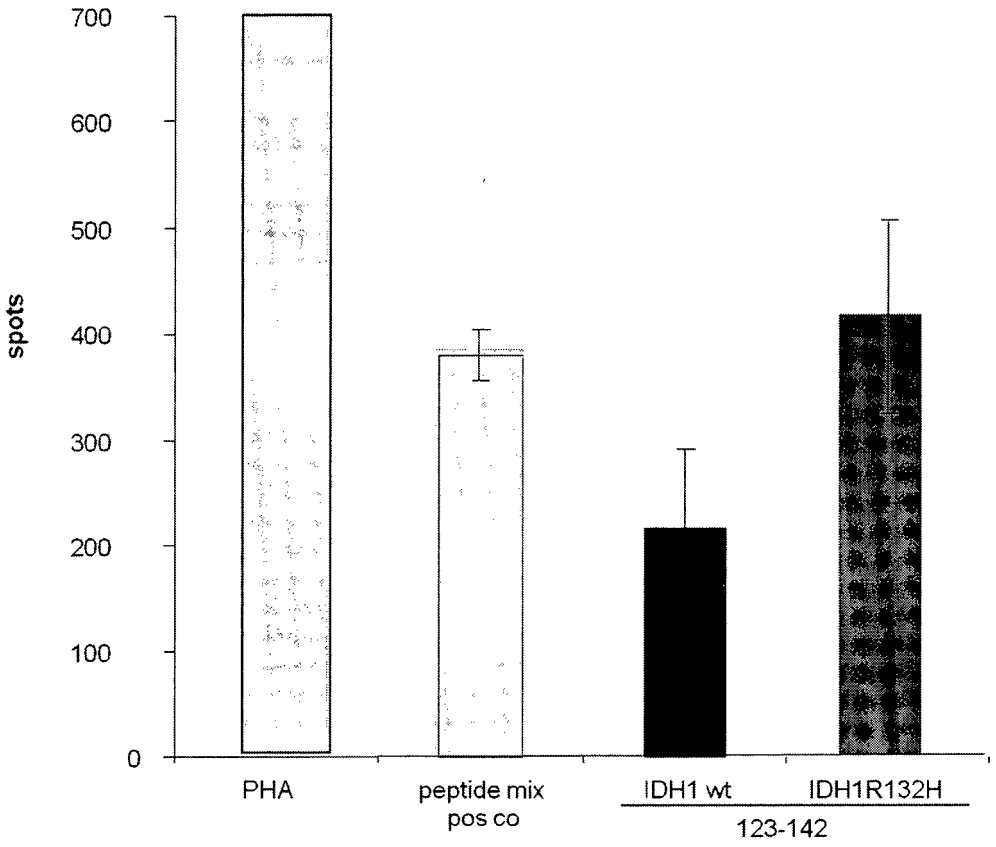

700
600
500
400
300
200
100
0
spots
PHA
peptide mix
pos co
IDH1 wt
IDH1R132H
123-142

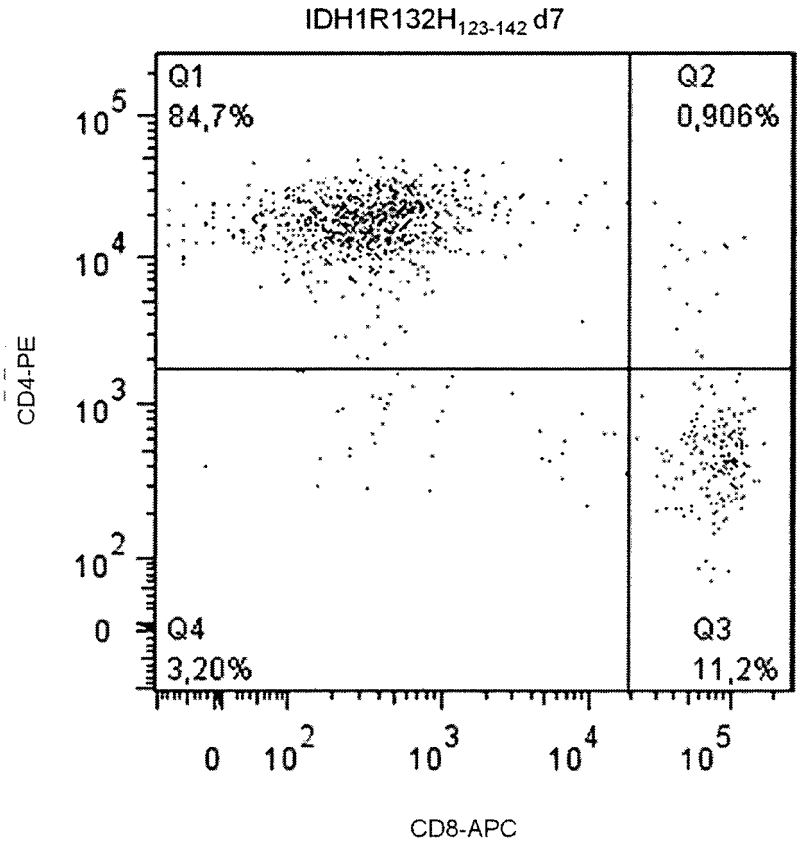

IDH1R132H123-142 d7
Q1
84,7%
Q2
0,906%
Q4
3,20%
Q3
11,2%
CD4-PE
CD8-APC

Fig. 1

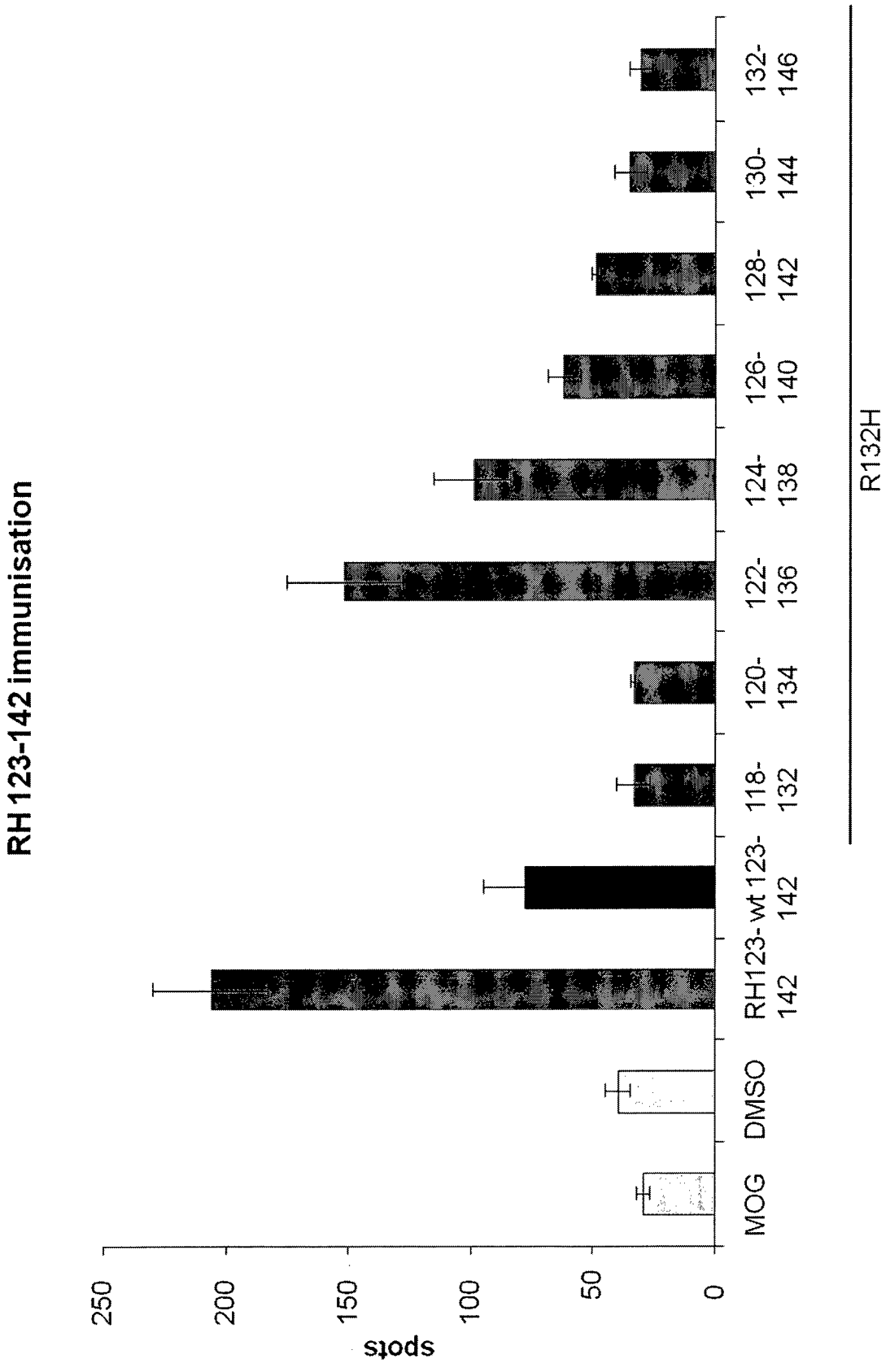

RH 123-142 immunisation
spots
250
200
150
100
50
0
MOG
DMSO
RH123-142
wt 123-142
118-132
120-134
122-136
124-138
126-140
128-142
130-144
132-146
R132H

Fig. 2(1)

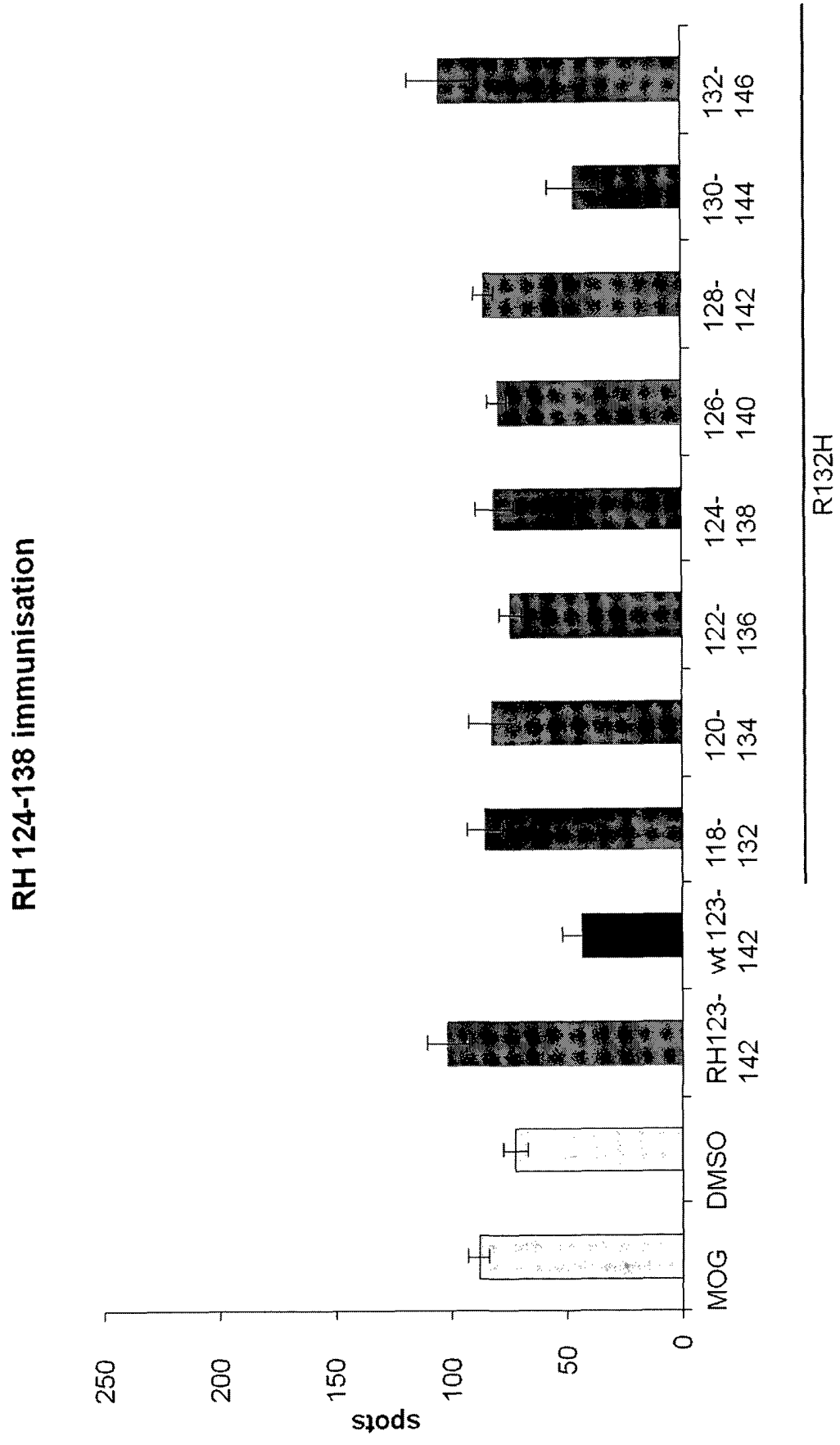

RH 124-138 immunisation
spots
250
200
150
100
50
0
MOG
DMSO
RH123-142
wt 123-142
118-132
120-134
122-136
124-138
126-140
128-142
130-144
132-146
R132H

Fig. 2(2)

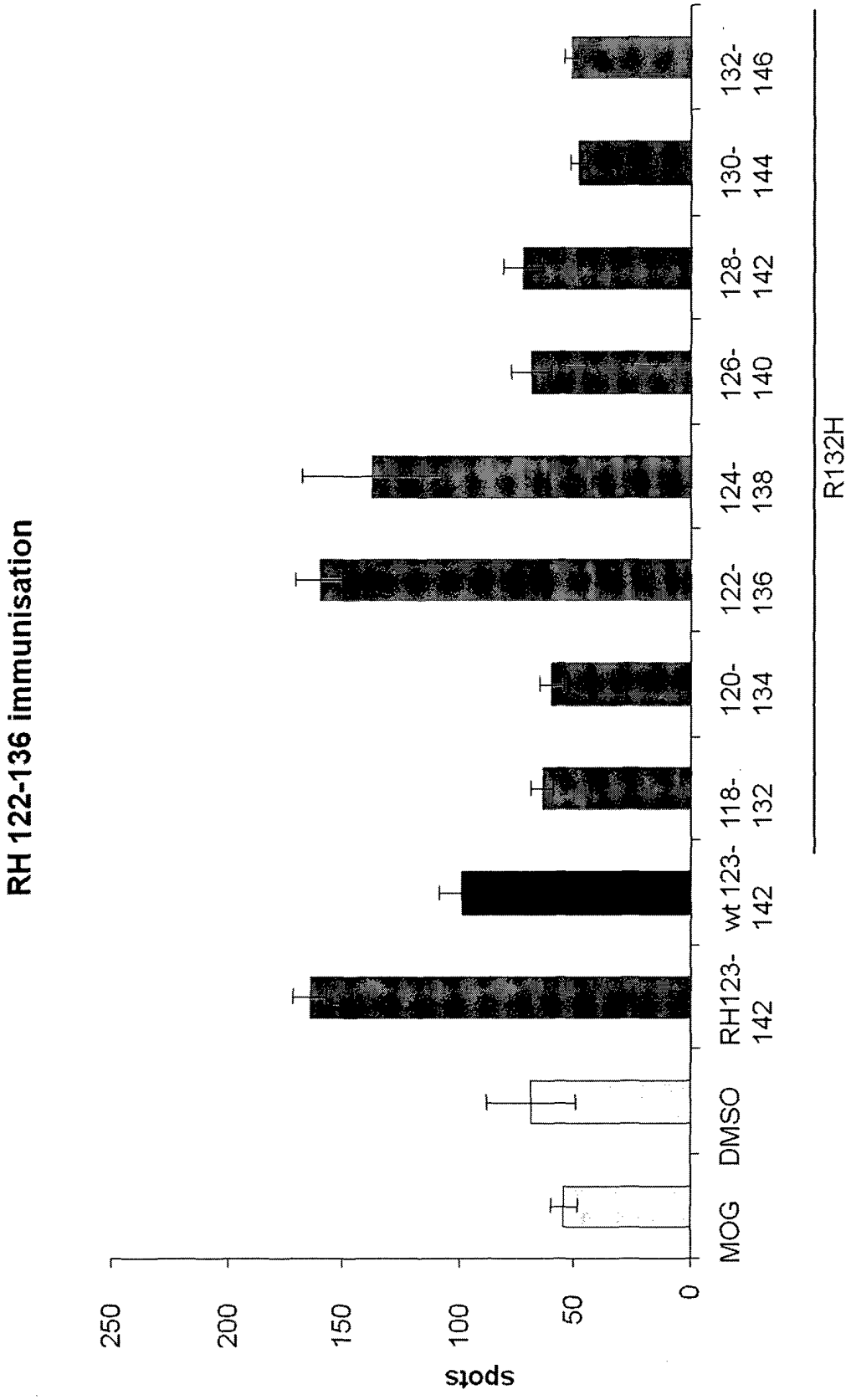

RH 122-136 immunisation
spots
250
200
150
100
50
0
MOG
DMSO
RH123-142
wt 123-142
118-132
120-134
122-136
124-138
126-140
128-142
130-144
132-146
R132H

Fig. 2(3)

