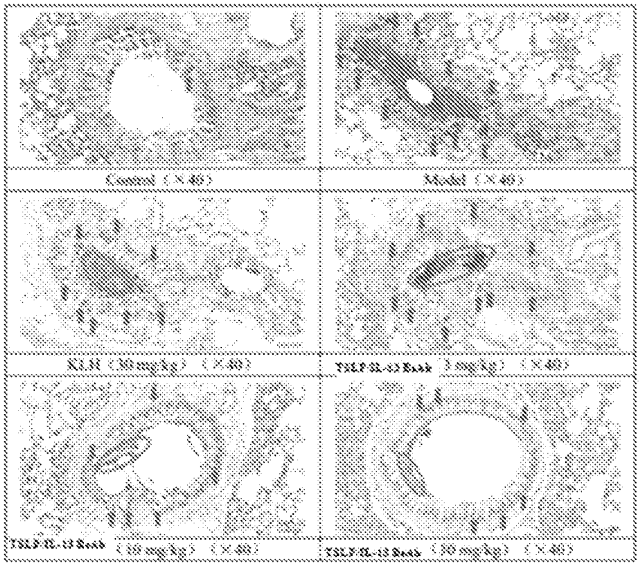

Control (× 40)
Model (× 40)
KLH (30 mg/kg) (× 40)
TSLP/IL-13 Bsab (3 mg/kg) (× 40)
TSLP/IL-13 Bsab (10 mg/kg) (× 40)
TSLP/IL-13 Bsab (30 mg/kg) (× 40)

FIG. 39

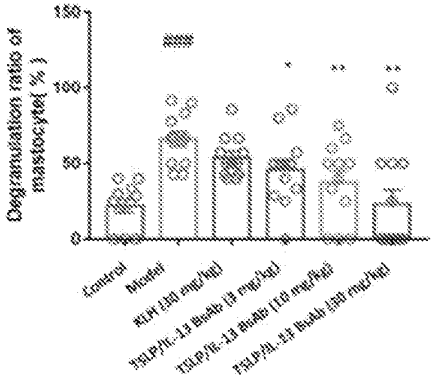

Degranulation ratio of mastocyte(%)
150
100
50
0
Control
Model
KLH (30 mg/kg)
TSLP/IL-13 BsAb (3 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
TSLP/IL-13 BsAb (30 mg/kg)

FIG. 40

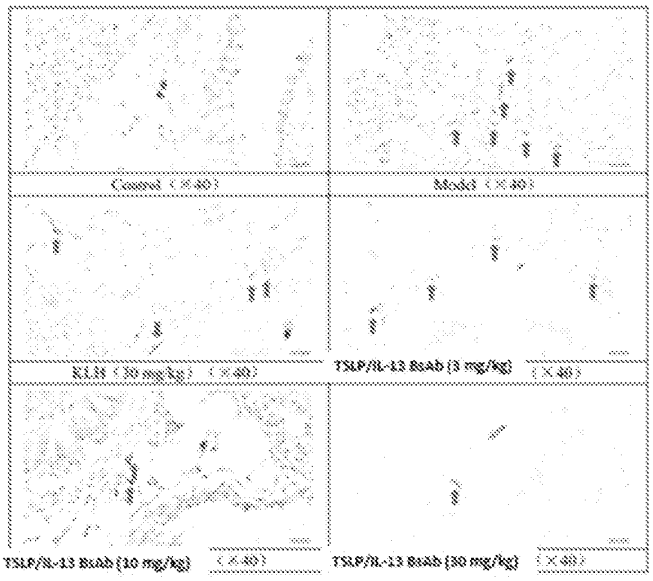

Control (×40)
Model (×40)
KLH (30 mg/kg) (×40)
TSLP/IL-13 BsAb (3 mg/kg) (×40)
TSLP/IL-13 BsAb (10 mg/kg) (×40)
TSLP/IL-13 BsAb (30 mg/kg) (×40)

FIG. 41

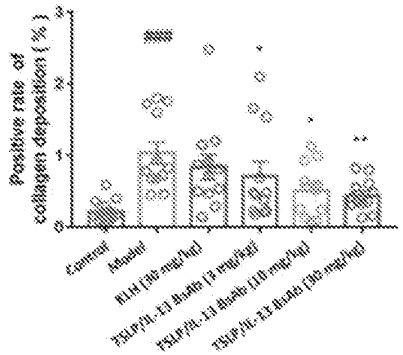

Positive rate of collagen deposition (%)
Control
Model
KLH (30 mg/kg)
TSLP/IL-13 BsAb (3 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
TSLP/IL-13 BsAb (30 mg/kg)

