FIGURE 1

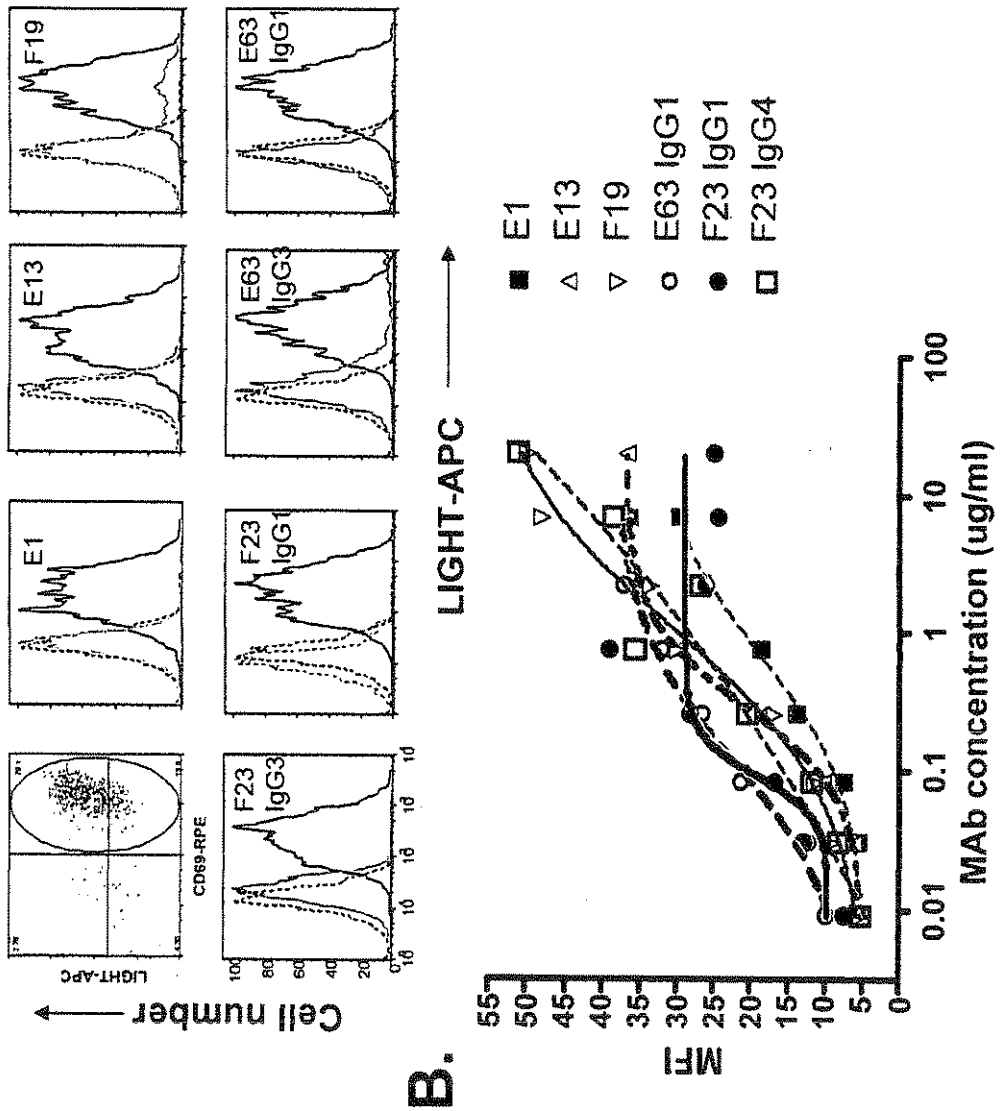
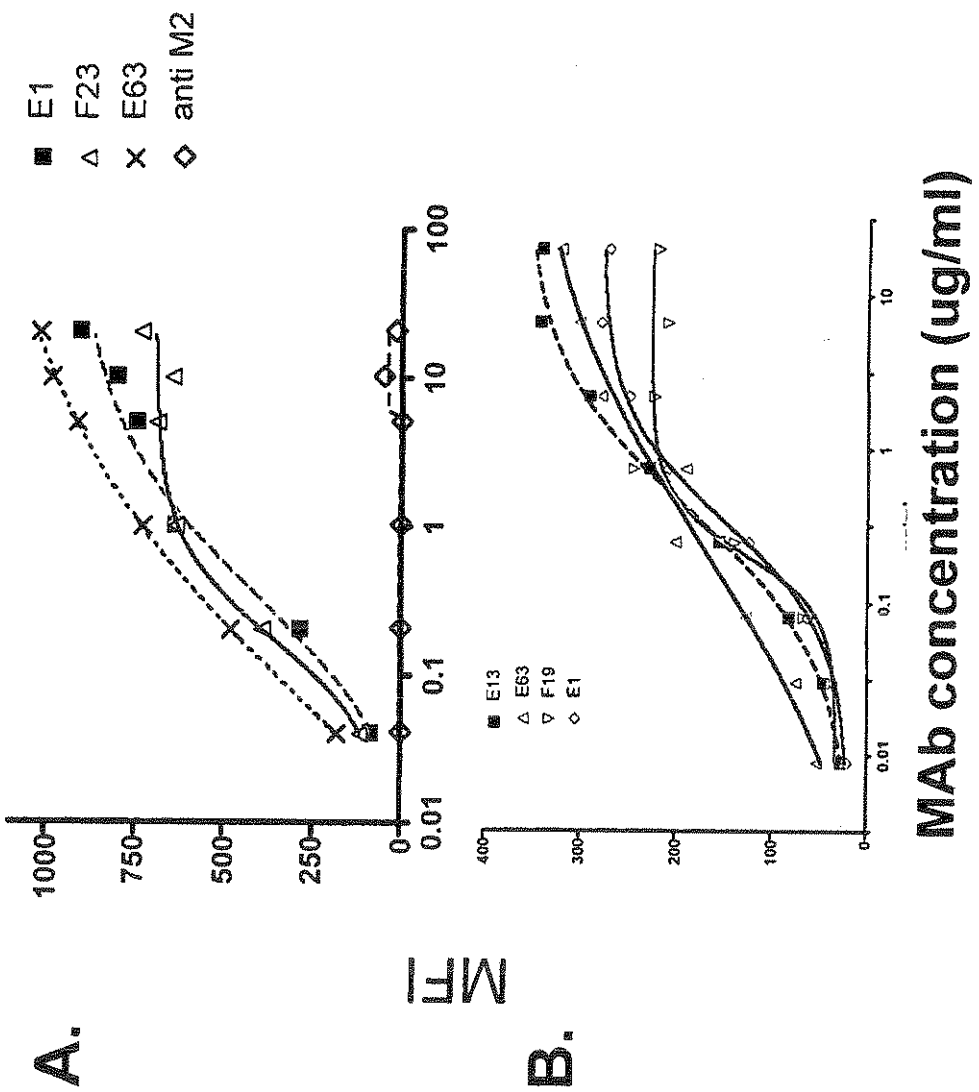

A.
Cell number
LIGHT-APC
CD69-RPE
E1
E13
F19
F23 IgG3
F23 IgG1
E63 IgG3
E63 IgG1
B.
LIGHT-APC
MFI
MAb concentration (ug/ml)
E1
E13
F19
E63 IgG1
F23 IgG1
F23 IgG4

FIGURE 2


A.
E1
F23
E63
anti M2
1000
750
500
250
0
0.01
0.1
1
10
100
MFI
B.
E13
E63
F19
E1
400
300
200
100
0
0.01
0.1
1
10
MAb concentration (ug/ml)

# FIGURE 3

| Name | Binding to HuLIGHT on EL4GFP HuLIGHT Cells | | Blocking Cell Surface LIGHT Binding to HVEM:Fc | | | | Blocking Cell Surface LIGHT Binding to LTBR:Fc | | | | Blocking CCL20 | Isotype | Epitope Group |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | relative affinity | EC50 (µg/ml) | Human | IC50 (µg/ml) | Mouse | IC50 (µg/ml) | Human | IC50 (µg/ml) | Mouse | IC50 (µg/ml) | | | |
| **124E 63** | +++ | 0.1 | ++++ | 0.19 | - | - | ++++ | 1.3 | +++ | 0.43 | + | IgG3 | A |
| **124E 1** | +++ | 0.32 | ++++ | 0.2 | +++ | 0.64 | +++ | 1.7 | +++ | 2.8 | + | IgG1 | A |
| **124F 23** | +++ | 0.18 | +++ | 0.29 | - | - | +++ | 2.1 | - | - | + | IgG4 | B |
| **124E13** | +++ | 0.3 | ++ | 0.41 | NA | NA | +++ | 1.8 | +++ | NA | + | IgG1 | A |
| **124F 19** | +++ | 0.21 | NA | NA | NA | NA | ++ | 4.2 | ++ | 3.9 | + | IgG1 | B |

# FIGURE 4

| | Coat mAb | | | | |
|---|---|---|---|---|---|
| Pre-Inc. mAb | E1 | E13 | E63 | F19 | F23 |
| E1 | 95 | 82 | 89 | 0 | 0 |
| E13 | 98 | 97 | 98 | 0 | 0 |
| E63 | 87 | 90 | 84 | 0 | 22 |
| F19 | 0 | 0 | 0 | 98 | 98 |
| F23 | 0 | 0 | 0 | 53 | 87 |

| | |
|---|---|
| hLIGHT Epitope #1 ("E antibodies") | E1, E13, E63 |
| hLIGHT Epitope #2 ("F antibodies") | F19, F23 |

FIGURE 5

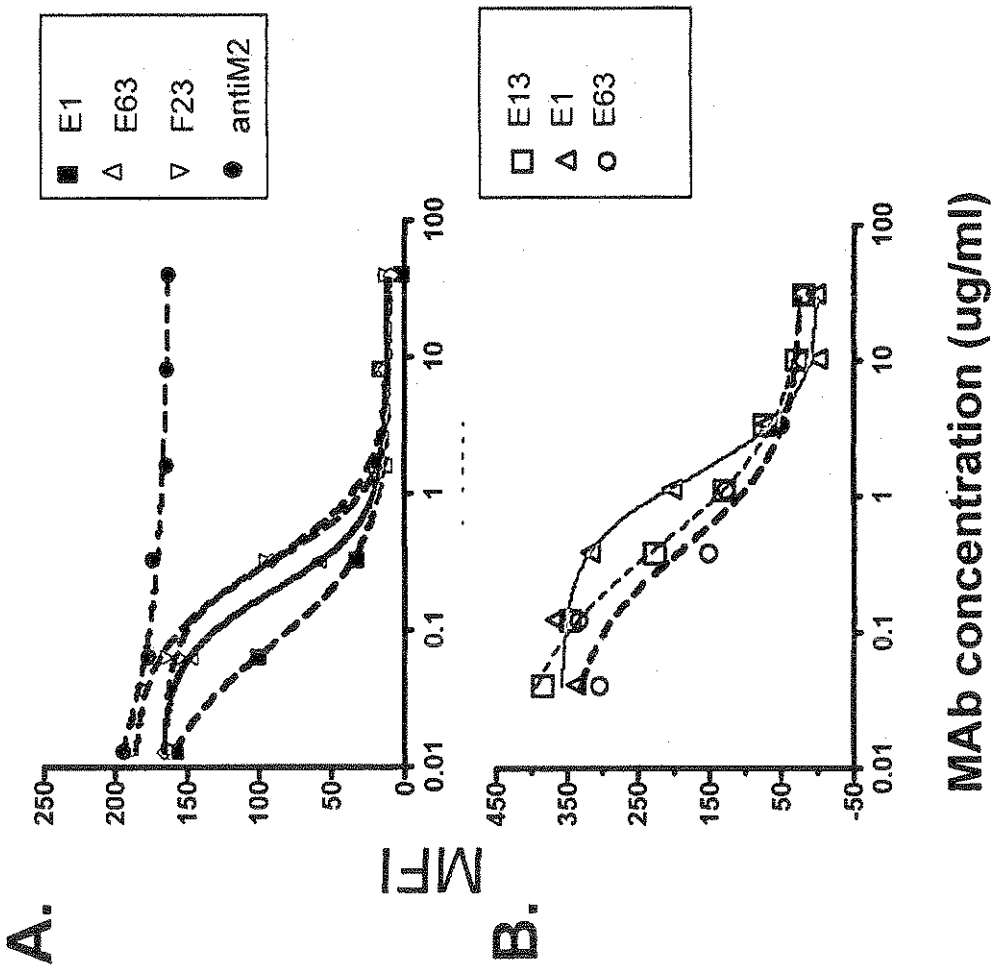

A.
E1
E63
F23
antiM2
MFI
250
200
150
100
50
0
0.01
0.1
1
10
100
B.
E13
E1
E63
450
350
250
150
50
-50
0.01
0.1
1
10
100
MAb concentration (ug/ml)