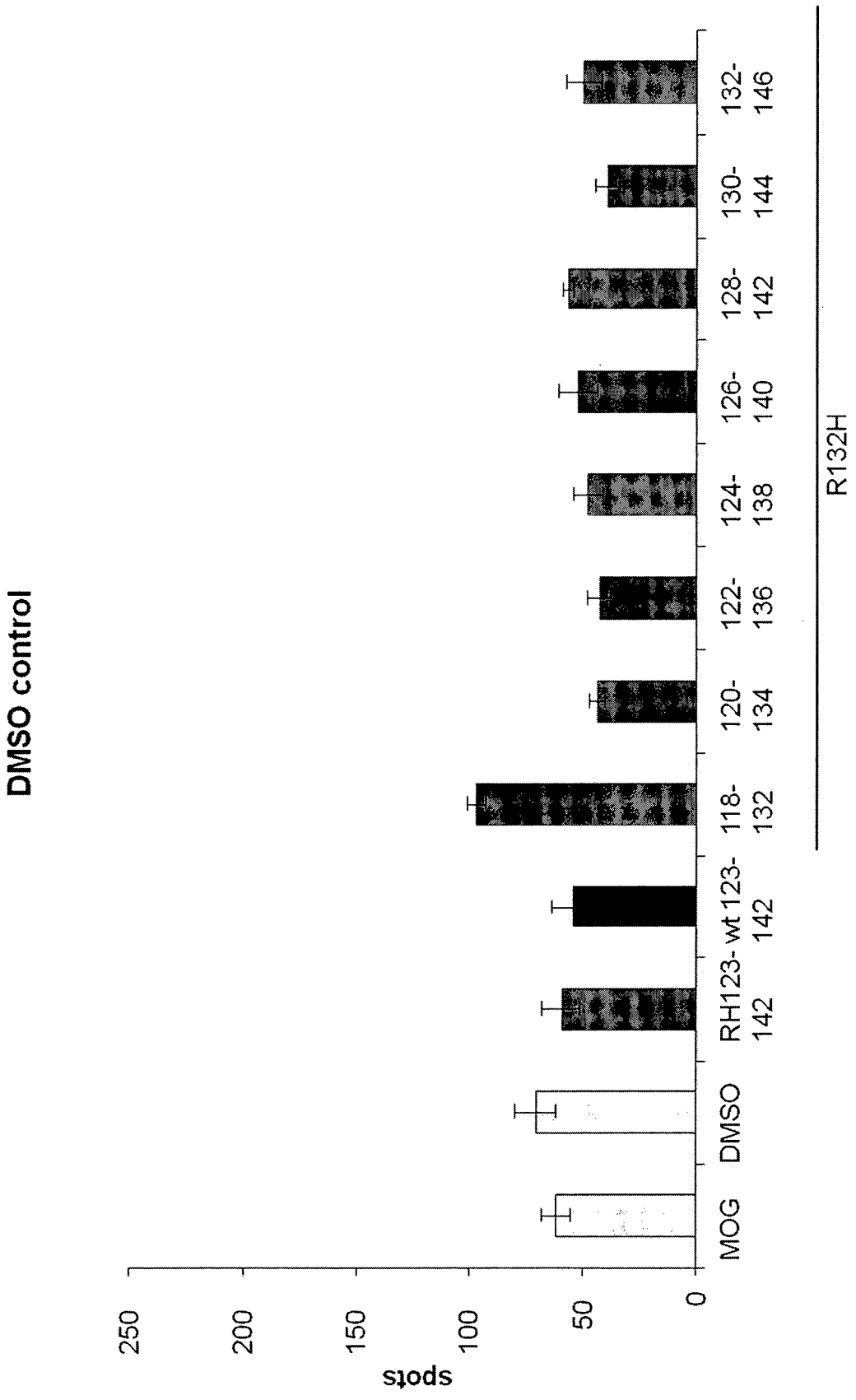

DMSO control
spots
250
200
150
100
50
0
MOG
DMSO
RH123-142
wt 123-142
118-132
120-134
122-136
124-138
126-140
128-142
130-144
132-146
R132H

Fig. 2(4)

Fig. 3

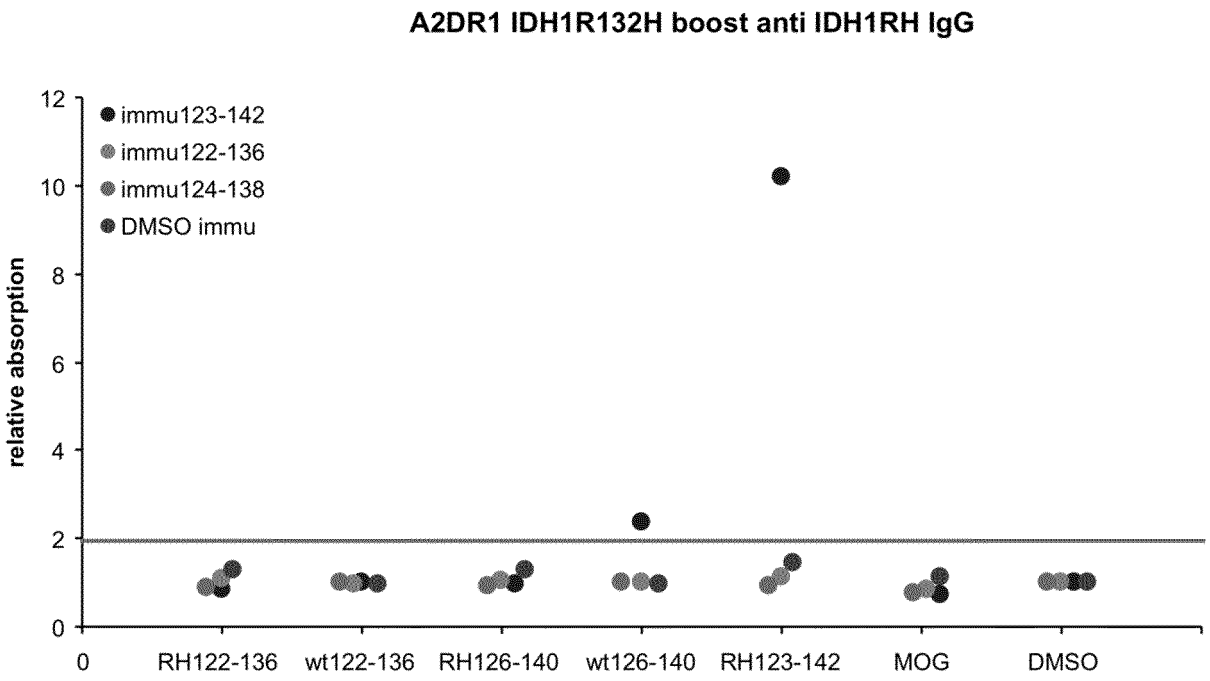

A2DR1 IDH1R132H boost anti IDH1RH IgG
immu123-142
immu122-136
immu124-138
DMSO immu
relative absorption
12
10
8
6
4
2
0
0
RH122-136
wt122-136
RH126-140
wt126-140
RH123-142
MOG
DMSO

Fig. 4

donor ID	MHC haplotype	IDH1 status	Glioma type	Anti-IDH1 (15mers) IgG
patTS060462	A*0301;2402 DRB1*1001;15	R132H	GBM	-
patTL260870	nd	?	GBM	$RH_{122-136}$
patJP270454	nd	R132H	OA °II	$RH_{126-140}$
patAW041083	nd	?	OA °II	-
patWG060257	nd	?	A °II	$RH_{126-140}$
patBS080462	nd	R132H	O °II	$RH_{122-136}$
patMA200158	nd	R132H	A °III	$RH_{122-136}$
patSG080572	nd	R132H	A °II	$RH_{126-140}$
AH	A*02;26 DRB1*07;15	-	-	-
TL	A*11;31 DRB1*03;04	-	-	-
TS	A*11;24 DRB1*01;13	-	-	-
glioma patients	**n.a.**	**R132H wt ?**	**°II – °IV**	**15.4 % (4/26) 0.0 % (0/20) 18.2 % (2/11)**
healthy donors	**various**	**wt**	**-**	**0 % (0/5)**

Fig. 5

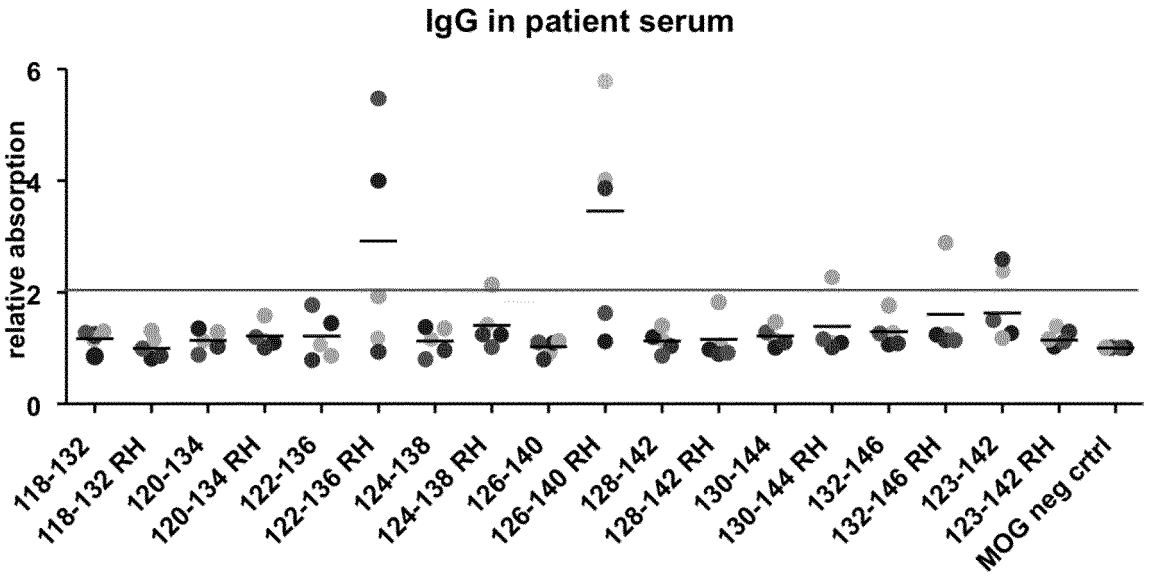

IgG in patient serum
relative absorption
6
4
2
0
118-132
118-132 RH
120-134
120-134 RH
122-136
122-136 RH
124-138
124-138 RH
126-140
126-140 RH
128-142
128-142 RH
130-144
130-144 RH
132-146
132-146 RH
123-142
123-142 RH
MOG neg crtrl

Fig. 6A

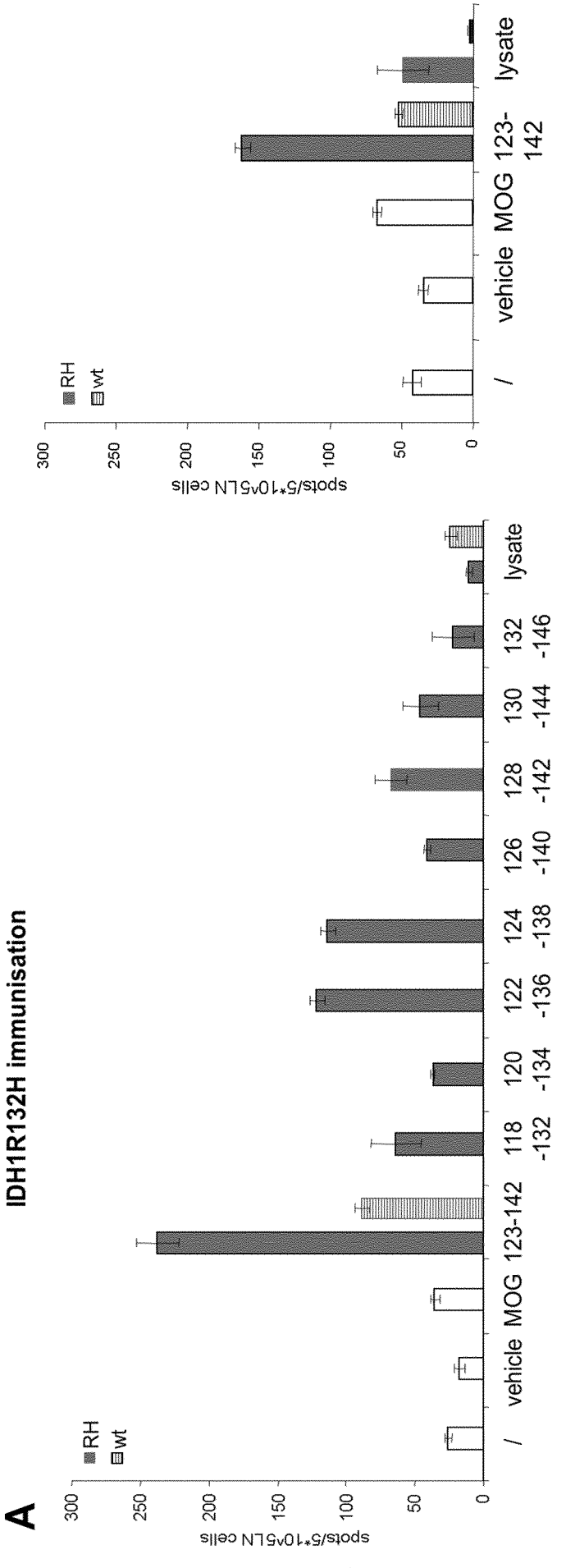

A
IDH1R132H immunisation
spots/5*10^5LN cells
300
250
200
150
100
50
0
RH
wt
/
vehicle
MOG 123-142
118 -132
120 -134
122 -136
124 -138
126 -140
128 -142
130 -144
132 -146
lysate
vehicle ctrl immunisation
spots/5*10^5LN cells
300
250
200
150
100
50
0
RH
wt
/
vehicle
MOG 123-142
lysate

Fig. 6B

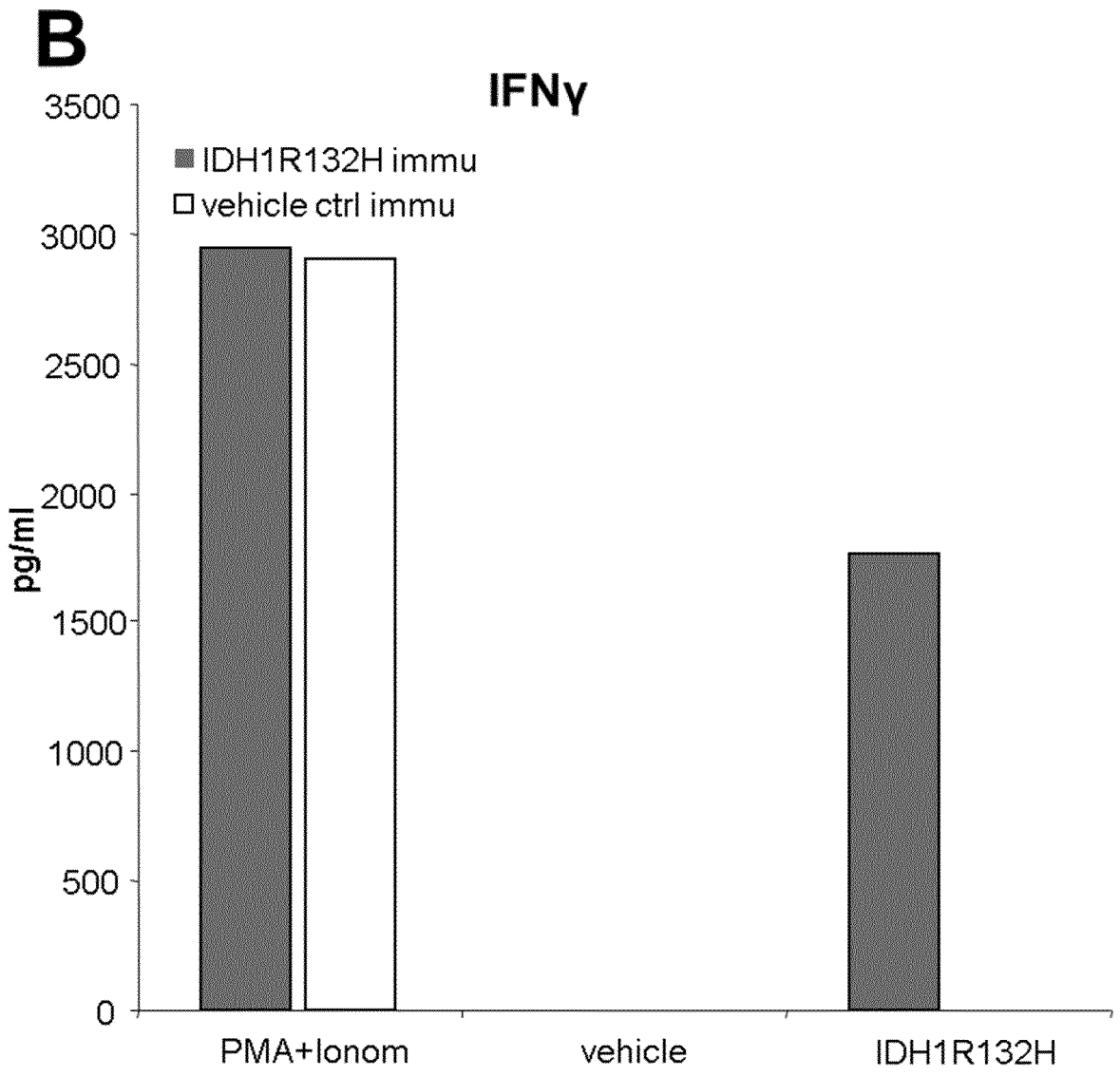

B
IFNγ
IDH1R132H immu
vehicle ctrl immu
pg/ml
3500
3000
2500
2000
1500
1000
500
0
PMA+Ionom
vehicle
IDH1R132H

