Figure 1

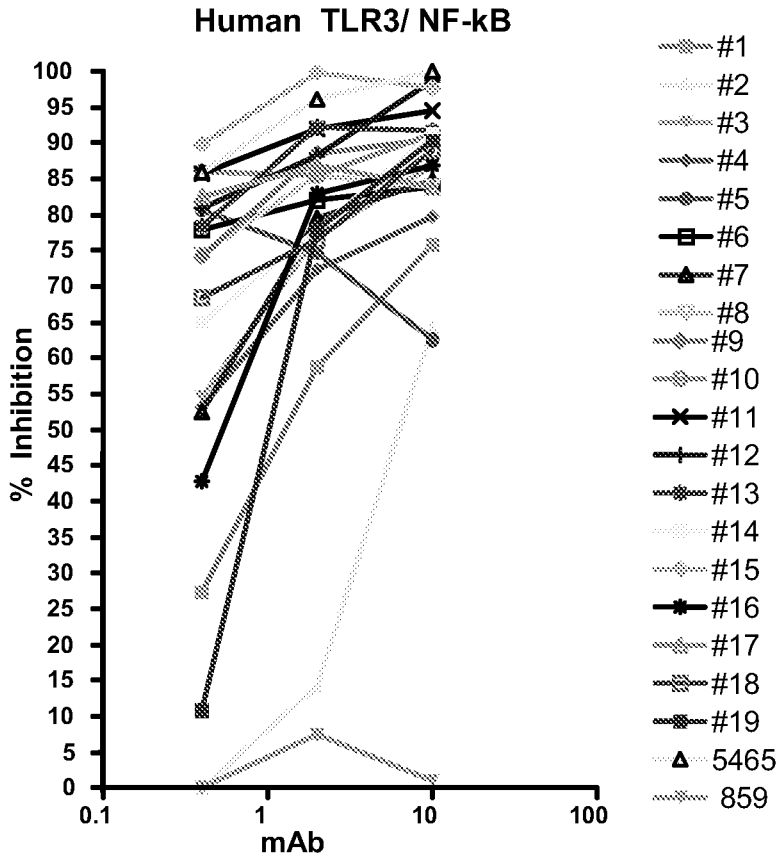

Human TLR3/ NF-kB
% Inhibition
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
0.1
1
10
100
mAb
#1
#2
#3
#4
#5
#6
#7
#8
#9
#10
#11
#12
#13
#14
#15
#16
#17
#18
#19
5465
859

Figure 2

Figure 2A

mAb [ug/ml]	IL6	IP-10	RANTES	MCP-1	IL8
#1 10	36	66	11	23	34
2	30	65	28	19	35
0.4	10	34	9	14	20
#2 10	35	52	13	11	35
2	41	76	22	26	33
0.4	21	57	19	13	13
#3 10	47	65	23	37	44
2	49	82	26	35	50
0.4	26	25	8	19	32
#4 10	98	100	100	83	87
2	46	81	31	29	50
0.4	42	54	17	28	45
#5 10	69	87	47	55	63
2	60	82	33	42	55
0.4	41	61	7	26	46
#6 10	70	89	49	56	66
2	57	81	29	38	58
0.4	58	80	29	35	56
#7 10	71	91	50	60	67
2	67	85	42	50	63
0.4	49	72	27	44	50
#8 10	61	78	29	41	41
2	39	37	3	32	34
0.4	46	67	14	31	46
#9 10	59	83	37	52	45
2	55	83	33	41	53
0.4	48	66	20	40	46
#10 10	75	91	60	60	65
2	62	82	37	48	58
0.4	53	73	30	48	51

Figure 2B

mAb [ug/ml]	IL6	IP-10	RANTES	MCP-1	IL8
#11 10	83	96	74	71	55
2	62	83	32	55	60
0.4	61	77	29	46	54
#12 10	74	91	52	57	27
2	69	88	39	53	53
0.4	55	79	28	43	51
#13 10	87	97	81	72	80
2	71	88	50	51	68
0.4	66	80	24	49	60
#14 10	84	90	59	70	80
2	72	85	40	57	66
0.4	61	80	35	46	57
#15 10	84	93	65	70	79
2	69	84	31	55	69
0.4	59	66	18	55	56
#16 10	75	84	42	54	65
2	-12	4	-20	-20	5
0.4	3	-17	-3	-17	6
#17 10	49	82	34	18	47
2	46	79	27	11	43
0.4	26	63	15	-1	34
#18 10	37	76	22	11	31
2	34	62	24	9	21
0.4	31	33	15	11	26
#19 10	32	41	11	9	39
2	32	59	12	14	36
0.4	33	47	5	-3	21
5465 10	78	94	63	48	68
2	56	79	36	29	55
0.4	57	77	25	33	47
859 10	16	57	3	10	17
2	29	55	10	10	10
0.4	1	36	-4	2	-3

Figure 3

Figure 3A

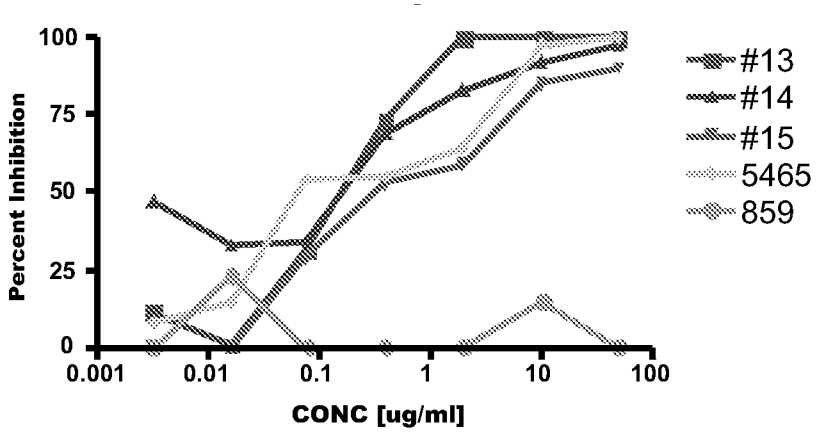


Figure 3B

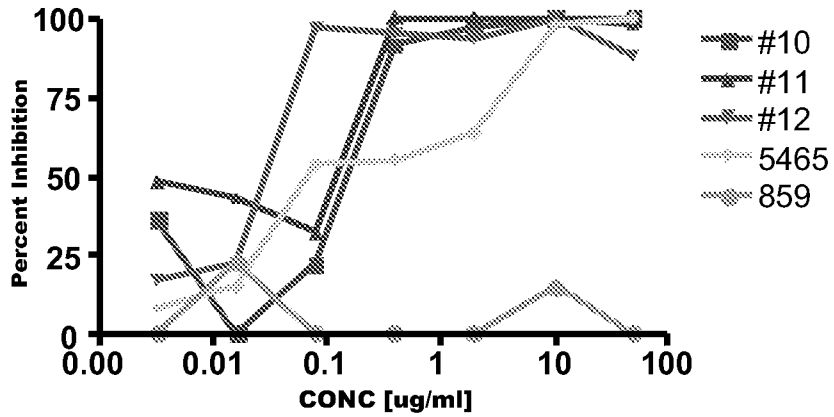


Figure 4

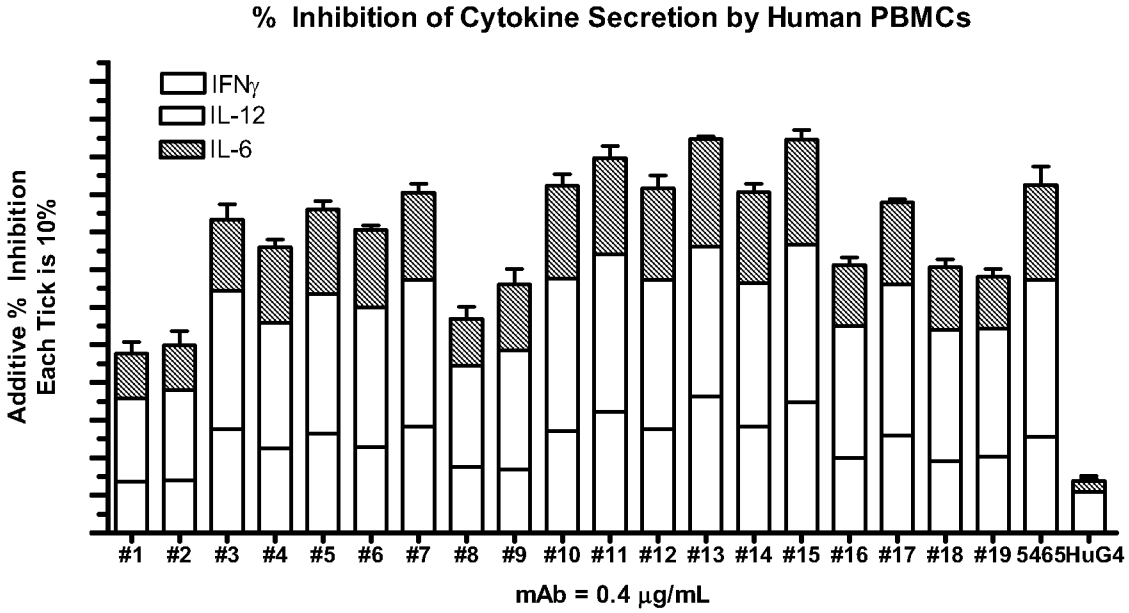

% Inhibition of Cytokine Secretion by Human PBMCs
IFNγ
IL-12
IL-6
Additive % Inhibition
Each Tick is 10%
#1 #2 #3 #4 #5 #6 #7 #8 #9 #10 #11 #12 #13 #14 #15 #16 #17 #18 #19 5465HuG4
mAb = 0.4 μg/mL