FIGURE 6

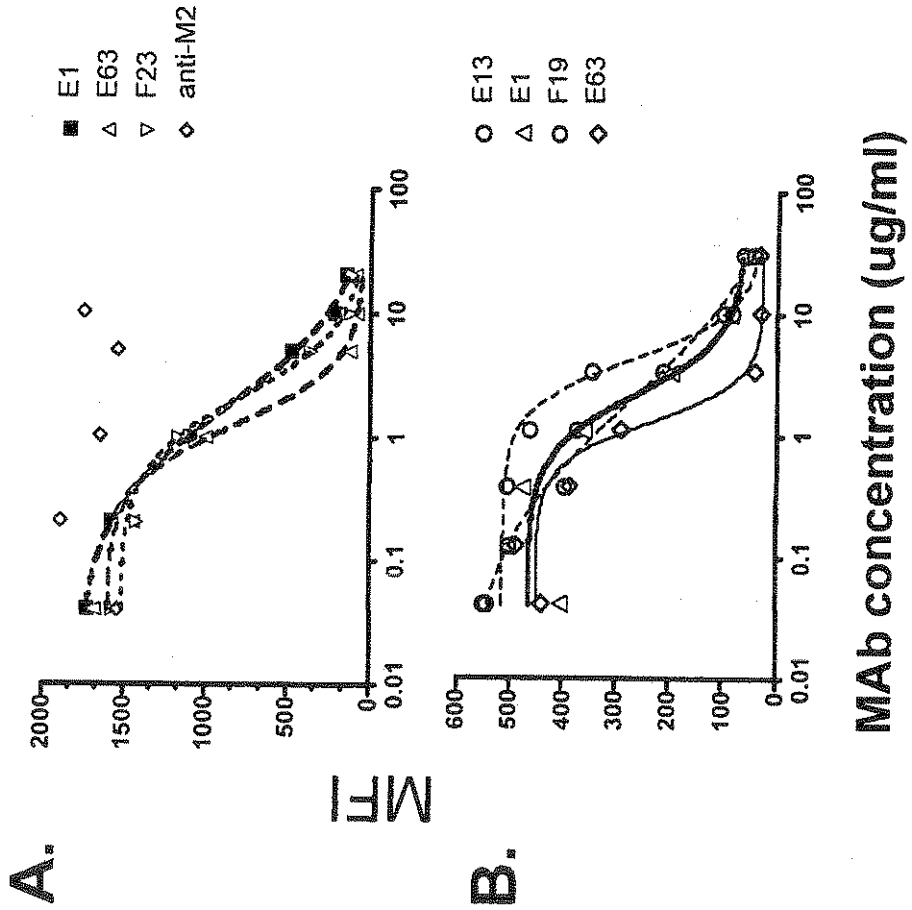

A.
E1
E63
F23
anti-M2
MTI
2000
1500
1000
500
0
0.01
0.1
1
10
100
B.
E13
E1
F19
E63
600
500
400
300
200
100
0
0.01
0.1
1
10
100
MAb concentration (ug/ml)

FIGURE 7

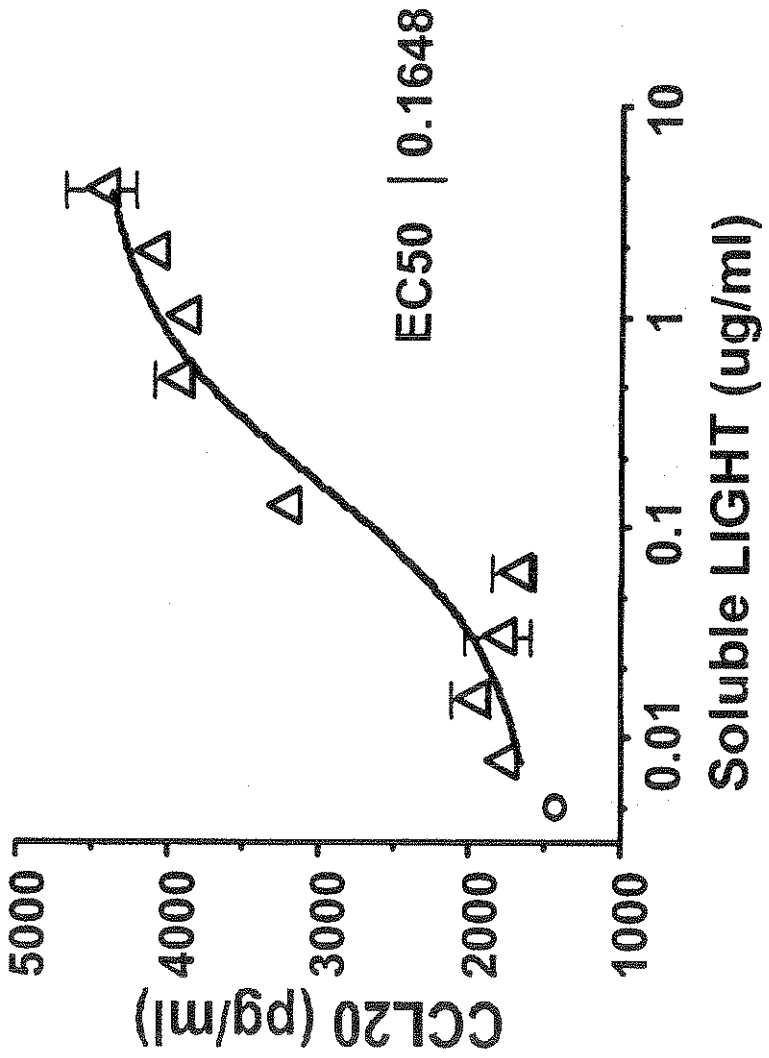

CCL20 (pg/ml)
5000
4000
3000
2000
1000
0
0.01
0.1
1
10
Soluble LIGHT (ug/ml)
EC50 | 0.1648

FIGURE 8

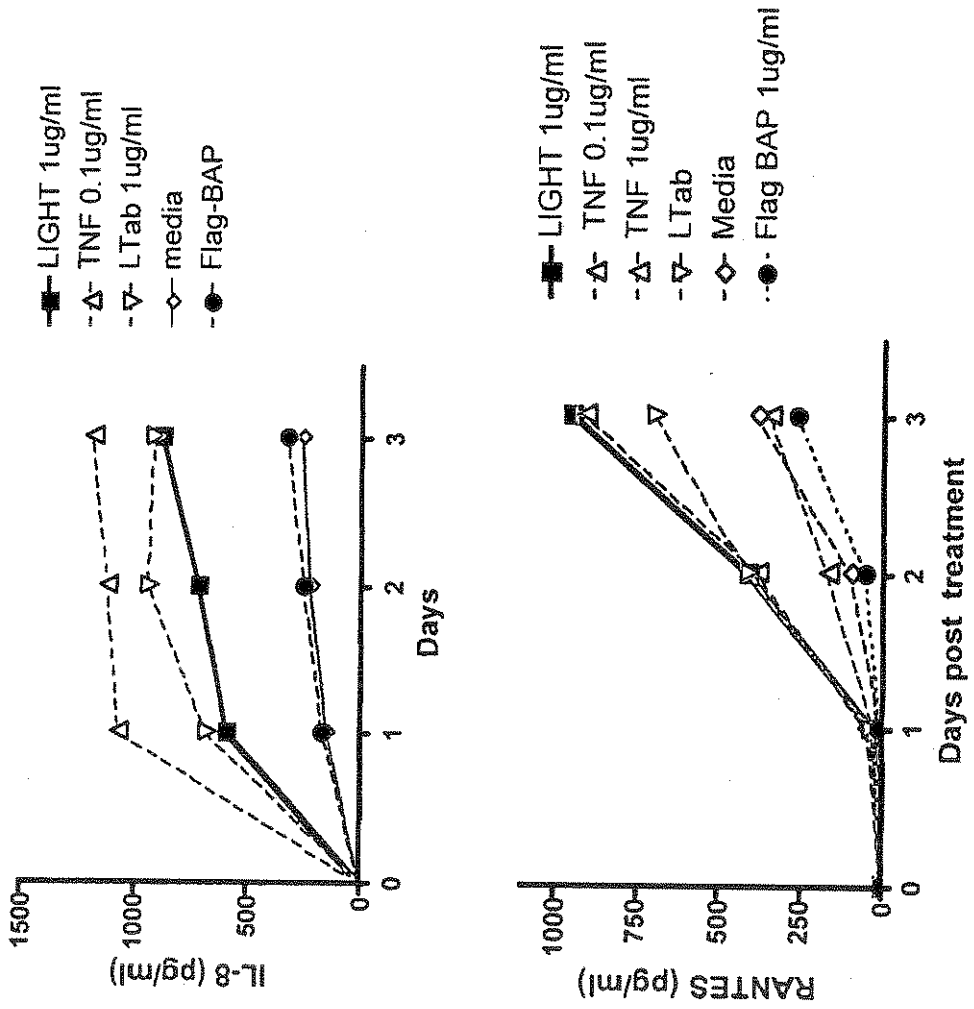

A.
LIGHT 1ug/ml
TNF 0.1ug/ml
LTab 1ug/ml
media
Flag-BAP
IL-8 (pg/ml)
1500
1000
500
0
0
1
2
3
Days
B.
LIGHT 1ug/ml
TNF 0.1ug/ml
TNF 1ug/ml
LTab
Media
Flag BAP 1ug/ml
RANTES (pg/ml)
1000
750
500
250
0
0
1
2
3
Days post treatment

FIGURE 9

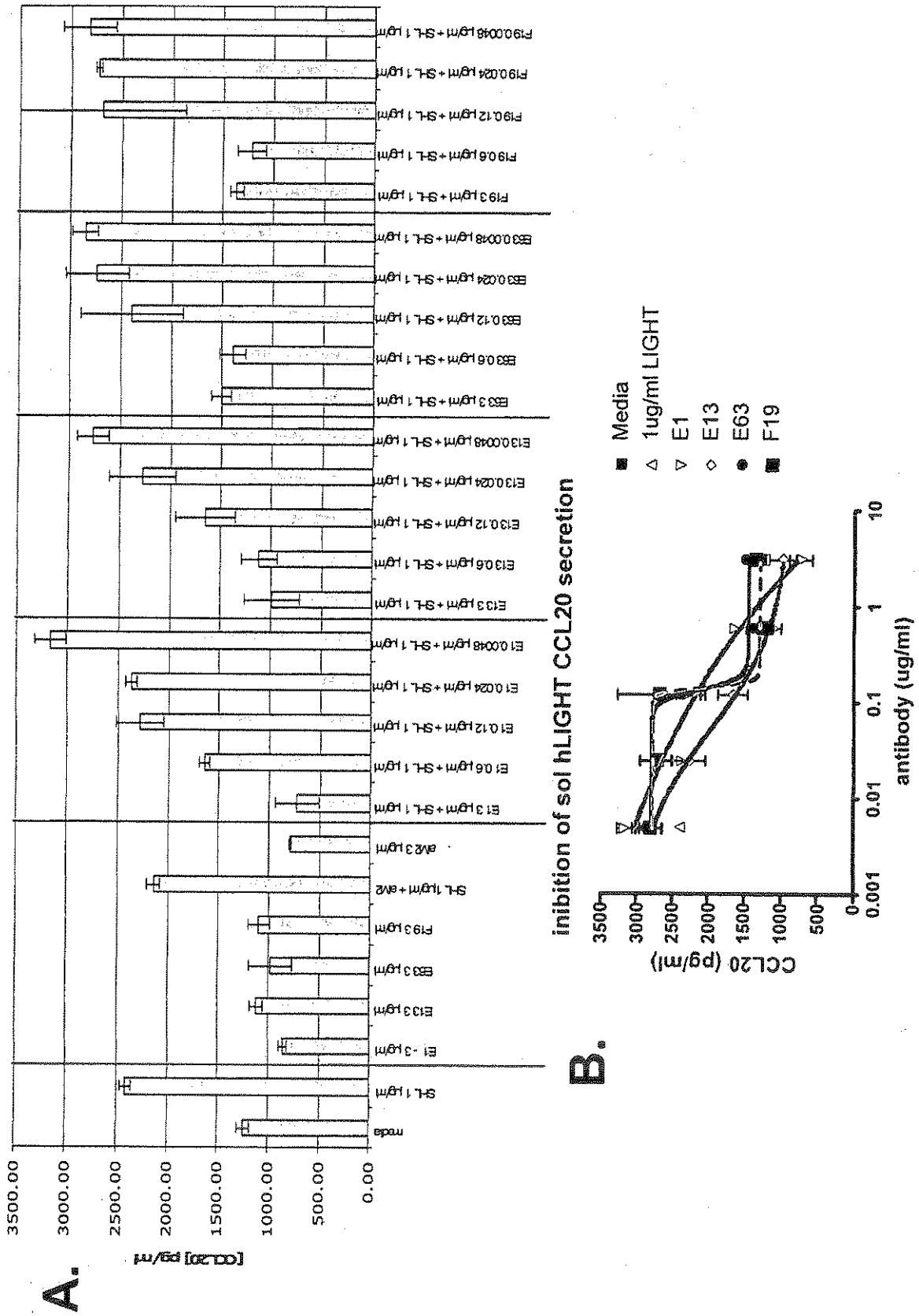
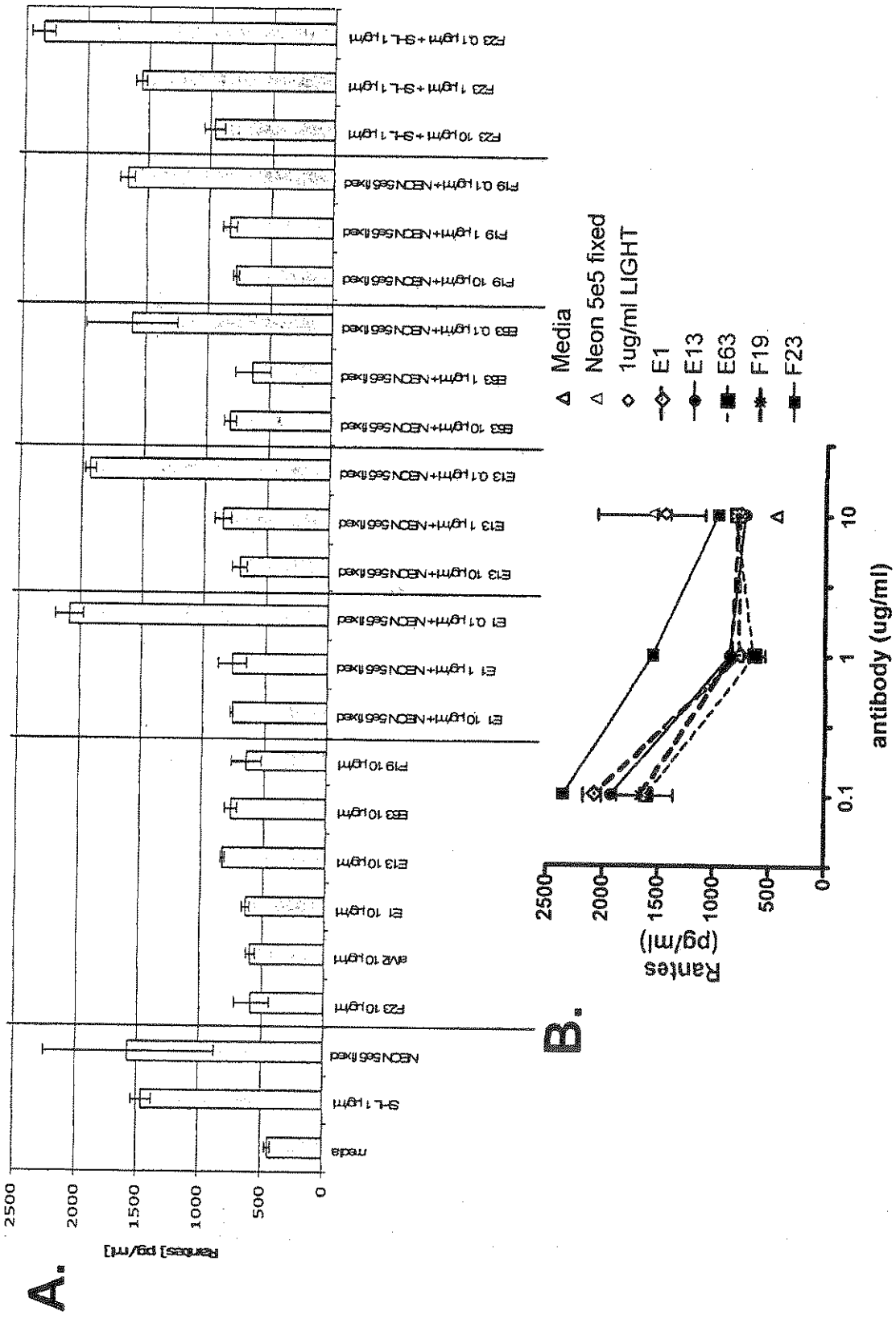