Fig. 6C

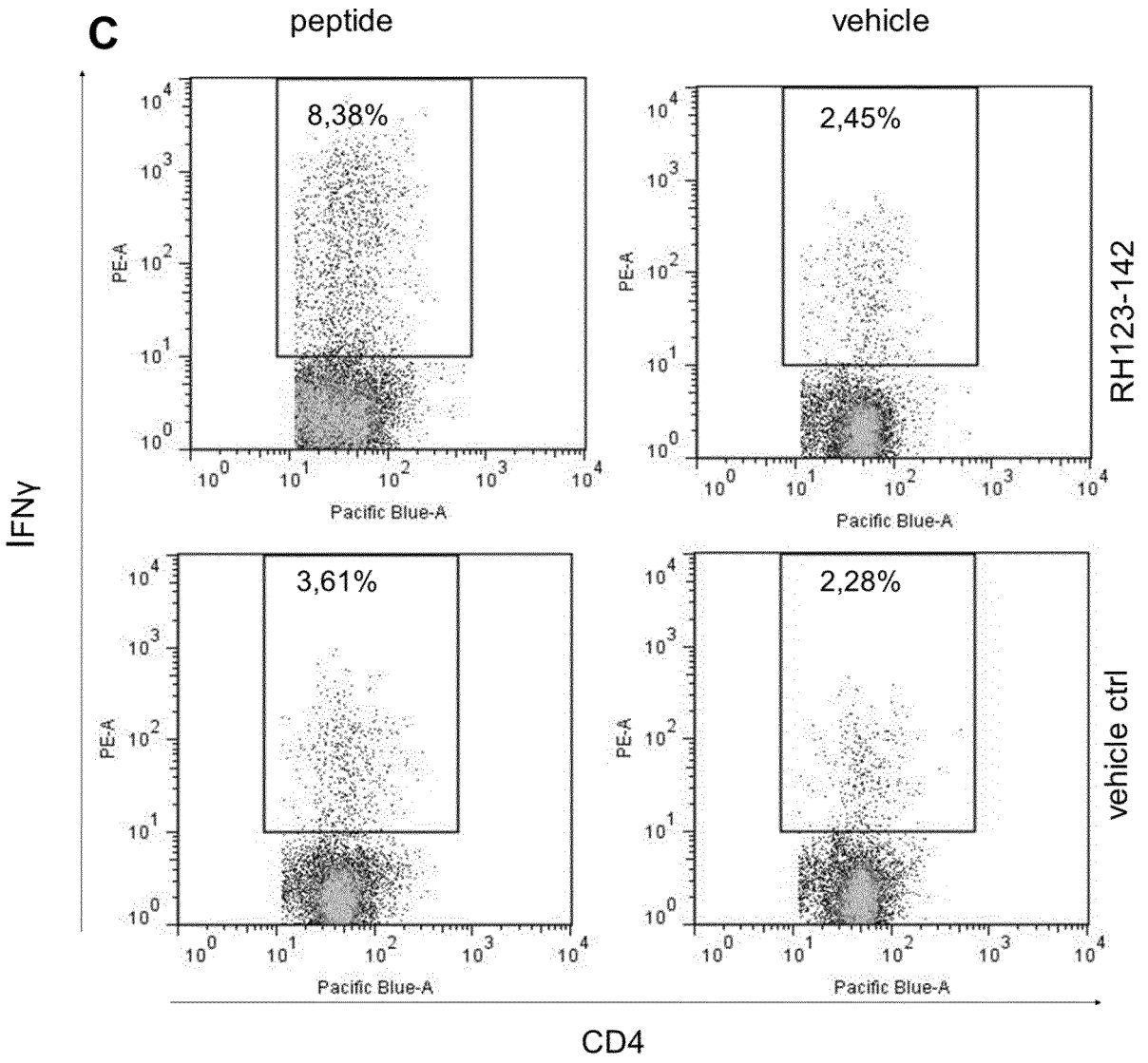

C
peptide
vehicle
8,38%
2,45%
3,61%
2,28%
RH123-142
vehicle ctrl
IFNγ
CD4
PE-A
Pacific Blue-A

Fig. 6C (continued)

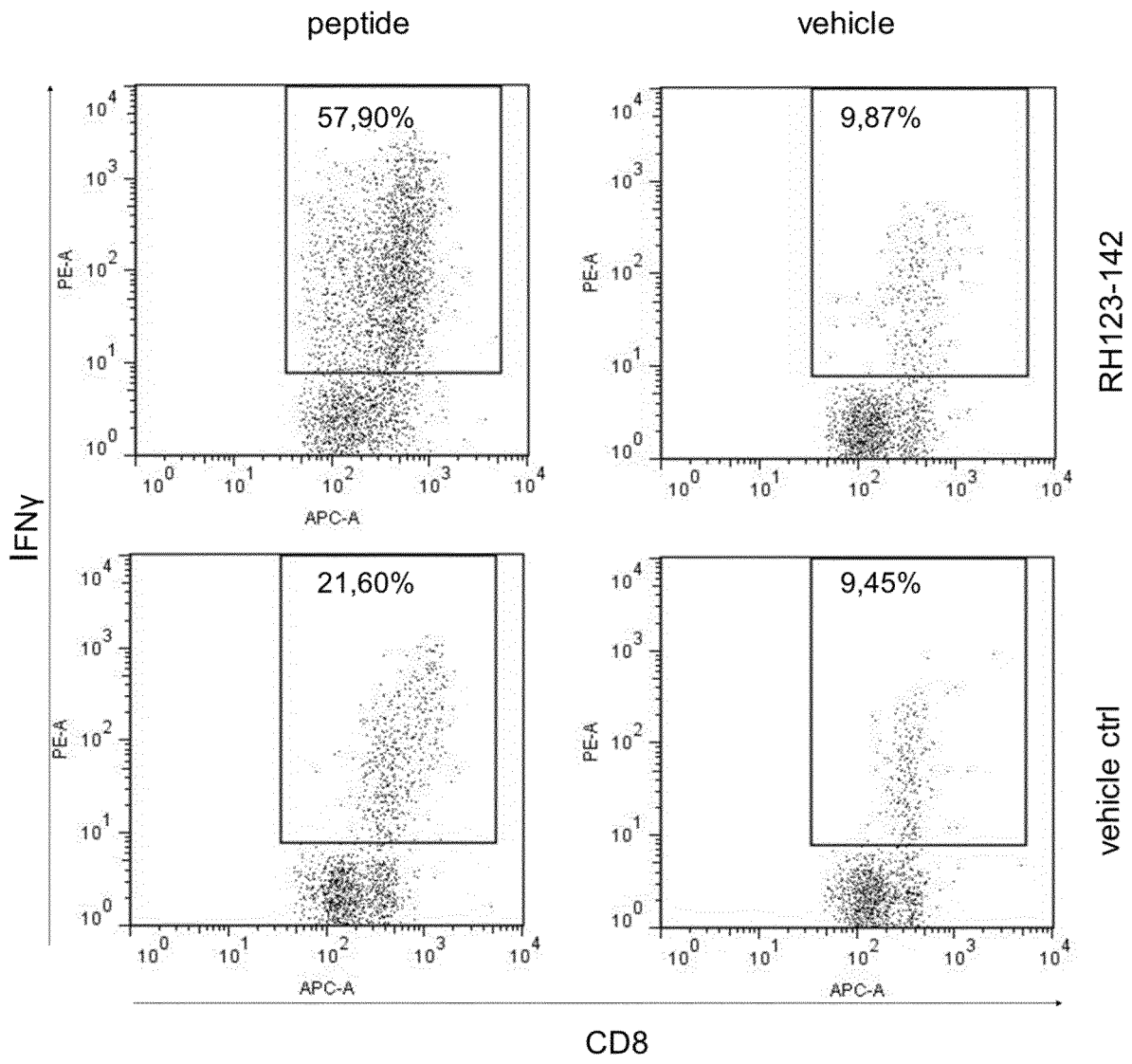


Fig. 7A

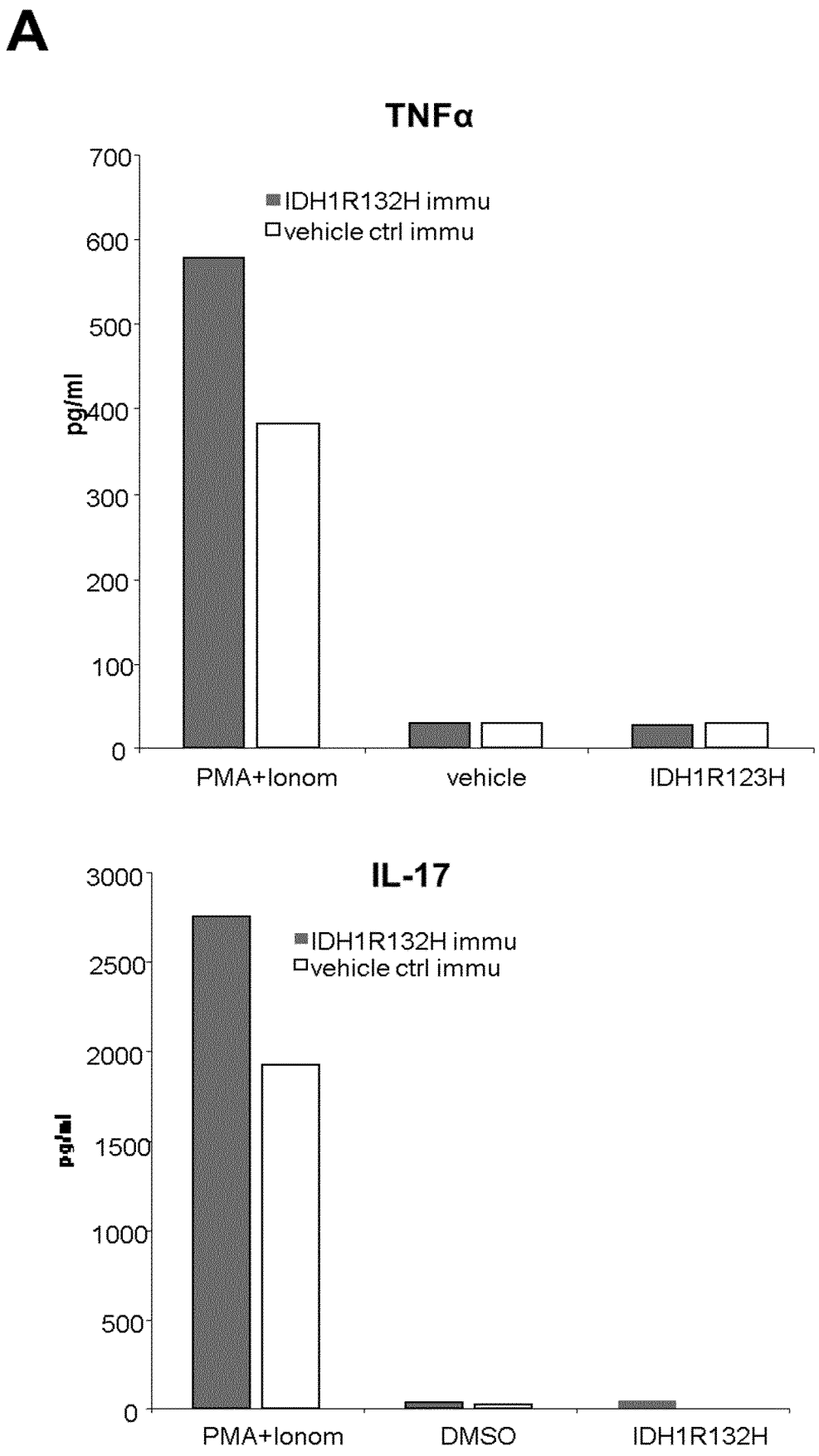

A
TNFα
700
600
500
400
300
200
100
0
pg/ml
IDH1R132H immu
vehicle ctrl immu
PMA+Ionom
vehicle
IDH1R123H
IL-17
3000
2500
2000
1500
1000
500
0
IDH1R132H immu
vehicle ctrl immu
PMA+Ionom
DMSO
IDH1R132H

Fig. 7B

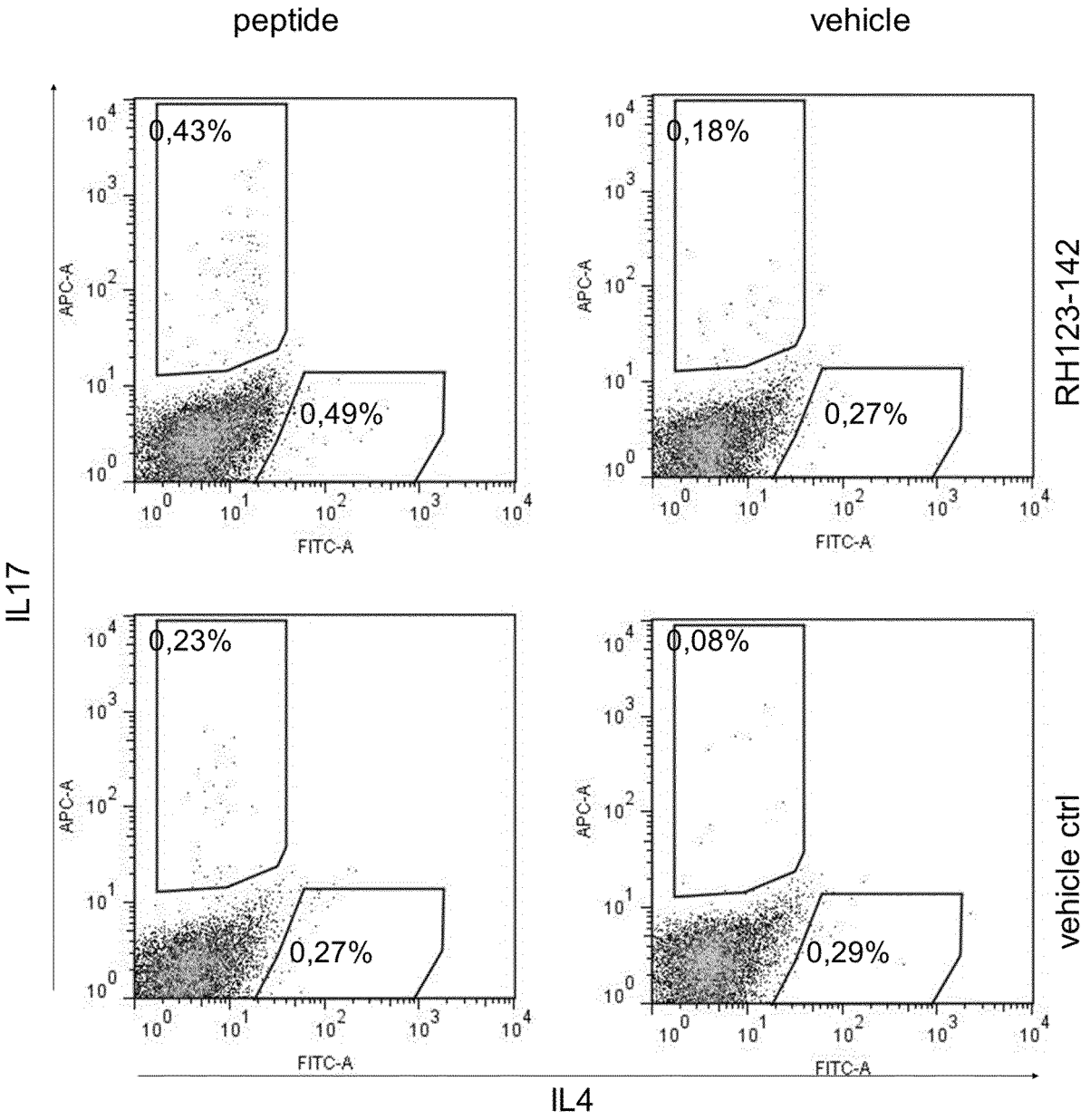

peptide
vehicle
0,43%
0,49%
0,18%
0,27%
0,23%
0,27%
0,08%
0,29%
APC-A
FITC-A
IL17
IL4
RH123-142
vehicle ctrl

Fig. 7B (continued)

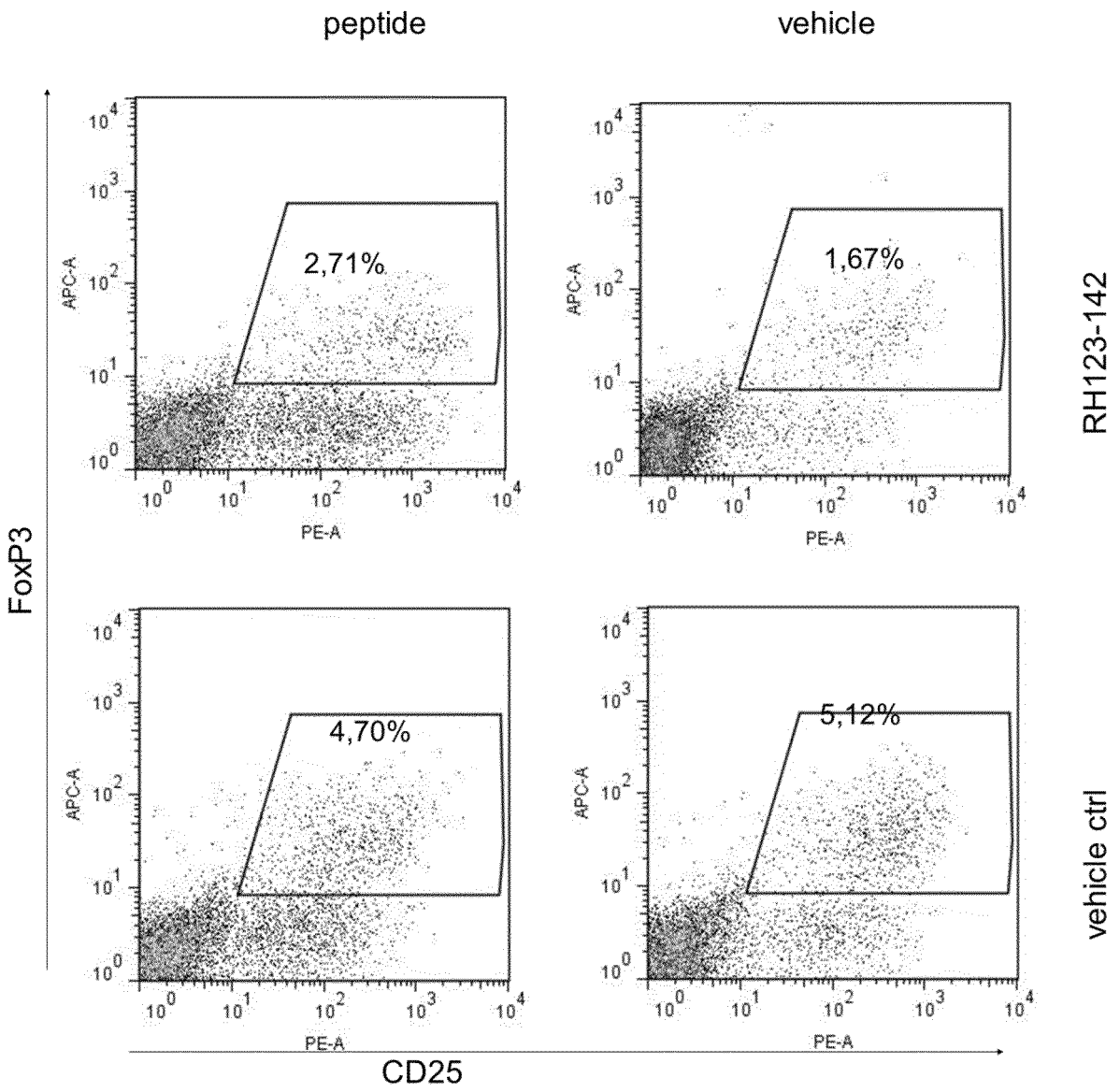
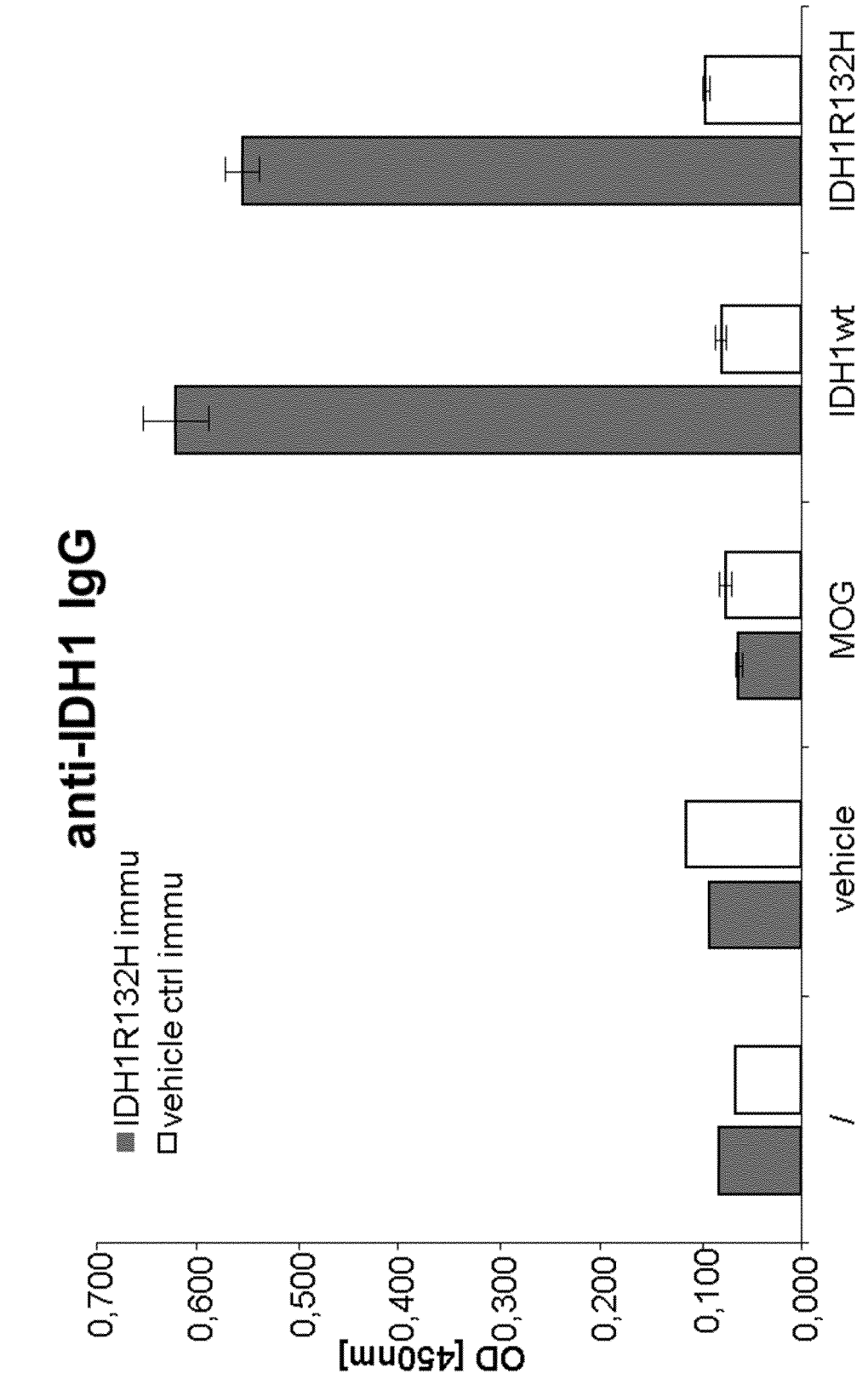