Figure 5

Figure 5A

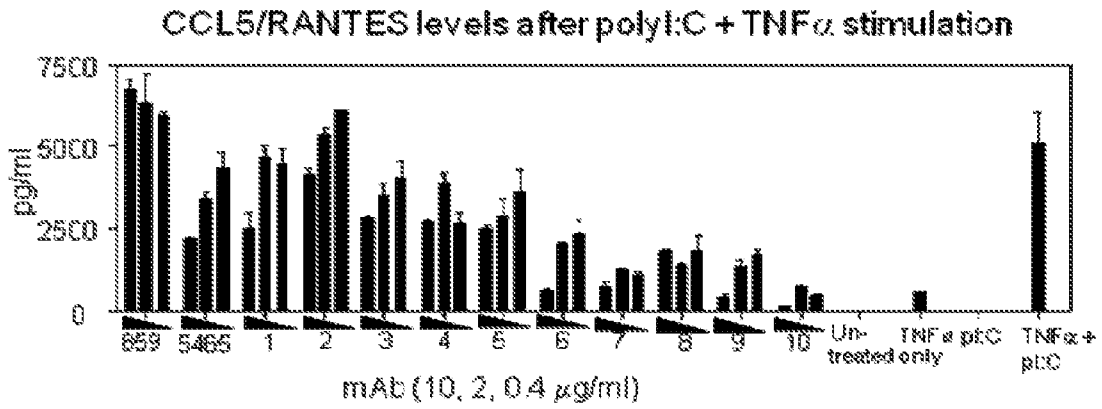


Figure 5B

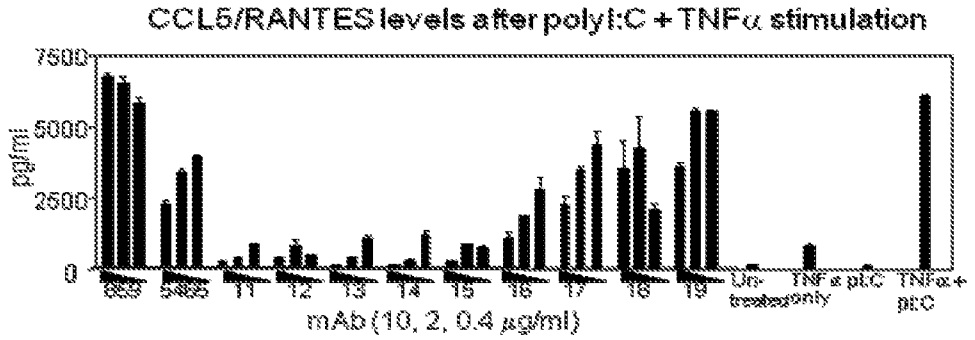


Figure 6

Figure 6A

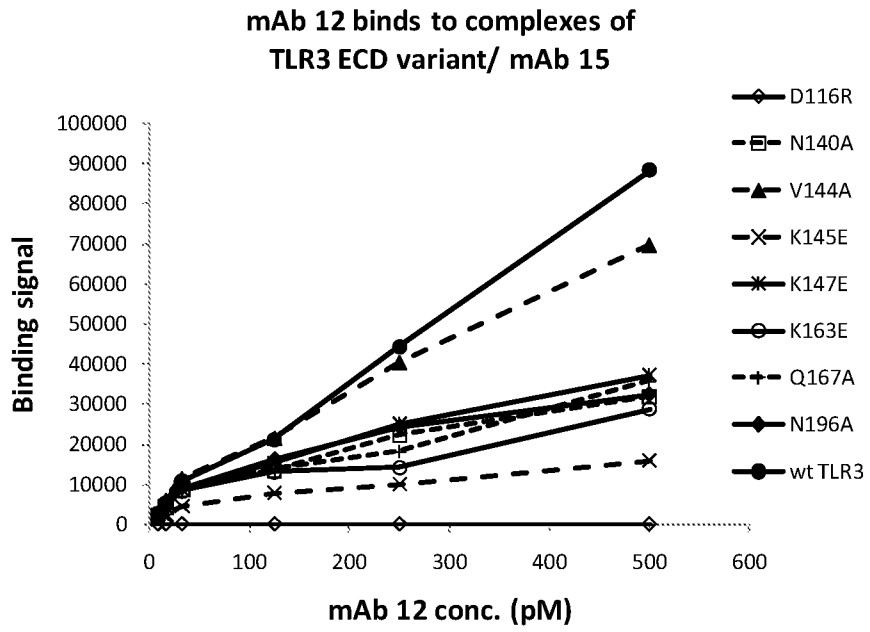


Figure 6B

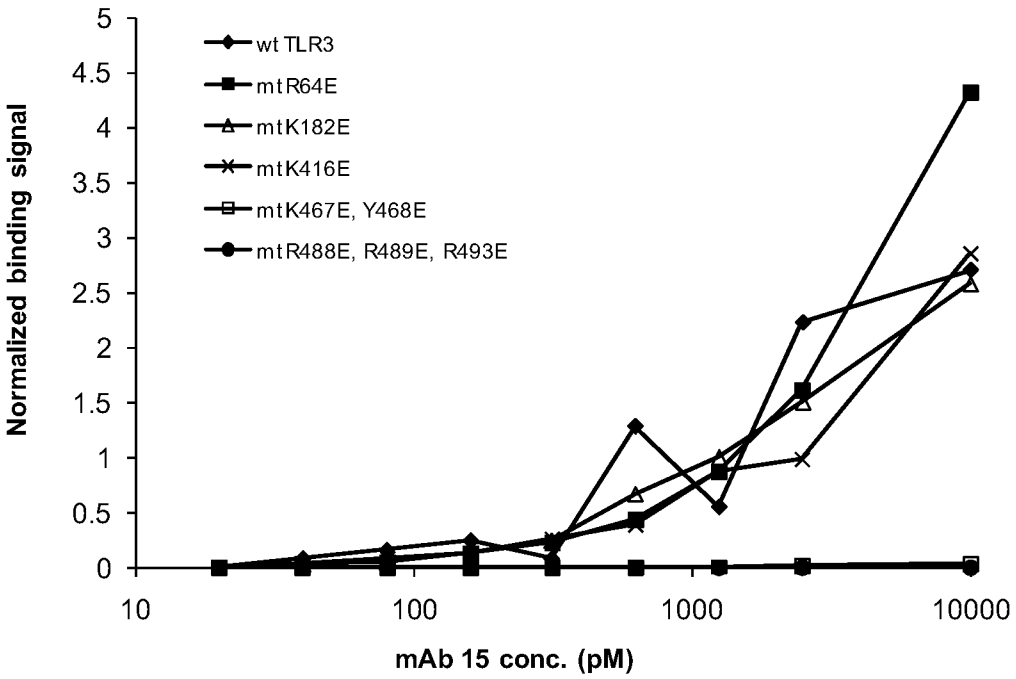

Normalized binding signal
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
10
100
1000
10000
mAb 15 conc. (pM)
wt TLR3
mtR64E
mtK182E
mtK416E
mtK467E, Y468E
mtR488E, R489E, R493E

Figure 6C

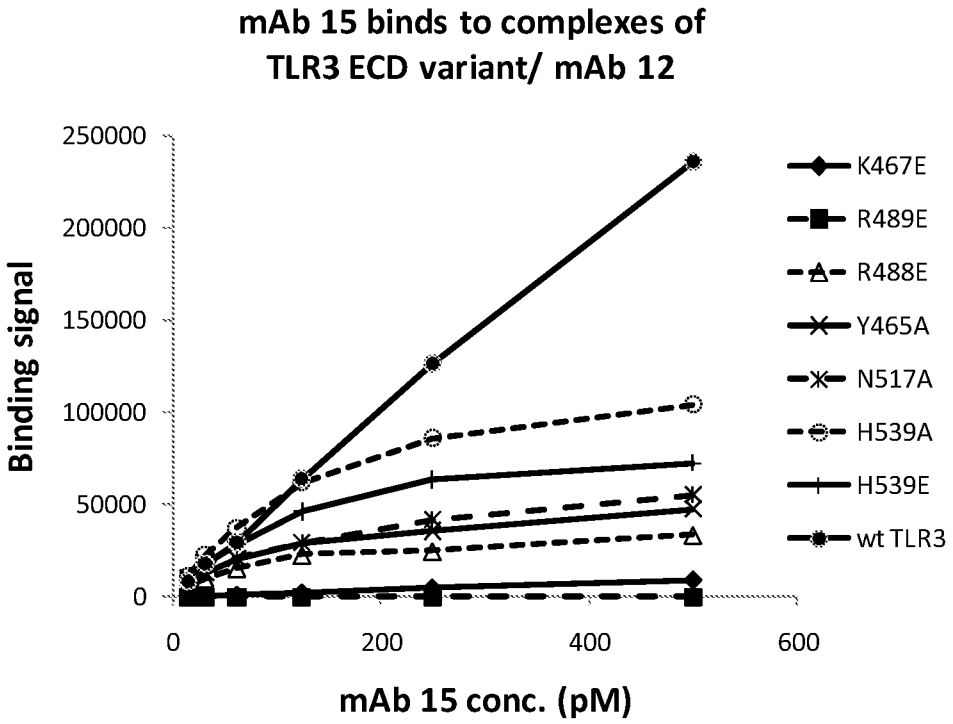

mAb 15 binds to complexes of
TLR3 ECD variant/ mAb 12
Binding signal
250000
200000
150000
100000
50000
0
0
200
400
600
mAb 15 conc. (pM)
K467E
R489E
R488E
Y465A
N517A
H539A
H539E
wt TLR3