FIG. 42

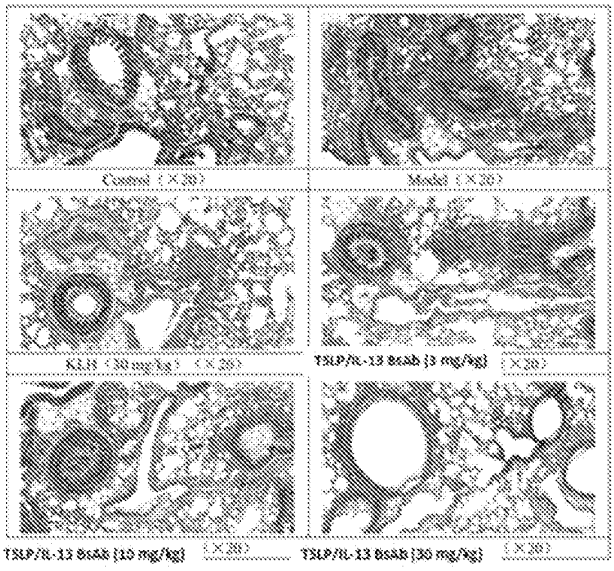

Control (×20)
Model (×20)
KLH (30 mg/kg) (×20)
TSLP/IL-13 BsAb (3 mg/kg) (×20)
TSLP/IL-13 BsAb (10 mg/kg) (×20)
TSLP/IL-13 BsAb (30 mg/kg) (×20)

FIG. 43

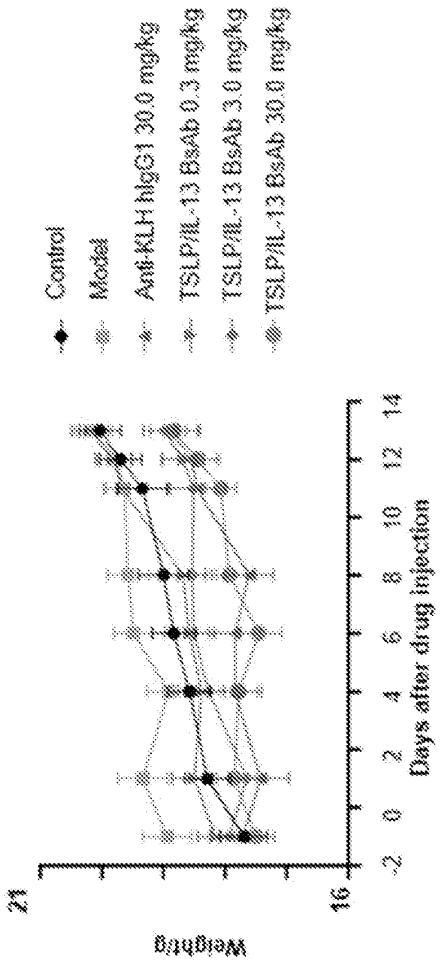

Control
Model
Anti-KLH hIgG1 30.0 mg/kg
TSLP/IL-13 BsAb 0.3 mg/kg
TSLP/IL-13 BsAb 3.0 mg/kg
TSLP/IL-13 BsAb 30.0 mg/kg
Weight/g
21
16
-2
0
2
4
6
8
10
12
14
Days after drug injection

FIG. 44

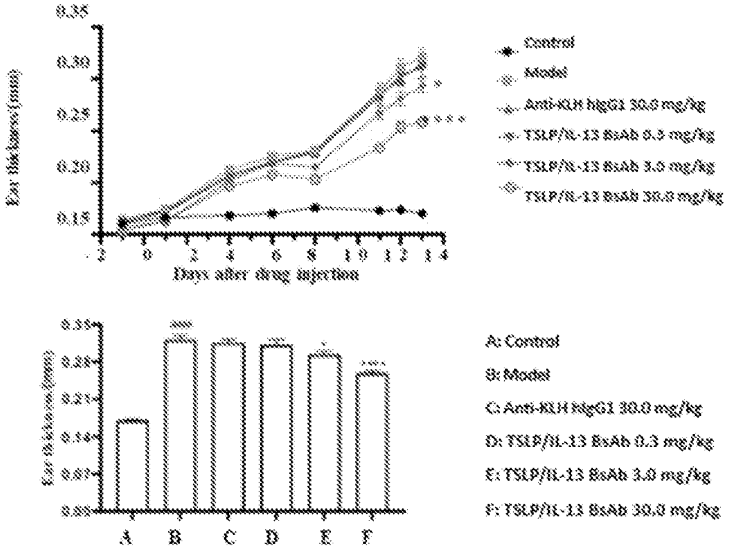

Ear thickness (mm)
Days after drug injection
Control
Model
Anti-KLH hIgG1 30.0 mg/kg
TSLP/IL-13 BsAb 0.3 mg/kg
TSLP/IL-13 BsAb 3.0 mg/kg
TSLP/IL-13 BsAb 30.0 mg/kg
A: Control
B: Model
C: Anti-KLH hIgG1 30.0 mg/kg
D: TSLP/IL-13 BsAb 0.3 mg/kg
E: TSLP/IL-13 BsAb 3.0 mg/kg
F: TSLP/IL-13 BsAb 30.0 mg/kg