A.
[CCL20] pg/ml
3500.00
3000.00
2500.00
2000.00
1500.00
1000.00
500.00
0.00
media
SHL 1ug/ml
E1 .3ug/ml
E133 ug/ml
E63 3 ug/ml
F193 ug/ml
SHL 1ug/ml + aIL2
aIL2 3 ug/ml
E1 3ug/ml + SHL 1 ug/ml
E1 0.06 ug/ml + SHL 1 ug/ml
E1 0.12 ug/ml + SHL 1 ug/ml
E1 0.024 ug/ml + SHL 1 ug/ml
E1 0.0048 ug/ml + SHL 1 ug/ml
E133 ug/ml + SHL 1 ug/ml
E13 0.06 ug/ml + SHL 1 ug/ml
E13 0.12 ug/ml + SHL 1 ug/ml
E13 0.024 ug/ml + SHL 1 ug/ml
E13 0.0048 ug/ml + SHL 1 ug/ml
E63 3 ug/ml + SHL 1 ug/ml
E63 0.6 ug/ml + SHL 1 ug/ml
E63 0.12 ug/ml + SHL 1 ug/ml
E63 0.024 ug/ml + SHL 1 ug/ml
E63 0.0048 ug/ml + SHL 1 ug/ml
F19 3 ug/ml + SHL 1 ug/ml
F19 0.6 ug/ml + SHL 1 ug/ml
F19 0.12 ug/ml + SHL 1 ug/ml
F19 0.024 ug/ml + SHL 1 ug/ml
F19 0.0048 ug/ml + SHL 1 ug/ml
inibition of sol hLIGHT CCL20 secretion
B.
Media
1ug/ml LIGHT
E1
E13
E63
F19
CCL20 (pg/ml)
3500
3000
2500
2000
1500
1000
500
0
0.001
0.01
0.1
1
10
antibody (ug/ml)

FIGURE 10


A.
Rantes] pg/ml]
2500
2000
1500
1000
500
0
media
SHL 1ug/ml
NEON5e6 fixed
F23 10ug/ml
aIv2 10ug/ml
E1 10ug/ml
E13 10ug/ml
E63 10ug/ml
F19 10ug/ml
E1 10ug/ml+NEON5e6fixed
E1 1ug/ml+NEON5e6fixed
E1 0.1ug/ml+NEON5e6fixed
E13 10ug/ml+NEON5e6fixed
E13 1ug/ml+NEON5e6fixed
E13 0.1ug/ml+NEON5e6fixed
E63 10ug/ml+NEON5e6fixed
E63 1ug/ml+NEON5e6fixed
E63 0.1ug/ml+NEON5e6fixed
F19 10ug/ml+NEON5e6fixed
F19 1ug/ml+NEON5e6fixed
F19 0.1ug/ml+NEON5e6fixed
F23 10ug/ml+SHL 1ug/ml
F23 1ug/ml+SHL 1ug/ml
F23 0.1ug/ml+SHL 1ug/ml
B.
Media
Neon 5e5 fixed
1ug/ml LIGHT
E1
E13
E63
F19
F23
Rantes (pg/ml)
2500
2000
1500
1000
500
0
0.1
1
10
antibody (ug/ml)

# FIGURE 11

| | | | Coated Ab | | | |
|---|---|---|---|---|---|---|
| Soluble Ab | E1 | B12 | F19 | R&D mAb | Abnova | E45 |
| E1 | 94 | 22 | 15 | 99 | 0 | 99 |
| B12 | 17 | 97 | 16 | 0 | 61 | 11 |
| F19 | 4 | 0 | 99 | 99 | 0 | 7 |
| R&D mAb | 47 | 0 | 86 | 92 | 0 | 78 |
| Abnova | 30 | 97 | 15 | 38 | 89 | 64 |
| E45 | 60 | 5 | 8 | 99 | 64 | 98 |
| AntiM2 | 0 | 0 | 0 | 0 | 0 | 0 |

FIGURE 12

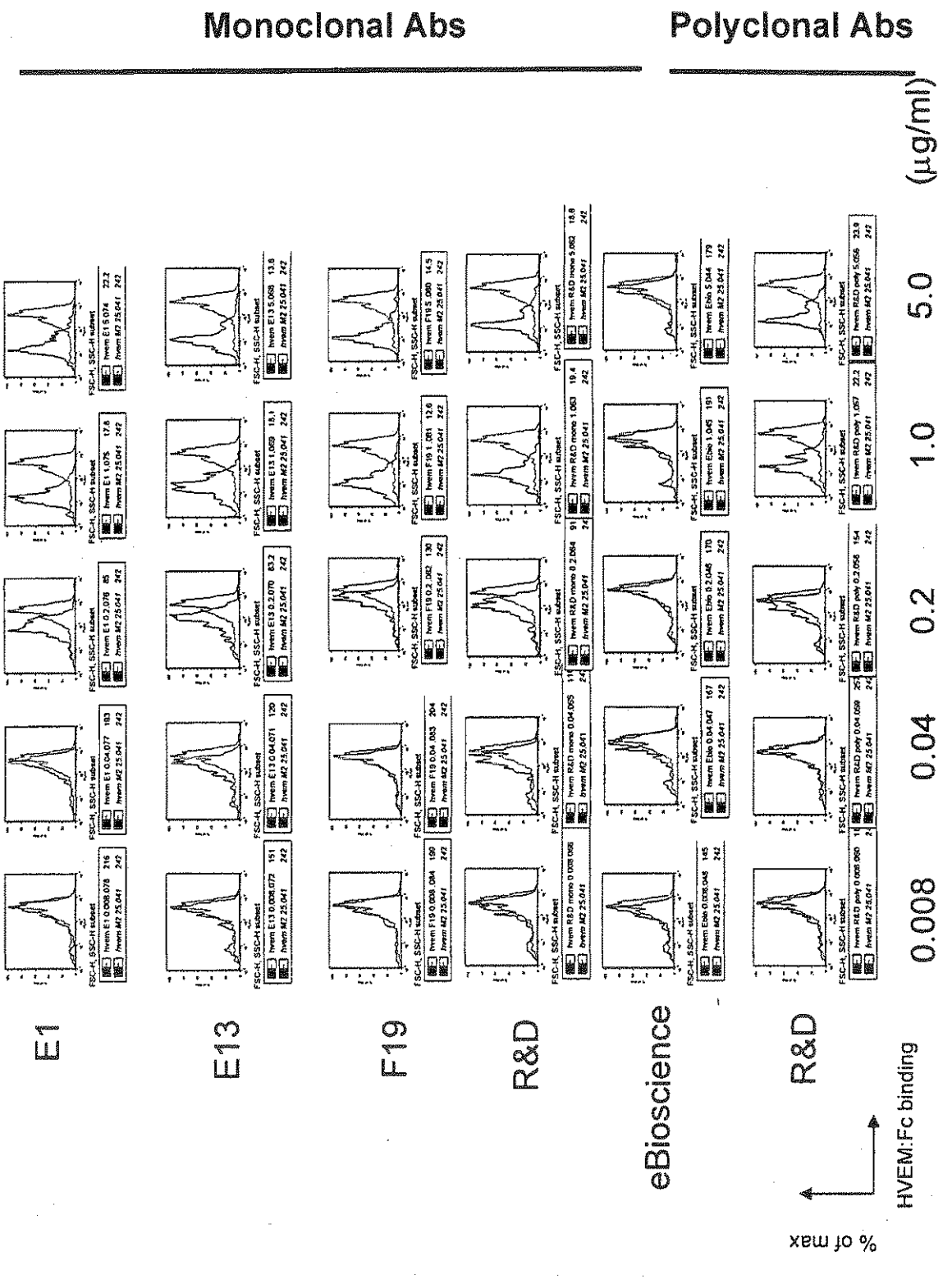

Monoclonal Abs
Polyclonal Abs
E1
E13
F19
R&D
eBioscience
R&D
0.008
0.04
0.2
1.0
5.0
(µg/ml)
HVEM:Fc binding
% of max

FIGURE 13

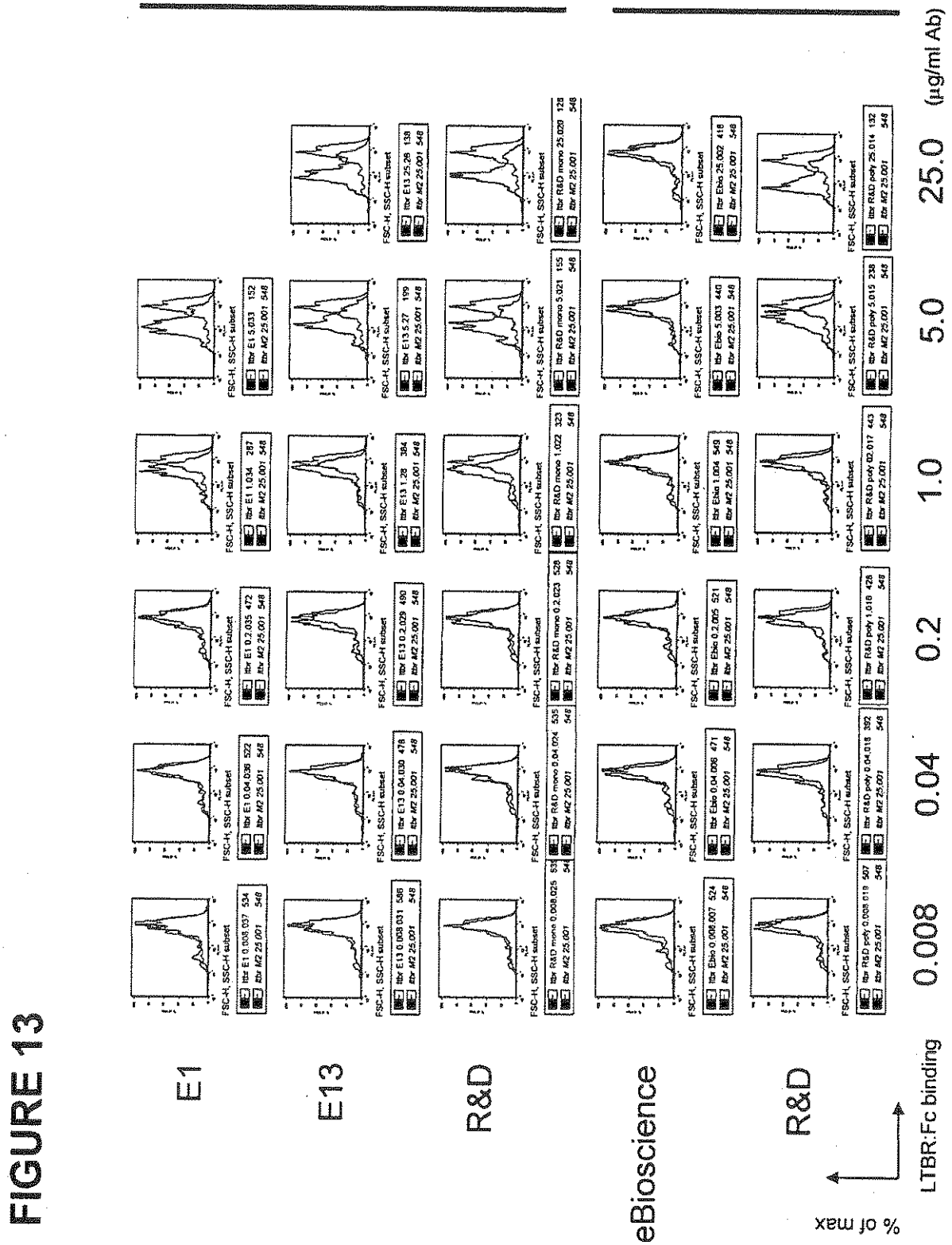

Monoclonal Abs
Polyclonal Abs
E1
E13
R&D
eBioscience
R&D
0.008
0.04
0.2
1.0
5.0
25.0
(µg/ml Ab)
LTBR:Fc binding
% of max