Fig. 8A


A
anti-IDH1 IgG
IDH1R132H immu
vehicle ctrl immu
OD [450nm]
0,700
0,600
0,500
0,400
0,300
0,200
0,100
0,000
/
vehicle
MOG
IDH1wt
IDH1R132H

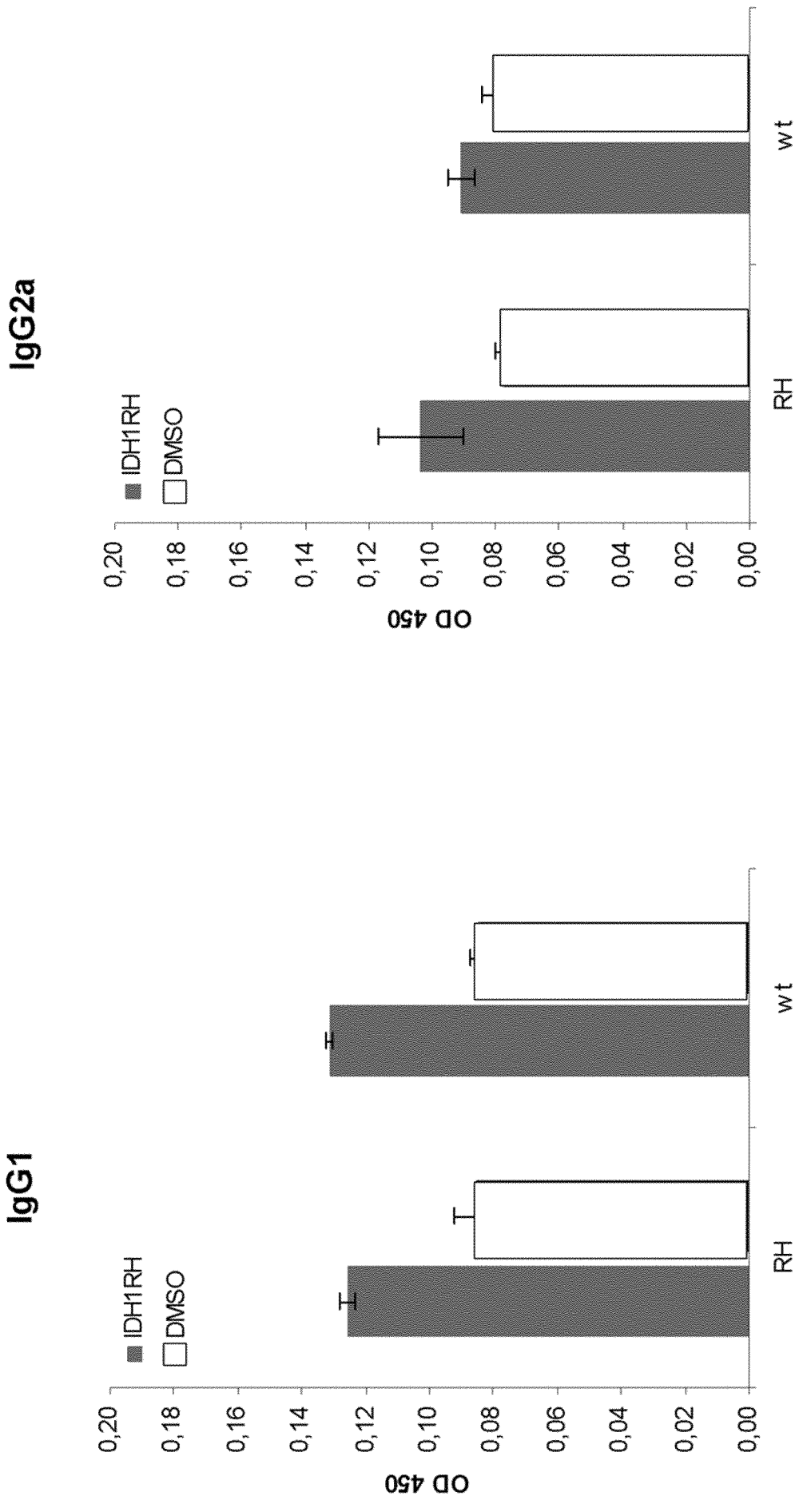

IgG2a
IDH1RH
DMSO
OD 450
0,20
0,18
0,16
0,14
0,12
0,10
0,08
0,06
0,04
0,02
0,00
RH
wt
IgG1
IDH1RH
DMSO
OD 450
0,20
0,18
0,16
0,14
0,12
0,10
0,08
0,06
0,04
0,02
0,00
RH
wt

Fig. 8B

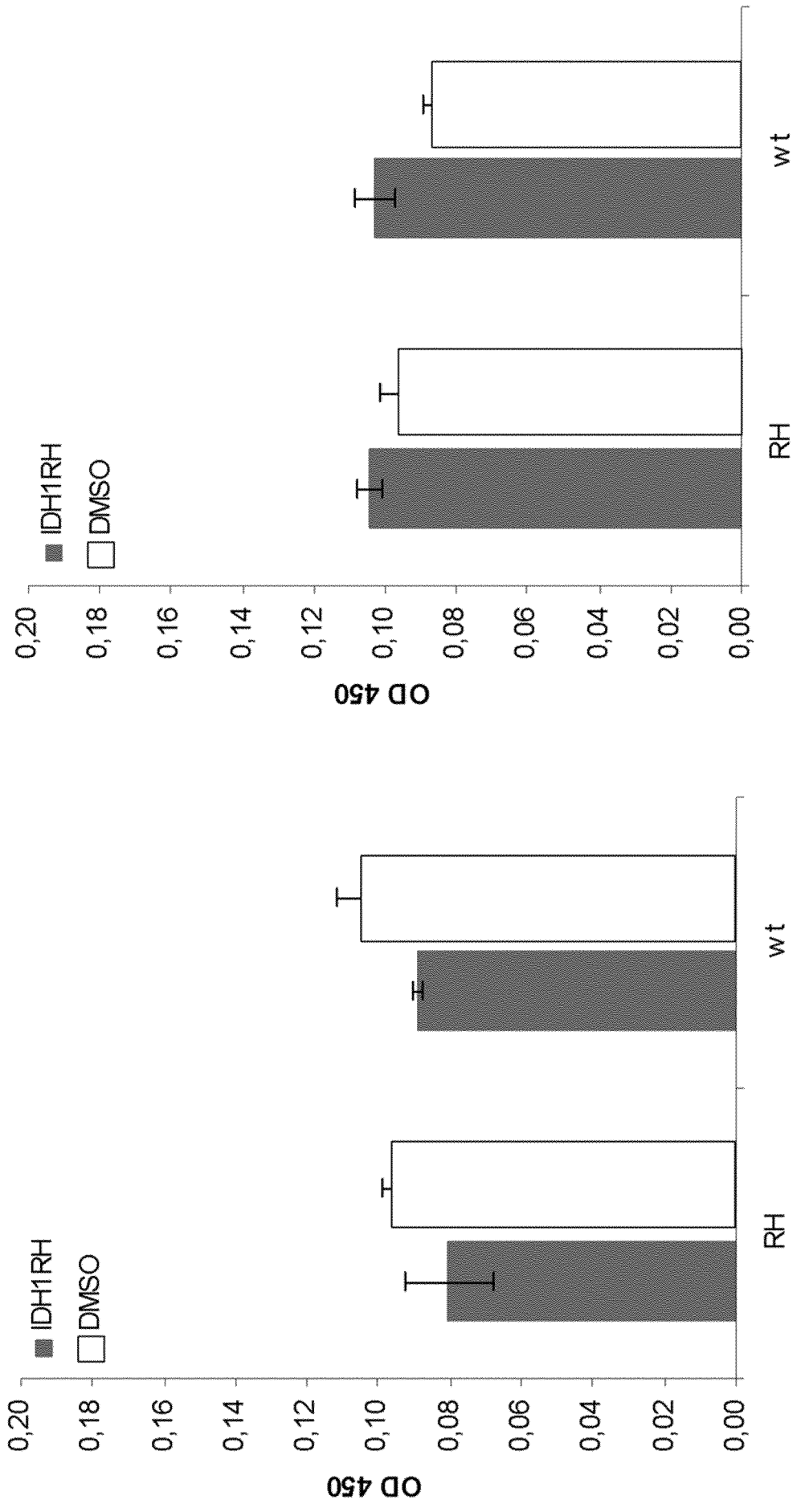
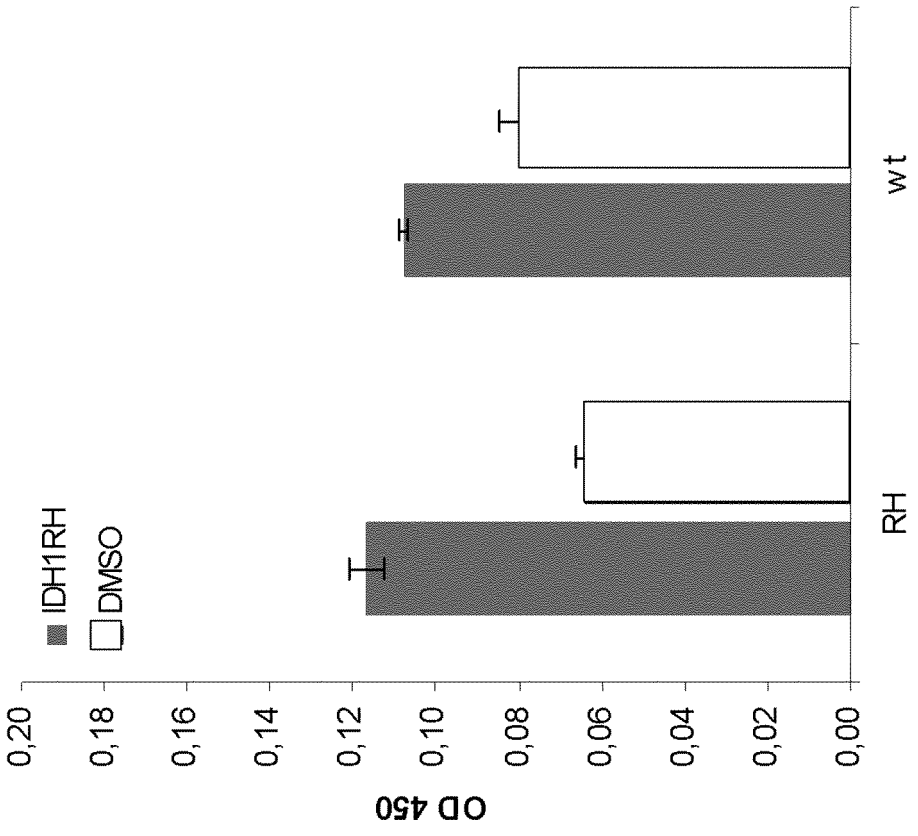


Fig. 8B (continued)

Fig. 8B (continued)



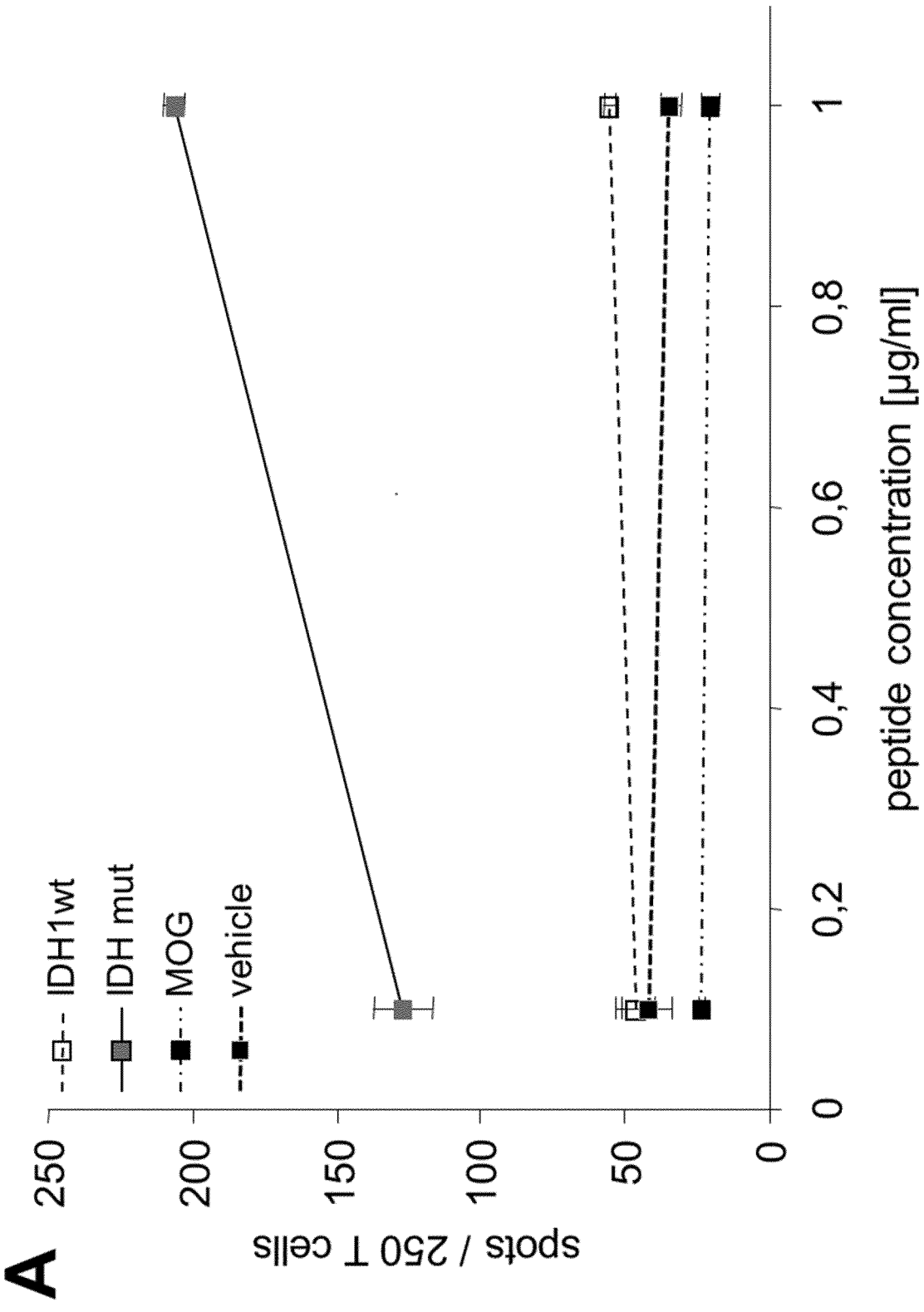

A
spots / 250 T cells
250
200
150
100
50
0
0
0,2
0,4
0,6
0,8
1
peptide concentration [µg/ml]
IDH1wt
IDH mut
MOG
vehicle

