Fig. 1

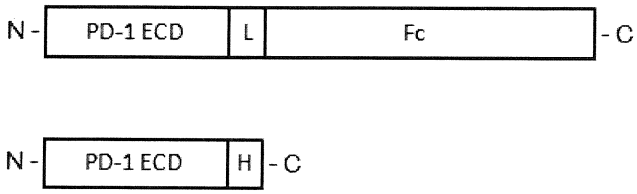

N -
PD-1 ECD
L
Fc
- C
N -
PD-1 ECD
H
- C

Fig. 2

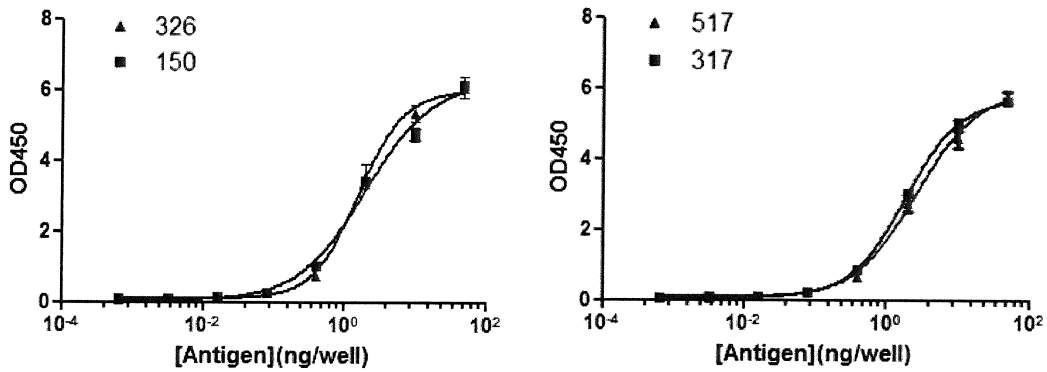

326
150
OD450
[Antigen](ng/well)
517
317
OD450
[Antigen](ng/well)