FIG. 45

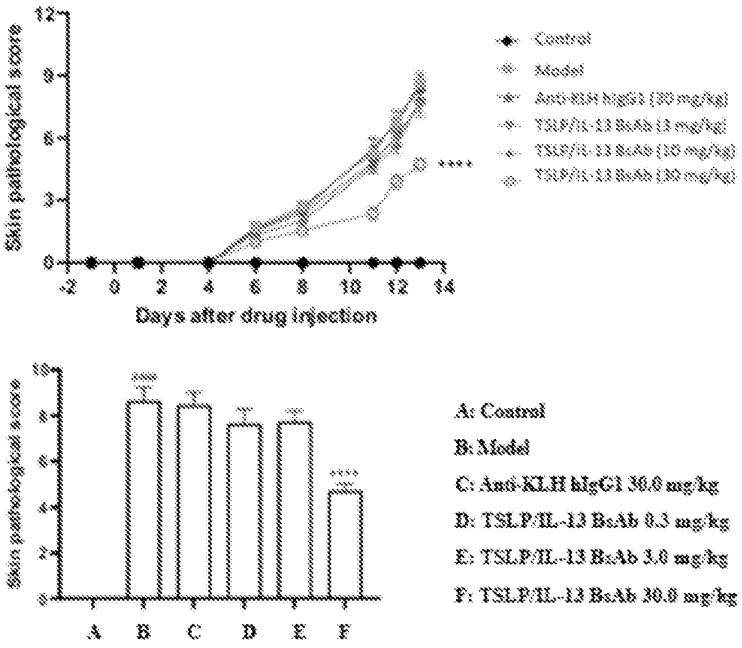

Skin pathological score
Days after drug injection
Control
Model
Anti-KLH hIgG1 (30 mg/kg)
TSLP/IL-13 BsAb (3 mg/kg)
TSLP/IL-13 BsAb (10 mg/kg)
TSLP/IL-13 BsAb (30 mg/kg)
A: Control
B: Model
C: Anti-KLH hIgG1 30.0 mg/kg
D: TSLP/IL-13 BsAb 0.3 mg/kg
E: TSLP/IL-13 BsAb 3.0 mg/kg
F: TSLP/IL-13 BsAb 30.0 mg/kg

FIG. 46

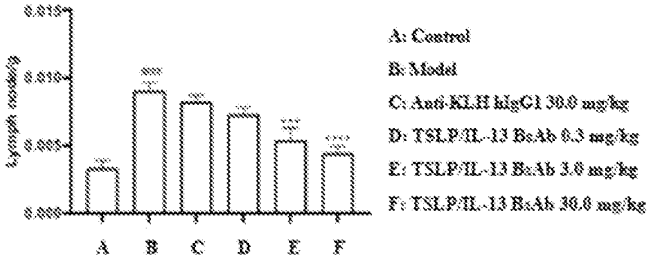

A: Control
B: Model
C: Anti-KLH hIgG1 30.0 mg/kg
D: TSLP/IL-13 BsAb 0.3 mg/kg
E: TSLP/IL-13 BsAb 3.0 mg/kg
F: TSLP/IL-13 BsAb 30.0 mg/kg
A B C D E F

FIG. 47

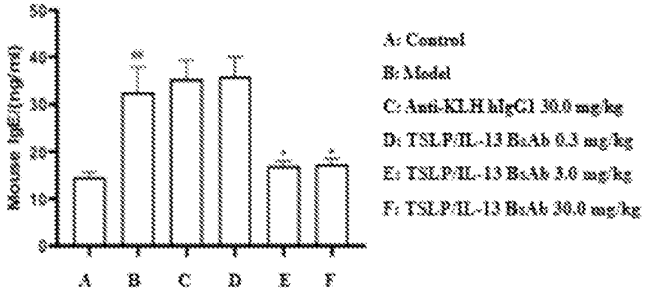

Mouse IgE (ng/ml)
A: Control
B: Model
C: Anti-KLH hIgG1 30.0 mg/kg
D: TSLP/IL-13 BsAb 0.3 mg/kg
E: TSLP/IL-13 BsAb 3.0 mg/kg
F: TSLP/IL-13 BsAb 30.0 mg/kg
A B C D E F