Fig. 9A

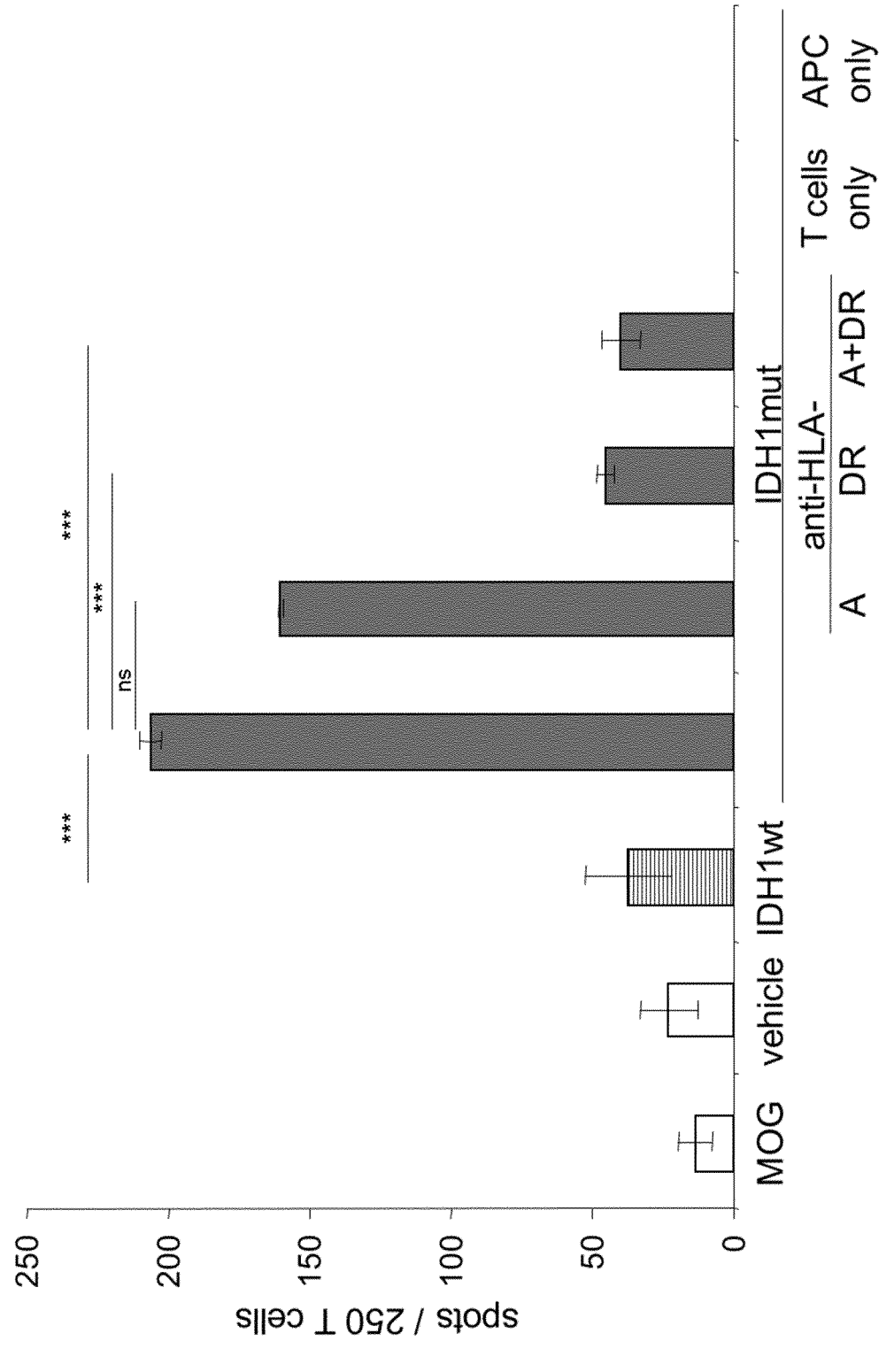

B
spots / 250 T cells
250
200
150
100
50
0
***
***
ns
***
MOG
vehicle
IDH1wt
IDH1mut
anti-HLA-
A
DR
A+DR
T cells only
APC only

Fig. 9B

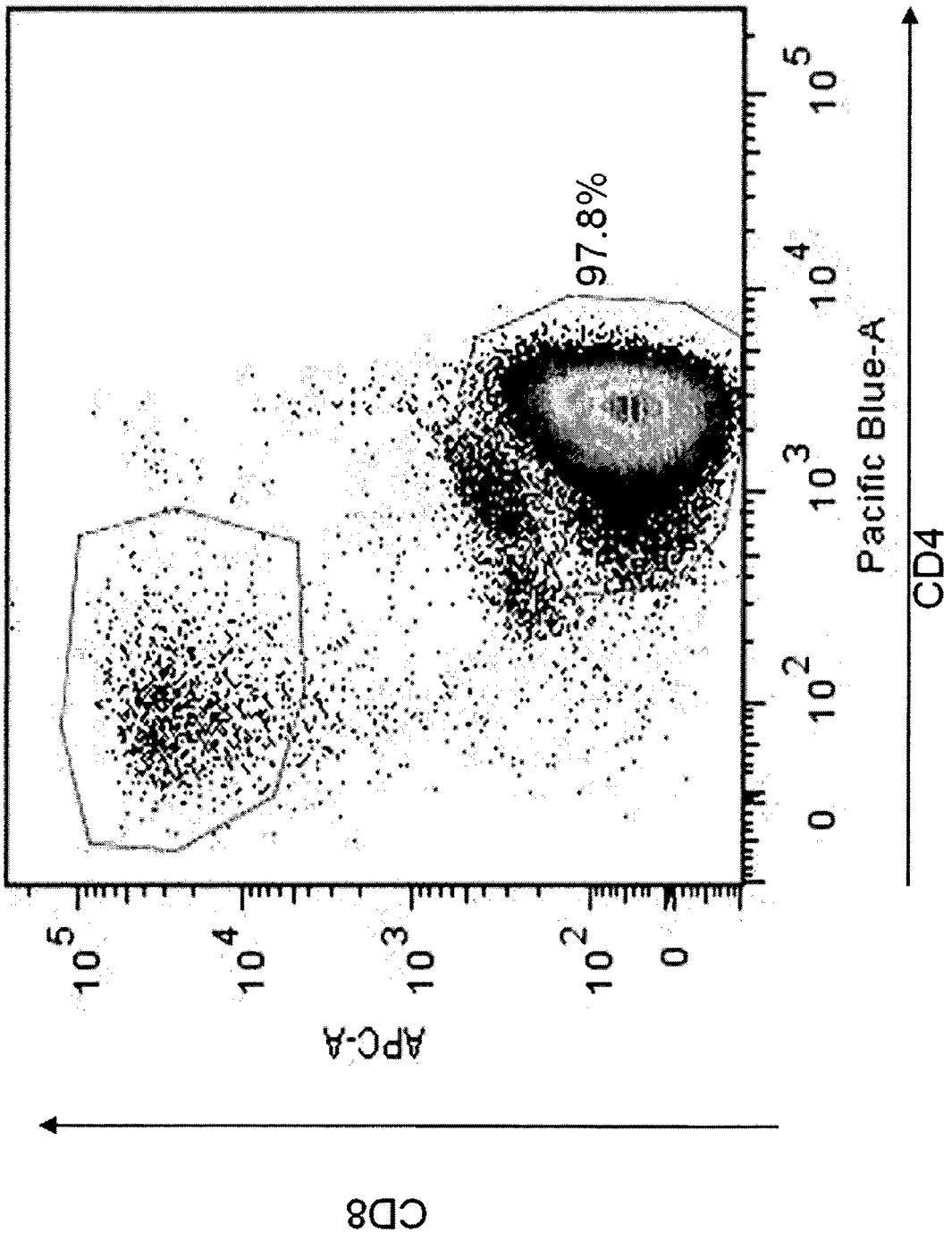


Fig. 9C

Fig. 9D

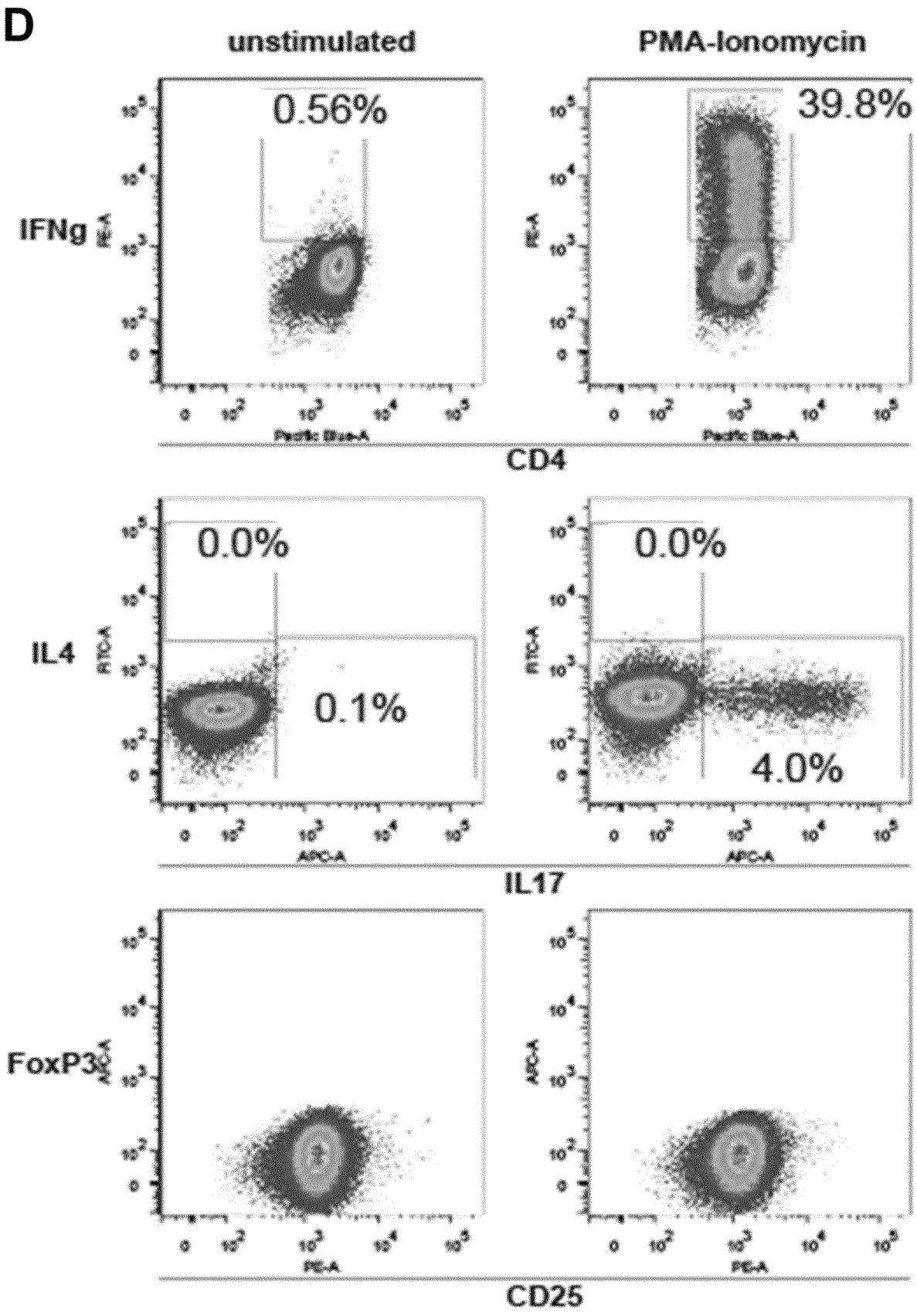

D
unstimulated
PMA-Ionomycin
0.56%
39.8%
IFNg
PE-A
Pacific Blue-A
CD4
0.0%
0.1%
0.0%
4.0%
IL4
IL17
PerCP-Cy5-5-A
APC-A
FoxP3
CD25

Fig. 9E

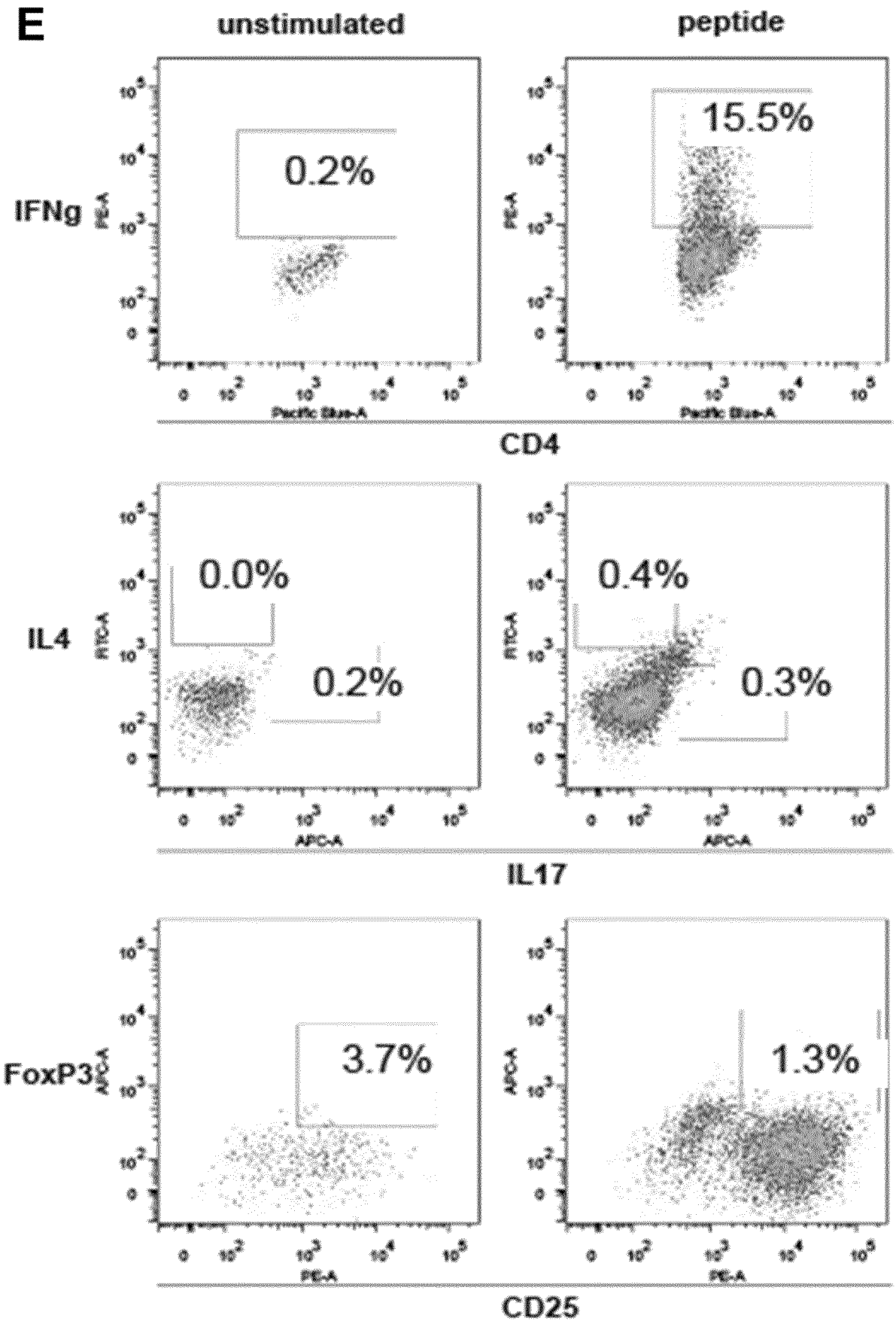

E
unstimulated
peptide
IFNg
0.2%
15.5%
PE-A
Pacific Blue-A
CD4
IL4
0.0%
0.2%
0.4%
0.3%
FITC-A
APC-A
IL17
FoxP3
3.7%
1.3%
APC-A
PE-A
CD25