Fig. 3

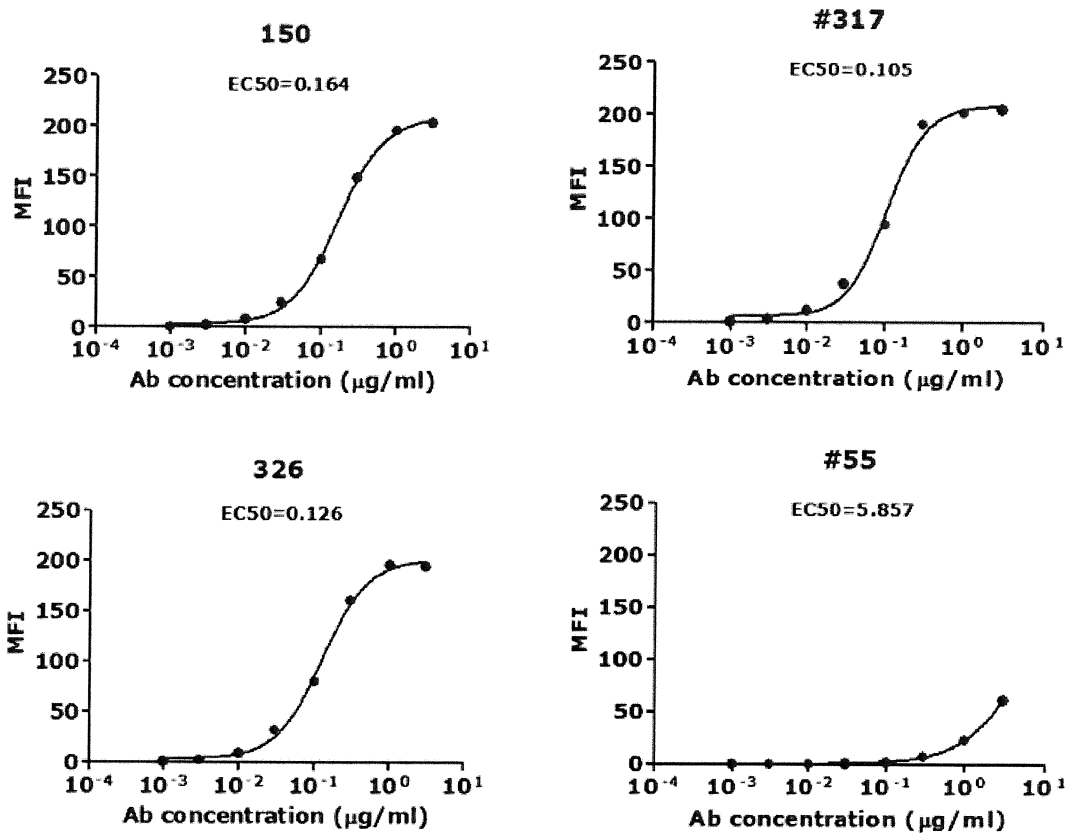

150
EC50=0.164
#317
EC50=0.105
326
EC50=0.126
#55
EC50=5.857
MFI
Ab concentration (µg/ml)

Fig. 4

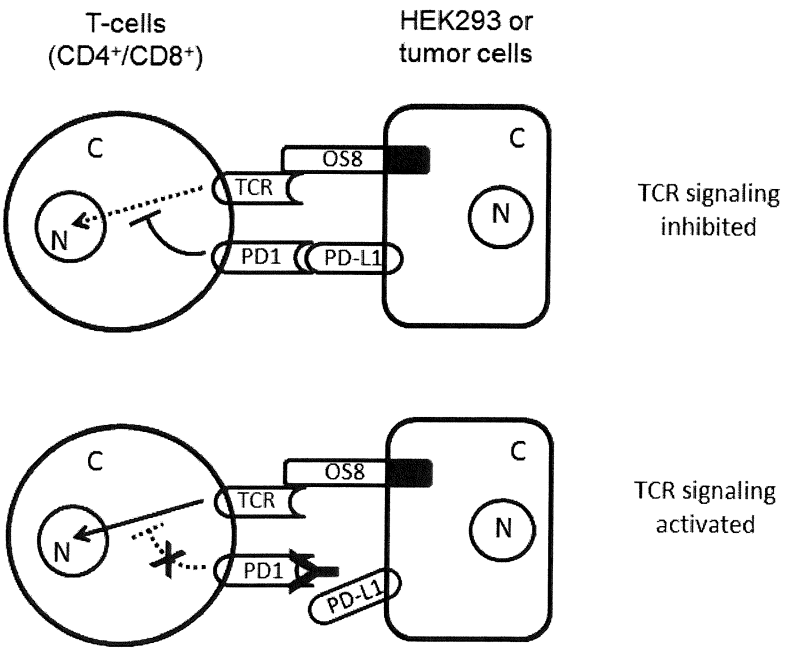

T-cells
(CD4+/CD8+)
HEK293 or
tumor cells
C
N
OS8
TCR
PD1
PD-L1
TCR signaling
inhibited
TCR signaling
activated

