FIGURE 1

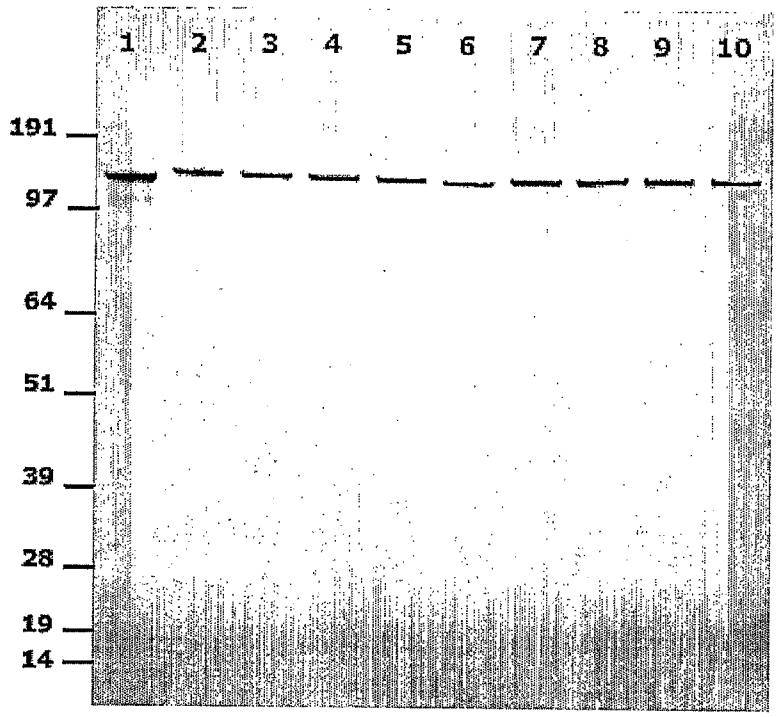


Figure 1 Non-reduced SDS-PAGE analysis of various HuMax-CD4 batches on 4-12% NuPAGE Bis-Tris gels. Lane 1, Internal Assay Control; Lane 2, MRS-CD4-001; Lane 3, MEV005; Lane 4, BN078; Lane 5, BO118; Lane 6, UNG-MRS-CD4; Lane 7, MOCK-MRS-CD4; Lane 8, M90-MRS-CD4; Lane 9, M50-MRS-CD4; Lane 10, MEV001. Migration of the markers (KDa) is indicated on the left.

FIGURE 2

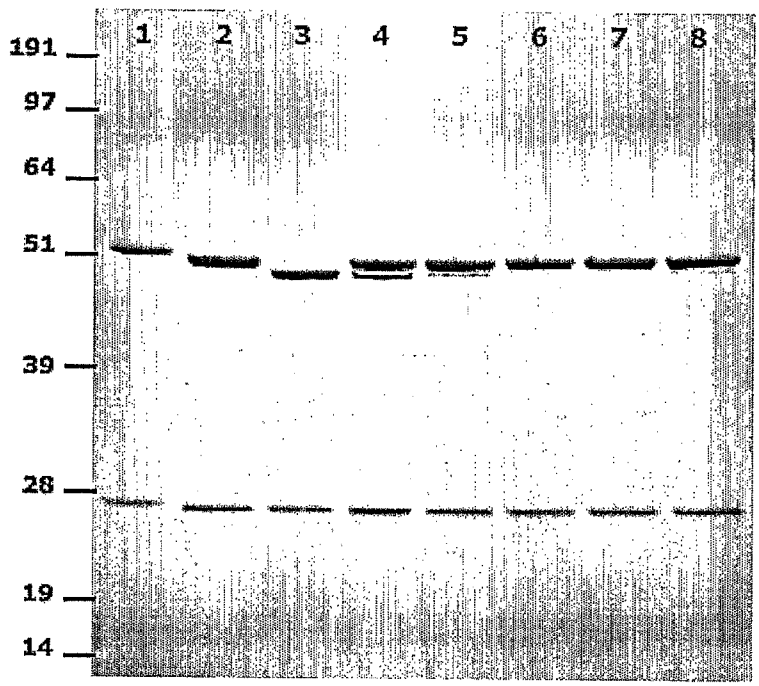


Figure 2A Reduced SDS-PAGE analysis of various HuMax-CD4 batches on 10% NuPAGE Bis-Tris gels. Lane 1, Internal Assay Control; Lane 2, MRS-CD4-001; Lane 3, UNG-MRS-CD4; Lane 4, MEV004; Lane 5, MEV005; Lane 6, MEV001; Lane 7, BN078; Lane 8, BO118. Migration of the markers (KDa) is indicated on the left.

FIGURE 3

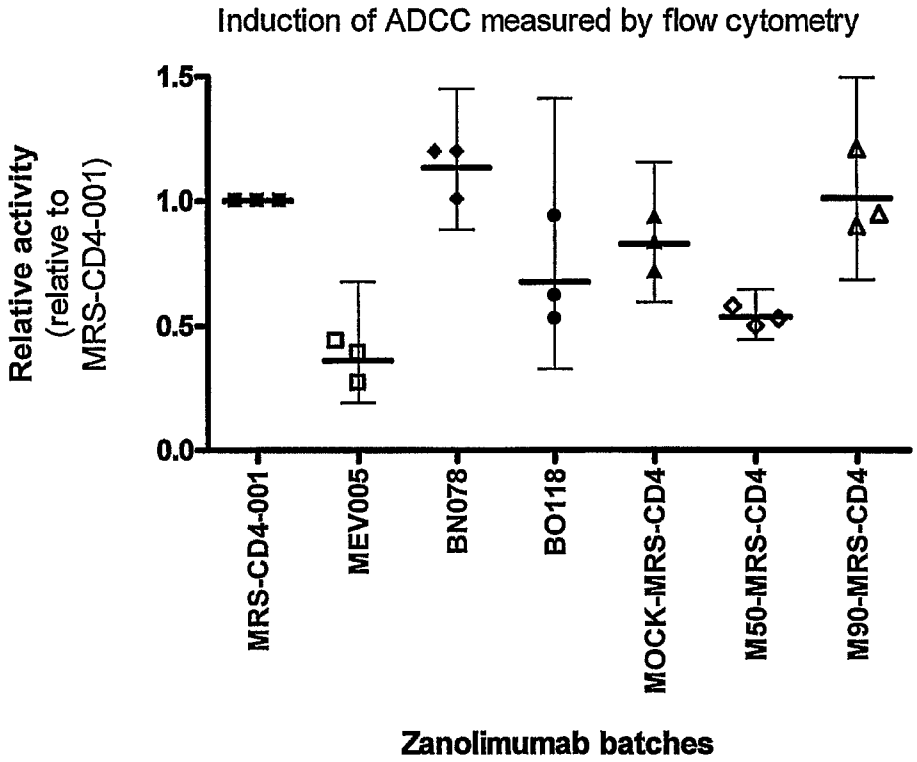
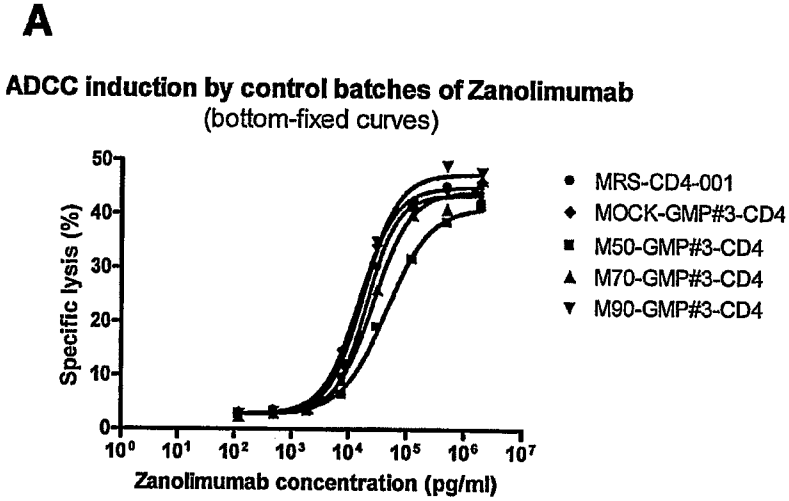