FIG. 48

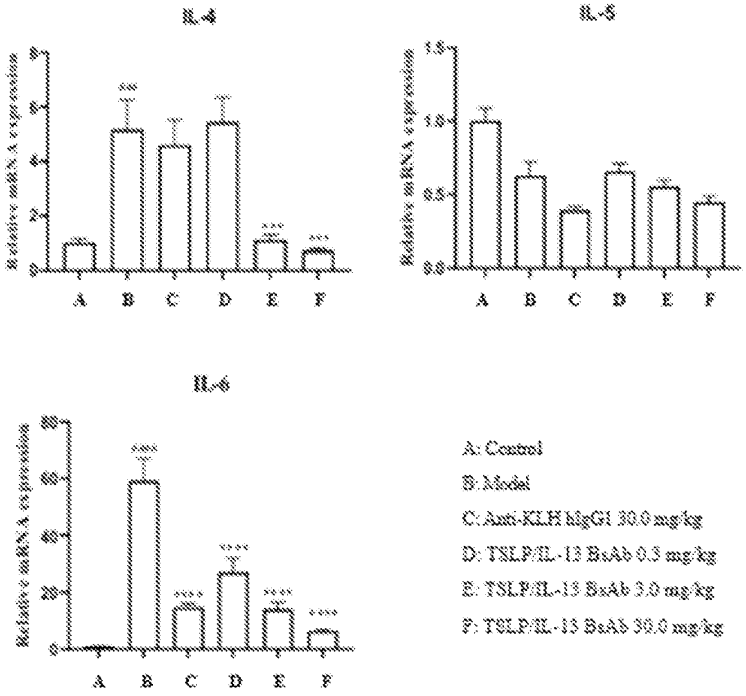

IL-4
IL-5
IL-6
A
B
C
D
E
F
A: Control
B: Model
C: Anti-KLH hIgG1 30.0 mg/kg
D: TSLP/IL-13 BsAb 0.3 mg/kg
E: TSLP/IL-13 BsAb 3.0 mg/kg
F: TSLP/IL-13 BsAb 30.0 mg/kg

FIG. 49

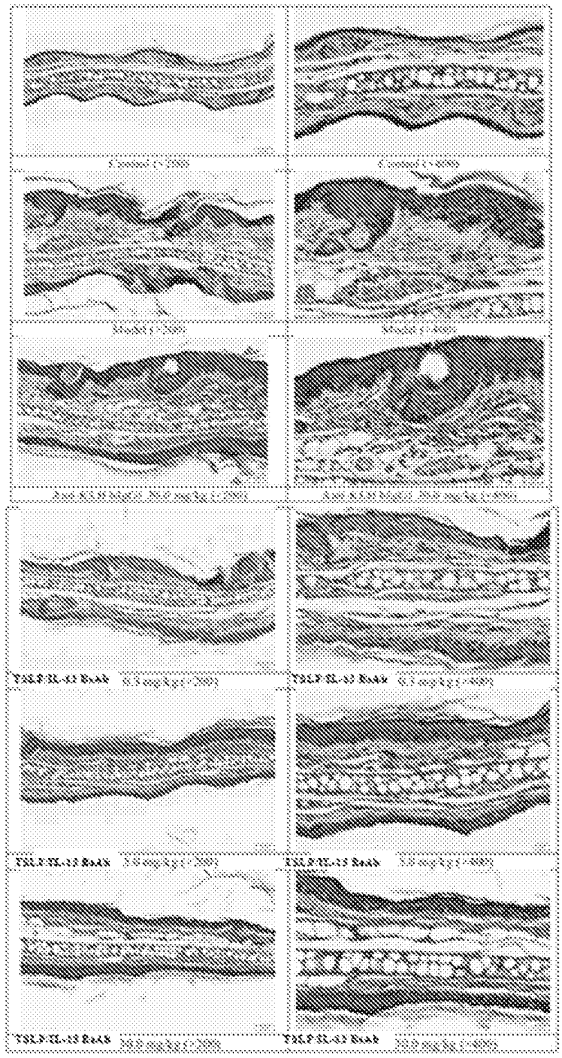


FIG. 50

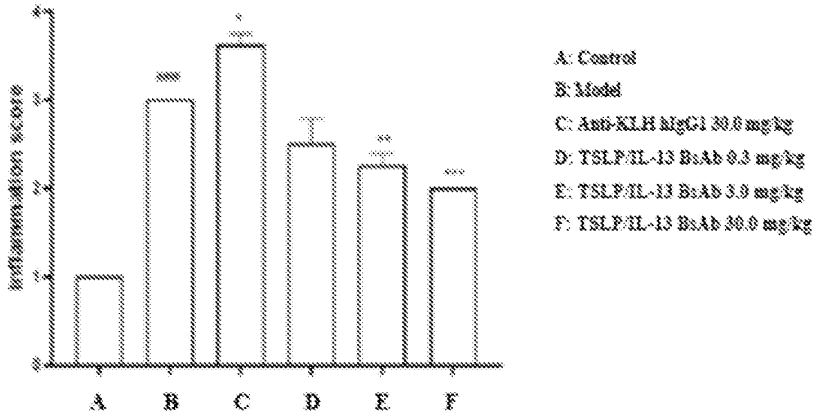

Inflammation score
A
B
C
D
E
F
A: Control
B: Model
C: Anti-KLH hIgG1 30.0 mg/kg
D: TSLP/IL-13 BsAb 0.3 mg/kg
E: TSLP/IL-13 BsAb 3.0 mg/kg
F: TSLP/IL-13 BsAb 30.0 mg/kg