Fig. 5

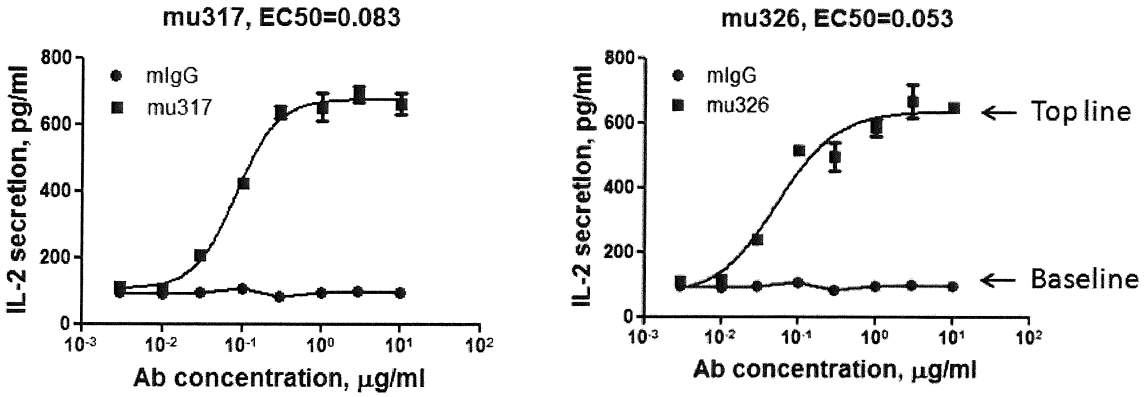
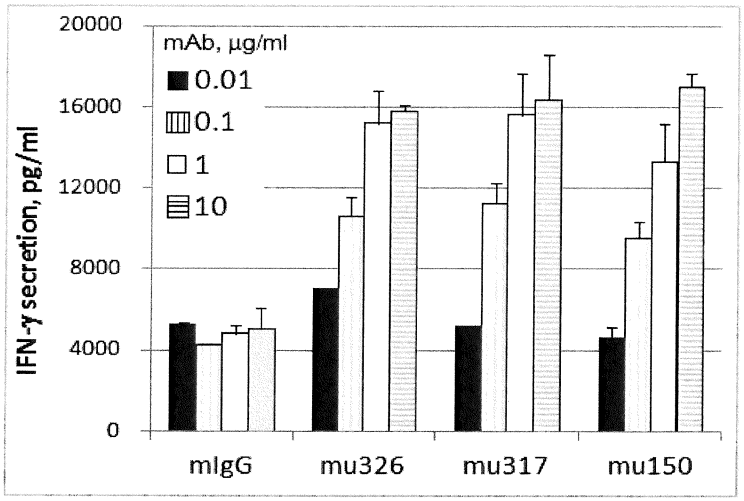

mu317, EC50=0.083
mIgG
mu317
IL-2 secretion, pg/ml
Ab concentration, µg/ml
mu326, EC50=0.053
mIgG
mu326
Top line
Baseline
IL-2 secretion, pg/ml
Ab concentration, µg/ml

Fig. 6 (A)


mAb, µg/ml
0.01
0.1
1
10
IFN-γ secretion, pg/ml
mIgG
mu326
mu317
mu150

(B)