Induction of ADCC measured by flow cytometry
Relative activity (relative to MRS-CD4-001)
1.5
1.0
0.5
0.0
MRS-CD4-001
MEV005
BN078
BO118
MOCK-MRS-CD4
M50-MRS-CD4
M90-MRS-CD4
Zanolimumab batches

FIGURE 4

A


ADCC induction by control batches of Zanolimumab
(bottom-fixed curves)
Specific lysis (%)
50
40
30
20
10
0
10⁰ 10¹ 10² 10³ 10⁴ 10⁵ 10⁶ 10⁷
Zanolimumab concentration (pg/ml)
MRS-CD4-001
MOCK-GMP#3-CD4
M50-GMP#3-CD4
M70-GMP#3-CD4
M90-GMP#3-CD4

B

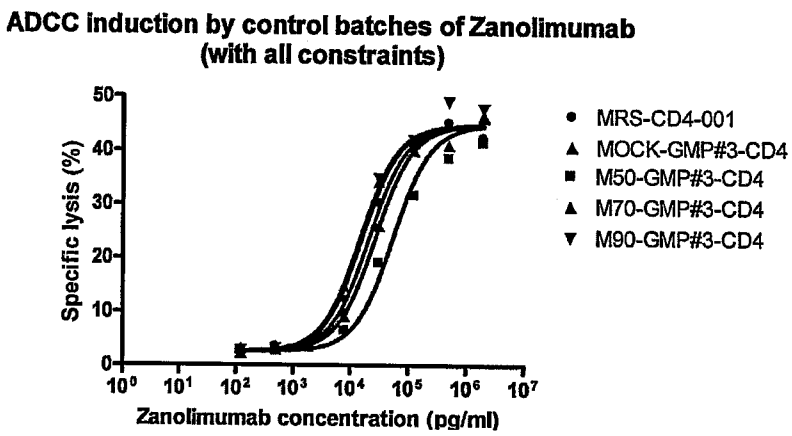

ADCC induction by control batches of Zanolimumab
(with all constraints)
Specific lysis (%)
50
40
30
20
10
0
10⁰ 10¹ 10² 10³ 10⁴ 10⁵ 10⁶ 10⁷
Zanolimumab concentration (pg/ml)
MRS-CD4-001
MOCK-GMP#3-CD4
M50-GMP#3-CD4
M70-GMP#3-CD4
M90-GMP#3-CD4

FIGURE 5

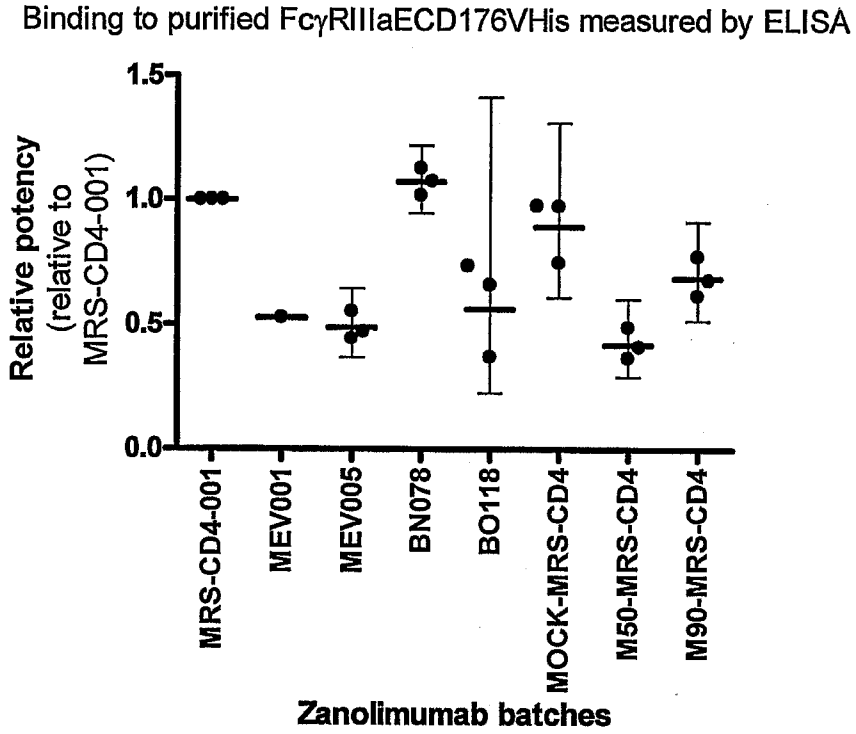

Binding to purified FcγRIIIaECD176VHis measured by ELISA
Relative potency (relative to MRS-CD4-001)
1.5
1.0
0.5
0.0
MRS-CD4-001
MEV001
MEV005
BN078
BO118
MOCK-MRS-CD4
M50-MRS-CD4
M90-MRS-CD4
Zanolimumab batches