FIG. 51

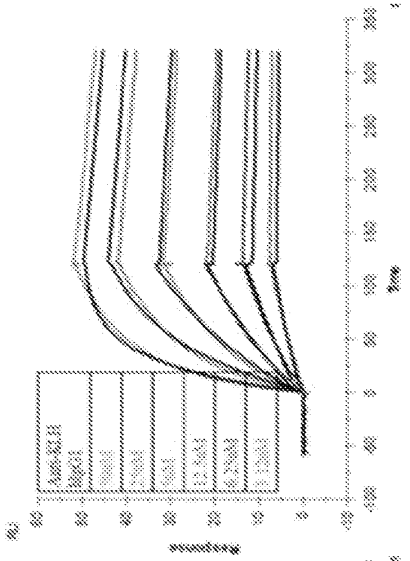


FIG. 52B

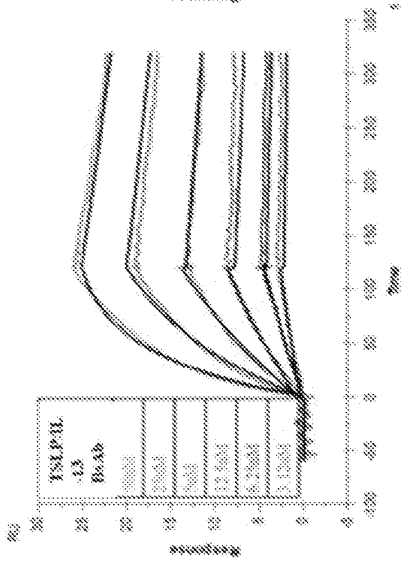


FIG. 52A

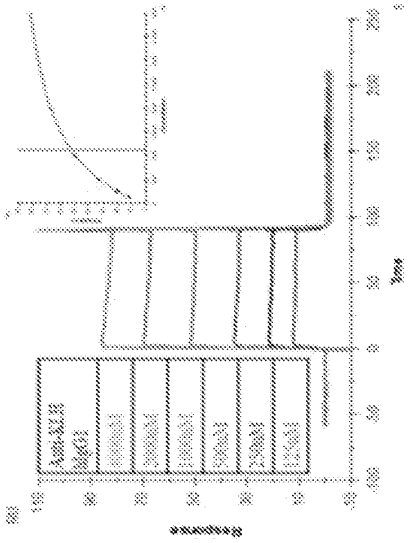


FIG. 53B

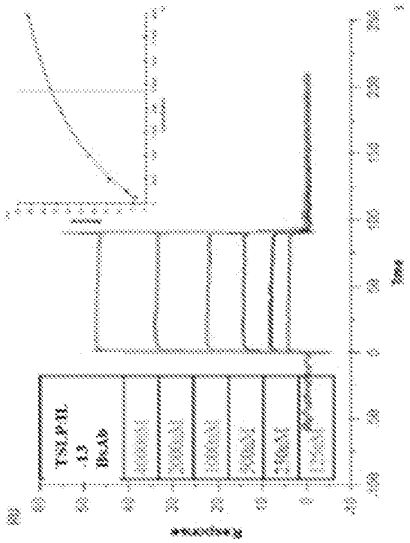


FIG. 53A

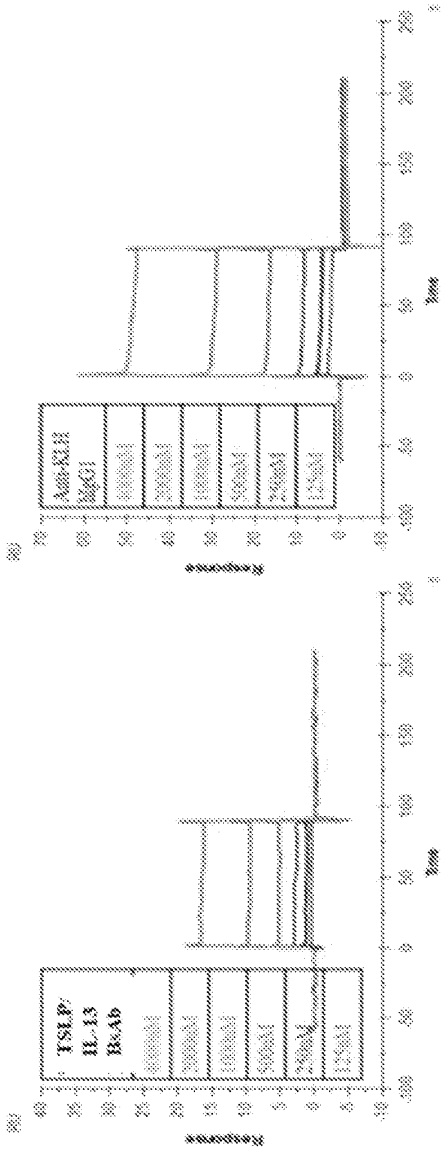