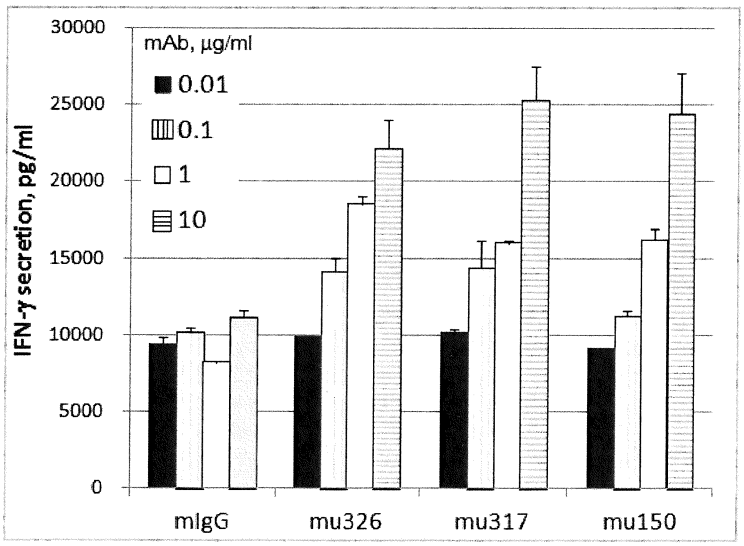

mAb, µg/ml
0.01
0.1
1
10
IFN-γ secretion, pg/ml
mIgG
mu326
mu317
mu150

Fig. 7

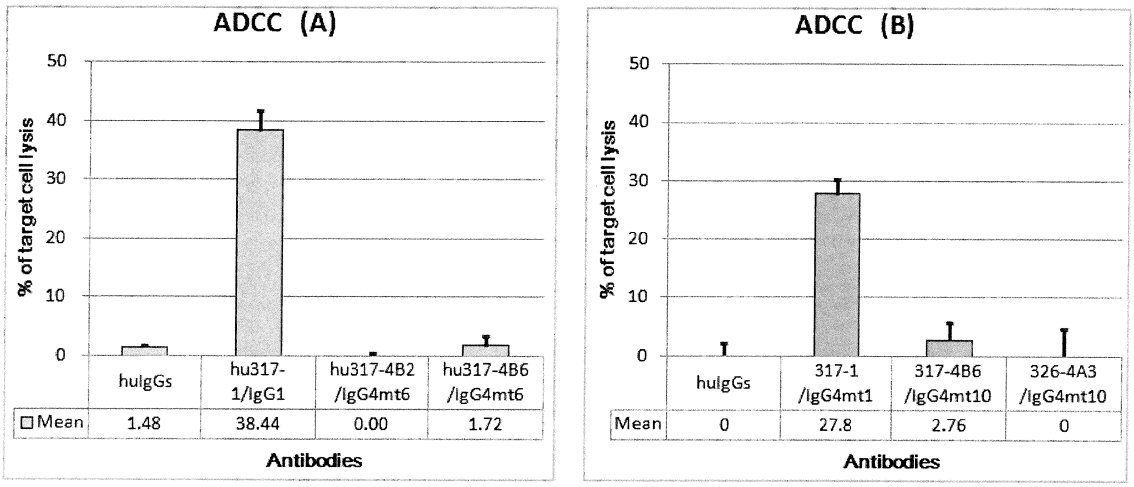
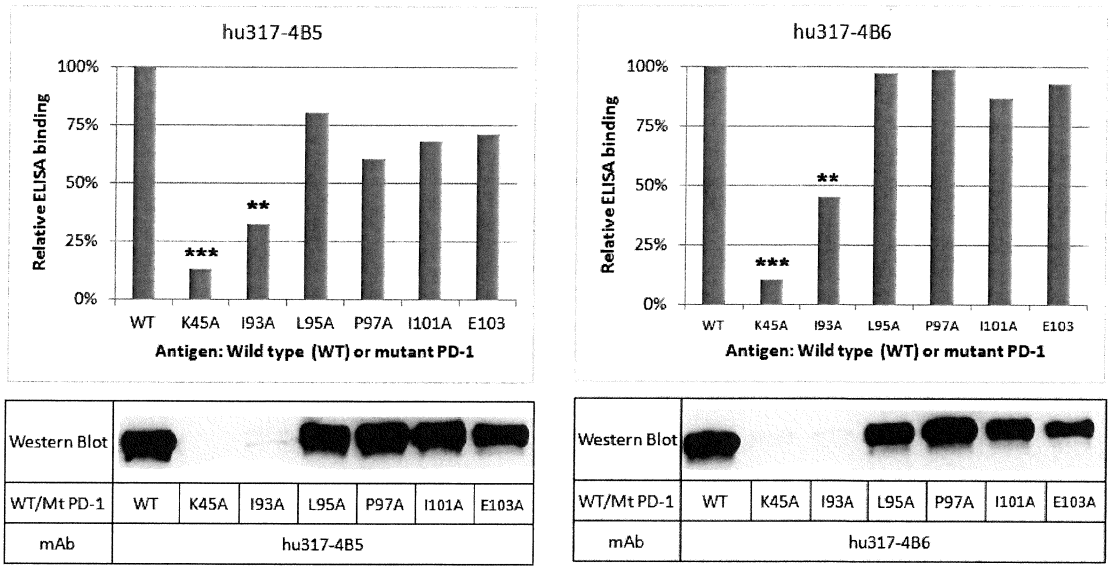