Figure 7

Figure 7A

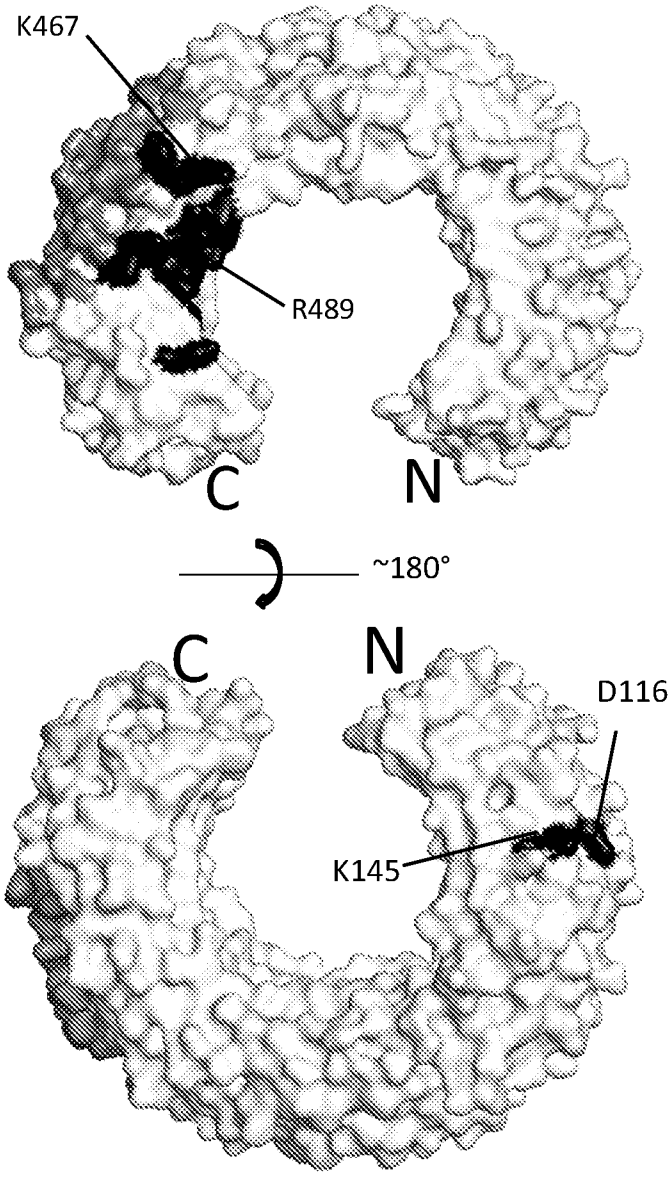


Figure 7B

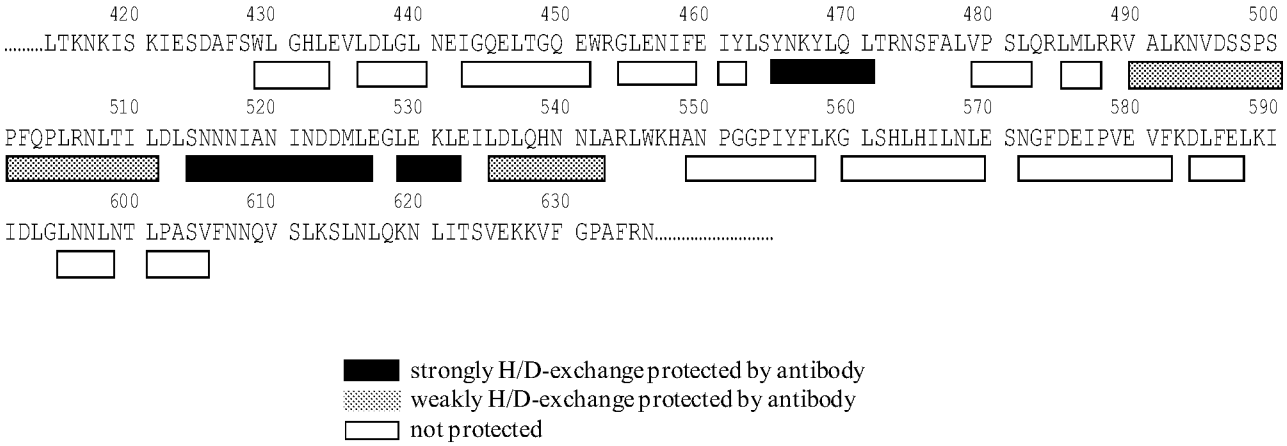
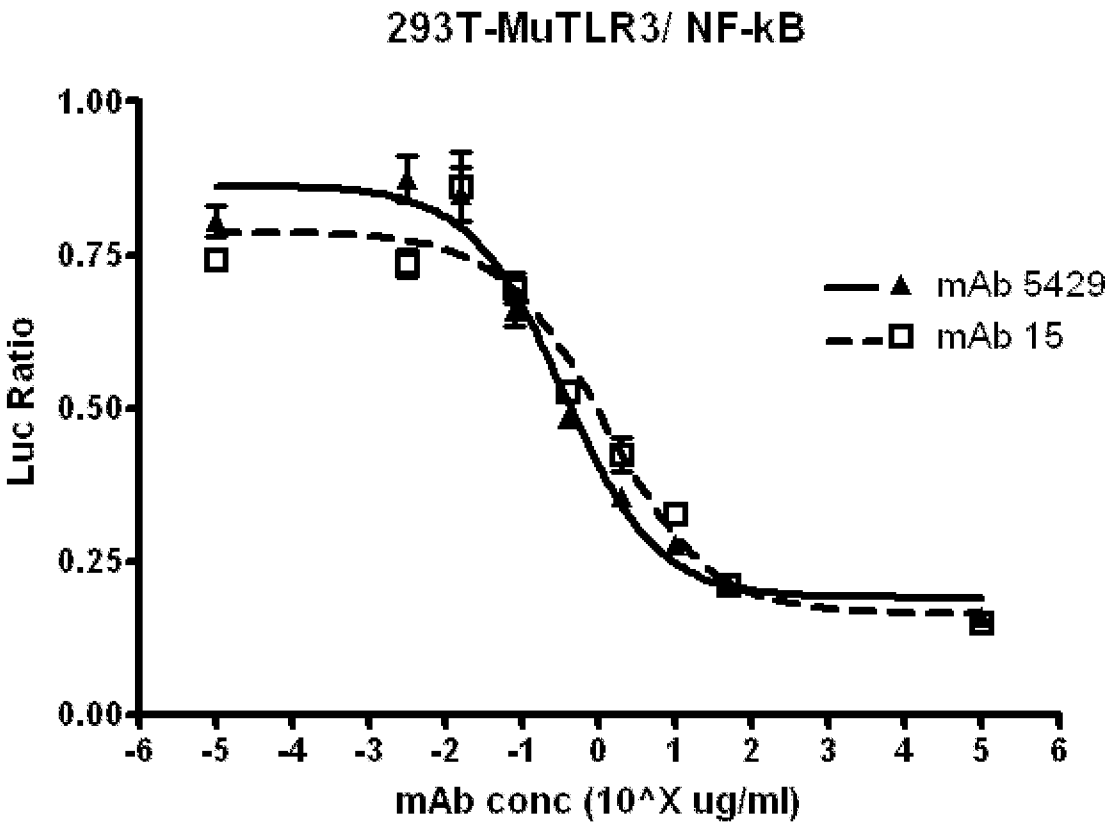

420 430 440 450 460 470 480 490 500
.....LTKNKIS KIESDAFSWL GHLEVLDLGL NEIGQELTGQ EWRGLENIFE IYLSYNKYLQ LTRNSFALVP SLQRLMLRRV ALKNVDSSPS
510 520 530 540 550 560 570 580 590
PFQPLRNLTI LDLSNNNIAN INDDMLEGLE KLEILDLQHN NLARLWKHAN PGGPIYFLKG LSHLHILNLE SNGFDEIPVE VFKDLFELKI
600 610 620 630
IDLGLNNLNT LPASVFNNQV SLKSLNLQKN LITSVEKKVF GPAFRN.....
strongly H/D-exchange protected by antibody
weakly H/D-exchange protected by antibody
not protected