Fig. 10A

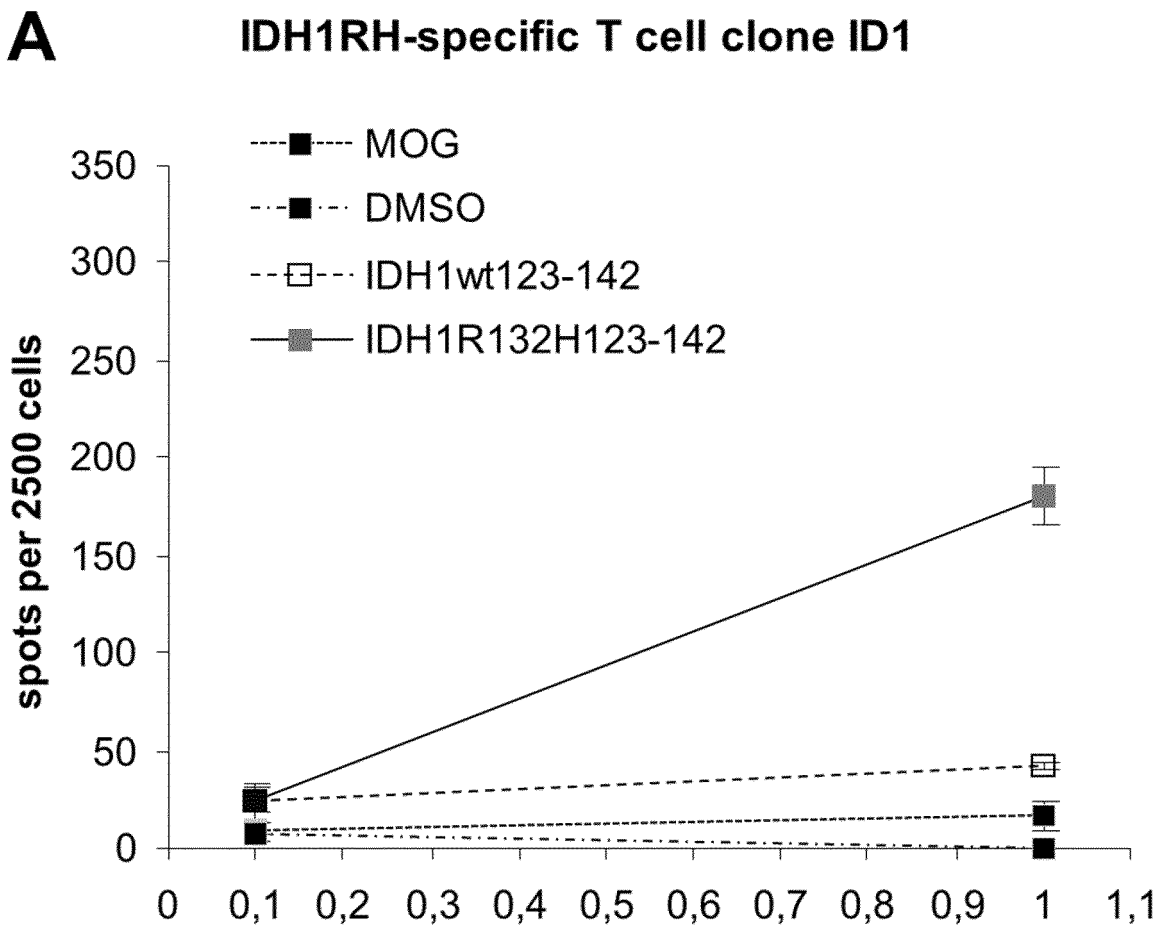
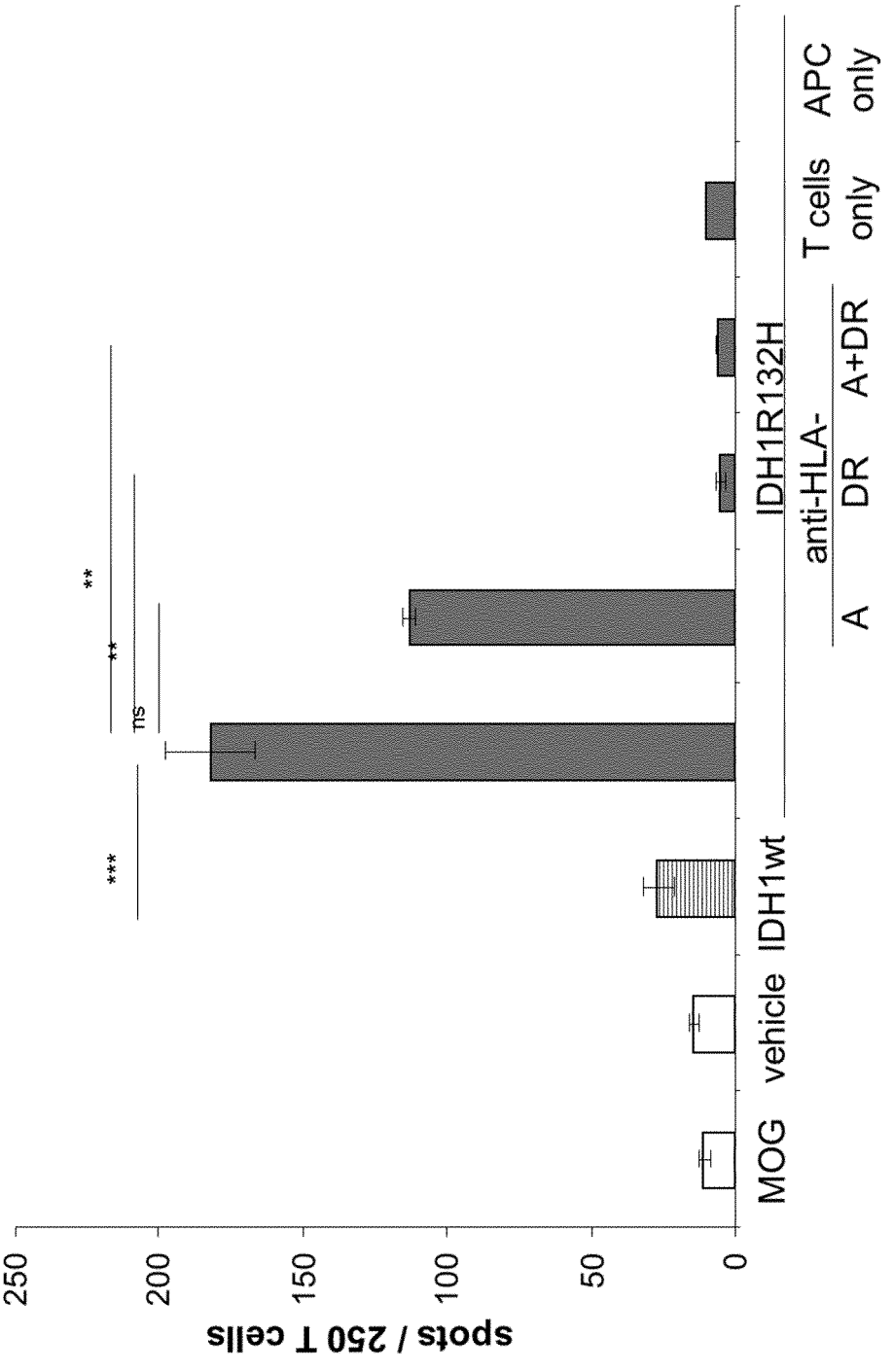

A
IDH1RH-specific T cell clone ID1
MOG
DMSO
IDH1wt123-142
IDH1R132H123-142
spots per 2500 cells
350
300
250
200
150
100
50
0
0
0,1
0,2
0,3
0,4
0,5
0,6
0,7
0,8
0,9
1
1,1

Fig. 10B


B
T cell clone ID1
spots / 250 T cells
250
200
150
100
50
0
***
**
ns
**
MOG
vehicle
IDH1wt
IDH1R132H
anti-HLA-
A
DR
A+DR
T cells only
APC only

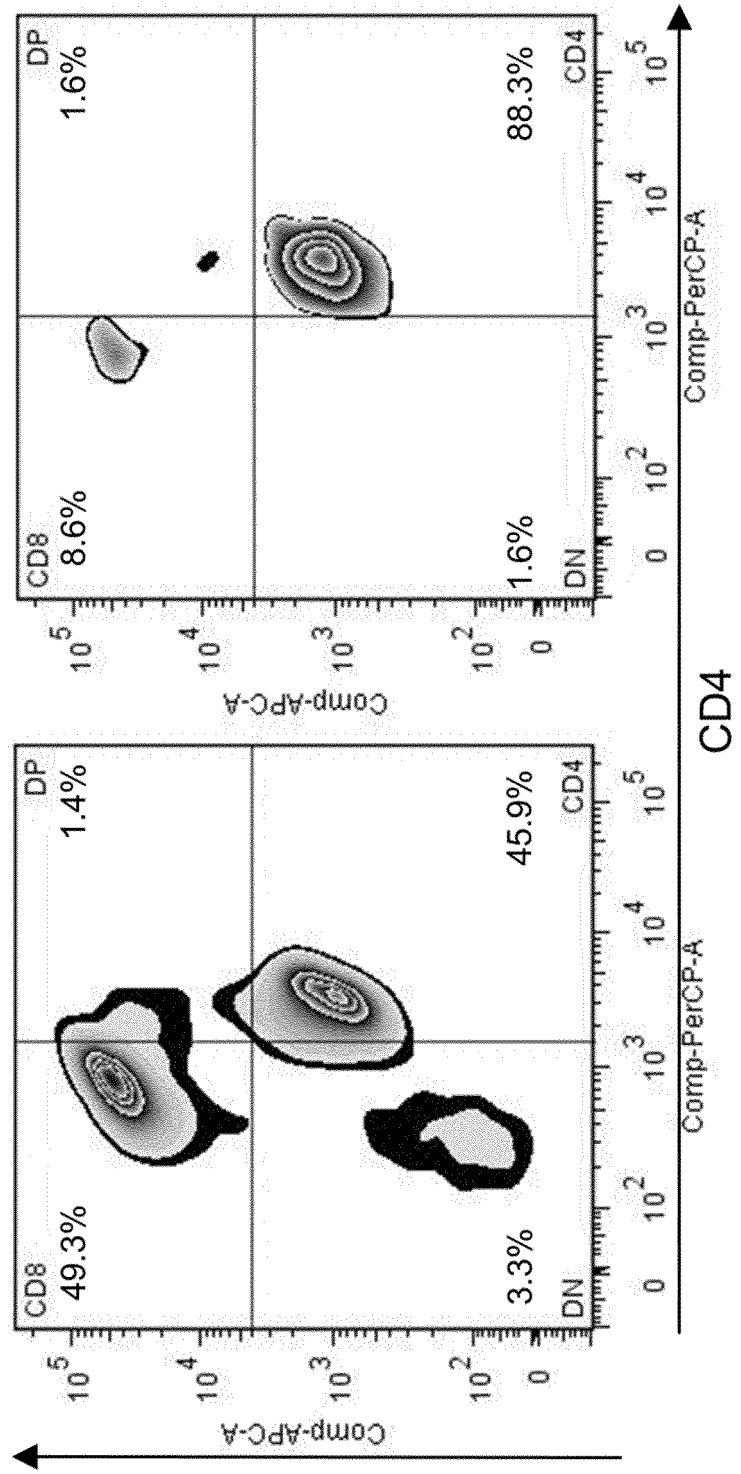

CD8
Comp-APC-A
CD4
Comp-PerCP-A
CD8
49.3%
DP
1.4%
45.9%
CD4
3.3%
DN
CD8
8.6%
DP
1.6%
88.3%
CD4
1.6%
DN

Fig. 11A

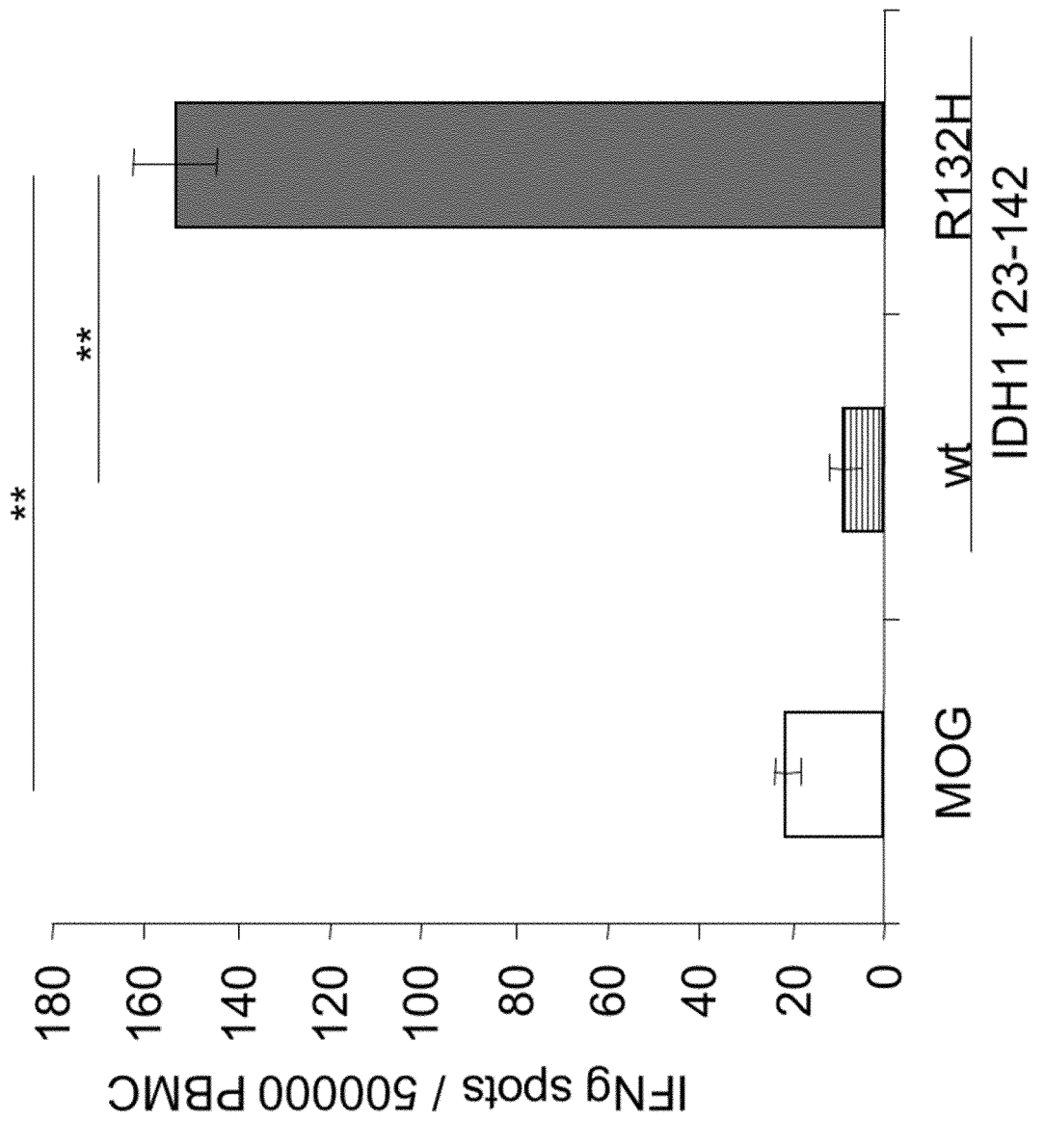

IFNg spots / 500000 PBMC
180
160
140
120
100
80
60
40
20
0
**
**
MOG
wt
R132H
IDH1 123-142

Fig. 11B

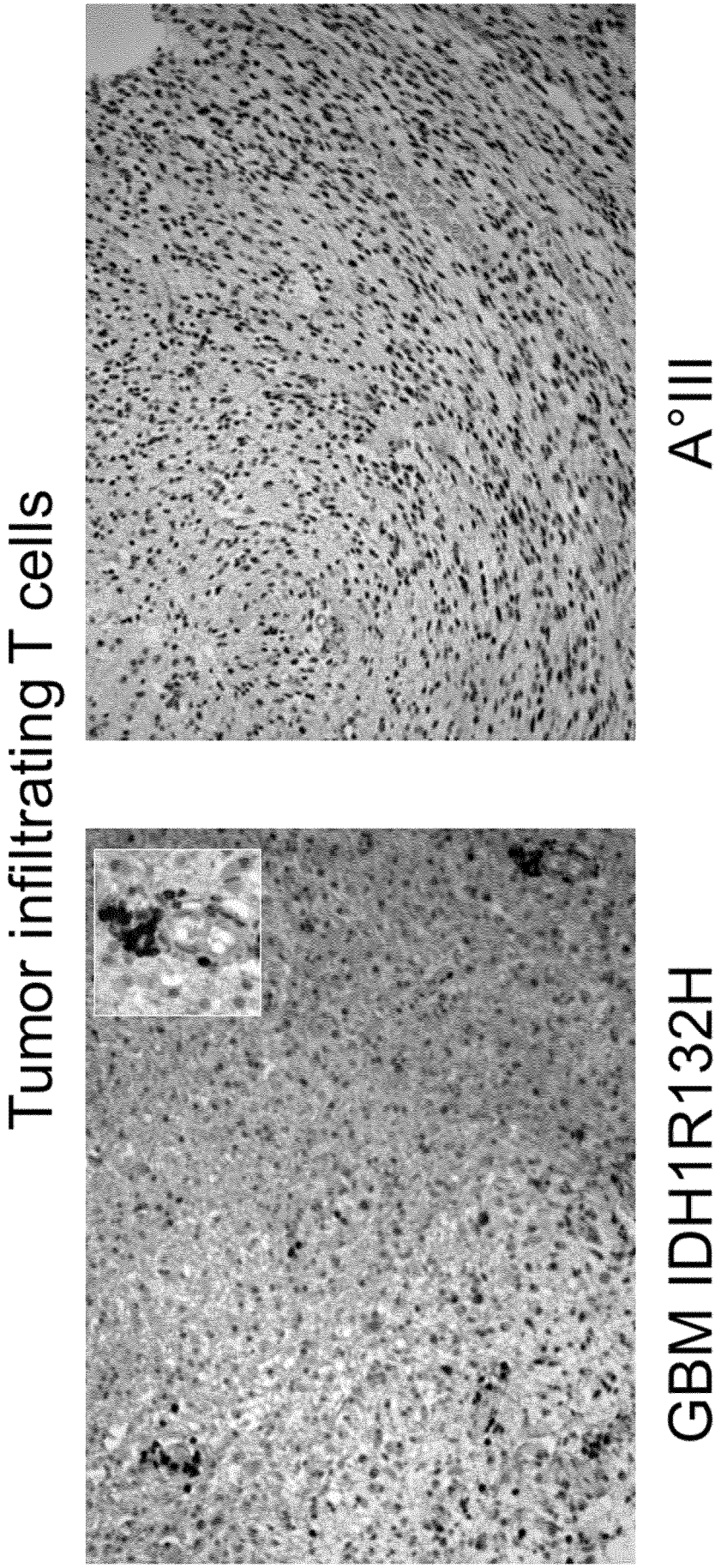


Fig. 11C

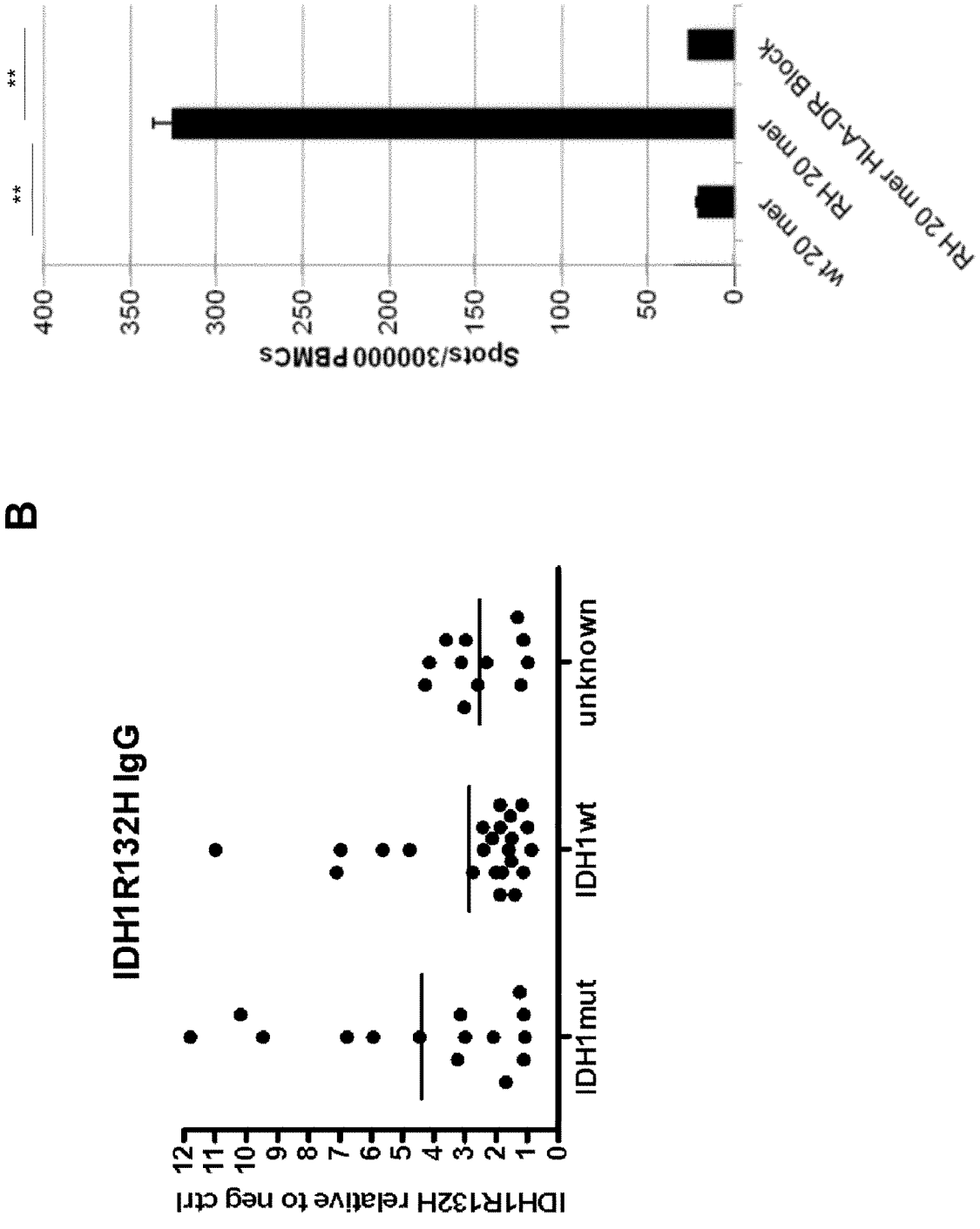

A
IDH1R132H IgG
IDH1R132H relative to neg ctrl
0
1
2
3
4
5
6
7
8
9
10
11
12
IDH1mut
IDH1wt
unknown
B
Spots/300000 PBMCs
0
50
100
150
200
250
300
350
400
**
**
wt 20 mer
RH 20 mer
RH 20 mer HLA-DR Block