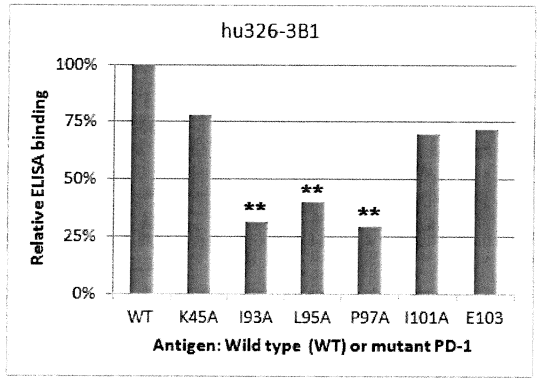
Fig. 8

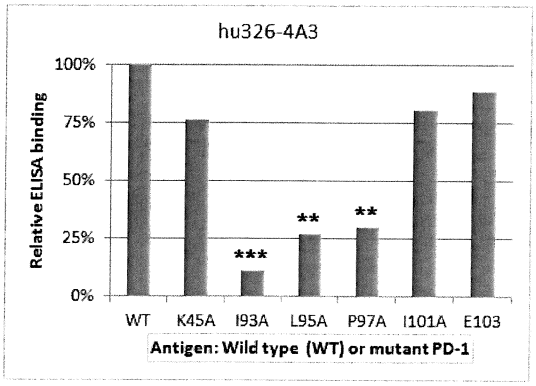


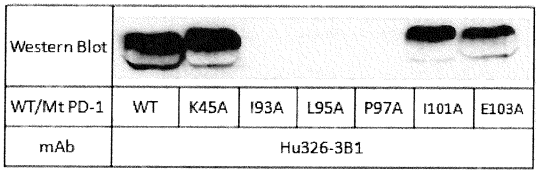
Western Blot							
WT/Mt PD-1	WT	K45A	I93A	L95A	P97A	I101A	E103A
mAb	hu317-4B5						

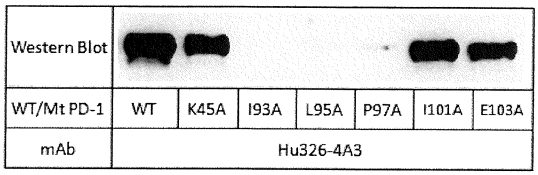
Western Blot							
WT/Mt PD-1	WT	K45A	I93A	L95A	P97A	I101A	E103A
mAb	hu317-4B6						

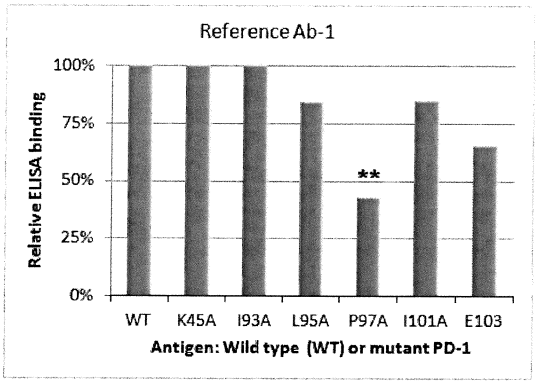
Fig. 8 (cont'd)

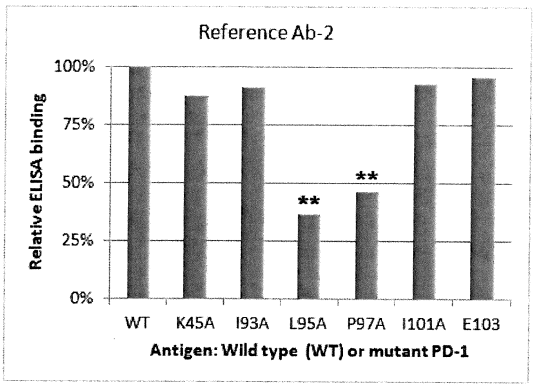

hu326-3B1
Relative ELISA binding
100%
75%
50%
25%
0%
**
**
**
WT
K45A
I93A
L95A
P97A
I101A
E103
Antigen: Wild type (WT) or mutant PD-1

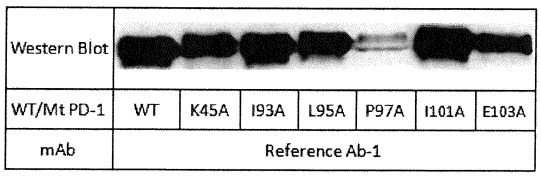

hu326-4A3
Relative ELISA binding
100%
75%
50%
25%
0%
***
**
**
WT
K45A
I93A
L95A
P97A
I101A
E103
Antigen: Wild type (WT) or mutant PD-1