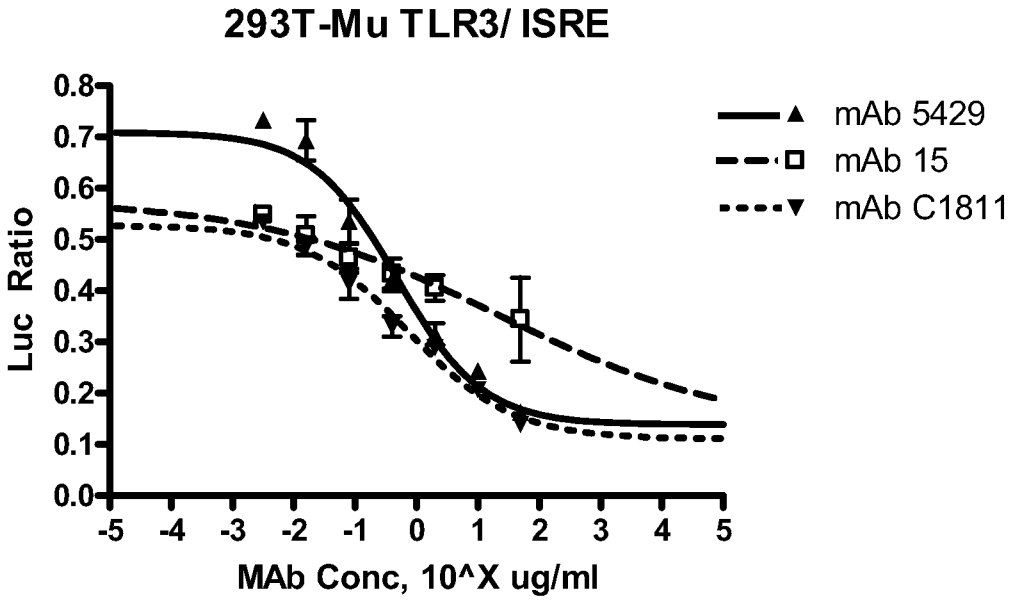
Figure 8

Figure 8A



IC50 (ug/ml)	5429	mAb 15
	0.3437	1.176

Figure 8B



	mAb 5429	mAb 15	mAb C1811
EC50 ug/ml	0.4856	22.13	0.7481

Figure 9

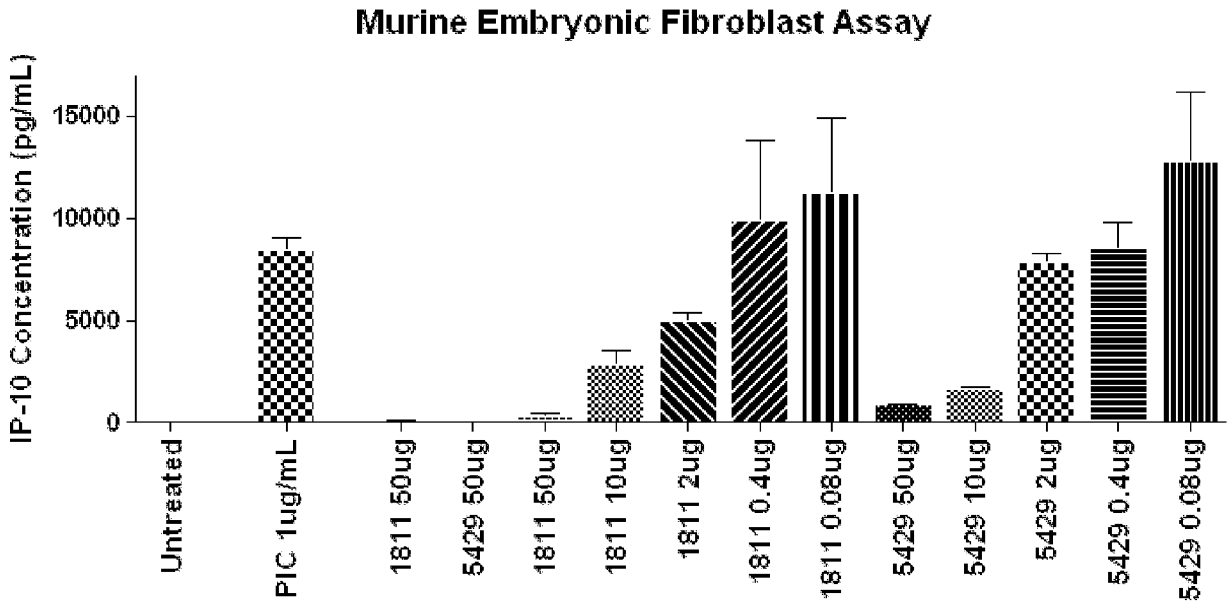

Murine Embryonic Fibroblast Assay
IP-10 Concentration (pg/mL)
15000
10000
5000
0
Untreated
PIC 1ug/mL
1811 50ug
5429 50ug
1811 50ug
1811 10ug
1811 2ug
1811 0.4ug
1811 0.08ug
5429 50ug
5429 10ug
5429 2ug
5429 0.4ug
5429 0.08ug

Figure 10

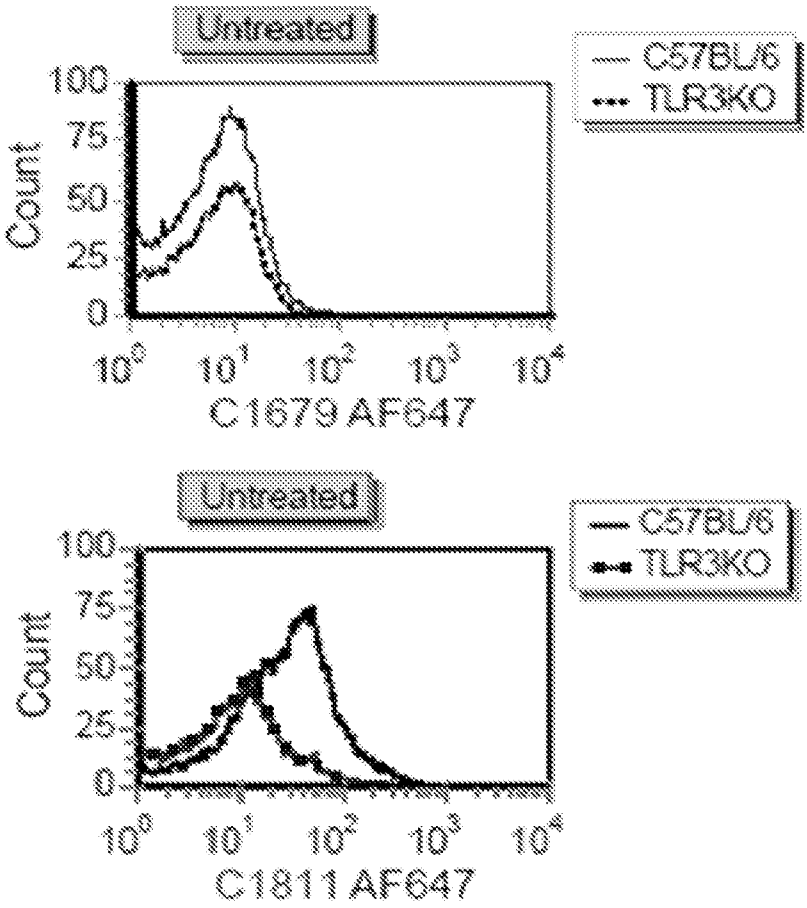

Untreated
C57BL/6
TLR3KO
Count
100
75
50
25
0
10^0
10^1
10^2
10^3
10^4
C1679 AF647
Untreated
C57BL/6
TLR3KO
Count
100
75
50
25
0
10^0
10^1
10^2
10^3
10^4
C1811 AF647