Fig. 12

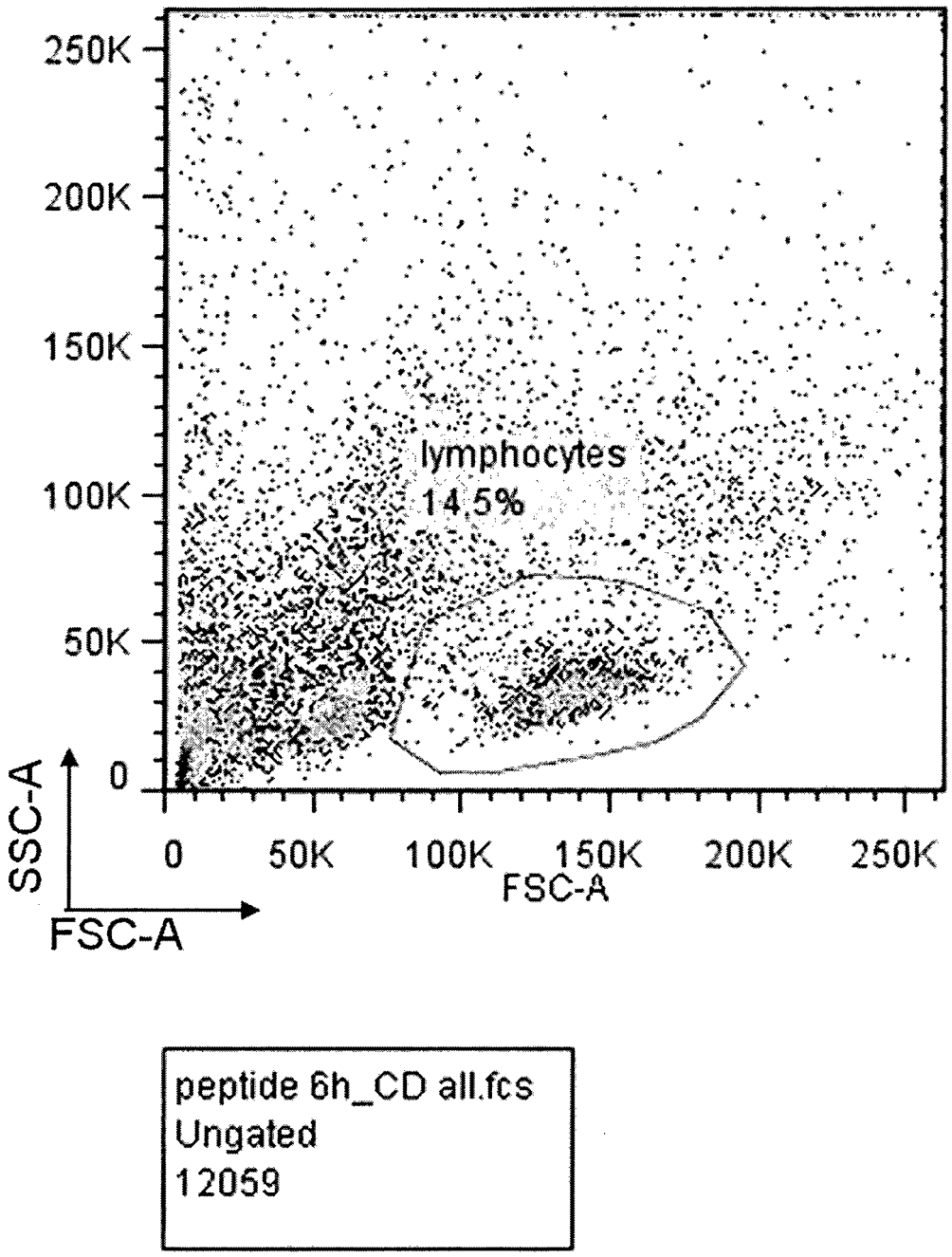

250K
200K
150K
100K
50K
0
lymphocytes
14.5%
SSC-A
FSC-A
0
50K
100K
150K
200K
250K
FSC-A
peptide 6h_CD all.fcs
Ungated
12059

Fig. 13(1)

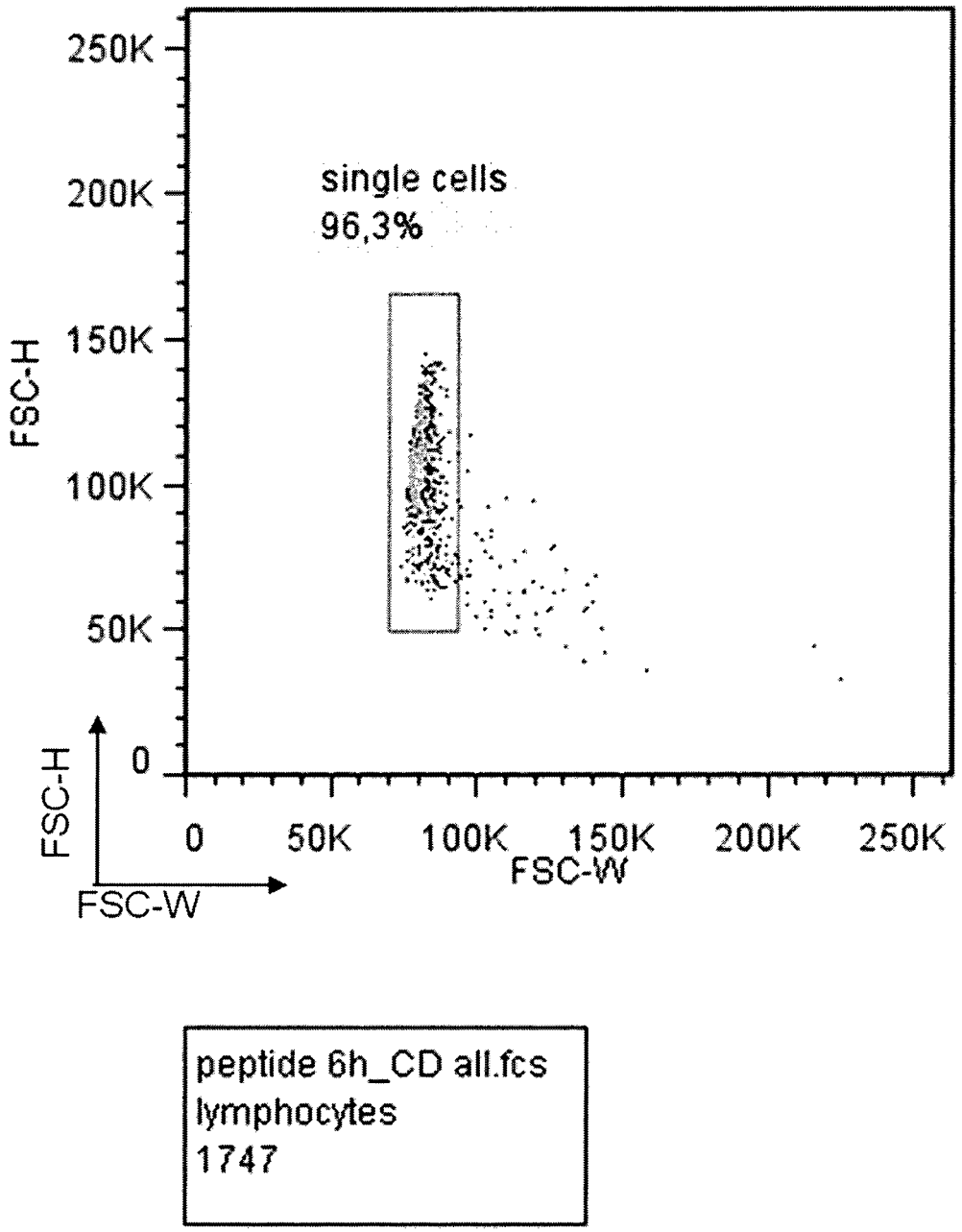

250K
200K
150K
100K
50K
0
FSC-H
single cells
96,3%
0
50K
100K
150K
200K
250K
FSC-W
FSC-H
FSC-W
peptide 6h_CD all.fcs
lymphocytes
1747

Fig. 13(2)

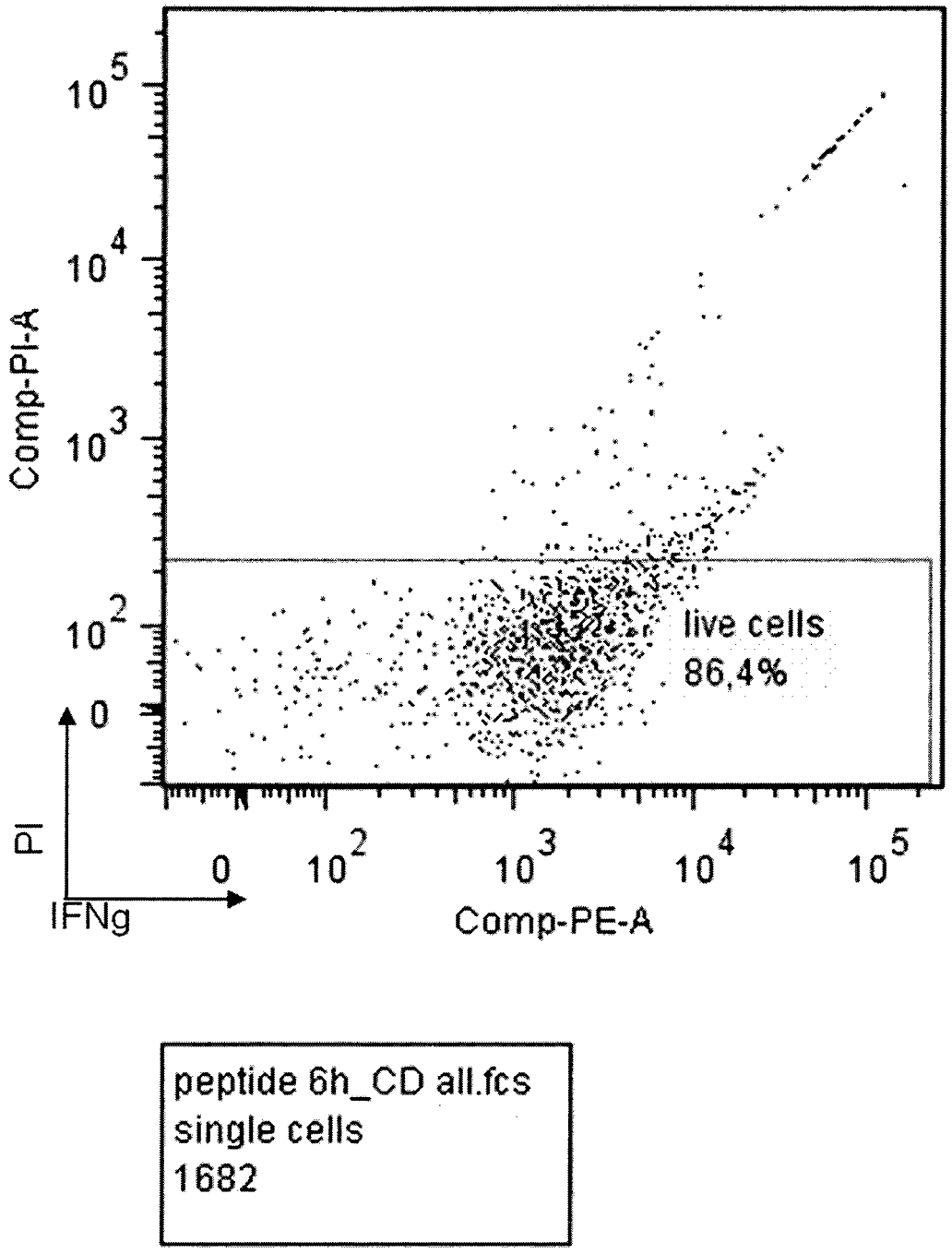

Comp-PI-A
10^5
10^4
10^3
10^2
0
live cells
86,4%
PI
IFNg
0
10^2
10^3
10^4
10^5
Comp-PE-A
peptide 6h_CD all.fcs
single cells
1682

Fig. 13(3)

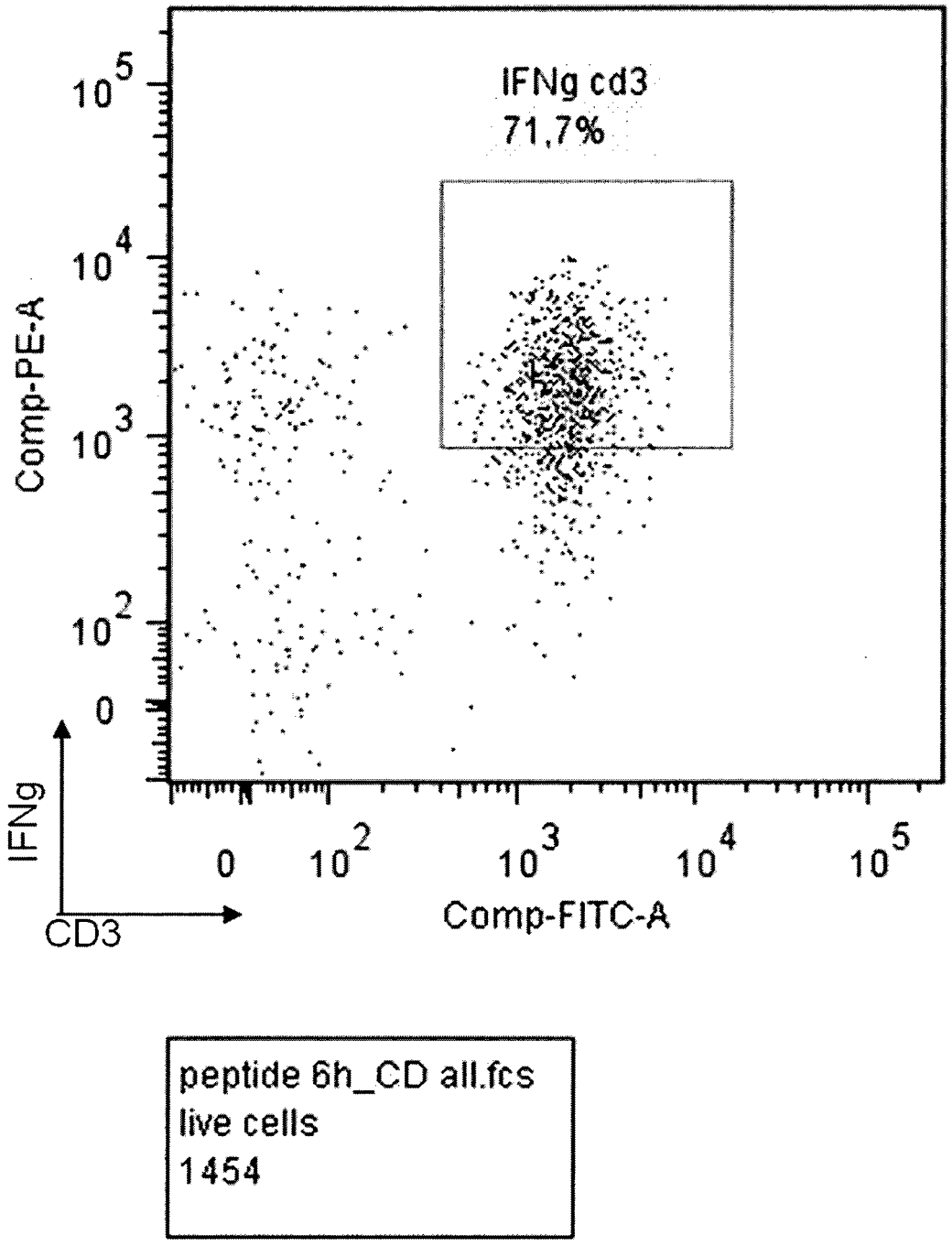

IFNg cd3
71,7%
Comp-PE-A
IFNg
CD3
Comp-FITC-A
peptide 6h_CD all.fcs
live cells
1454

Fig. 13(4)