Western Blot
WT/Mt PD-1
WT
K45A
I93A
L95A
P97A
I101A
E103A
mAb
Hu326-3B1


Western Blot
WT/Mt PD-1
WT
K45A
I93A
L95A
P97A
I101A
E103A
mAb
Hu326-4A3


Reference Ab-1
Relative ELISA binding
100%
75%
50%
25%
0%
**
WT
K45A
I93A
L95A
P97A
I101A
E103
Antigen: Wild type (WT) or mutant PD-1


Reference Ab-2
Relative ELISA binding
100%
75%
50%
25%
0%
**
**
WT
K45A
I93A
L95A
P97A
I101A
E103
Antigen: Wild type (WT) or mutant PD-1


Western Blot
WT/Mt PD-1
WT
K45A
I93A
L95A
P97A
I101A
E103A
mAb
Reference Ab-1

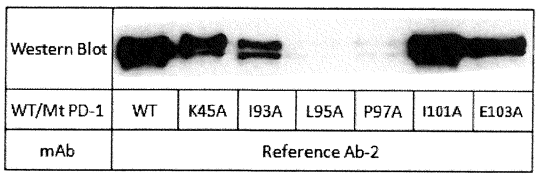

Western Blot
WT/Mt PD-1
WT
K45A
I93A
L95A
P97A
I101A
E103A
mAb
Reference Ab-2

Fig. 9.