FIGURE 14

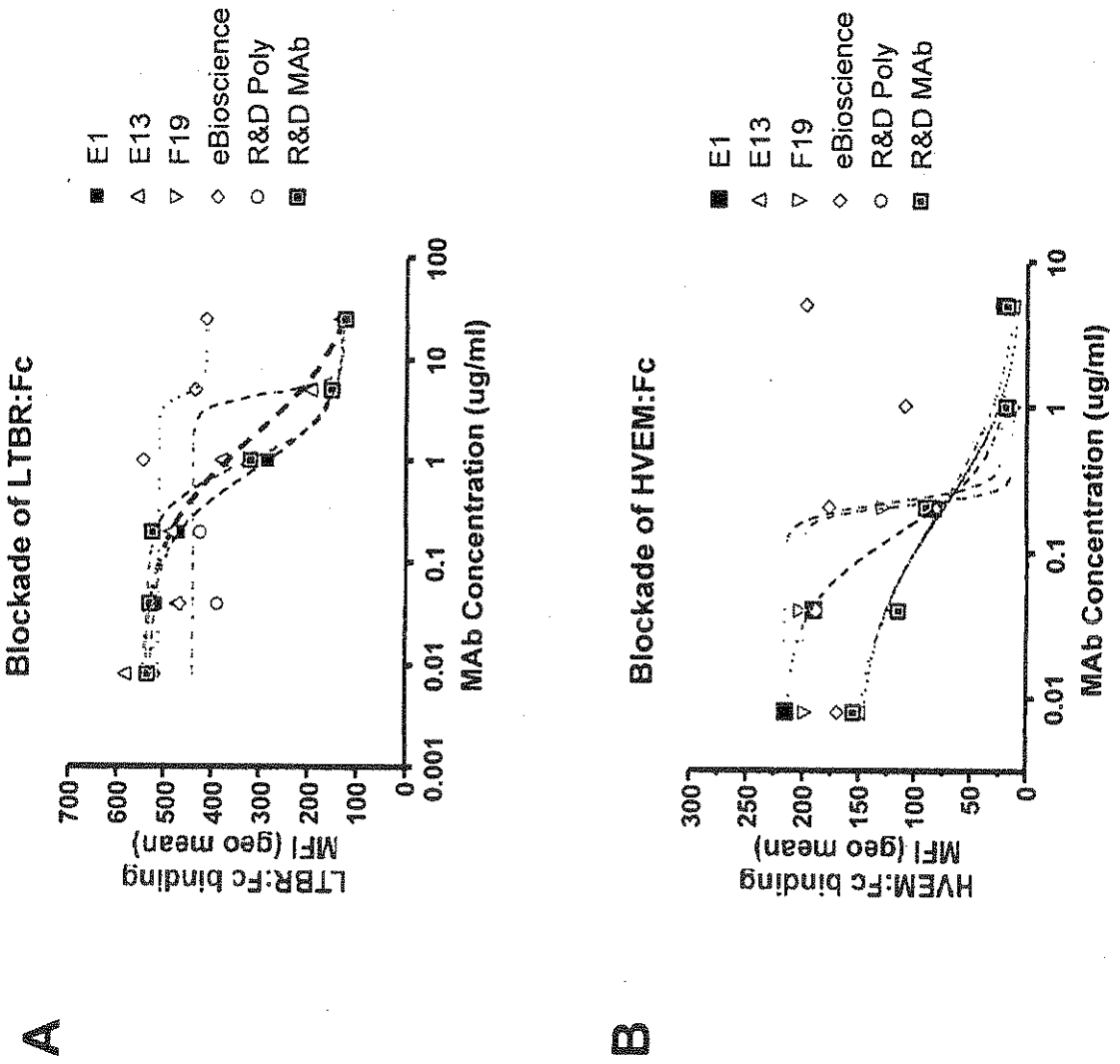
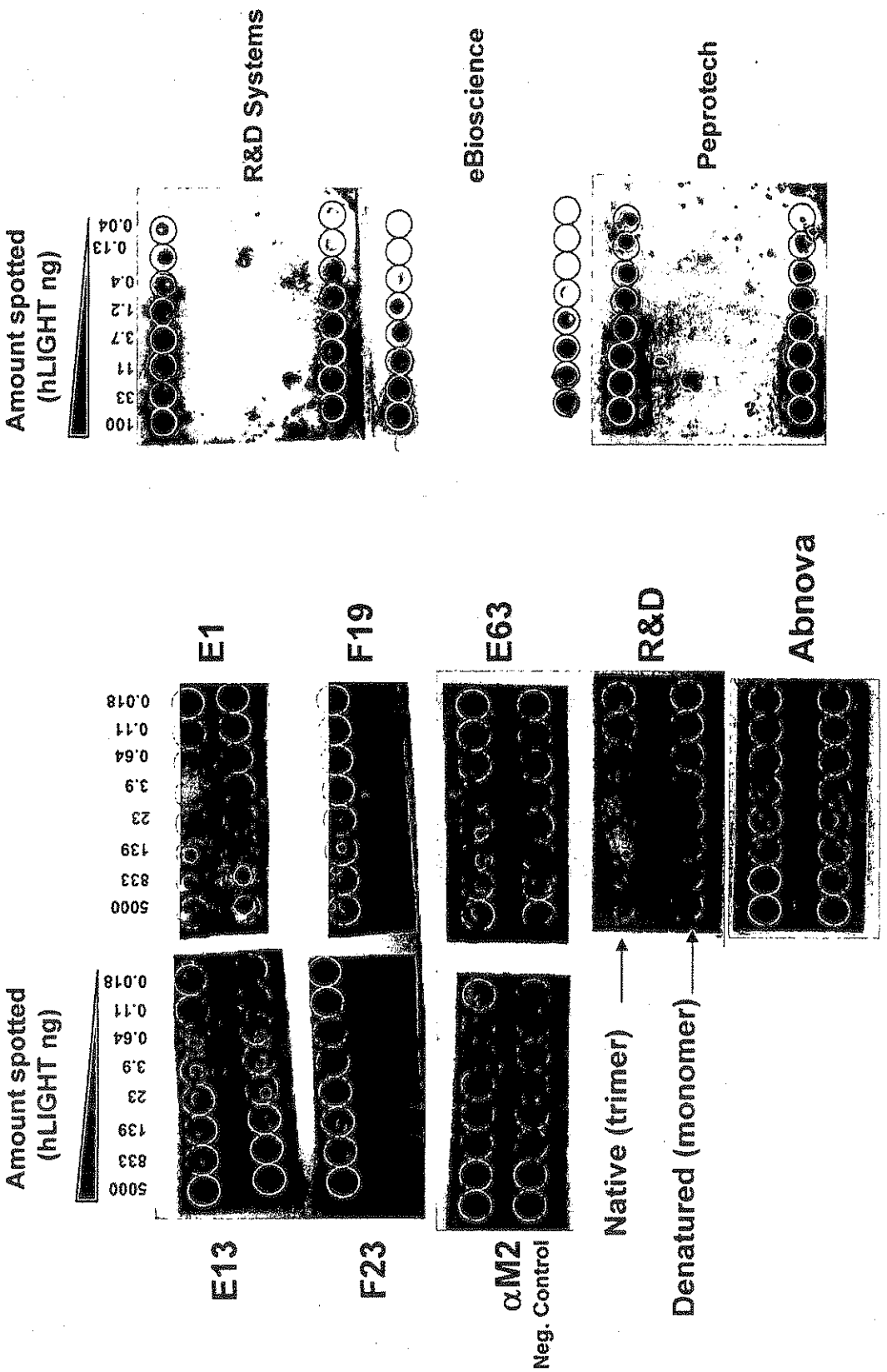

A
Blockade of LTBR:Fc
LTBR:Fc binding
MFI (geo mean)
MAb Concentration (ug/ml)
E1
E13
F19
eBioscience
R&D Poly
R&D MAb
B
Blockade of HVEM:Fc
HVEM:Fc binding
MFI (geo mean)
MAb Concentration (ug/ml)
E1
E13
F19
eBioscience
R&D Poly
R&D MAb

FIGURE 15


A
Monoclonal Abs
B
Polyclonal Abs
Amount spotted (hLIGHT ng)
5000
833
139
23
3.9
0.64
0.11
0.018
E13
F23
αM2
Neg. Control
E1
F19
E63
R&D
Abnova
Native (trimer)
Denatured (monomer)
Amount spotted (hLIGHT ng)
100
33
11
3.7
1.2
0.4
0.13
0.04
R&D Systems
eBioscience
Peprotech

# FIGURE 16

| | Antibody | Native-trimer * | Denatured-monomer * |
|---|---|---|---|
| Monoclonals | E1 (human mAb) | 23 | 139 |
| | E13 (human mAb) | 0.64 | 0.64 |
| | E63 (human mAb) | 3.9 | 139 |
| | F19 (human mAb) | 23 | >5000 |
| | F23 (human mAb) | 23 | >5000 |
| | Abnova (mouse mAb) | 0.64 | 0.64 |
| | R&D systems (mouse mAb) | 23 | 139 |
| Polyclonals | R&D systems (goat pAb) | 0.04 | 0.13 |
| | eBiosciences (rabbit pAb) | 0.4 | 1.2 |
| | Peprotech (rabbit pAb) | 0.04 | 0.13 |

*Limit of detection (lowest amt of LIGHT detected (ng))

FIGURE 17

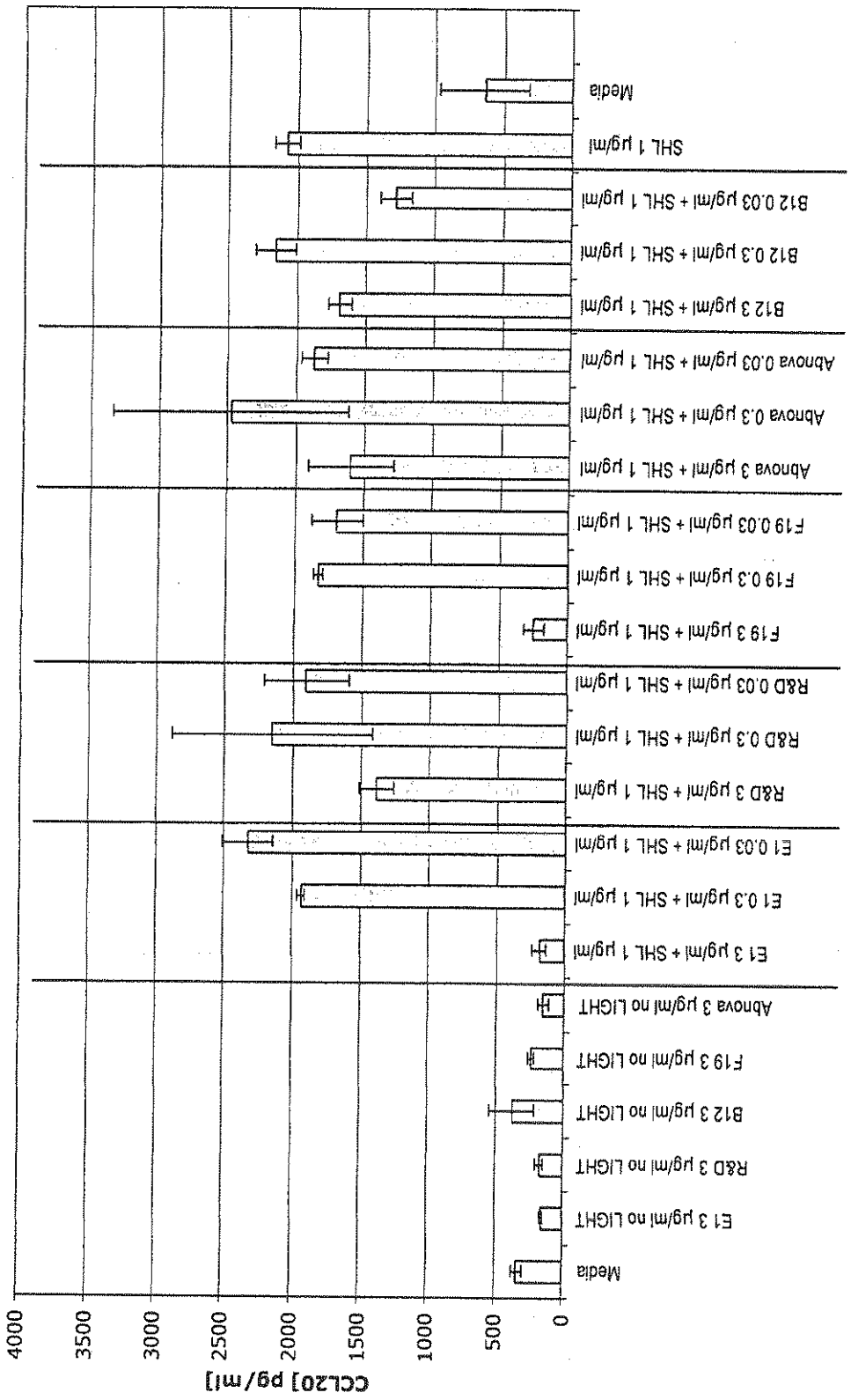

CCL20] pg/ml]
0
500
1000
1500
2000
2500
3000
3500
4000
Media
E1 3 µg/ml no LIGHT
R8D 3 µg/ml no LIGHT
B12 3 µg/ml no LIGHT
F19 3 µg/ml no LIGHT
Abnova 3 µg/ml no LIGHT
E1 3 µg/ml + SHL 1 µg/ml
E1 0.3 µg/ml + SHL 1 µg/ml
E1 0.03 µg/ml + SHL 1 µg/ml
R8D 3 µg/ml + SHL 1 µg/ml
R8D 0.3 µg/ml + SHL 1 µg/ml
R8D 0.03 µg/ml + SHL 1 µg/ml
F19 3 µg/ml + SHL 1 µg/ml
F19 0.3 µg/ml + SHL 1 µg/ml
F19 0.03 µg/ml + SHL 1 µg/ml
Abnova 3 µg/ml + SHL 1 µg/ml
Abnova 0.3 µg/ml + SHL 1 µg/ml
Abnova 0.03 µg/ml + SHL 1 µg/ml
B12 3 µg/ml + SHL 1 µg/ml
B12 0.3 µg/ml + SHL 1 µg/ml
B12 0.03 µg/ml + SHL 1 µg/ml
SHL 1 µg/ml
Media