Figure 11

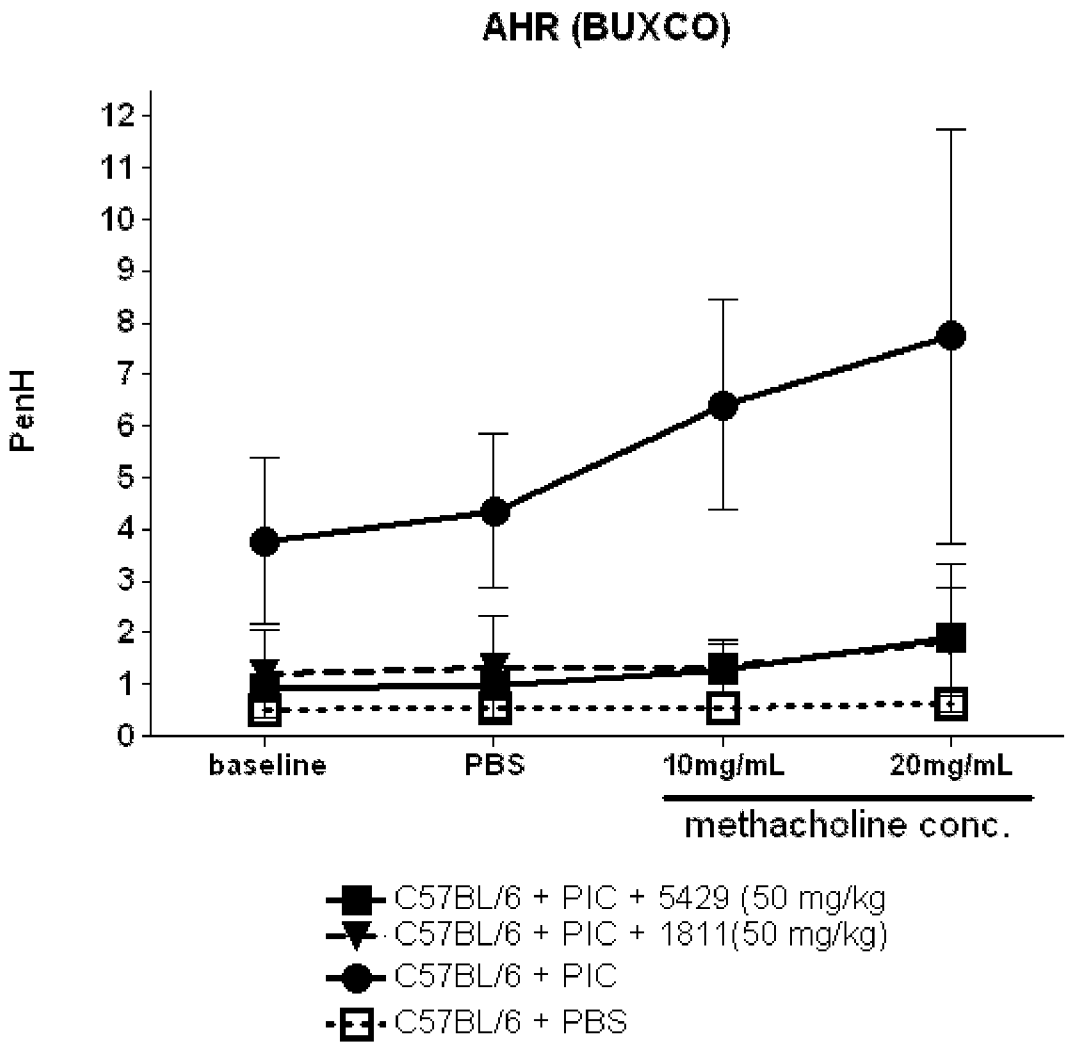

AHR (BUXCO)
PenH
12
11
10
9
8
7
6
5
4
3
2
1
0
baseline
PBS
10mg/mL
20mg/mL
methacholine conc.
C57BL/6 + PIC + 5429 (50 mg/kg
C57BL/6 + PIC + 1811(50 mg/kg)
C57BL/6 + PIC
C57BL/6 + PBS

Figure 12

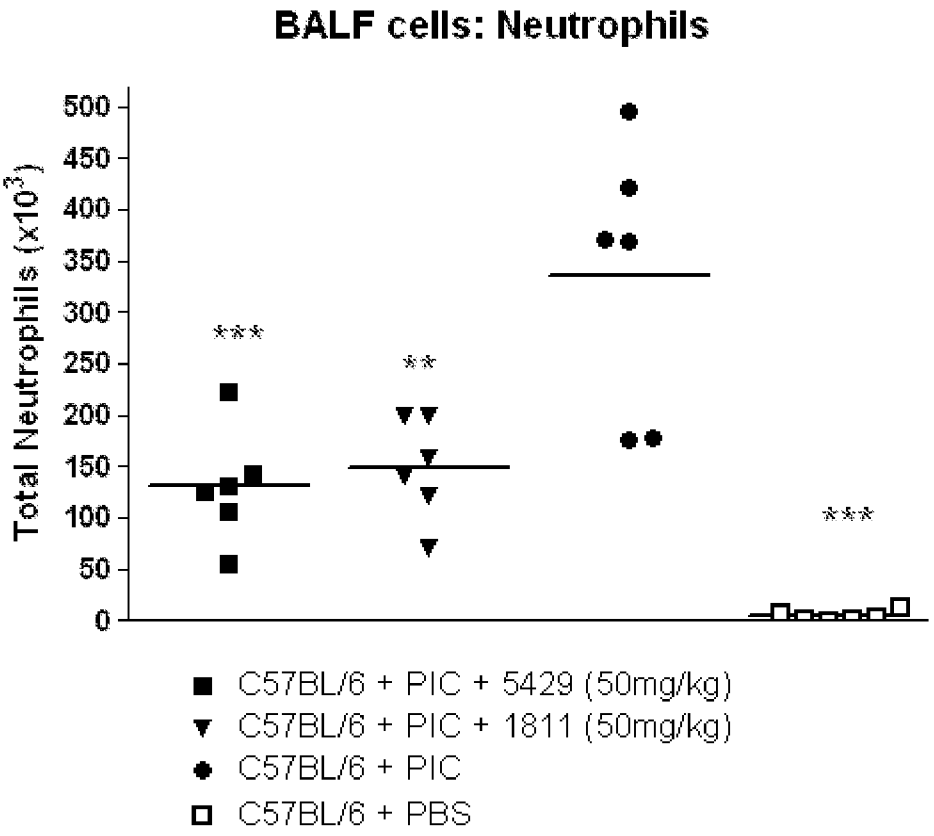

BALF cells: Neutrophils
Total Neutrophils (x10^3)
500
450
400
350
300
250
200
150
100
50
0
***
**
***
C57BL/6 + PIC + 5429 (50mg/kg)
C57BL/6 + PIC + 1811 (50mg/kg)
C57BL/6 + PIC
C57BL/6 + PBS

Figure 13

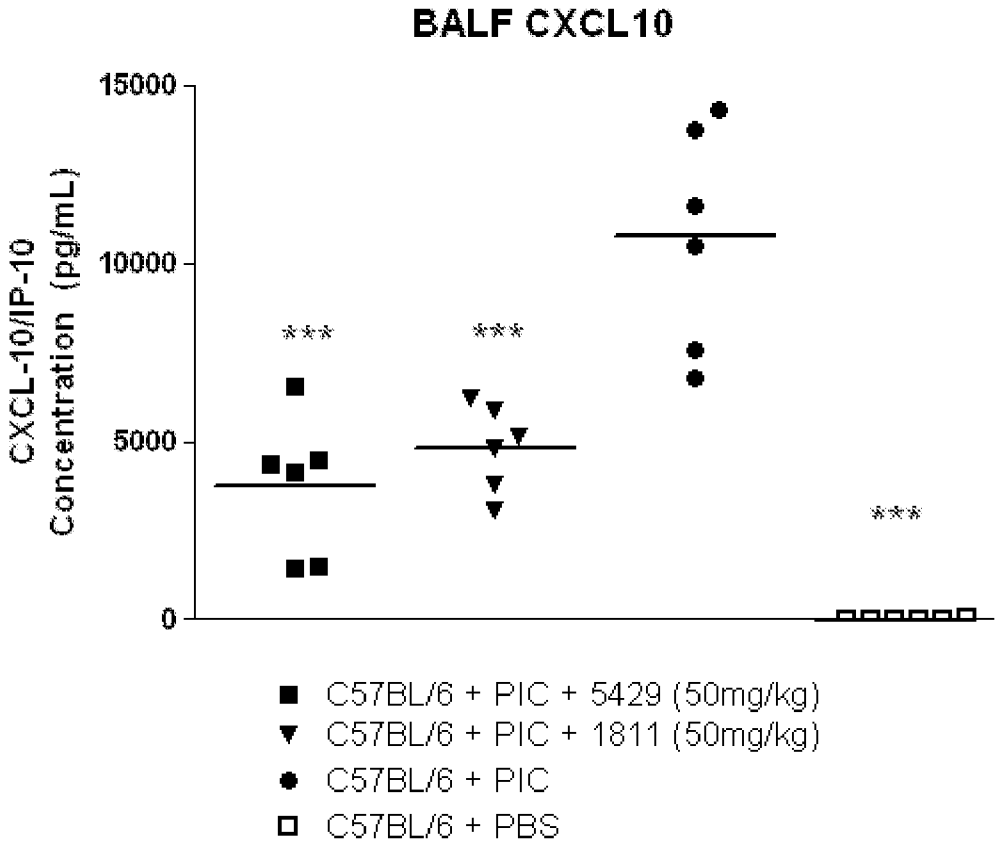
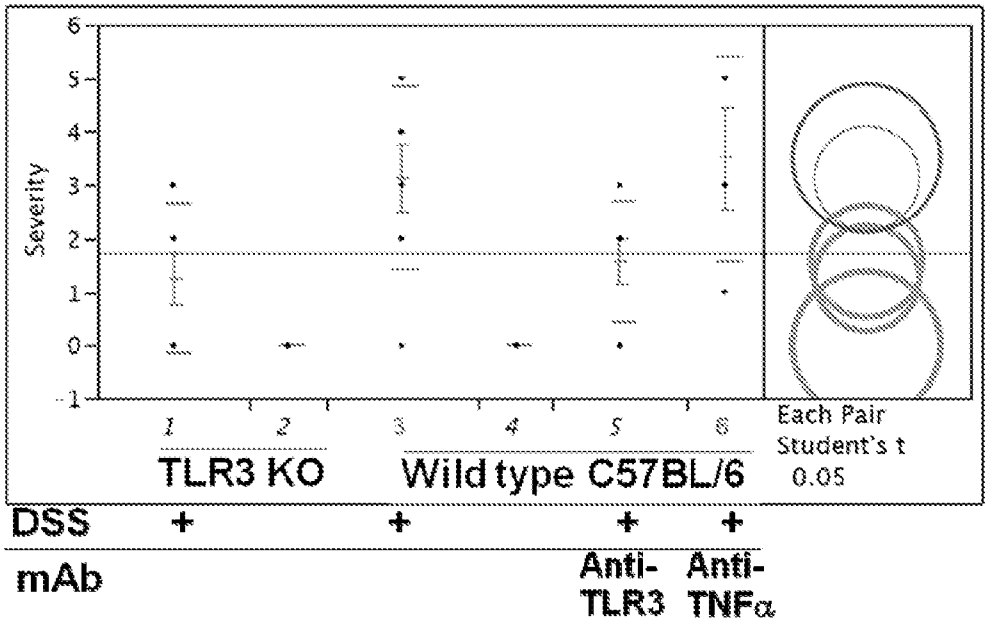

BALF CXCL10
CXCL-10/IP-10 Concentration (pg/mL)
15000
10000
5000
0
***
***
***
C57BL/6 + PIC + 5429 (50mg/kg)
C57BL/6 + PIC + 1811 (50mg/kg)
C57BL/6 + PIC
C57BL/6 + PBS