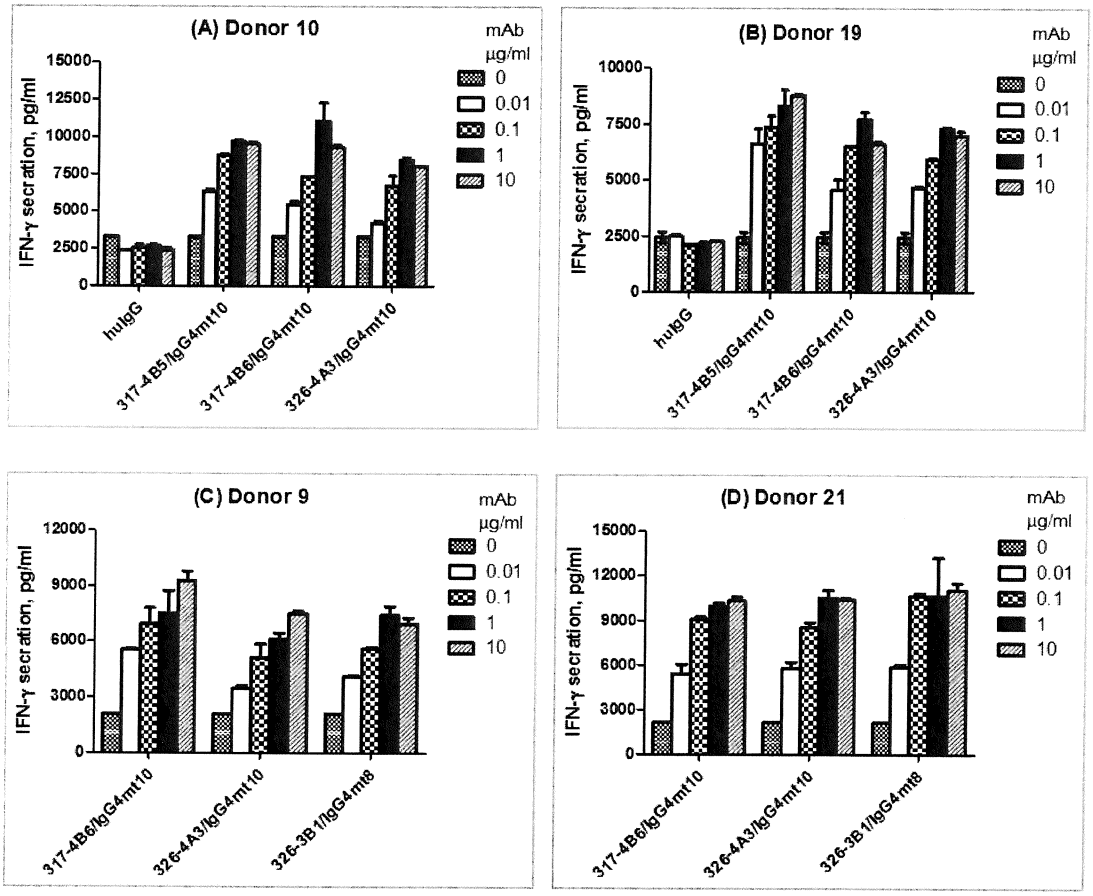

(A) Donor 10
IFN-γ secration, pg/ml
15000
12500
10000
7500
5000
2500
0
huIgG
317-4B5/IgG4mt10
317-4B6/IgG4mt10
326-4A3/IgG4mt10
mAb µg/ml
0
0.01
0.1
1
10
(B) Donor 19
IFN-γ secration, pg/ml
10000
7500
5000
2500
0
huIgG
317-4B5/IgG4mt10
317-4B6/IgG4mt10
326-4A3/IgG4mt10
mAb µg/ml
0
0.01
0.1
1
10
(C) Donor 9
IFN-γ secration, pg/ml
12000
9000
6000
3000
0
317-4B6/IgG4mt10
326-4A3/IgG4mt10
326-3B1/IgG4mt8
mAb µg/ml
0
0.01
0.1
1
10
(D) Donor 21
IFN-γ secration, pg/ml
15000
12000
9000
6000
3000
0
317-4B6/IgG4mt10
326-4A3/IgG4mt10
326-3B1/IgG4mt8
mAb µg/ml
0
0.01
0.1
1
10