FIGURE 6

FcγRIIIaECD176VHis binding by control batches of Zanolimumab

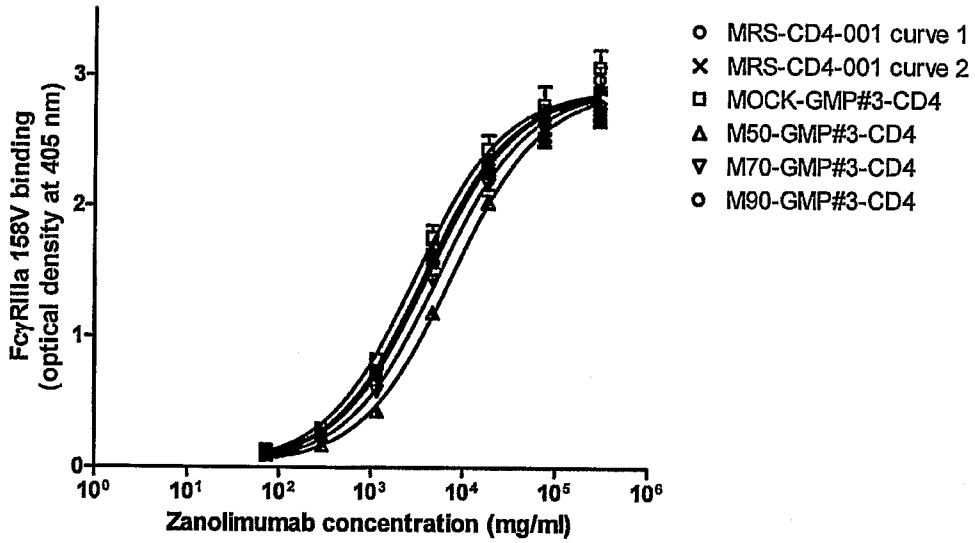


FIGURE 7

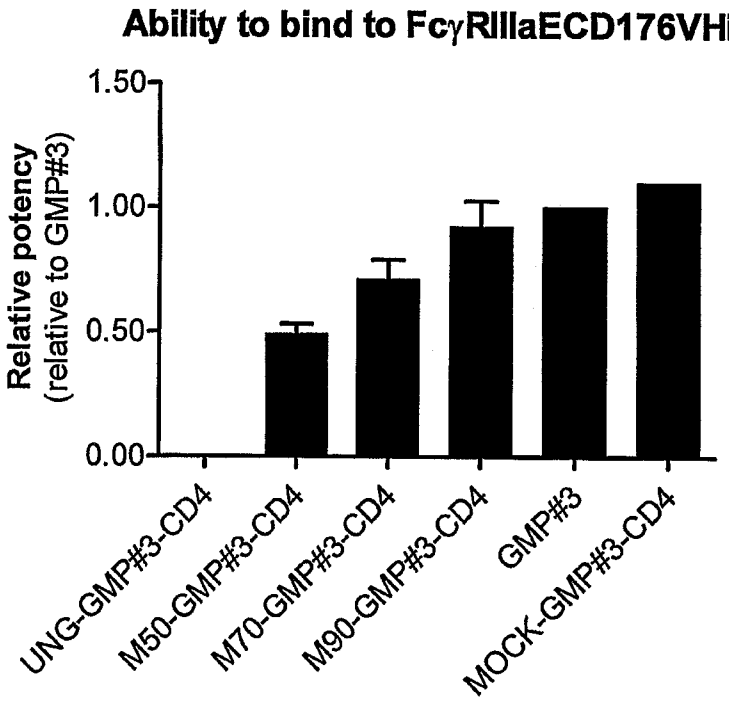

Ability to bind to FcγRIIIaECD176VHis
Relative potency
(relative to GMP#3)
1.50
1.00
0.50
0.00
UNG-GMP#3-CD4
M50-GMP#3-CD4
M70-GMP#3-CD4
M90-GMP#3-CD4
GMP#3
MOCK-GMP#3-CD4

FIGURE 8

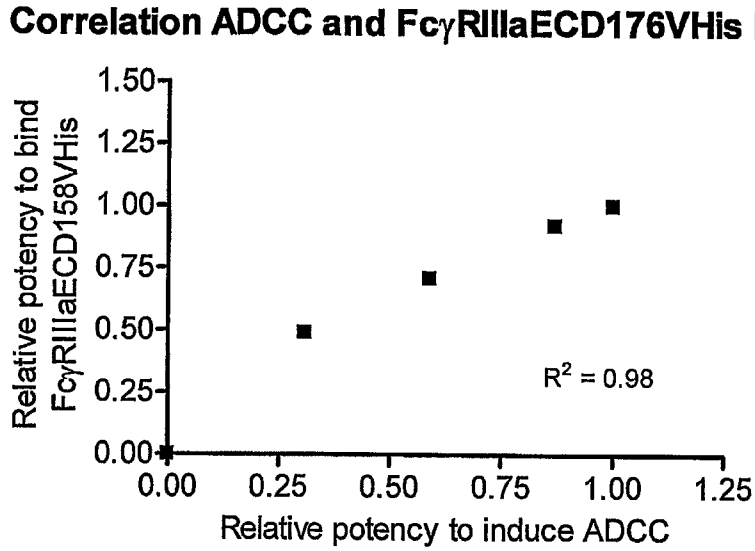

Correlation ADCC and FcγRIIIaECD176VHis binding
Relative potency to bind FcγRIIIaECD158VHis
1.50
1.25
1.00
0.75
0.50
0.25
0.00
R2 = 0.98
0.00
0.25
0.50
0.75
1.00
1.25
Relative potency to induce ADCC

FIGURE 9

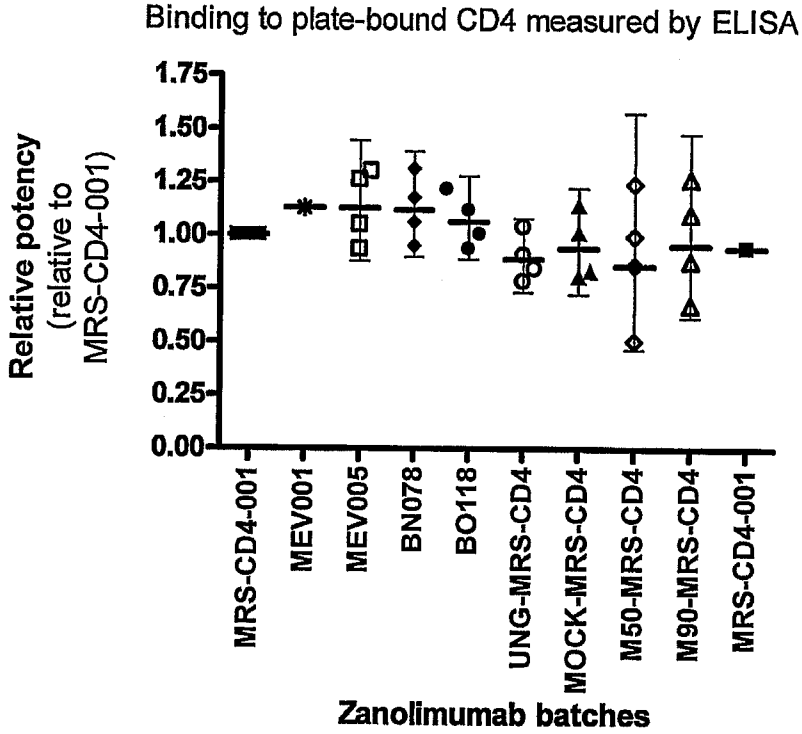

Binding to plate-bound CD4 measured by ELISA
Relative potency (relative to MRS-CD4-001)
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
MRS-CD4-001
MEV001
MEV005
BN078
BO118
UNG-MRS-CD4
MOCK-MRS-CD4
M50-MRS-CD4
M90-MRS-CD4
MRS-CD4-001
Zanolimumab batches