FIG. 54A

FIG. 54B

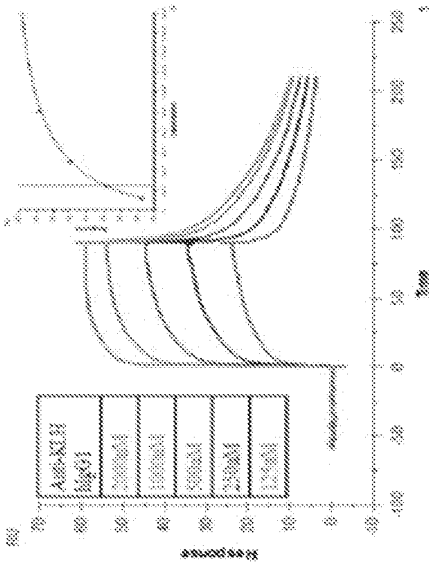


FIG. 55B

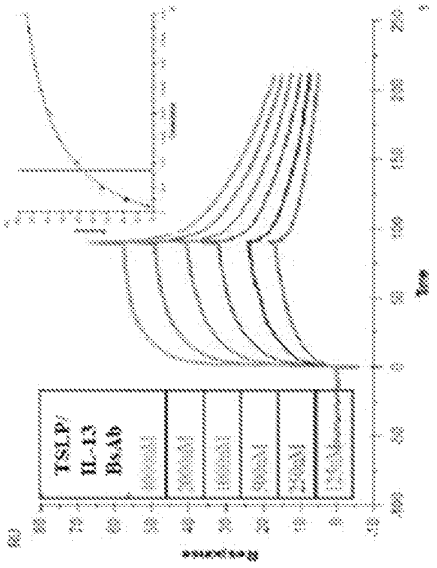


FIG. 55A

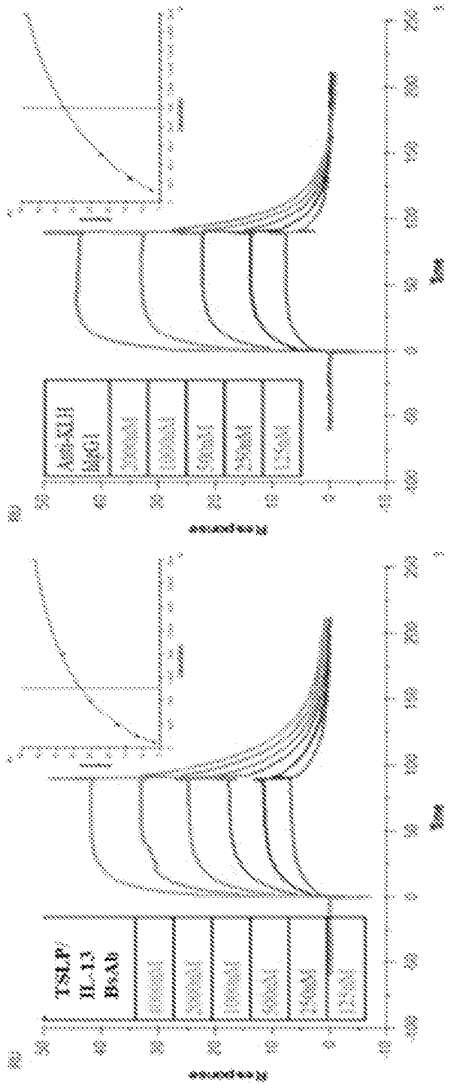


FIG. 56A

FIG. 56B

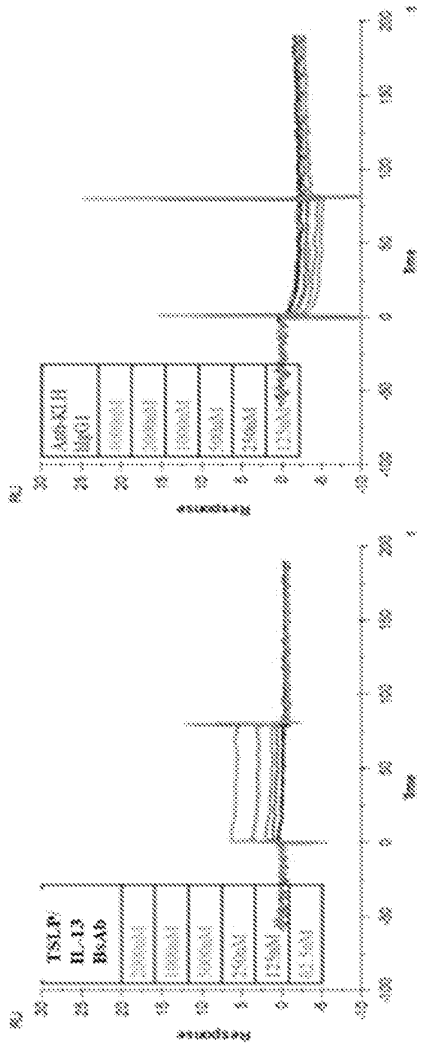


FIG. 57A