Fig. 10

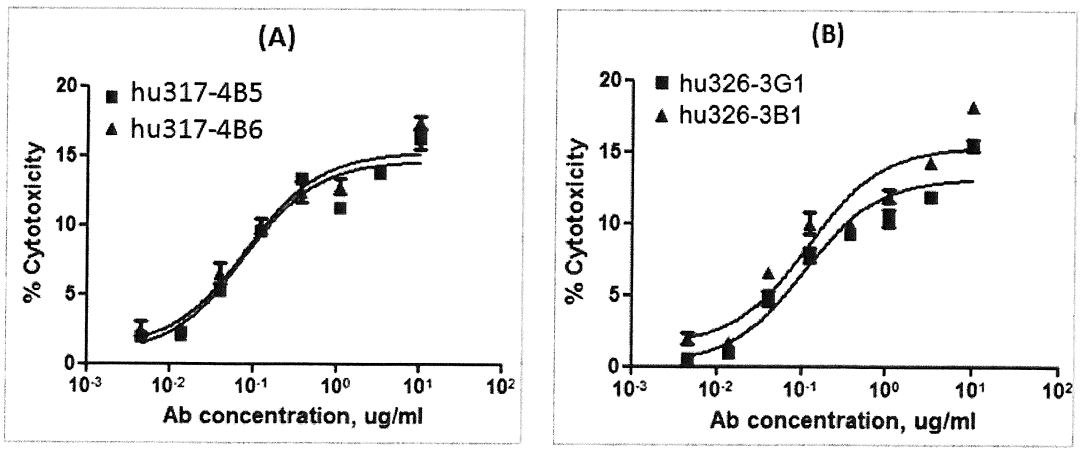
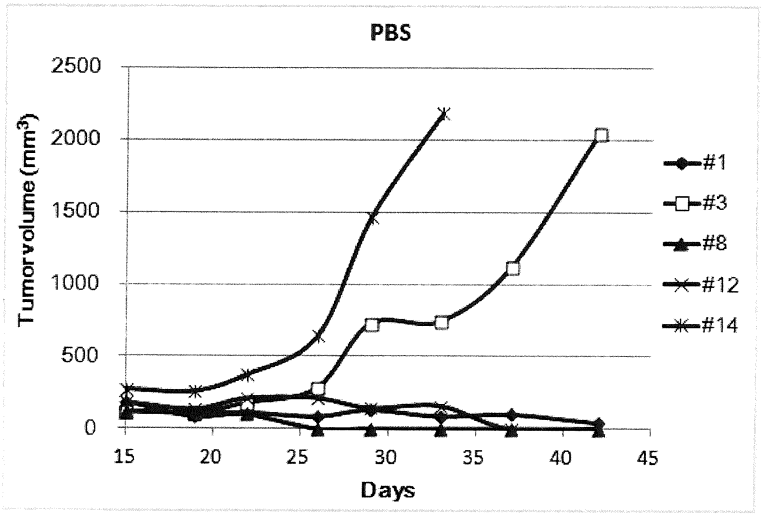
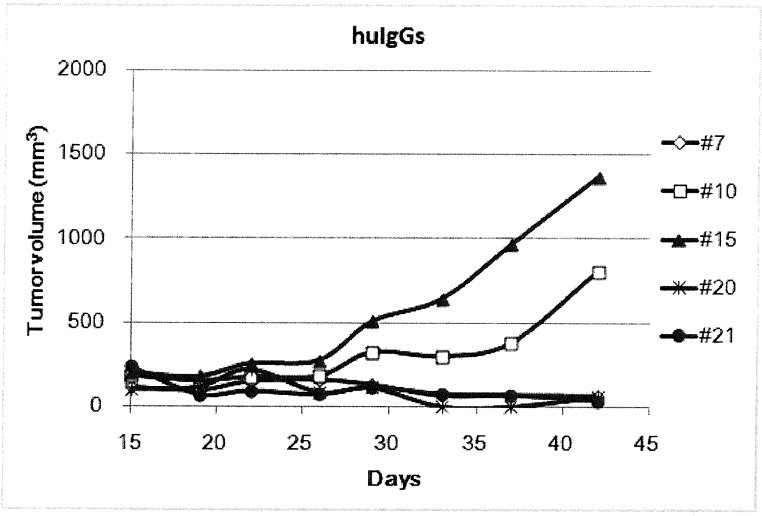
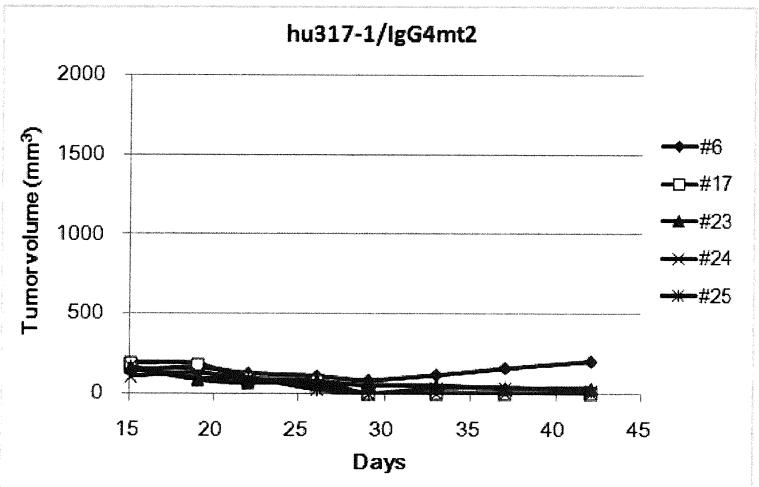

(A)
hu317-4B5
hu317-4B6
% Cytotoxicity
20
15
10
5
0
10-3
10-2
10-1
100
101
102
Ab concentration, ug/ml
(B)
hu326-3G1
hu326-3B1
% Cytotoxicity
20
15
10
5
0
10-3
10-2
10-1
100
101
102
Ab concentration, ug/ml

Fig. 11


PBS
Tumor volume (mm3)
2500
2000
1500
1000
500
0
15
20
25
30
35
40
45
Days
#1
#3
#8
#12
#14


huIgGs
Tumor volume (mm3)
2000
1500
1000
500
0
15
20
25
30
35
40
45
Days
#7
#10
#15
#20
#21


hu317-1/IgG4mt2
Tumor volume (mm3)
2000
1500
1000
500
0
15
20
25
30
35
40
45
Days
#6
#17
#23
#24
#25