FIGURE 18

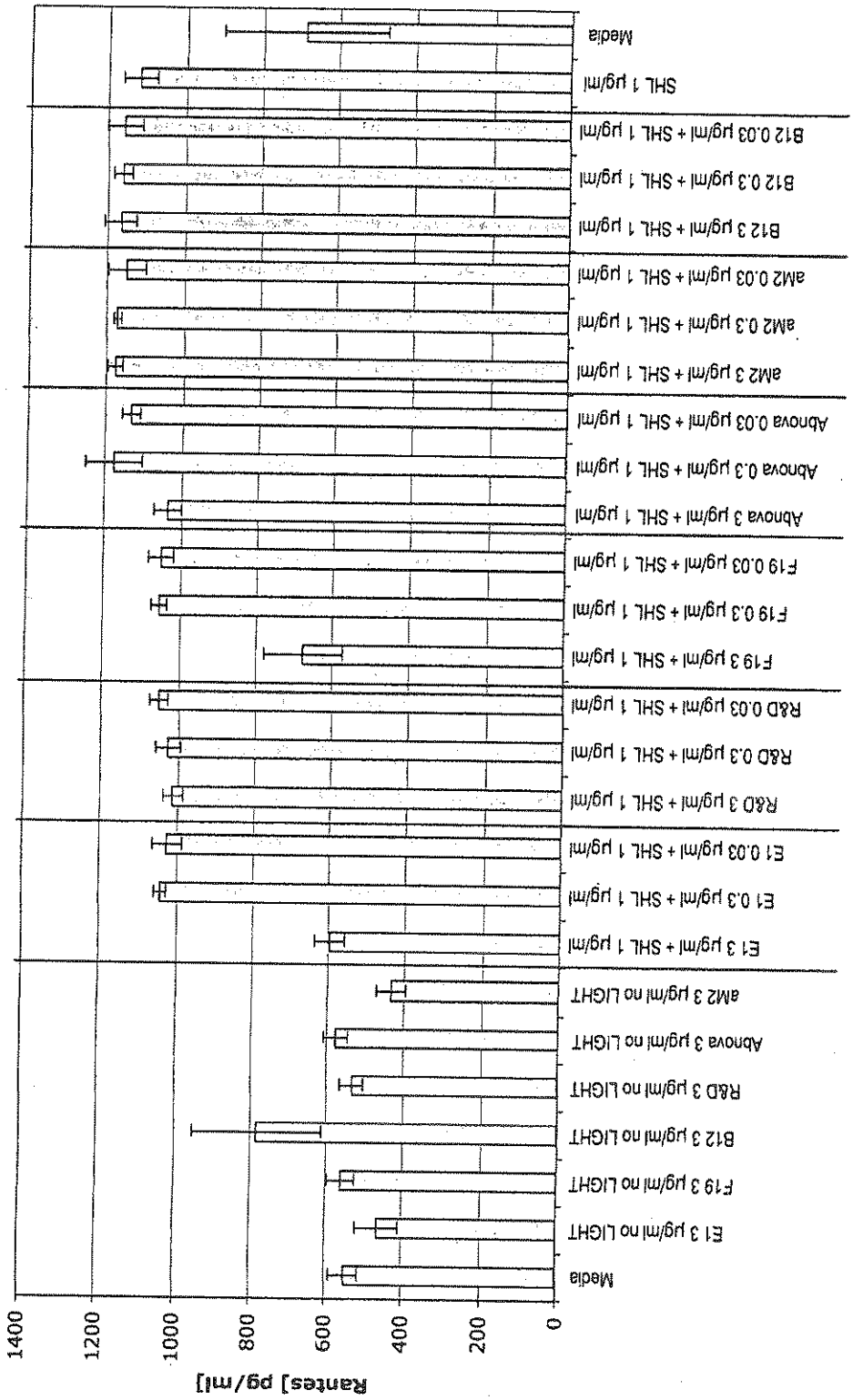
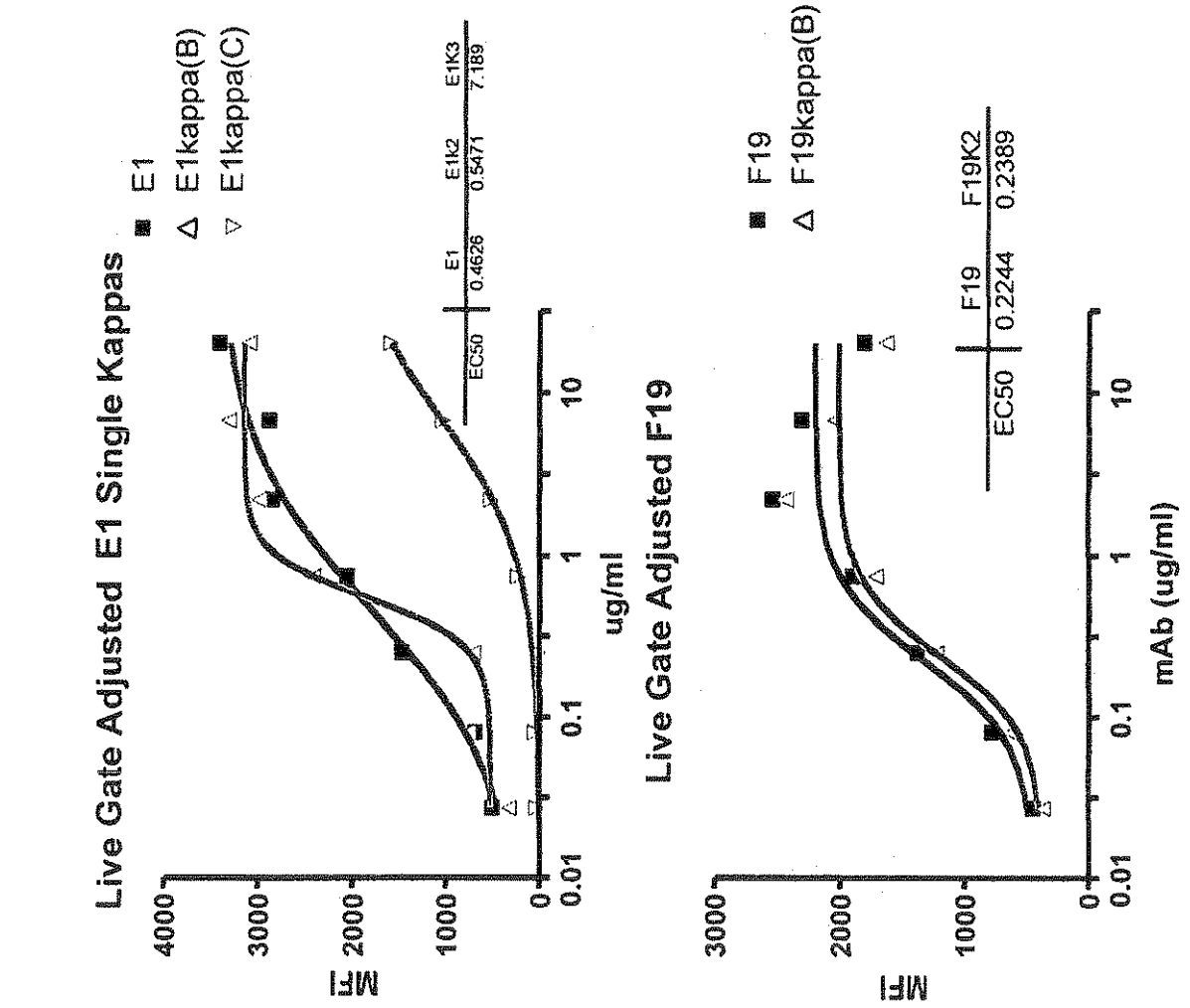

Rantes] pg/ml]
0
200
400
600
800
1000
1200
1400
Media
E1 3 ug/ml no LIGHT
F19 3 ug/ml no LIGHT
B12 3 ug/ml no LIGHT
R8D 3 ug/ml no LIGHT
Abnova 3 ug/ml no LIGHT
aM2 3 ug/ml no LIGHT
E1 3 ug/ml + SHL 1 ug/ml
E1 0.3 ug/ml + SHL 1 ug/ml
E1 0.03 ug/ml + SHL 1 ug/ml
R8D 3 ug/ml + SHL 1 ug/ml
R8D 0.3 ug/ml + SHL 1 ug/ml
R8D 0.03 ug/ml + SHL 1 ug/ml
F19 3 ug/ml + SHL 1 ug/ml
F19 0.3 ug/ml + SHL 1 ug/ml
F19 0.03 ug/ml + SHL 1 ug/ml
Abnova 3 ug/ml + SHL 1 ug/ml
Abnova 0.3 ug/ml + SHL 1 ug/ml
Abnova 0.03 ug/ml + SHL 1 ug/ml
aM2 3 ug/ml + SHL 1 ug/ml
aM2 0.3 ug/ml + SHL 1 ug/ml
aM2 0.03 ug/ml + SHL 1 ug/ml
B12 3 ug/ml + SHL 1 ug/ml
B12 0.3 ug/ml + SHL 1 ug/ml
B12 0.03 ug/ml + SHL 1 ug/ml
SHL 1 ug/ml
Media

FIGURE 19


A
Live Gate Adjusted E1 Single Kappas
E1
E1kappa(B)
E1kappa(C)
MFI
4000
3000
2000
1000
0
0.01
0.1
1
10
ug/ml
EC50
E1
0.4626
E1K2
0.5471
E1K3
7.189
B
Live Gate Adjusted F19
F19
F19kappa(B)
MFI
3000
2000
1000
0
0.01
0.1
1
10
mAb (ug/ml)
EC50
F19
0.2244
F19K2
0.2389

# FIGURE 20

| | | Coated Ab | | |
|---|---|---|---|---|
| Soluble Ab | E1 | E1kappa(B) | F19 | F19kappa(B) |
| E1 | 90 | 91 | 0 | 0 |
| E1kappa(B) | 92 | 92 | 0 | 0 |
| F19 | 0 | 0 | 98 | 98 |
| F19kappa(B) | 0 | 24 | 98 | 98 |
| AntiM2 | 0 | 0 | 0 | 0 |

FIGURE 21

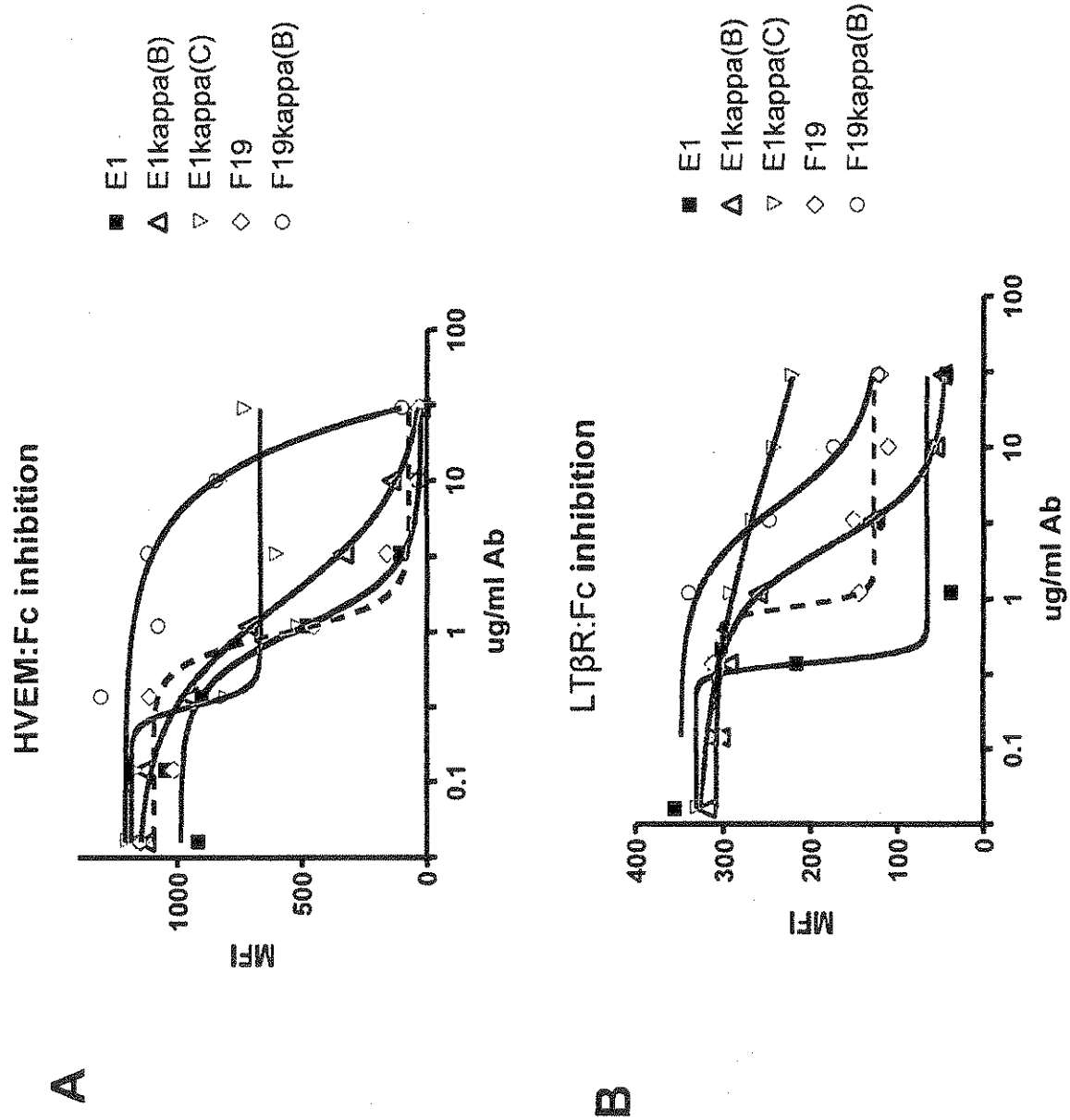

A
HVEM:Fc inhibition
E1
E1kappa(B)
E1kappa(C)
F19
F19kappa(B)
MFI
1000
500
0
0.1
1
10
100
ug/ml Ab
B
LTβR:Fc inhibition
E1
E1kappa(B)
E1kappa(C)
F19
F19kappa(B)
MFI
400
300
200
100
0
0.1
1
10
100
ug/ml Ab