FIG. 57B

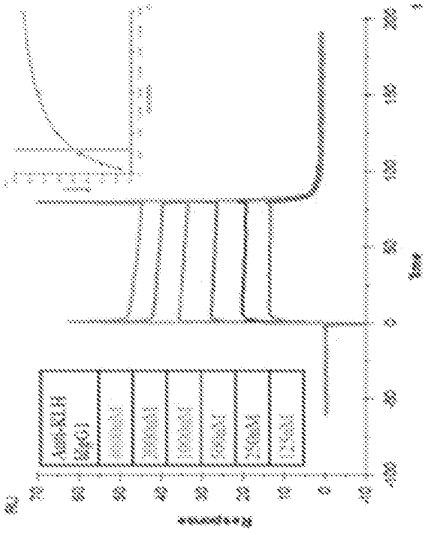


FIG. 58B

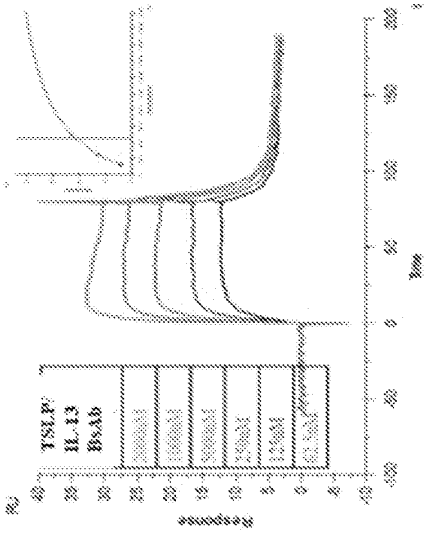


FIG. 58A

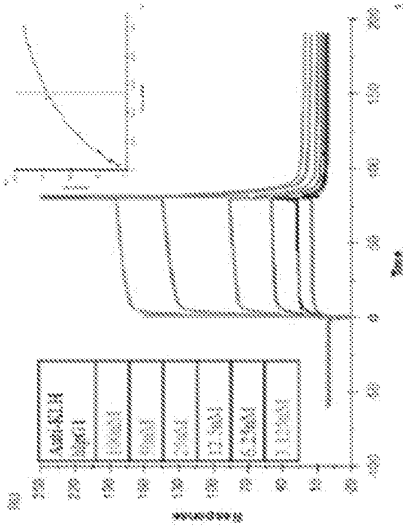


FIG. 59B

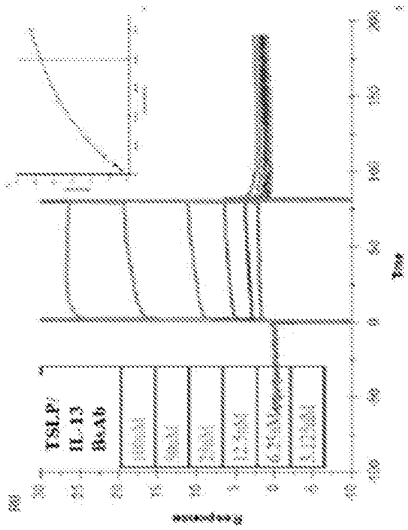
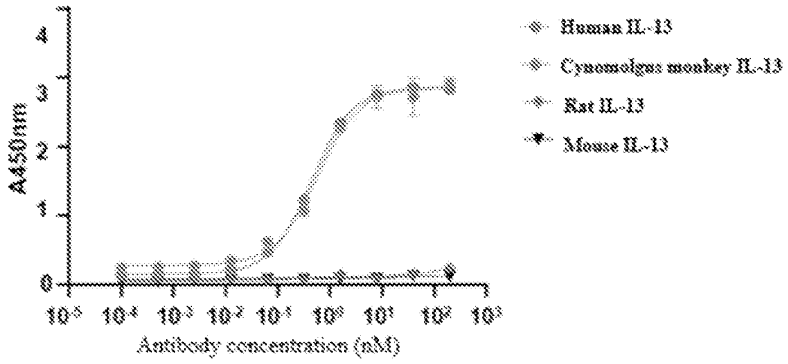