FIGURE 10

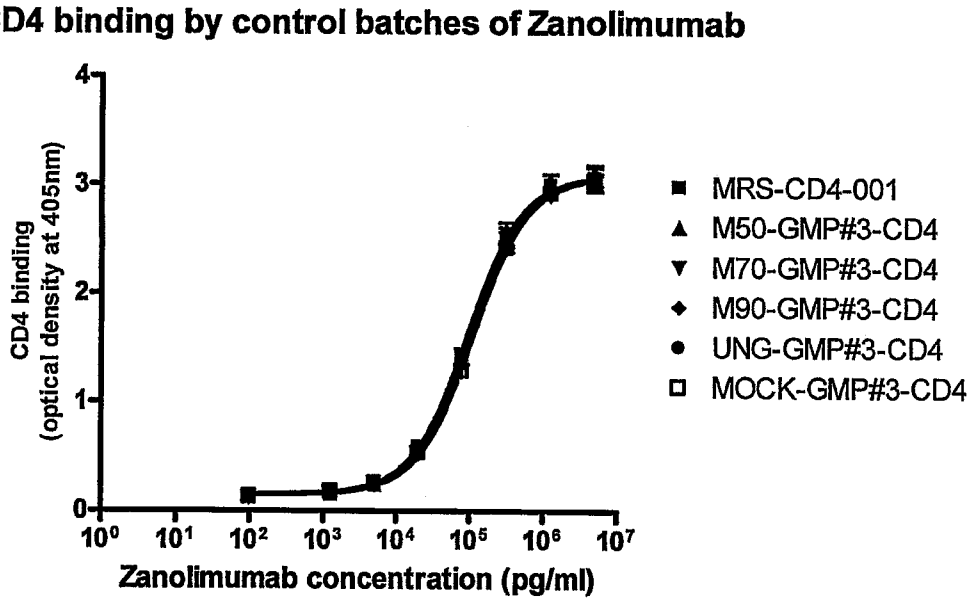

CD4 binding by control batches of Zanolimumab
CD4 binding (optical density at 405nm)
0
1
2
3
4
10^0 10^1 10^2 10^3 10^4 10^5 10^6 10^7
Zanolimumab concentration (pg/ml)
MRS-CD4-001
M50-GMP#3-CD4
M70-GMP#3-CD4
M90-GMP#3-CD4
UNG-GMP#3-CD4
MOCK-GMP#3-CD4

FIGURE 11

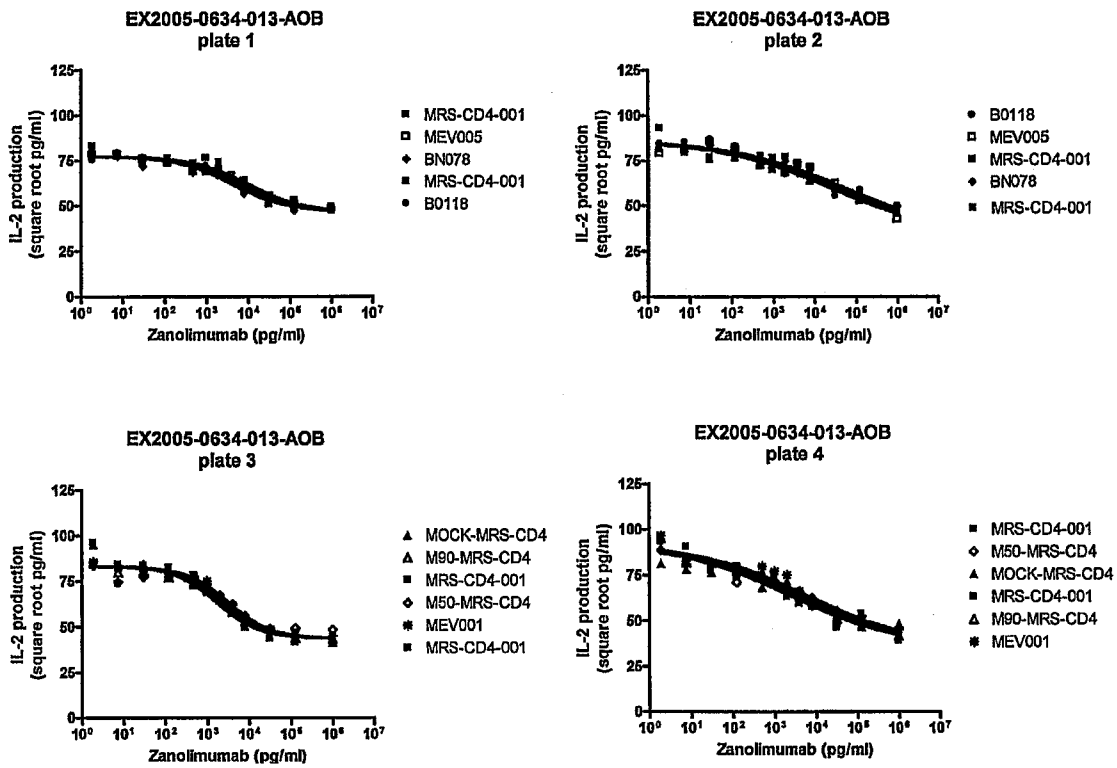

EX2005-0634-013-AOB
plate 1
IL-2 production (square root pg/ml)
Zanolimumab (pg/ml)
MRS-CD4-001
MEV005
BN078
MRS-CD4-001
B0118
EX2005-0634-013-AOB
plate 2
IL-2 production (square root pg/ml)
Zanolimumab (pg/ml)
B0118
MEV005
MRS-CD4-001
BN078
MRS-CD4-001
EX2005-0634-013-AOB
plate 3
IL-2 production (square root pg/ml)
Zanolimumab (pg/ml)
MOCK-MRS-CD4
M90-MRS-CD4
MRS-CD4-001
M50-MRS-CD4
MEV001
MRS-CD4-001
EX2005-0634-013-AOB
plate 4
IL-2 production (square root pg/ml)
Zanolimumab (pg/ml)
MRS-CD4-001
M50-MRS-CD4
MOCK-MRS-CD4
MRS-CD4-001
M90-MRS-CD4
MEV001

FIGURE 12

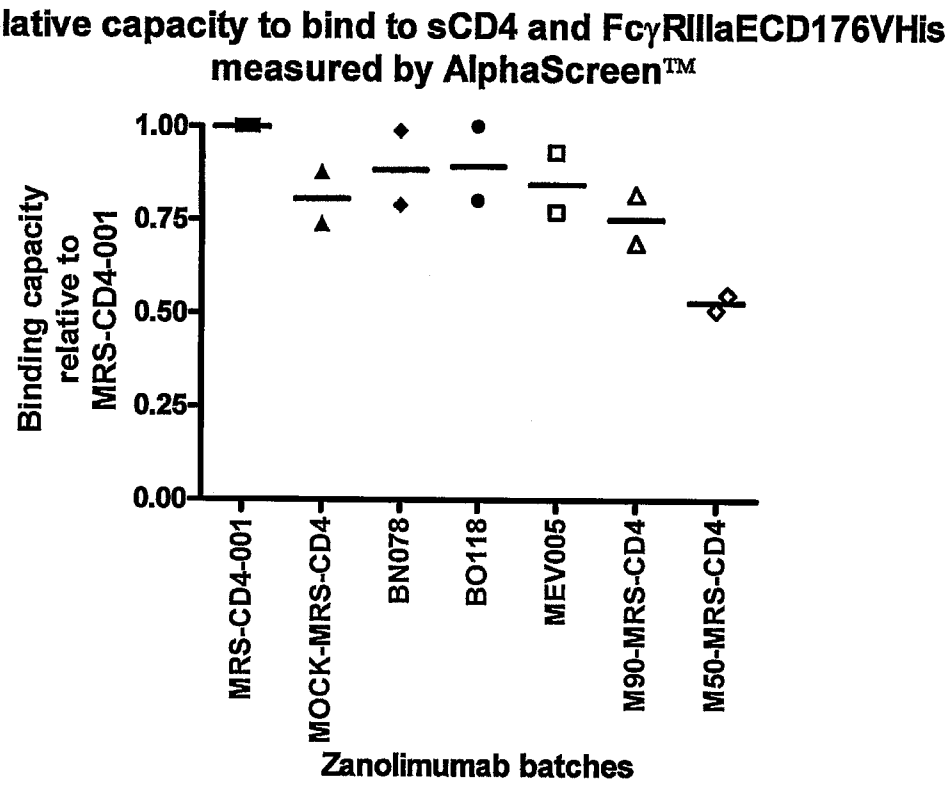

Relative capacity to bind to sCD4 and FcγRIIIaECD176VHis measured by AlphaScreen™
Binding capacity relative to MRS-CD4-001
1.00
0.75
0.50
0.25
0.00
MRS-CD4-001
MOCK-MRS-CD4
BN078
BO118
MEV005
M90-MRS-CD4
M50-MRS-CD4
Zanolimumab batches