Figure 14



BLINDED scoring based on: Single cell necrosis, Epithelial ulceration, Epithelial sloughing, Cryptal abscess, Cryptal cell proliferation, LP Granulation tissue Submucosal granulation tissue, Submucosal neutrophils, Submucosal edema

Figure 15

Figure 15A

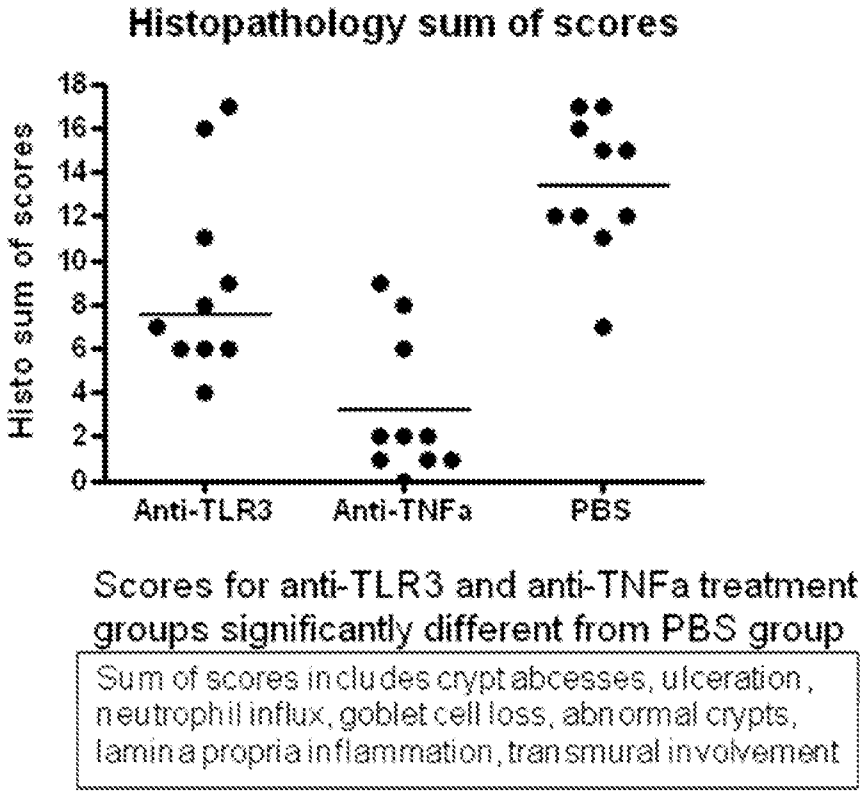


Figure 15B

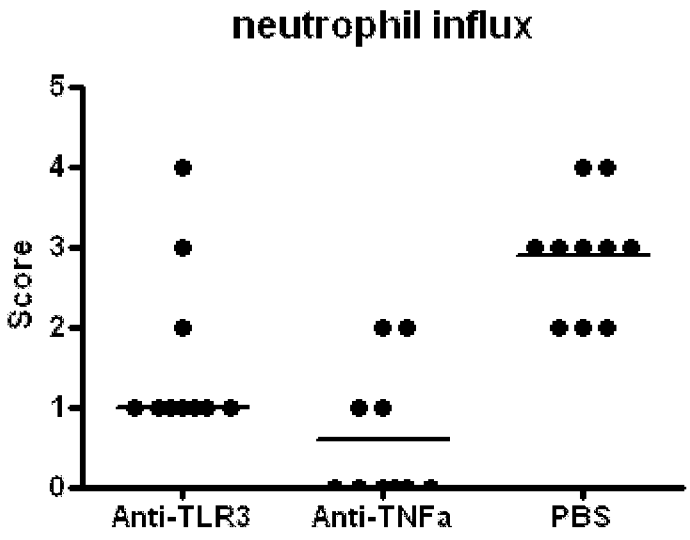


Figure 16

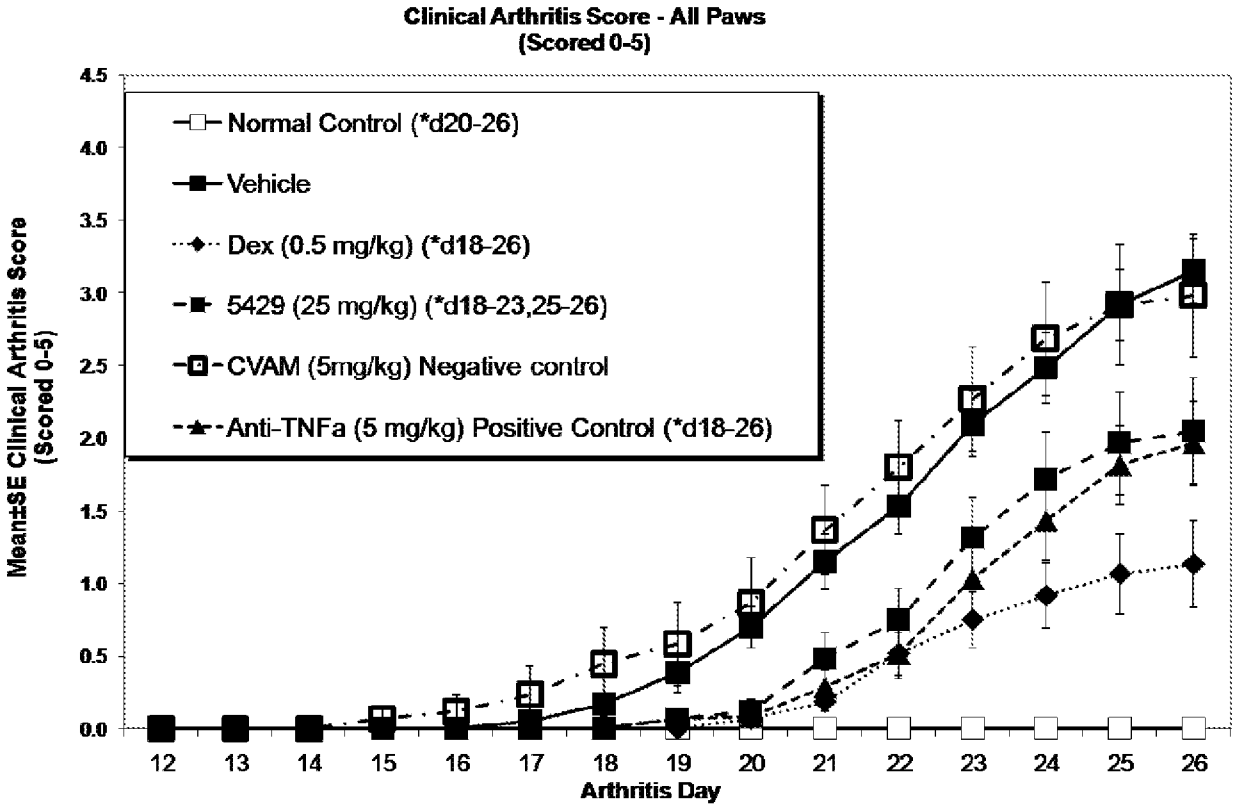

Clinical Arthritis Score - All Paws
(Scored 0-5)
Mean±SE Clinical Arthritis Score
(Scored 0-5)
Normal Control (*d20-26)
Vehicle
Dex (0.5 mg/kg) (*d18-26)
5429 (25 mg/kg) (*d18-23,25-26)
CVAM (5mg/kg) Negative control
Anti-TNFa (5 mg/kg) Positive Control (*d18-26)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
Arthritis Day