FIG. 59A



	Human IL-13	Cynomolgus monkey IL-13
EC_{50} (nM)	0.45	0.56

FIG. 60

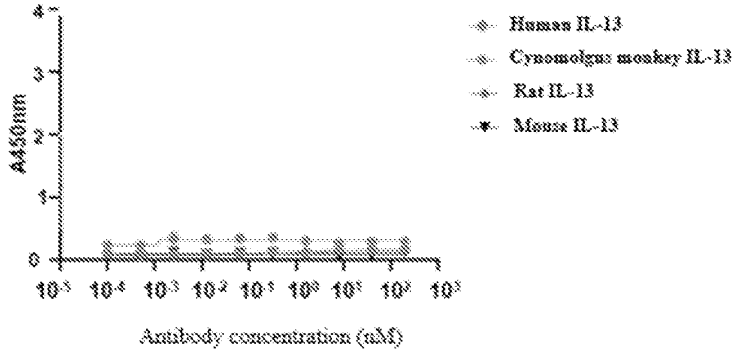
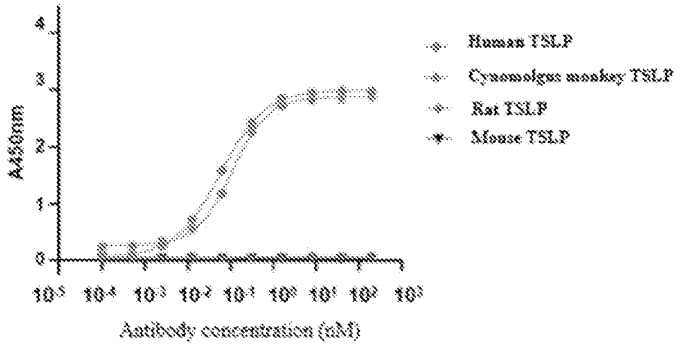


FIG. 61



	Human TSLP	Cynomolgus monkey TSLP
EC_{50} (nM)	0.05	0.11

FIG. 62

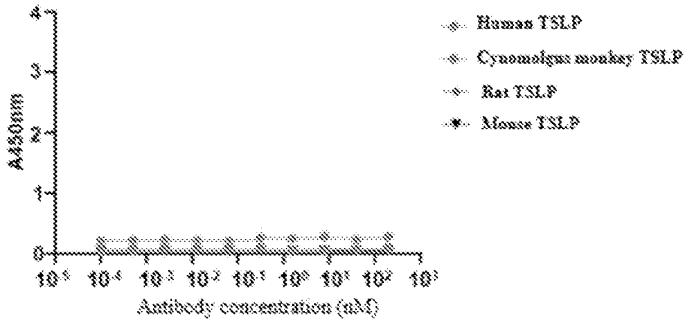


FIG. 63

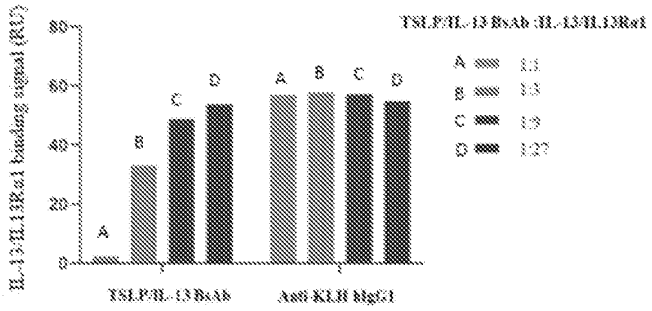
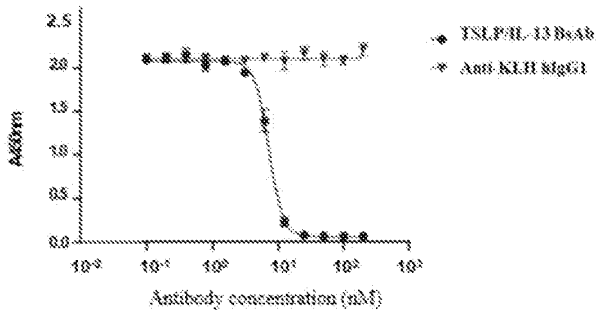
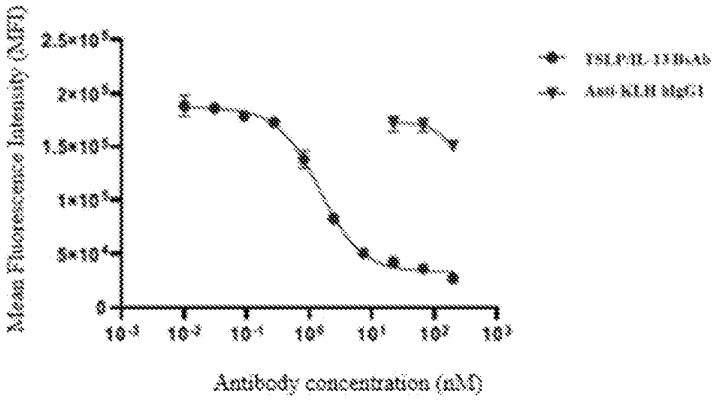


FIG. 64



	TSLP/IL-13 BsAb
IC_{50} (nM)	7.26

FIG. 65



	TSLP/IL-13 BsAb
IC_{50} (nM)	1.46

FIG. 66