FIGURE 22

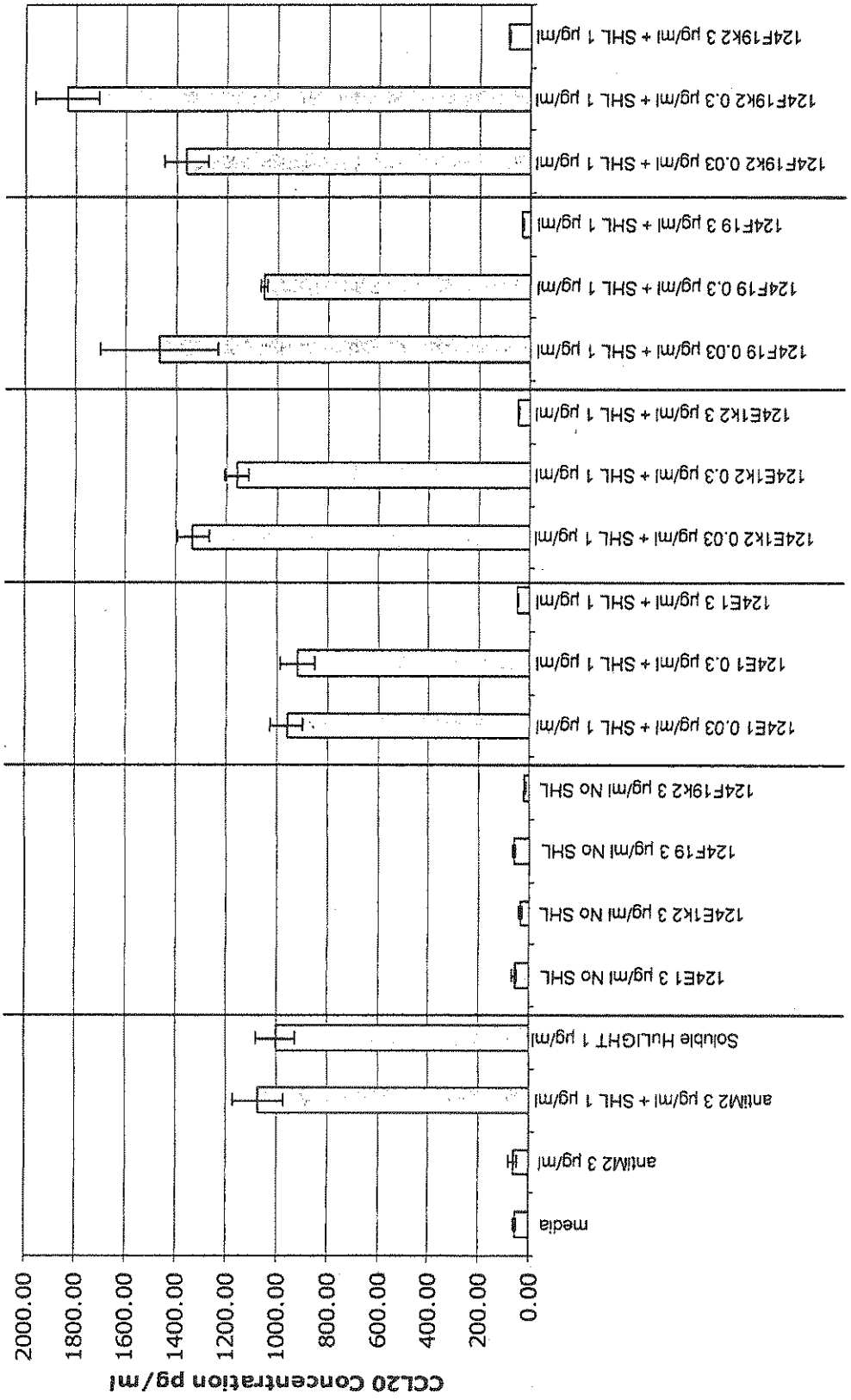
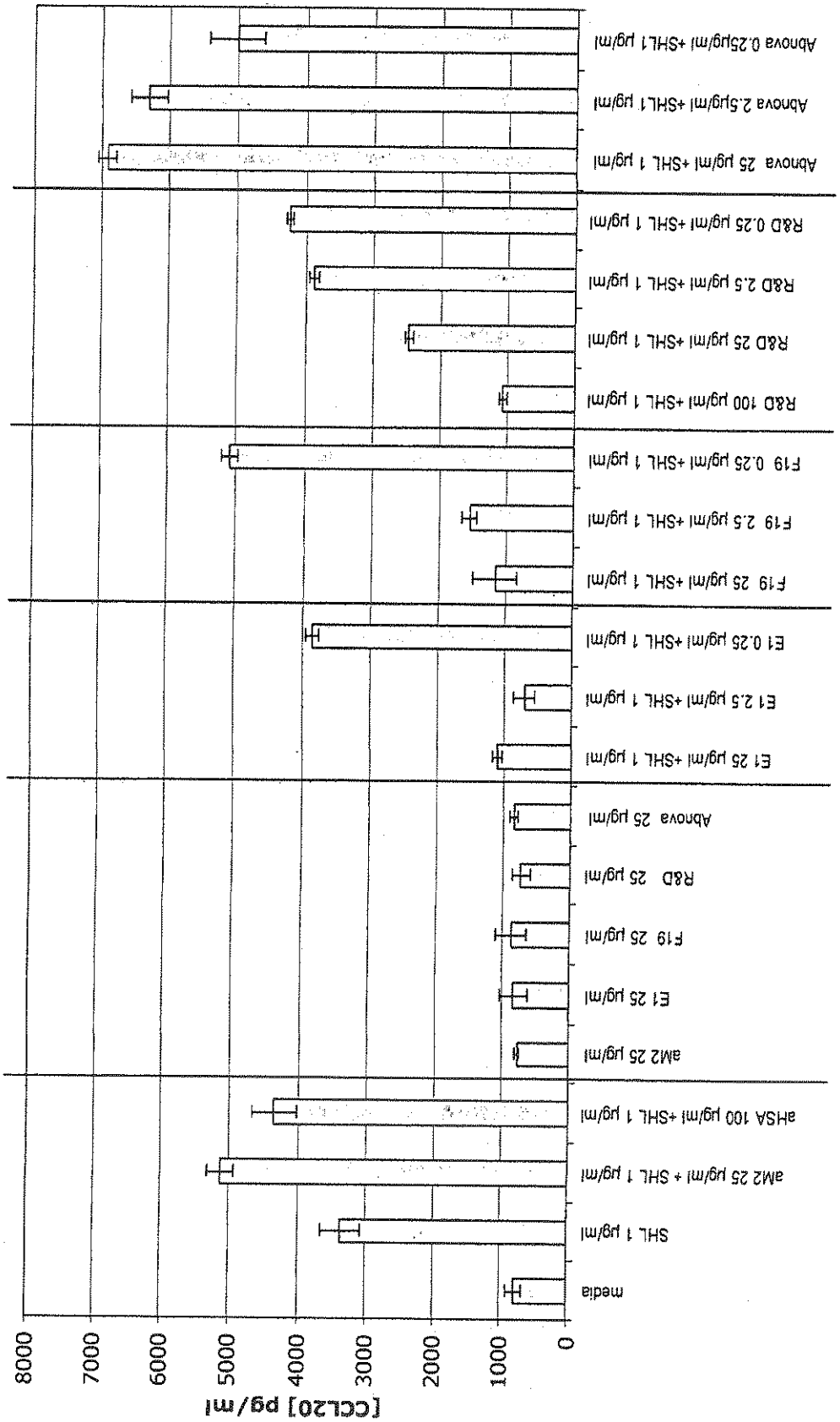

CCL20 Concentration pg/ml
2000.00
1800.00
1600.00
1400.00
1200.00
1000.00
800.00
600.00
400.00
200.00
0.00
media
antiM2 3 µg/ml
antiM2 3 µg/ml + SHL 1 µg/ml
Soluble HuLIGHT 1 µg/ml
124E1 3 µg/ml No SHL
124E1K2 3 µg/ml No SHL
124F19 3 µg/ml No SHL
124F19K2 3 µg/ml No SHL
124E1 0.03 µg/ml + SHL 1 µg/ml
124E1 0.3 µg/ml + SHL 1 µg/ml
124E1 3 µg/ml + SHL 1 µg/ml
124E1K2 0.03 µg/ml + SHL 1 µg/ml
124E1K2 0.3 µg/ml + SHL 1 µg/ml
124E1K2 3 µg/ml + SHL 1 µg/ml
124F19 0.03 µg/ml + SHL 1 µg/ml
124F19 0.3 µg/ml + SHL 1 µg/ml
124F19 3 µg/ml + SHL 1 µg/ml
124F19K2 0.03 µg/ml + SHL 1 µg/ml
124F19K2 0.3 µg/ml + SHL 1 µg/ml
124F19K2 3 µg/ml + SHL 1 µg/ml

FIGURE 23


[CCL20] pg/ml
8000
7000
6000
5000
4000
3000
2000
1000
0
media
SHL 1 µg/ml
aM2 25 µg/ml + SHL 1 µg/ml
aHSA 100 µg/ml +SHL 1 µg/ml
aM2 25 µg/ml
E1 25 µg/ml
F19 25 µg/ml
R8D 25 µg/ml
Abnova 25 µg/ml
E1 25 µg/ml +SHL 1 µg/ml
E1 2.5 µg/ml +SHL 1 µg/ml
E1 0.25 µg/ml +SHL 1 µg/ml
F19 25 µg/ml +SHL 1 µg/ml
F19 2.5 µg/ml +SHL 1 µg/ml
F19 0.25 µg/ml +SHL 1 µg/ml
R8D 100 µg/ml +SHL 1 µg/ml
R8D 25 µg/ml +SHL 1 µg/ml
R8D 2.5 µg/ml +SHL 1 µg/ml
R8D 0.25 µg/ml +SHL 1 µg/ml
Abnova 25 µg/ml +SHL 1 µg/ml
Abnova 2.5µg/ml +SHL1 µg/ml
Abnova 0.25µg/ml +SHL1 µg/ml

# FIGURE 24

## A.

## Extracellular: a.a. 214

Population Diversity TNFSF14 SNP aa 214

| Population | Individual Group | Allele Frequency A | G |
|---|---|---|---|
| WICGR8_asian_pooled | | 0.120 | 0.880 |
| WICGR6_caucasian_pooled | | 0.020 | 0.980 |
| CEPH | | 0.080 | 0.920 |
| HapMap-CEU | European | 0.042 | 0.958 |
| HapMap-HCB | Asian | 0.011 | 0.989 |
| HapMap-JPT | Asian | 0.136 | 0.864 |
| HapMap-YRI | Sub-Saharan African | 0.033 | 0.967 |
| AGI_ASP population | African American | 0.050 | 0.950 |

| dbSNP allele | Protein residue | Amino acid pos |
|---|---|---|
| G | Glu [E] | 214 |
| A | Lys [K] | 214 |

## B.

## Cytoplasmic: a.a. 32

Population Diversity TNFSF14 SNP aa 32

| Population | Individual Group | Allele Frequency C | T |
|---|---|---|---|
| AFD_EUR_PANEL | European | 1.000 | |
| AFD_AFR_PANEL | African American | 1.000 | |
| AFD_CHN_PANEL | Asian | 0.979 | 0.021 |
| HapMap-CEU | European | 1.000 | |
| HapMap-HCB | Asian | 0.989 | 0.011 |
| HapMap-JPT | Asian | 1.000 | |
| HapMap-YRI | Sub-Saharan African | 1.000 | |

| dbSNP allele | Protein residue | Amino acid pos |
|---|---|---|
| T | Leu [L] | 32 |
| C | Ser [S] | 32 |

FIGURE 25

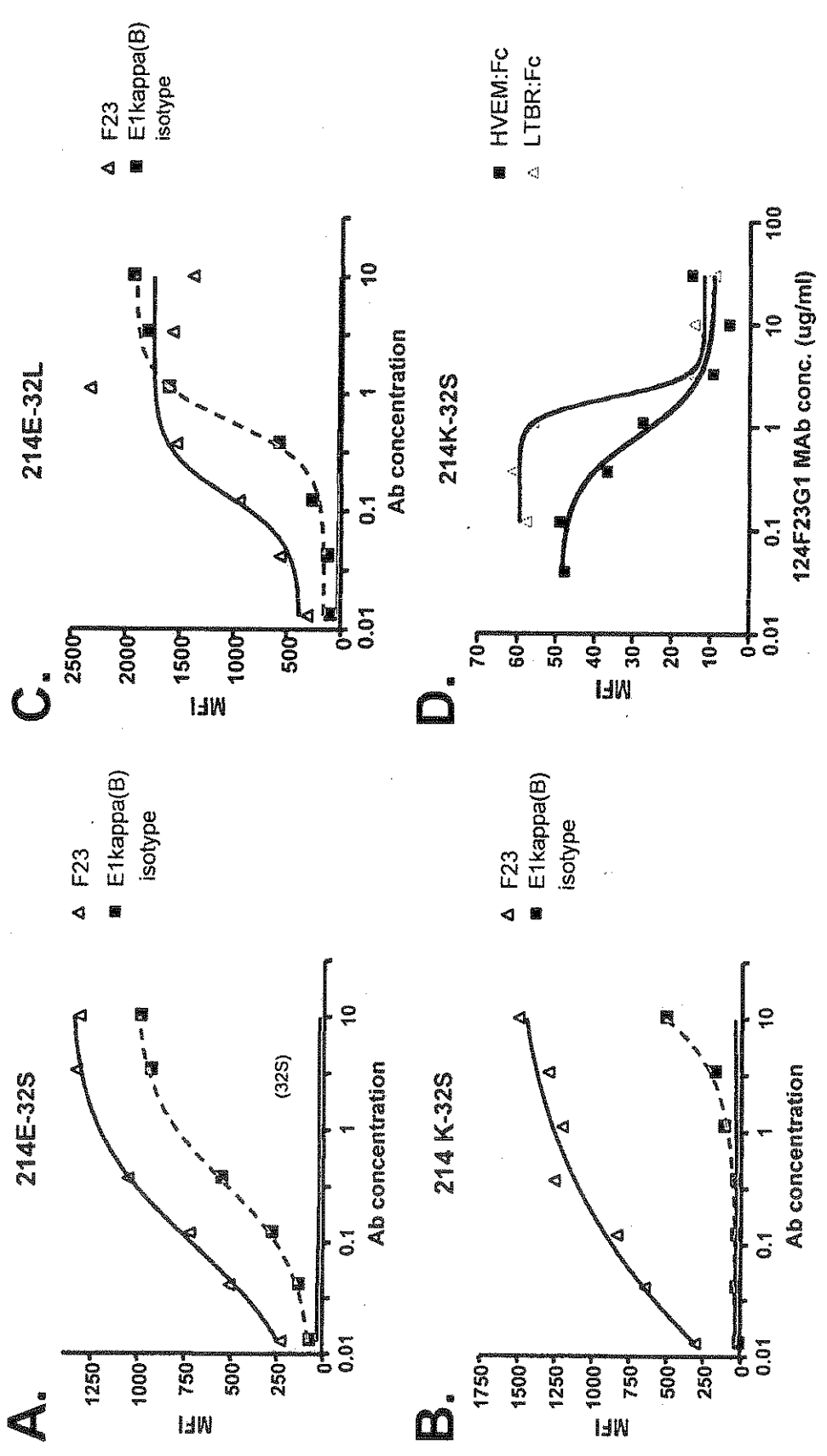

A.
214E-32S
F23
E1kappa(B) isotype
MFI
Ab concentration
(32S)
B.
214 K-32S
C.
214E-32L
D.
214K-32S
HVEM:Fc
LTBR:Fc
124F23G1 MAb conc. (ug/ml)