FIGURE 13

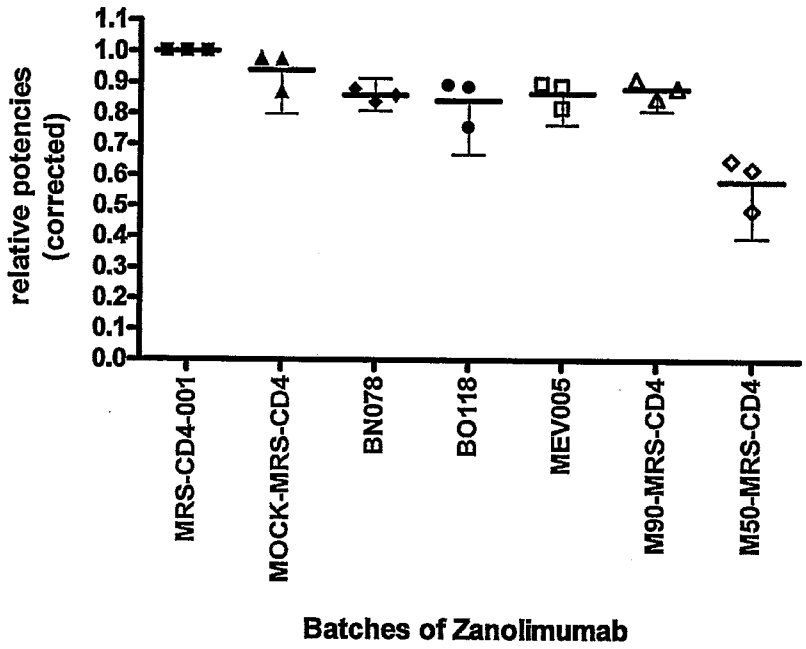

relative potencies (corrected)
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
MRS-CD4-001
MOCK-MRS-CD4
BN078
BO118
MEV005
M90-MRS-CD4
M50-MRS-CD4
Batches of Zanolimumab

FIGURE 14

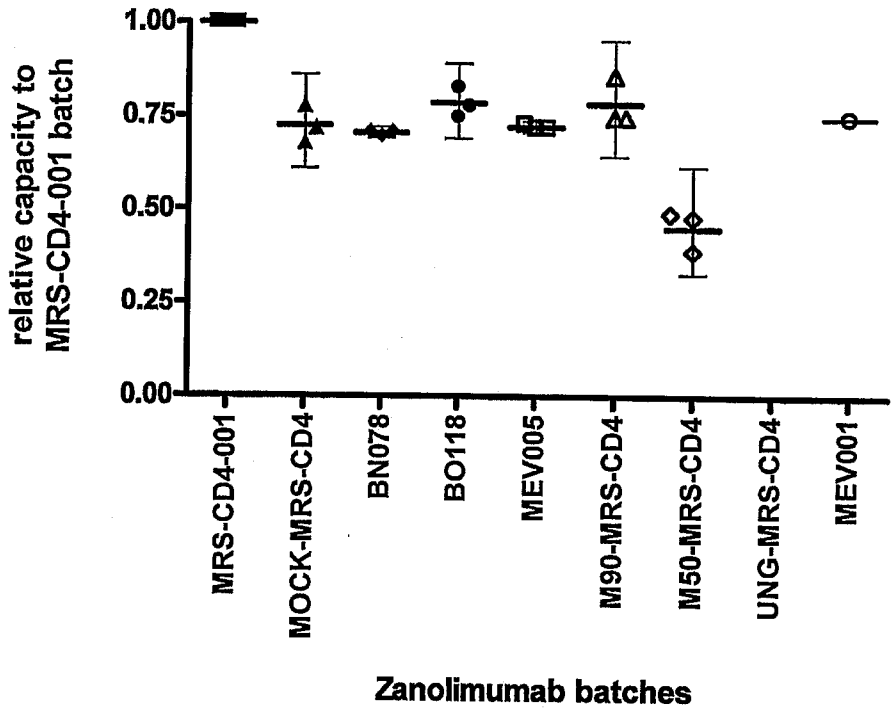

relative capacity to MRS-CD4-001 batch
1.00
0.75
0.50
0.25
0.00
MRS-CD4-001
MOCK-MRS-CD4
BN078
BO118
MEV005
M90-MRS-CD4
M50-MRS-CD4
UNG-MRS-CD4
MEV001
Zanolimumab batches