Figure 17

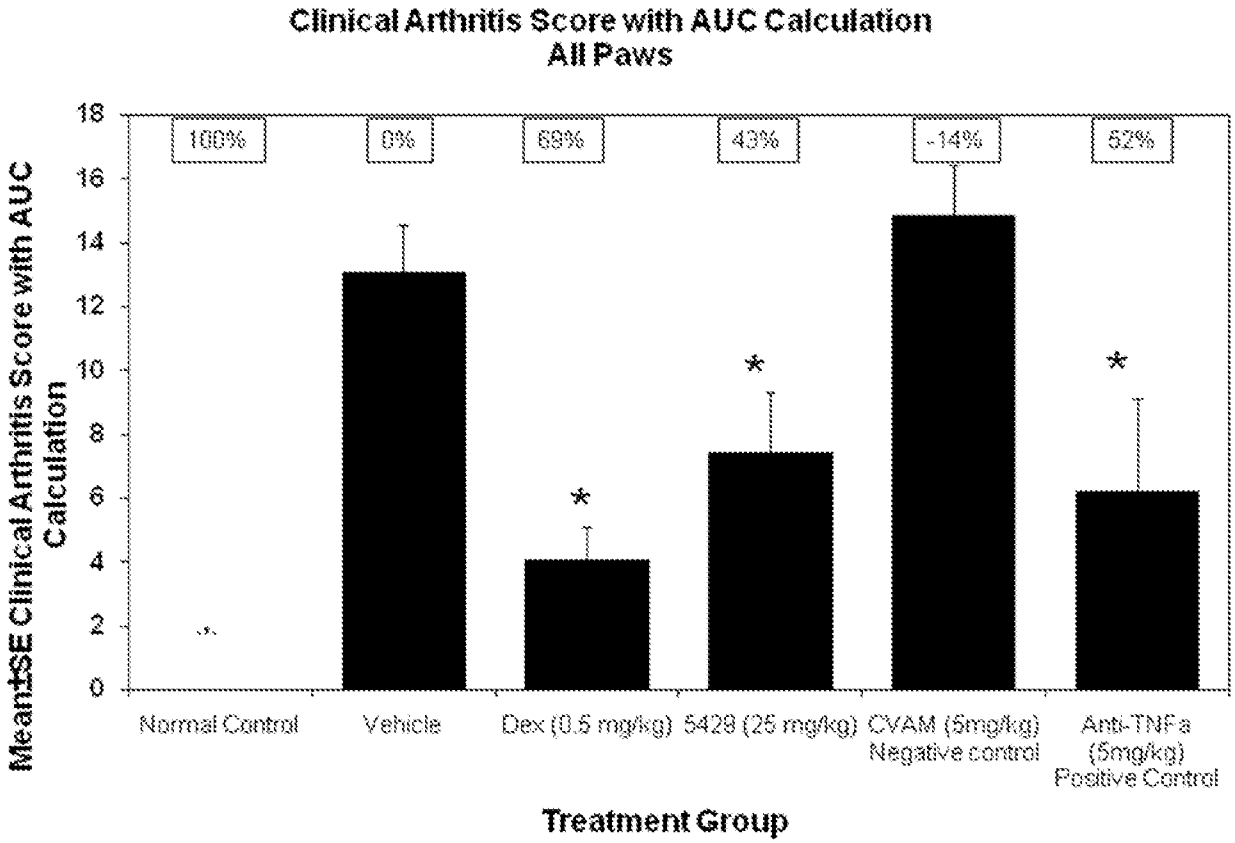

Clinical Arthritis Score with AUC Calculation
All Paws
Mean±SE Clinical Arthritis Score with AUC Calculation
18
16
14
12
10
8
6
4
2
0
100%
0%
69%
43%
-14%
52%
*
*
*
Normal Control
Vehicle
Dex (0.5 mg/kg)
5428 (25 mg/kg)
CVAM (5mg/kg) Negative control
Anti-TNFa (5mg/kg) Positive Control
Treatment Group

Figure 18

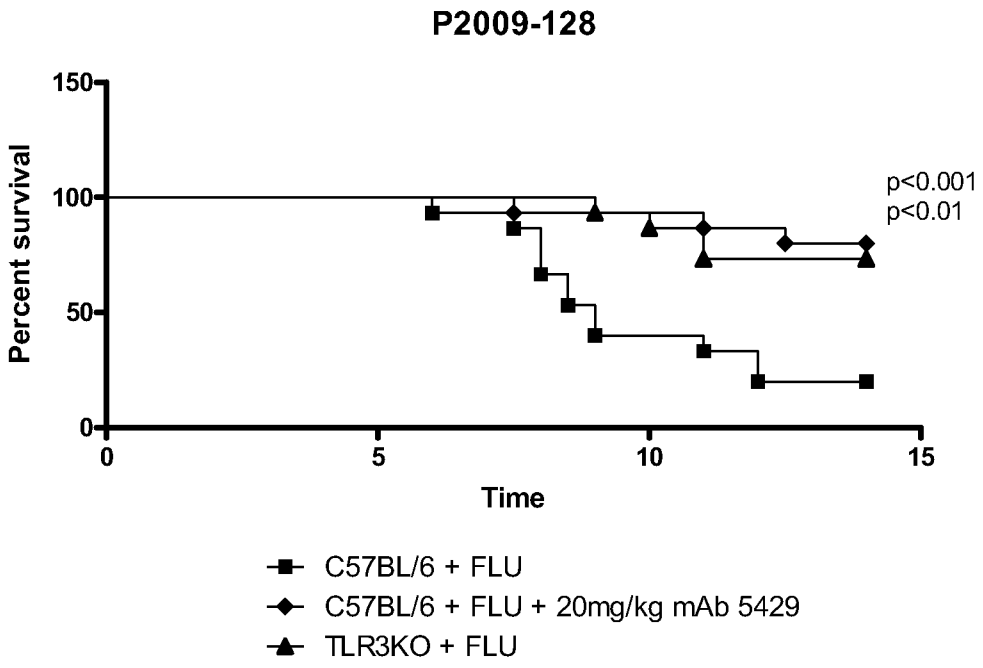
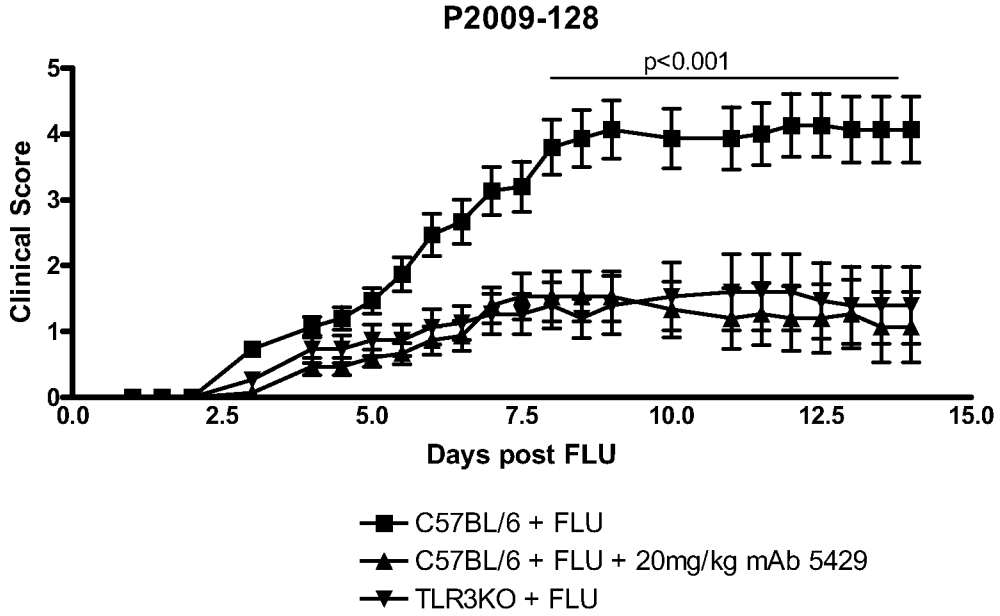

P2009-128
150
100
50
0
Percent survival
0
5
10
15
Time
p<0.001
p<0.01
C57BL/6 + FLU
C57BL/6 + FLU + 20mg/kg mAb 5429
TLR3KO + FLU

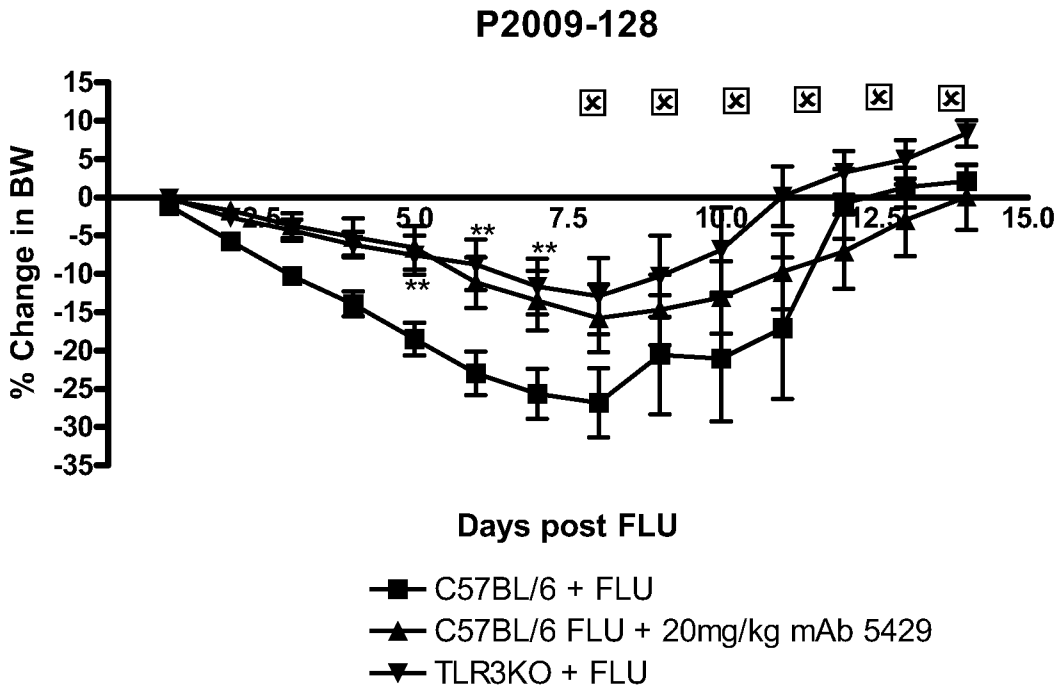
Figure 19

Clinical Score following administration of influenza A/PR/8/34.[3]



Significant Differences of mAb Treated and KO groups vs. C57BL/6 +flu after day 8

Figure 20



Significant differences between mAb treated and KO groups vs. C57BL/6 +flu, $p<0.01$ at day 5, 6, and 7

Figure 21

Figure 21A.