FIGURE 26

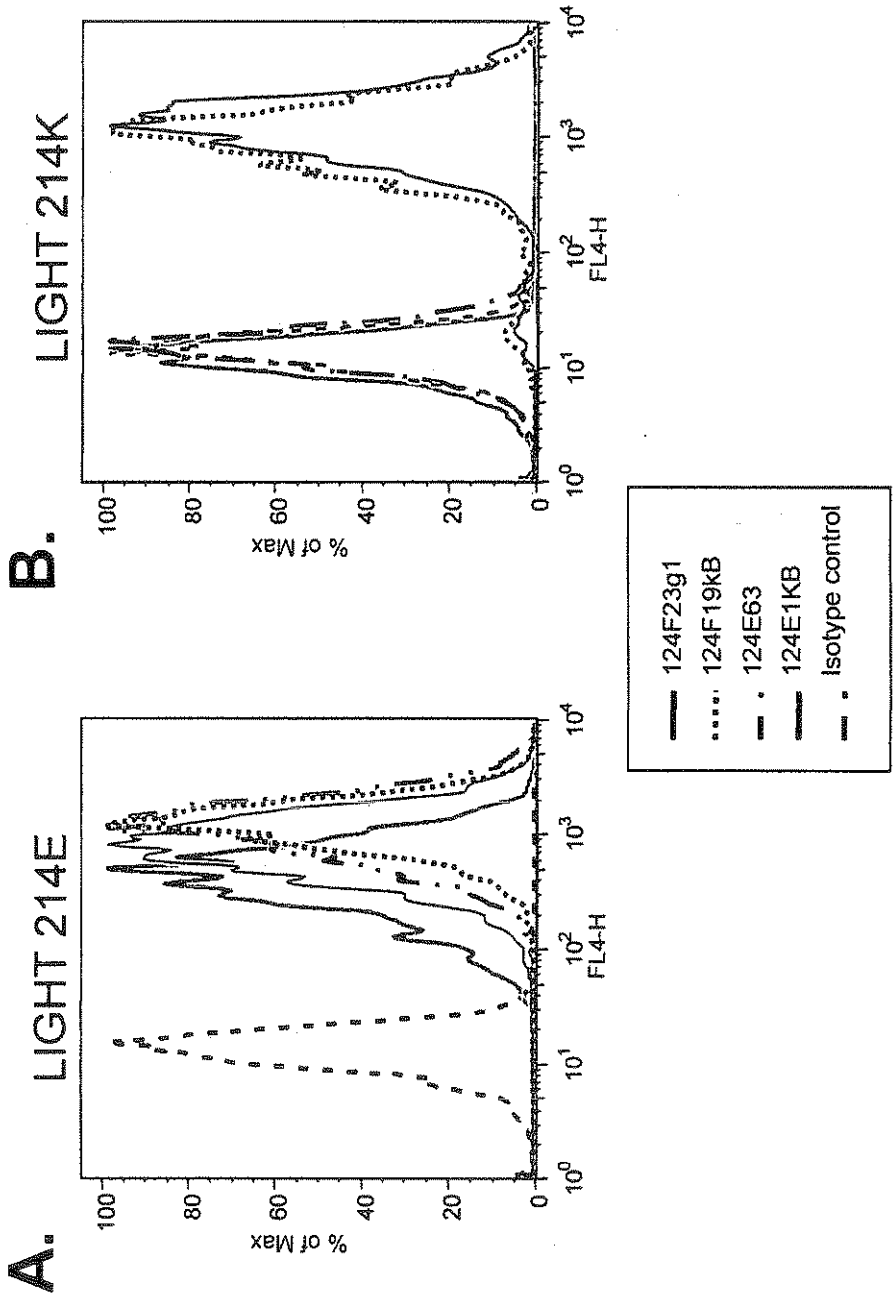
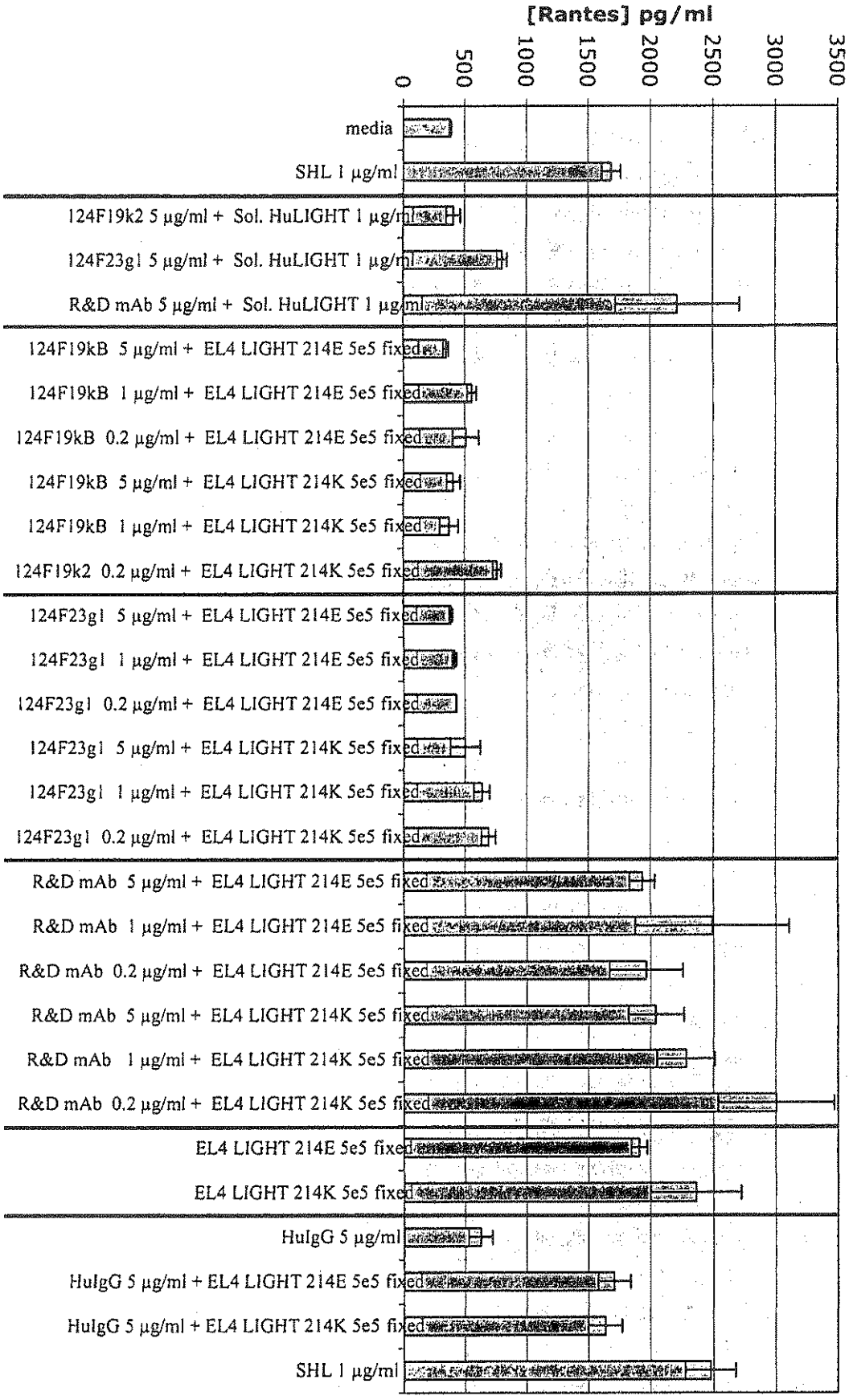
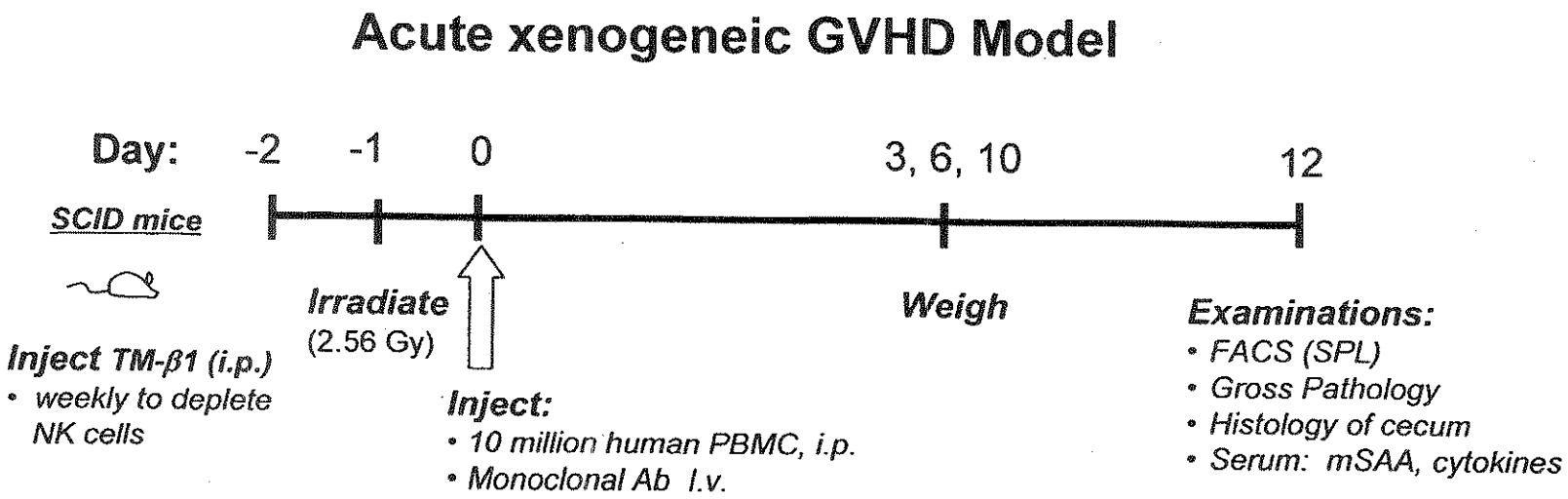

A.
LIGHT 214E
B.
LIGHT 214K
% of Max
FL4-H
124F23g1
124F19kB
124E63
124E1KB
Isotype control

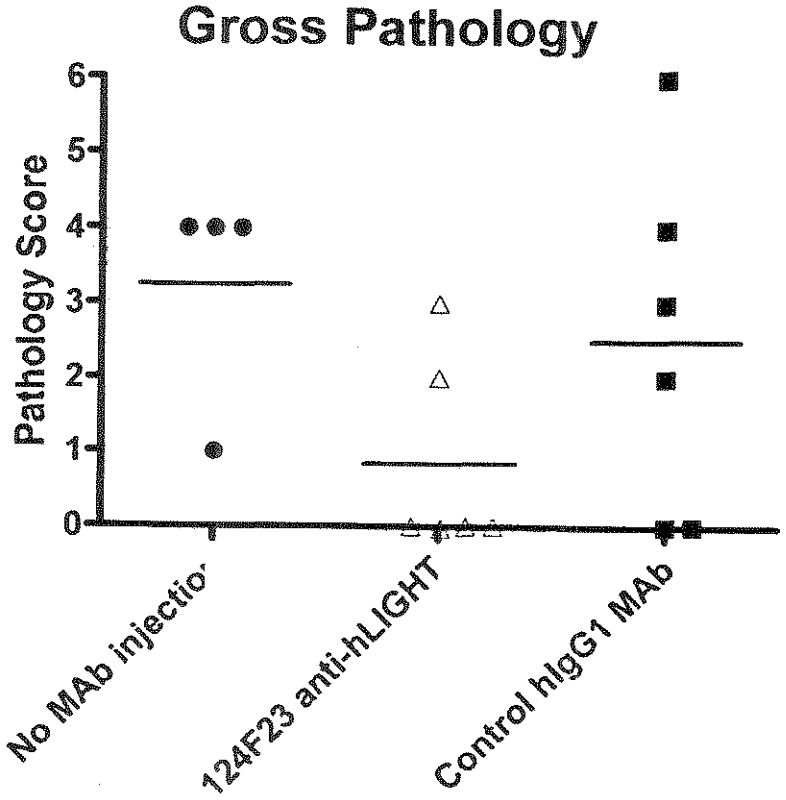
FIGURE 27


[Rantes] pg/ml
0
500
1000
1500
2000
2500
3000
3500
media
SHL 1 µg/ml
124F19k2 5 µg/ml + Sol. HuLIGHT 1 µg/ml
124F23g1 5 µg/ml + Sol. HuLIGHT 1 µg/ml
R&D mAb 5 µg/ml + Sol. HuLIGHT 1 µg/ml
124F19kB 5 µg/ml + EL4 LIGHT 214E 5e5 fixed
124F19kB 1 µg/ml + EL4 LIGHT 214E 5e5 fixed
124F19kB 0.2 µg/ml + EL4 LIGHT 214E 5e5 fixed
124F19kB 5 µg/ml + EL4 LIGHT 214K 5e5 fixed
124F19kB 1 µg/ml + EL4 LIGHT 214K 5e5 fixed
124F19k2 0.2 µg/ml + EL4 LIGHT 214K 5e5 fixed
124F23g1 5 µg/ml + EL4 LIGHT 214E 5e5 fixed
124F23g1 1 µg/ml + EL4 LIGHT 214E 5e5 fixed
124F23g1 0.2 µg/ml + EL4 LIGHT 214E 5e5 fixed
124F23g1 5 µg/ml + EL4 LIGHT 214K 5e5 fixed
124F23g1 1 µg/ml + EL4 LIGHT 214K 5e5 fixed
124F23g1 0.2 µg/ml + EL4 LIGHT 214K 5e5 fixed
R&D mAb 5 µg/ml + EL4 LIGHT 214E 5e5 fixed
R&D mAb 1 µg/ml + EL4 LIGHT 214E 5e5 fixed
R&D mAb 0.2 µg/ml + EL4 LIGHT 214E 5e5 fixed
R&D mAb 5 µg/ml + EL4 LIGHT 214K 5e5 fixed
R&D mAb 1 µg/ml + EL4 LIGHT 214K 5e5 fixed
R&D mAb 0.2 µg/ml + EL4 LIGHT 214K 5e5 fixed
EL4 LIGHT 214E 5e5 fixed
EL4 LIGHT 214K 5e5 fixed
HuIgG 5 µg/ml
HuIgG 5 µg/ml + EL4 LIGHT 214E 5e5 fixed
HuIgG 5 µg/ml + EL4 LIGHT 214K 5e5 fixed
SHL 1 µg/ml

# FIGURE 28


Acute xenogeneic GVHD Model
Day:
-2
-1
0
3, 6, 10
12
SCID mice
Irradiate
(2.56 Gy)
Weigh
Examinations:
• FACS (SPL)
• Gross Pathology
• Histology of cecum
• Serum: mSAA, cytokines
Inject TM-β1 (i.p.)
• weekly to deplete NK cells
Inject:
• 10 million human PBMC, i.p.
• Monoclonal Ab I.v.