FIGURE 15

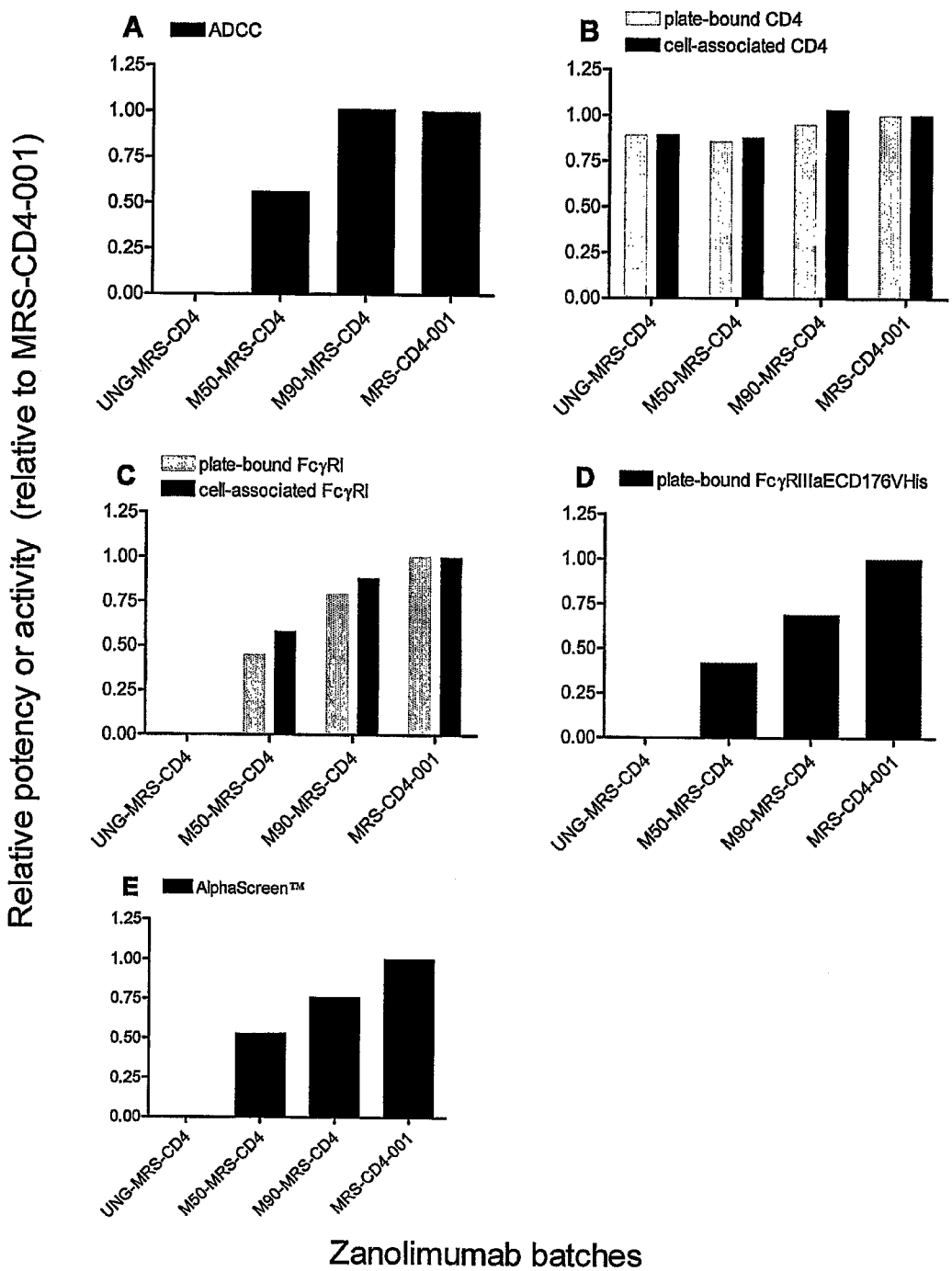

A
ADCC
B
plate-bound CD4
cell-associated CD4
C
plate-bound FcγRI
cell-associated FcγRI
D
plate-bound FcγRIIIaECD176VHis
E
AlphaScreen™
1.25
1.00
0.75
0.50
0.25
0.00
UNG-MRS-CD4
M50-MRS-CD4
M90-MRS-CD4
MRS-CD4-001
Relative potency or activity (relative to MRS-CD4-001)
Zanolimumab batches

FIGURE 16

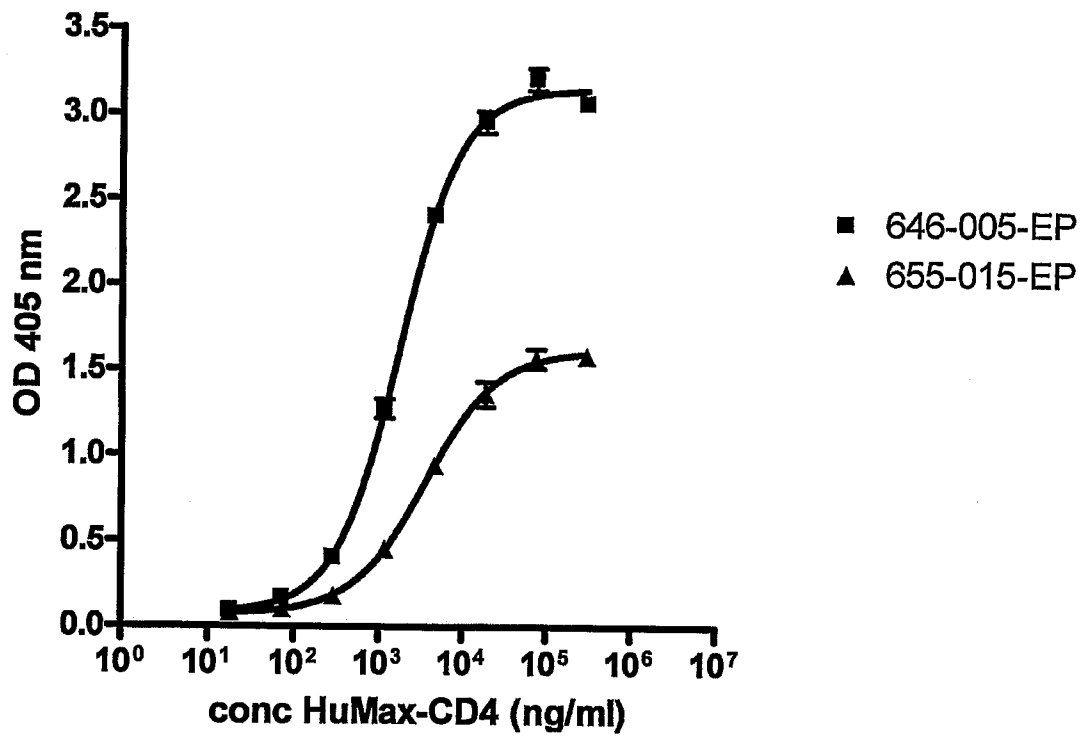

3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
OD 405 nm
10^0 10^1 10^2 10^3 10^4 10^5 10^6 10^7
conc HuMax-CD4 (ng/ml)
646-005-EP
655-015-EP