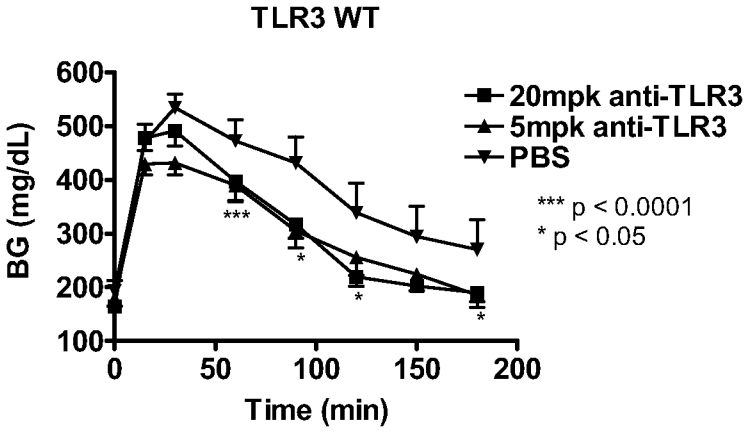


Figure 21B

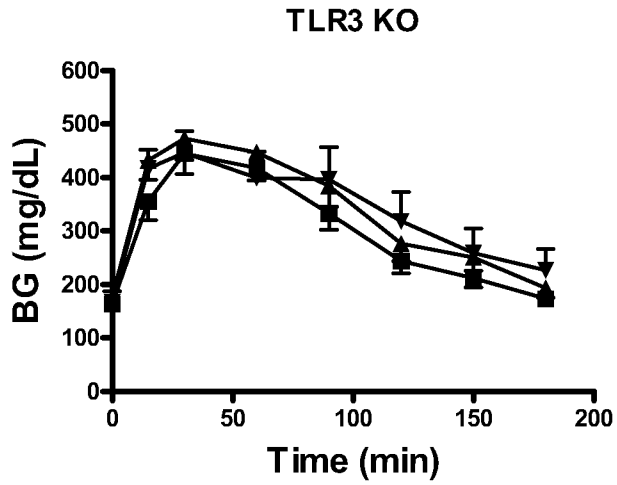


Figure 22

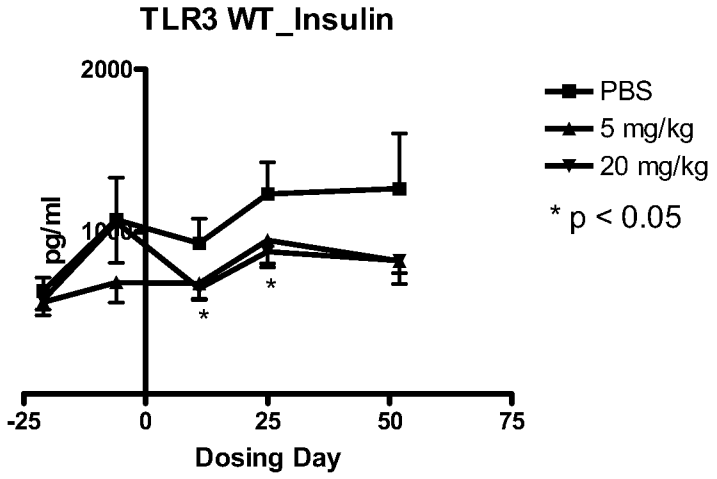

TLR3 WT_Insulin
2000
pg/ml
-25
0
25
50
75
Dosing Day
PBS
5 mg/kg
20 mg/kg
* p < 0.05

Figure 23

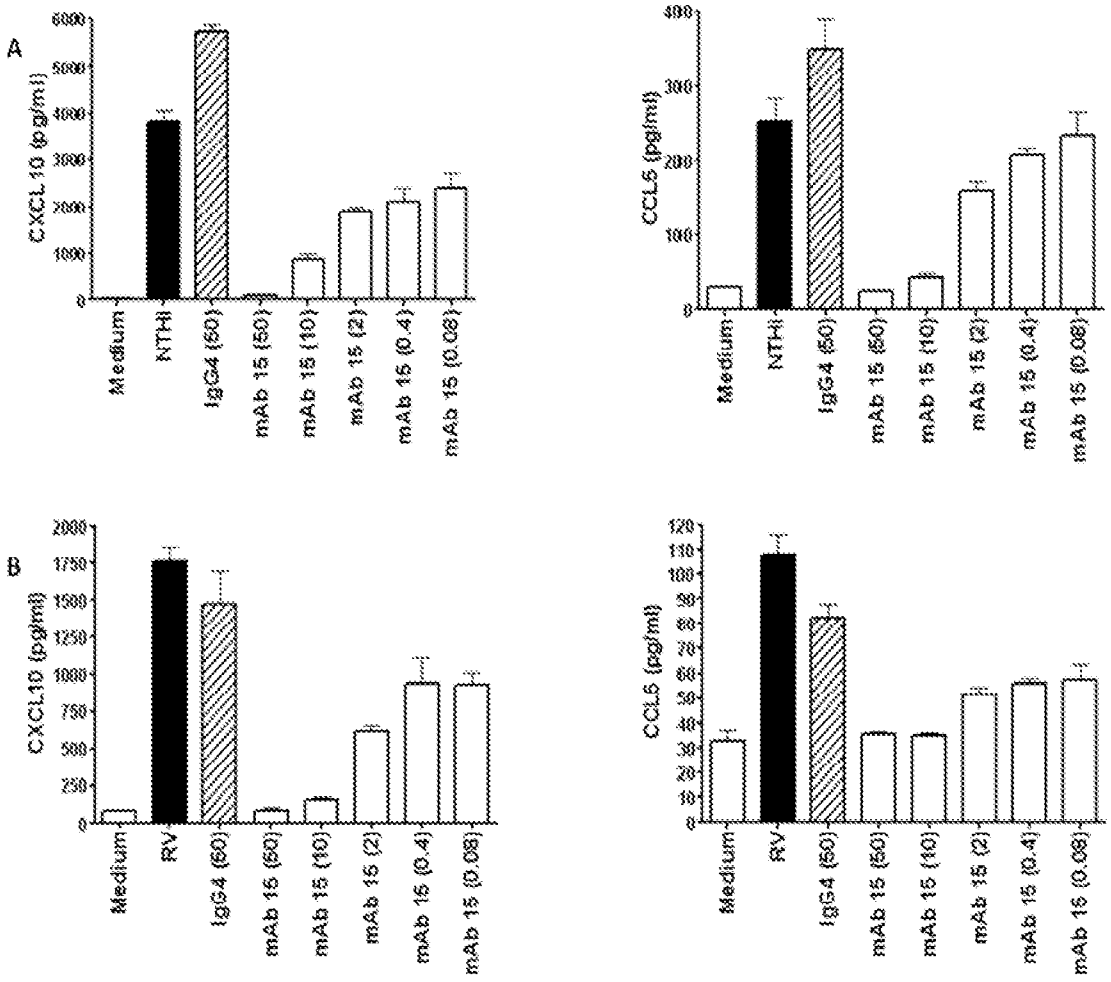

A
CXCL 10 (pg/ml)
CCL5 (pg/ml)
B
CXCL10 (pg/ml)
CCL5 (pg/ml)
Medium
NTHI
RV
IgG4 (60)
mAb 15 (60)
mAb 15 (10)
mAb 15 (2)
mAb 15 (0.4)
mAb 15 (0.08)

Figure 24

Figure 24A

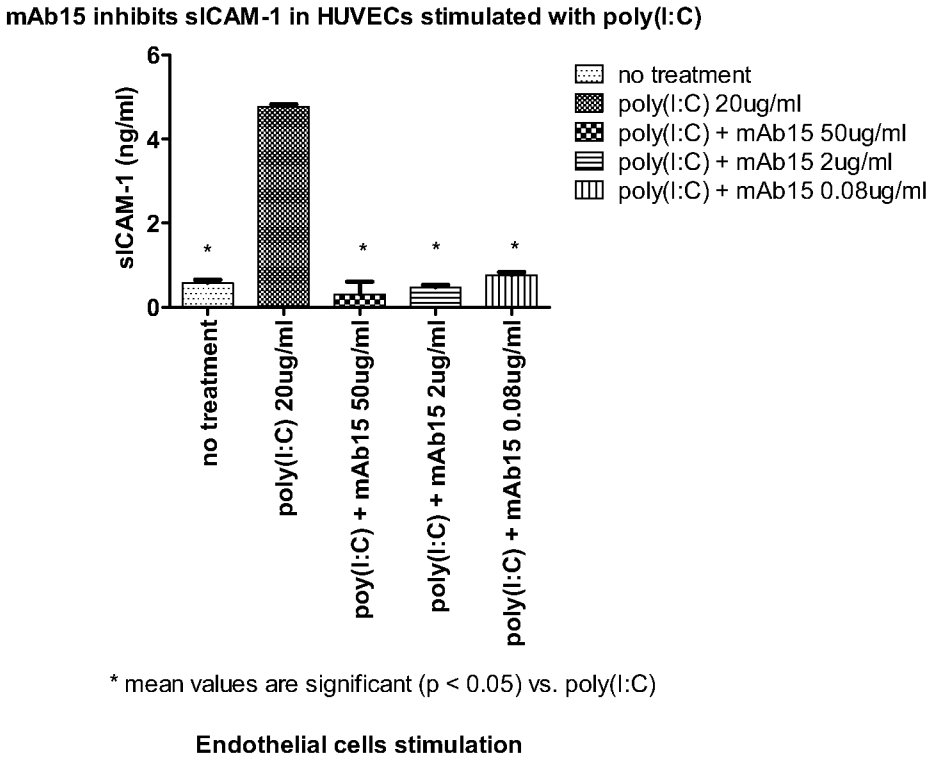


Figure 24B