# FIGURE 29




## Pathology score breakdown

**Categories scored:**

- Diarrhea
- Peritoneal inflammation & Ascites
- Intestinal inflammation

**Scored 0-3** (none, mild, mod., severe)

- Final score is total of each category
- Maximum score of 9

FIGURE 30

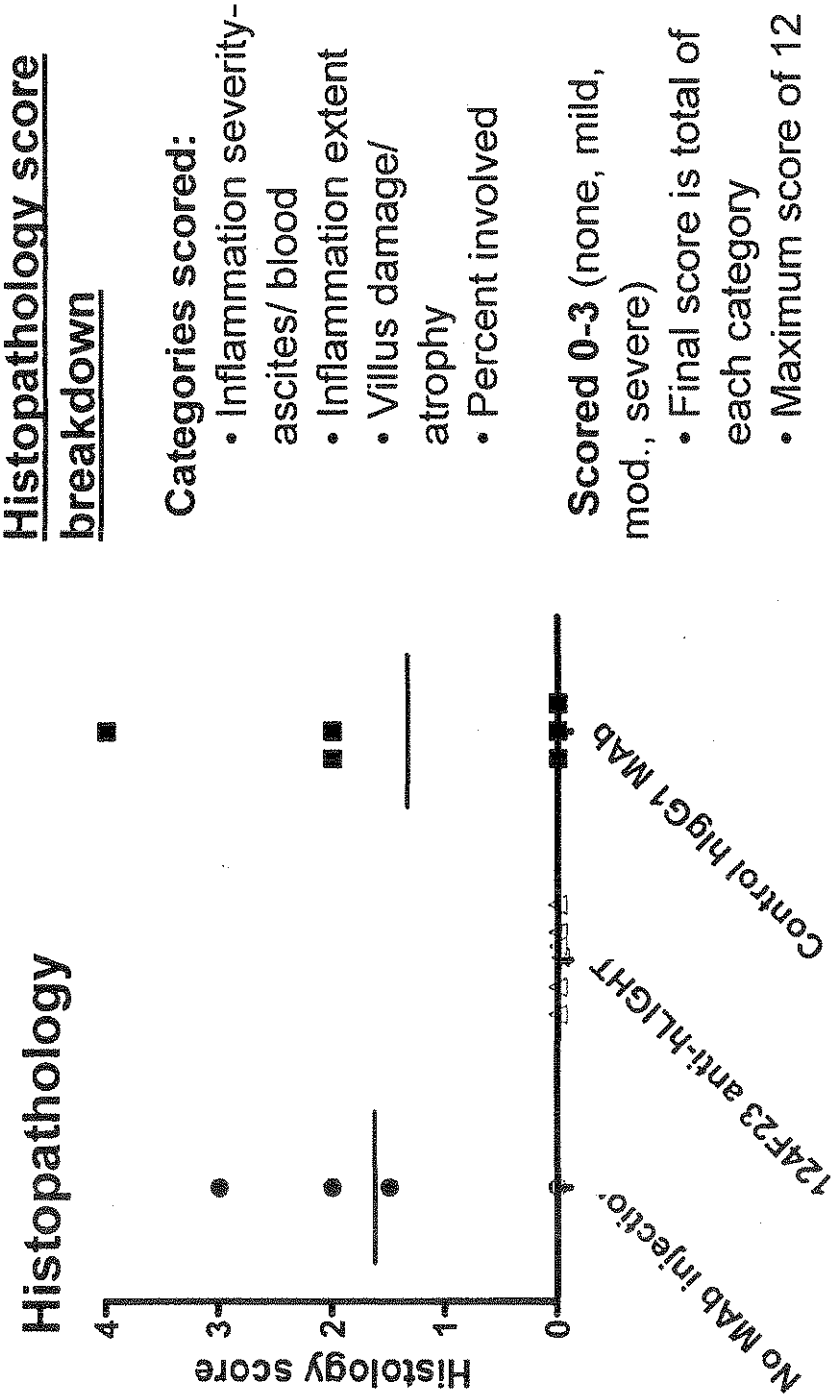

Histopathology
Histology score
4
3
2
1
0
No MAb injection
12AF23 anti-hLIGHT
Control hIgG1 MAb
Histopathology score breakdown
Categories scored:
• Inflammation severity- ascites/ blood
• Inflammation extent
• Villus damage/ atrophy
• Percent involved
Scored 0-3 (none, mild, mod., severe)
• Final score is total of each category
• Maximum score of 12

FIGURE 31

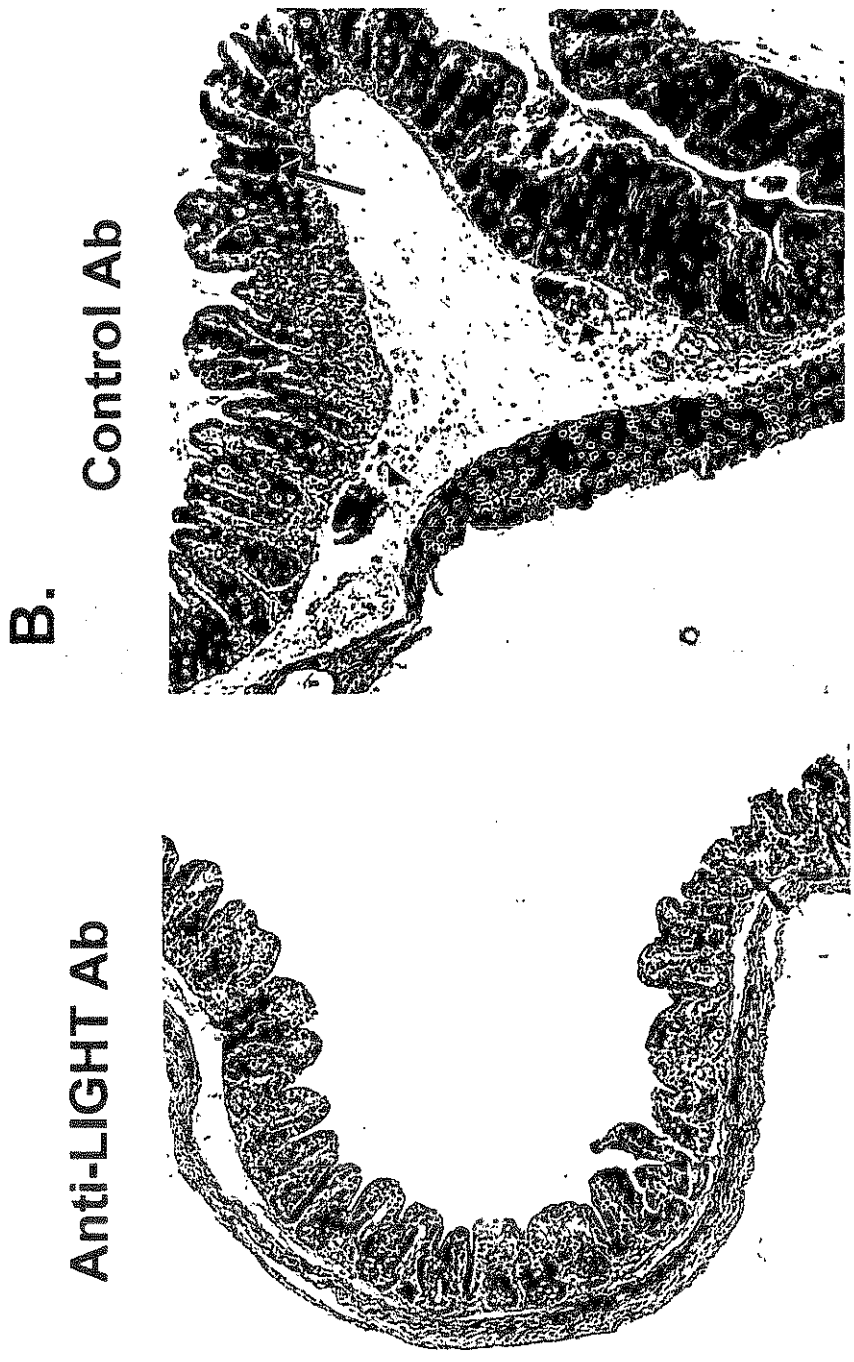
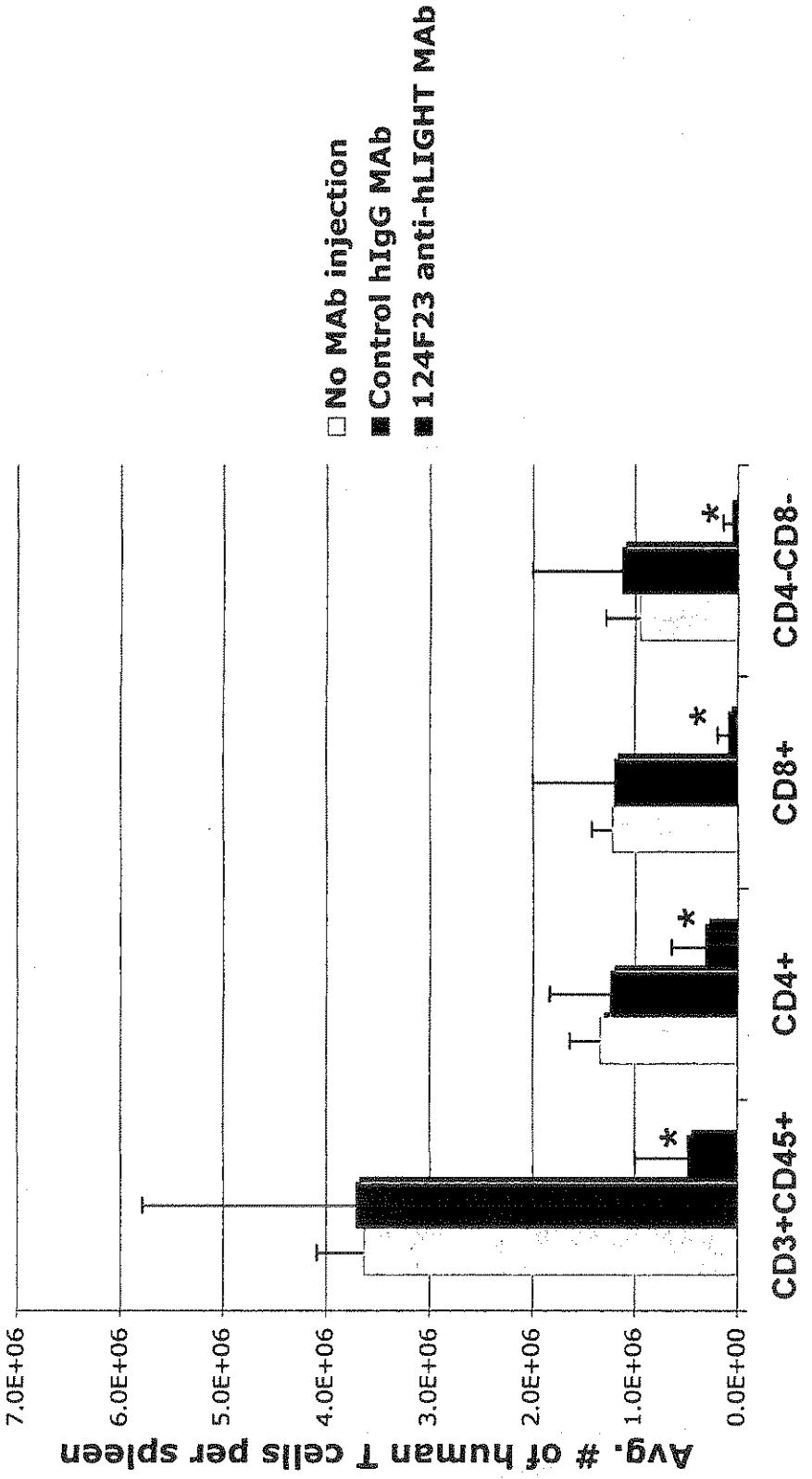


FIGURE 32


No MAb injection
Control hIgG MAb
124F23 anti-hLIGHT MAb
Avg. # of human T cells per spleen
7.0E+06
6.0E+06
5.0E+06
4.0E+06
3.0E+06
2.0E+06
1.0E+06
0.0E+00
CD3+CD45+
CD4+
CD8+
CD4-CD8-
*