FIGURE 17

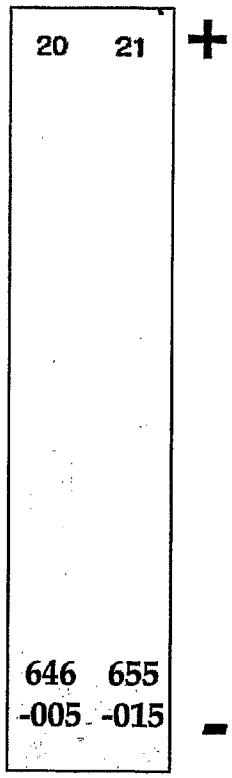


FIGURE 18

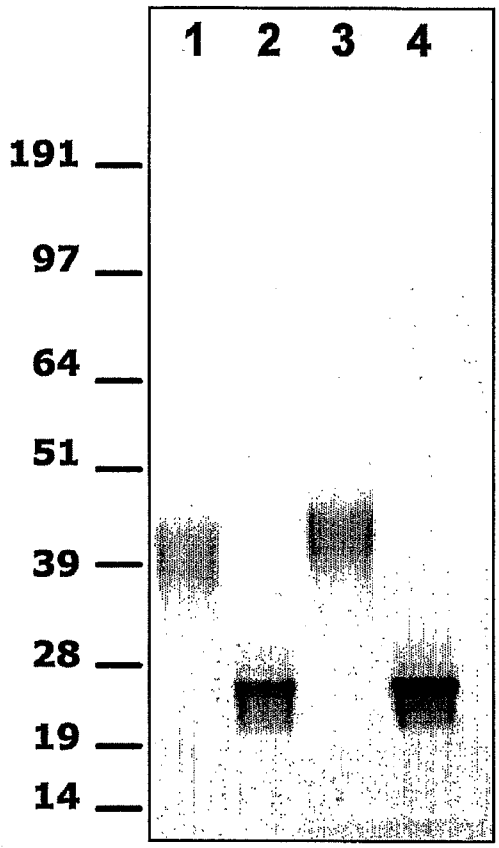


FIGURE 19

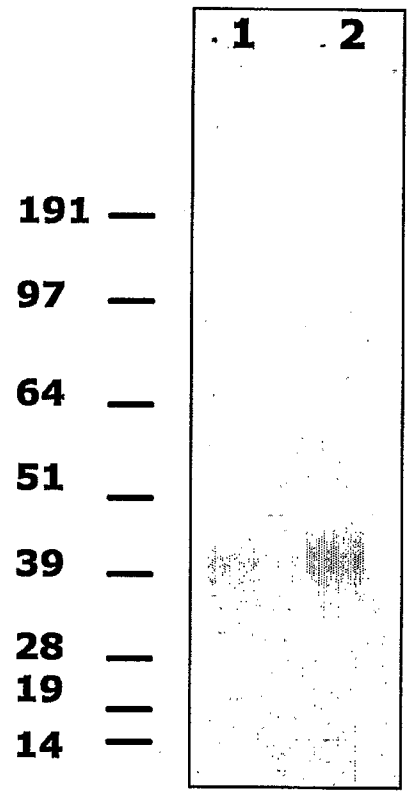


FIGURE 20

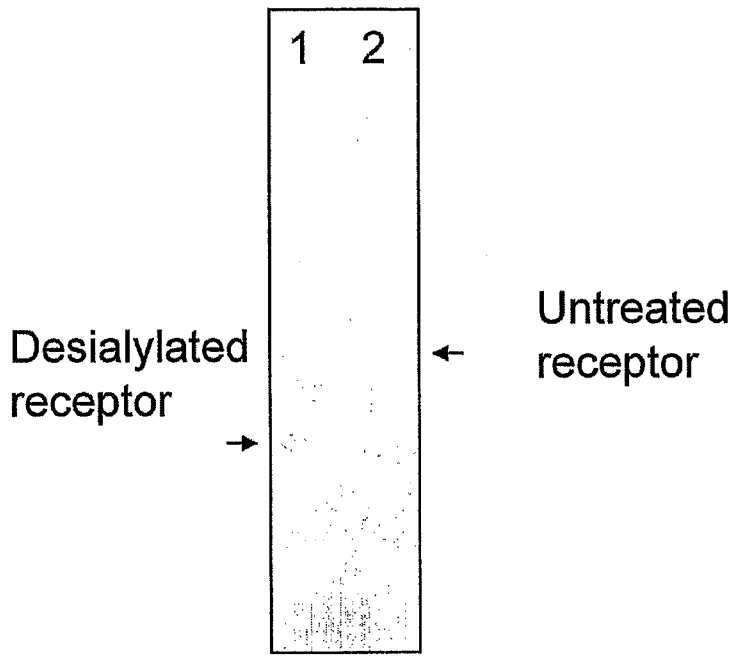


FIGURE 21

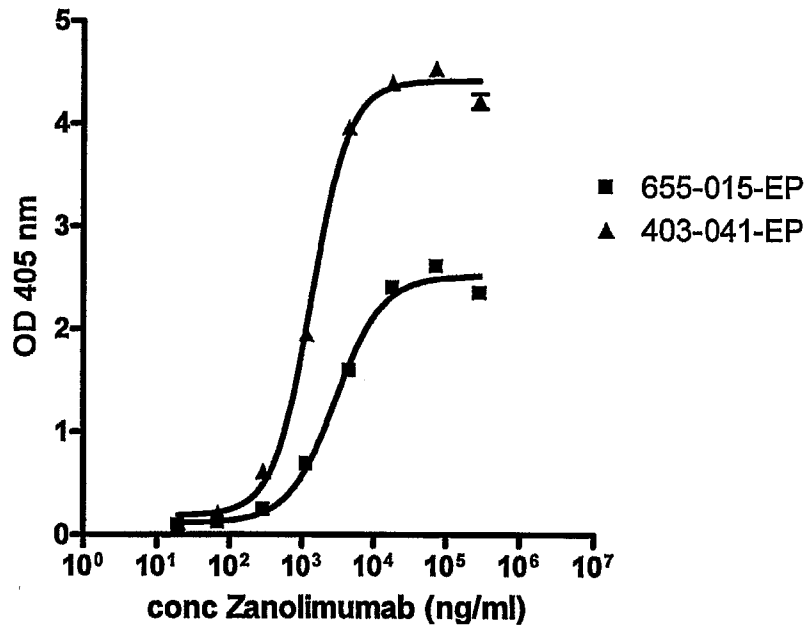

OD 405 nm
0
1
2
3
4
5
10^0 10^1 10^2 10^3 10^4 10^5 10^6 10^7
conc Zanolimumab (ng/ml)
655-015-EP
403-041-EP

FIGURE 22

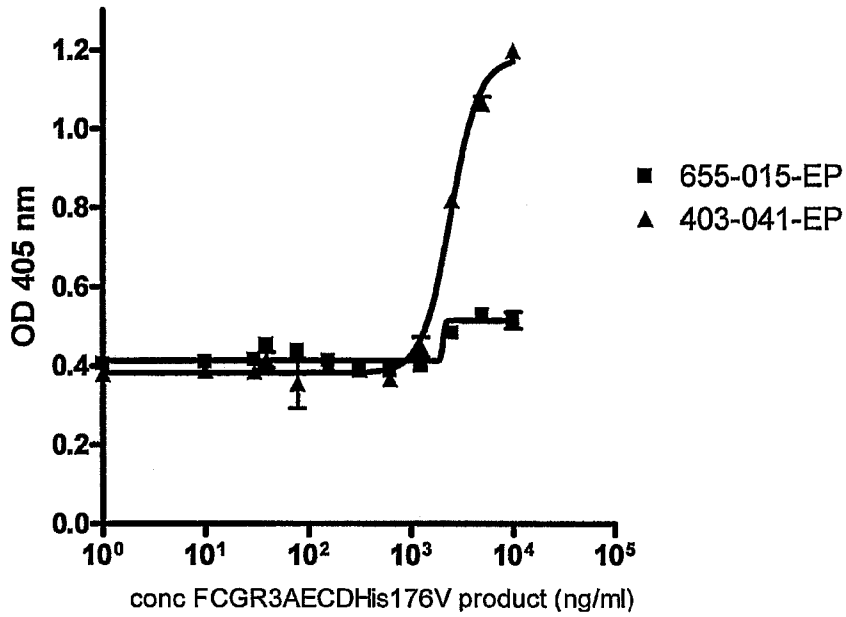
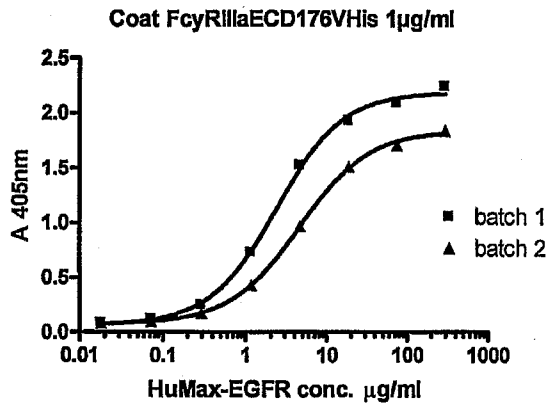

1.2
1.0
0.8
0.6
0.4
0.2
0.0
OD 405 nm
10^0
10^1
10^2
10^3
10^4
10^5
conc FCGR3AECDHis176V product (ng/ml)
655-015-EP
403-041-EP

FIGURE 23


Coat FcyRIIIaECD176VHis 1µg/ml
A 405nm
2.5
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
1000
HuMax-EGFR conc. µg/ml
batch 1
batch 2

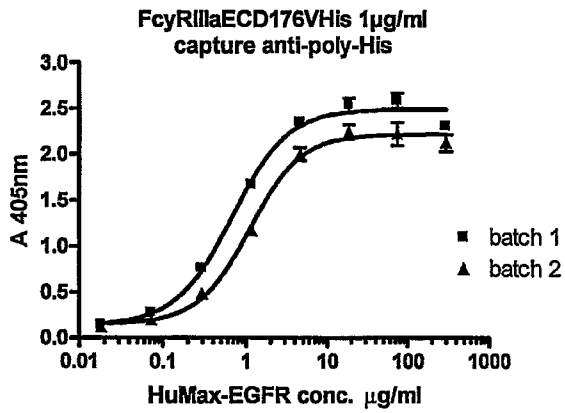

FcyRIIIaECD176VHis 1µg/ml
capture anti-poly-His
A 405nm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
1000
HuMax-EGFR conc. µg/ml
batch 1
batch 2

Figure 24

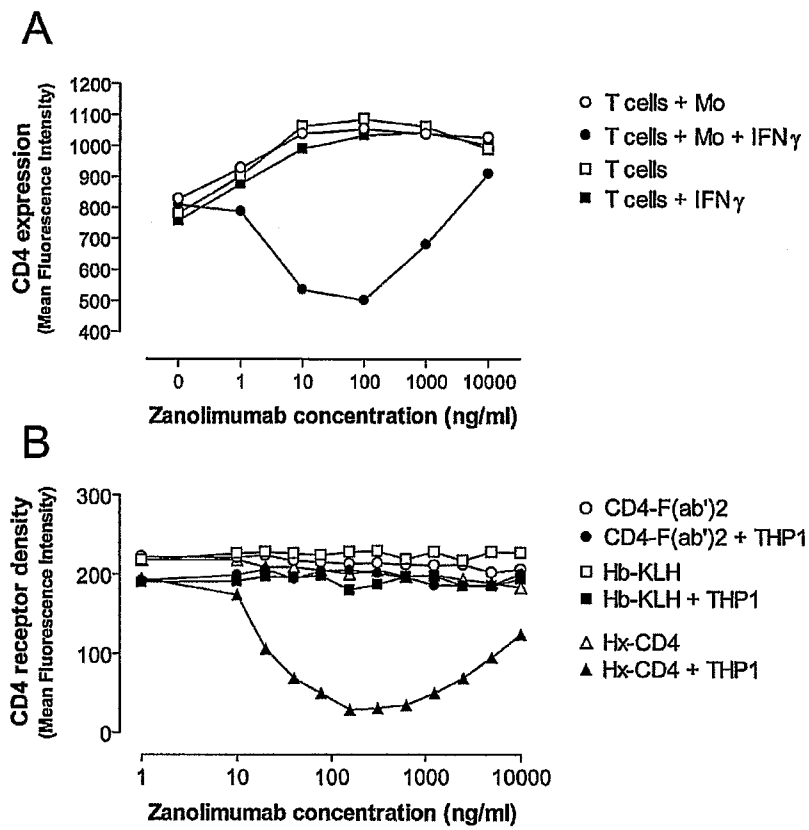

A
CD4 expression
(Mean Fluorescence Intensity)
1200
1100
1000
900
800
700
600
500
400
0
1
10
100
1000
10000
Zanolimumab concentration (ng/ml)
T cells + Mo
T cells + Mo + IFNγ
T cells
T cells + IFNγ
B
CD4 receptor density
(Mean Fluorescence Intensity)
300
200
100
0
1
10
100
1000
10000
Zanolimumab concentration (ng/ml)
CD4-F(ab')2
CD4-F(ab')2 + THP1
Hb-KLH
Hb-KLH + THP1
Hx-CD4
Hx-CD4 + THP1

FIGURE 25

Sequence listing

SEQ ID No: 1

```
  1 MWFLTTLLLW VPVDGQVDTT KAVITLQPPW VSVFQEETVT LHCEVLHLPG SSSTQWFLNG
 61 TATQTSTPSY RITSASVNDS GEYRCQRGLS GRSDPIQLEI HRGWLLLQVS SRVFTEGEPL
121 ALRCHAWKDK LVYNVLYYRN GKAFKFFHWN SNLTILKTNI SHNGTYHCSG MGKHRYTSAG
181 ISVTVKELFP APVLNASVTS PLLEGNLVTL SCETKLLLQR PGLQLYFSFY MGSKTLRGRN
241 TSSEYQILTA RREDSGLYWC EAATEDGNVL KRSPELELQV LGLQLPTPVW FHHHHHHH
```

SEQ ID No: 2

```
  1 MWQLLLPTAL LLLVSAGMRT EDLPKAVVFL EPQWYRVLEK DSVTLKCQGA YSPEDNSTQW
 61 FHNESLISSQ ASSYFIDAAT VDDSGEYRCQ TNLSTLSDPV QLEVHIGWLL LQAPRWVFKE
121 EDPIHLRCHS WKNTALHKVT YLQNGKGRKY FHHNSDFYIP KATLKDSGSY FCRGLVGSKN
181 VSSETVNITI TQGLAVSTIS HHHHHH
```

SEQ ID No: 3

```
  1 MWQLLLPTAL LLLVSAGMRT EDLPKAVVFL EPQWYRVLEK DSVTLKCQGA YSPEDNSTQW
 61 FHNESLISSQ ASSYFIDAAT VDDSGEYRCQ TNLSTLSDPV QLEVHIGWLL LQAPRWVFKE
121 EDPIHLRCHS WKNTALHKVT YLQNGKGRKY FHHNSDFYIP KATLKDSGSY FCRGLFGSKN
181 VSSETVNITI TQGLAVSTIS HHHHHH
```

SEQ ID No: 4

```
1 GATCCCGGGG CCGCCACCAT GTGGTTCTTG ACAACTCTGC
```

SEQ ID No: 5

```
1 CCGTACGTTA GTGATGGTGA TGGTGATGAT GAAACCAGAC AGGAGTTGG
```

SEQ ID No: 6

```
1 GAAGACTTAA GGCAGCGGCA GAA
```

SEQ ID No: 7

```
1 TCGGACATCT CATGACTTTC TTT
```

SEQ ID No: 8

```
1 GATCCCGGGG CCGCCACCAT GTGGCAGCTG CTCCTCCCAA
```

SEQ ID No: 9

```
1 CGAATTCTTA GTGATGGTGA TGGTGATGTG AGATGGTTGA CACTGCCAA
```

SEQ ID No: 10

```
1 TACTTCTGCA GGGGGCTTTT CGGGAGTAAA AATGTGTCT
```

SEQ ID No: 11

1 AGACACATTT TTACTCCCGA AAAGCCCCCT GCAGAAGTA