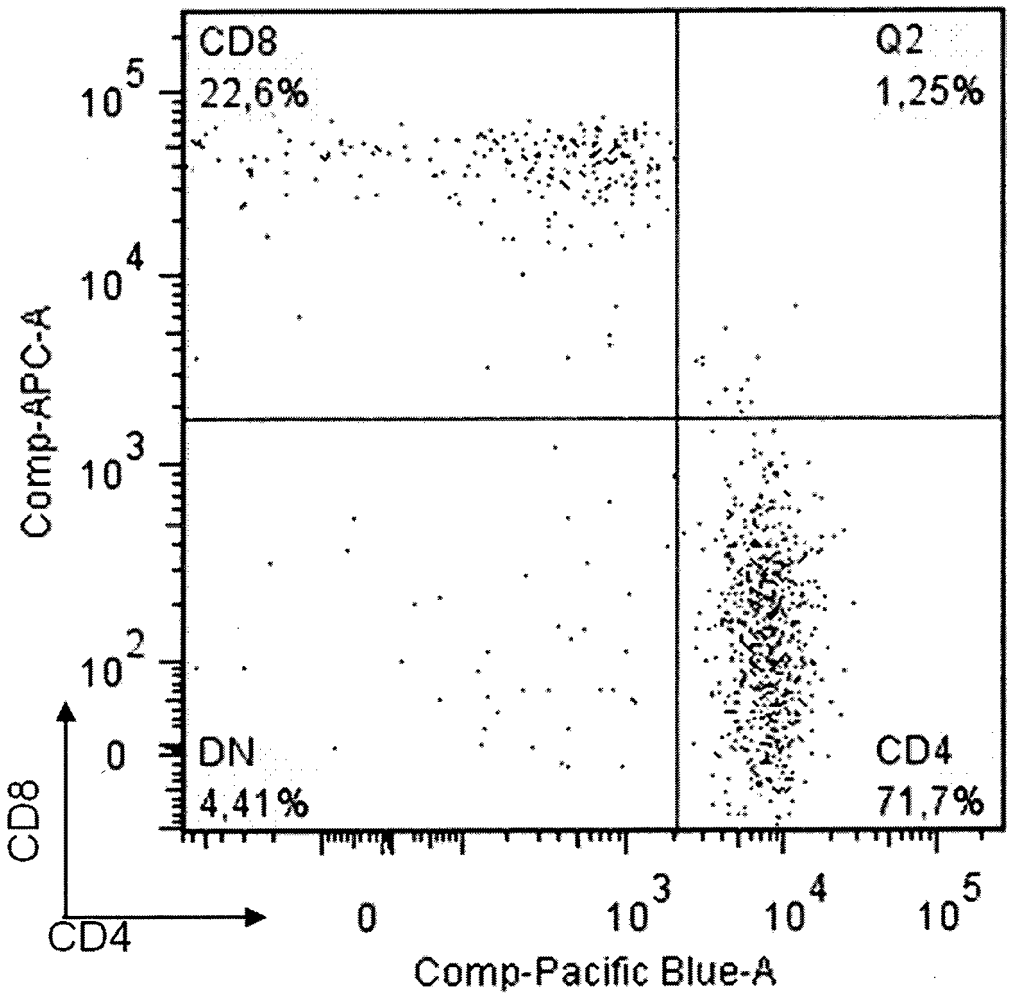

CD8
22,6%
Q2
1,25%
DN
4,41%
CD4
71,7%
Comp-APC-A
Comp-Pacific Blue-A
CD8
CD4
0
10^3
10^4
10^5
peptide 6h_CD all.fcs
IFNg cd3
1043

Fig. 13(5)

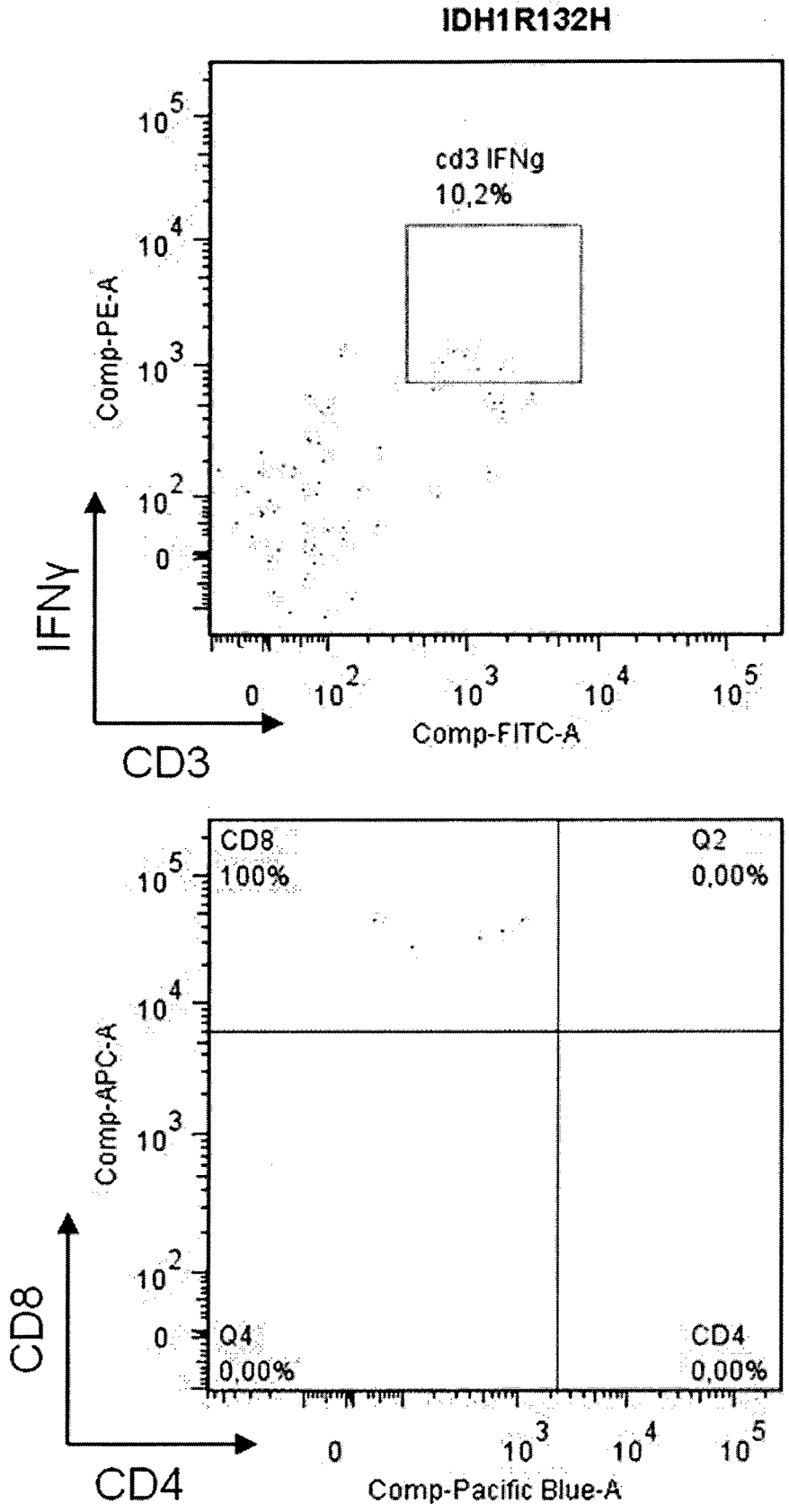

IDH1R132H
cd3 IFNg
10,2%
Comp-PE-A
IFNγ
CD3
Comp-FITC-A
CD8
100%
Q2
0,00%
Q4
0,00%
CD4
0,00%
Comp-APC-A
CD8
CD4
Comp-Pacific Blue-A

Fig. 14 A(1)

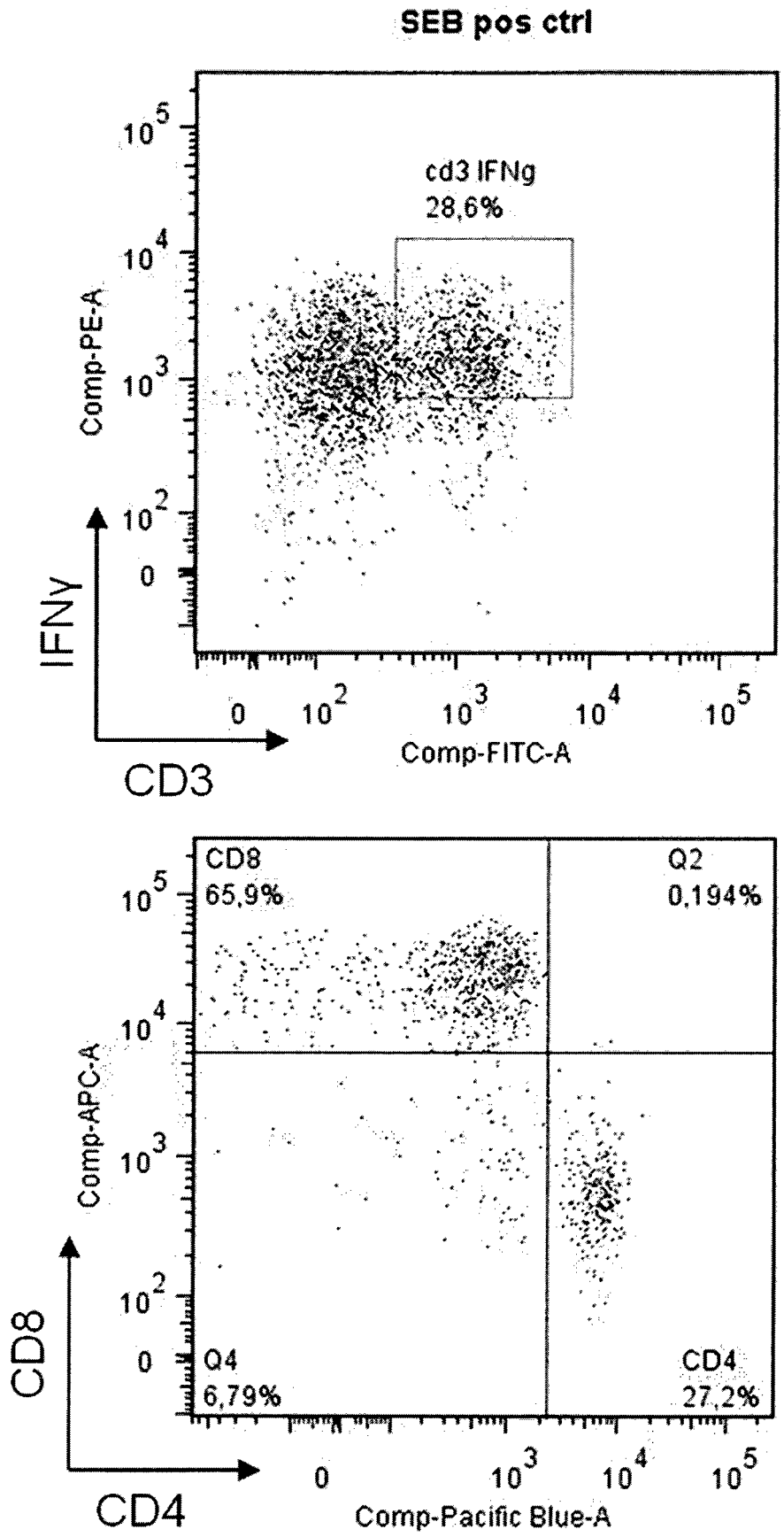

SEB pos ctrl
cd3 IFNg
28,6%
Comp-PE-A
IFNγ
CD3
Comp-FITC-A
CD8
65,9%
Q2
0,194%
Q4
6,79%
CD4
27,2%
Comp-APC-A
CD8
CD4
Comp-Pacific Blue-A

Fig. 14 A(2)

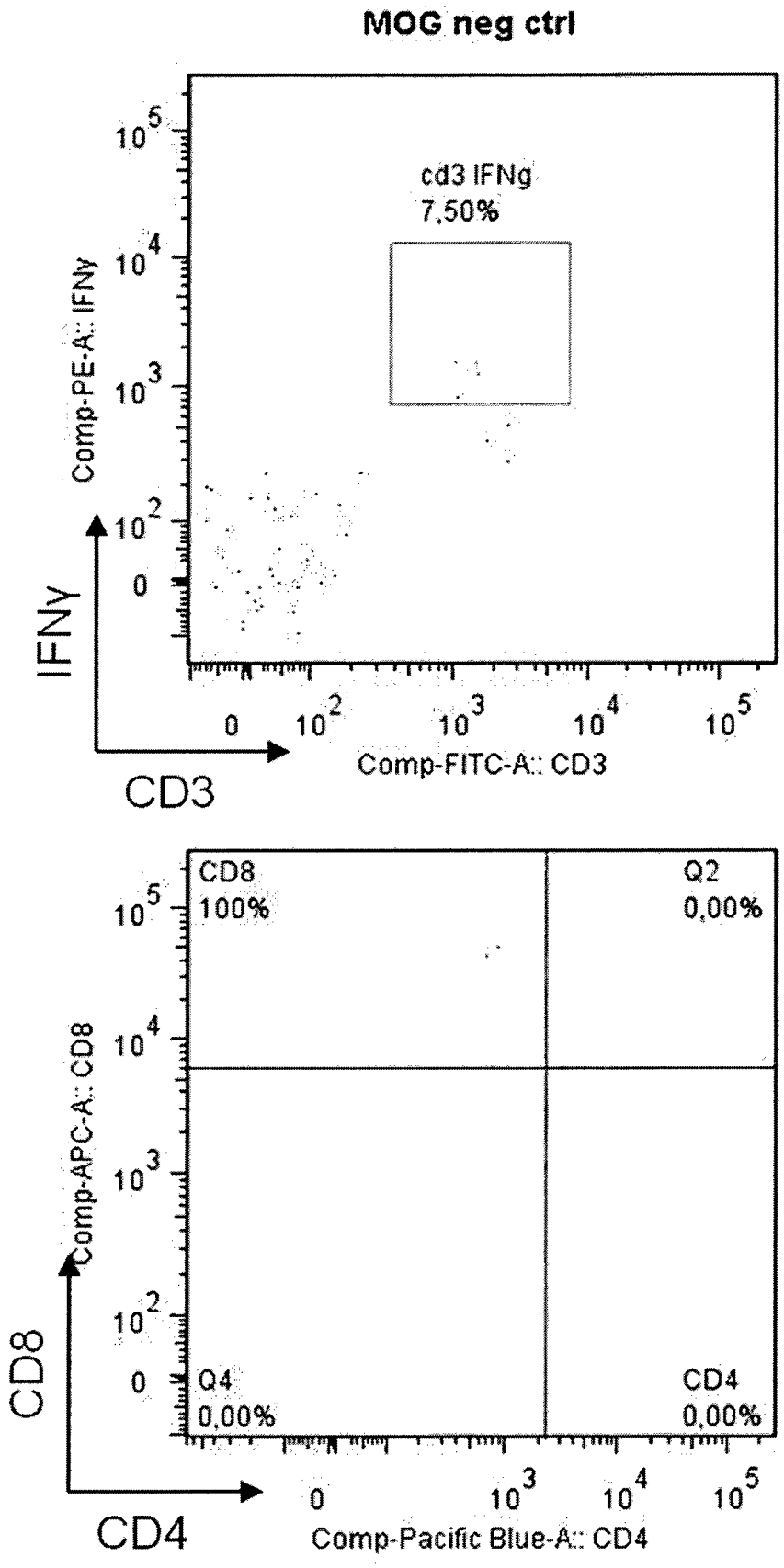

MOG neg ctrl
cd3 IFNg
7,50%
Comp-PE-A:: IFNγ
IFNγ
CD3
Comp-FITC-A:: CD3
CD8
100%
Q2
0,00%
Q4
0,00%
CD4
0,00%
Comp-APC-A:: CD8
CD8
CD4
Comp-Pacific Blue-A:: CD4

Fig. 14 A(3)

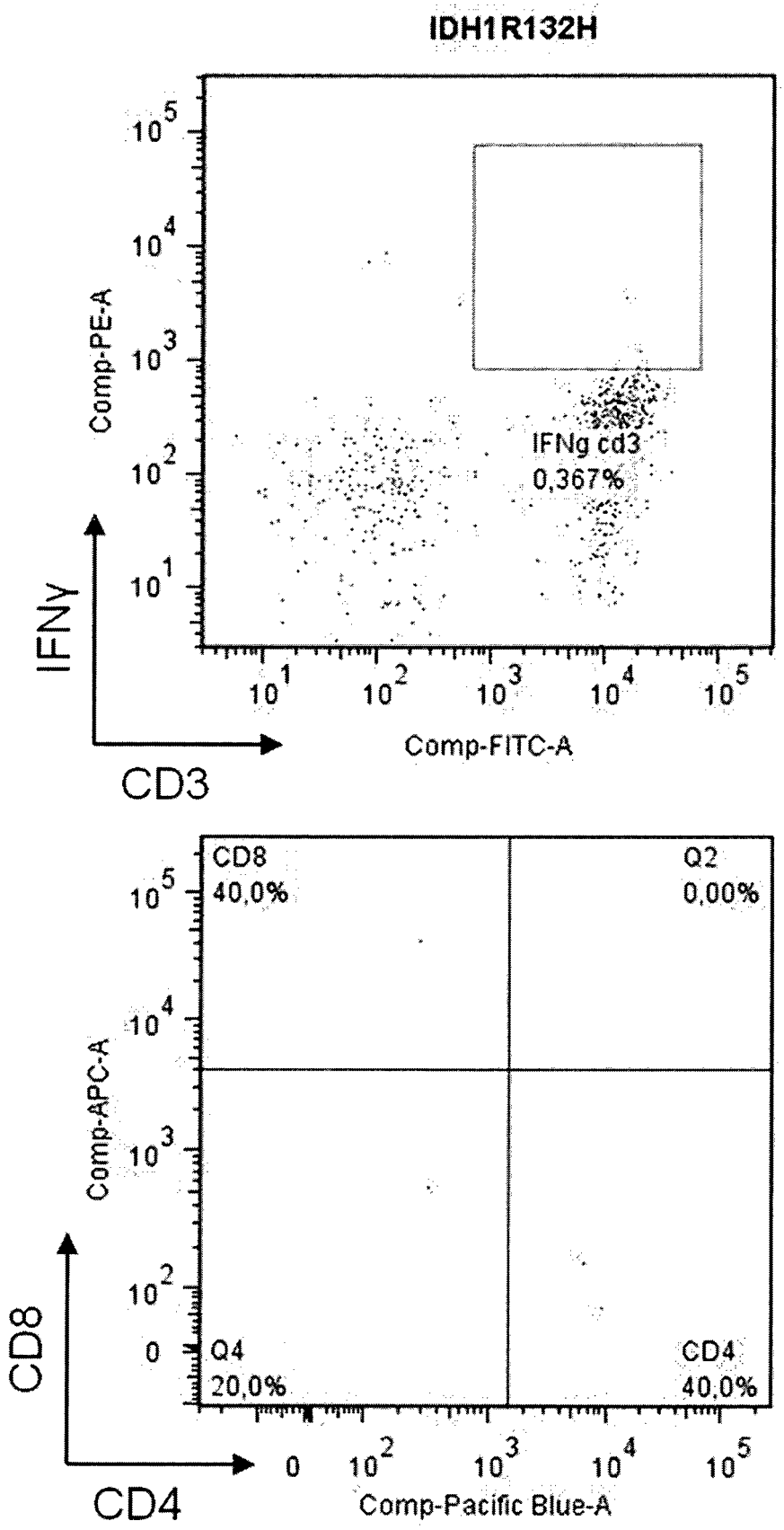

IDH1R132H
Comp-PE-A
IFNg cd3
0,367%
IFNγ
CD3
Comp-FITC-A
CD8
40,0%
Q2
0,00%
Comp-APC-A
Q4
20,0%
CD4
40,0%
CD8
CD4
Comp-Pacific Blue-A

Fig. 14 B(1)

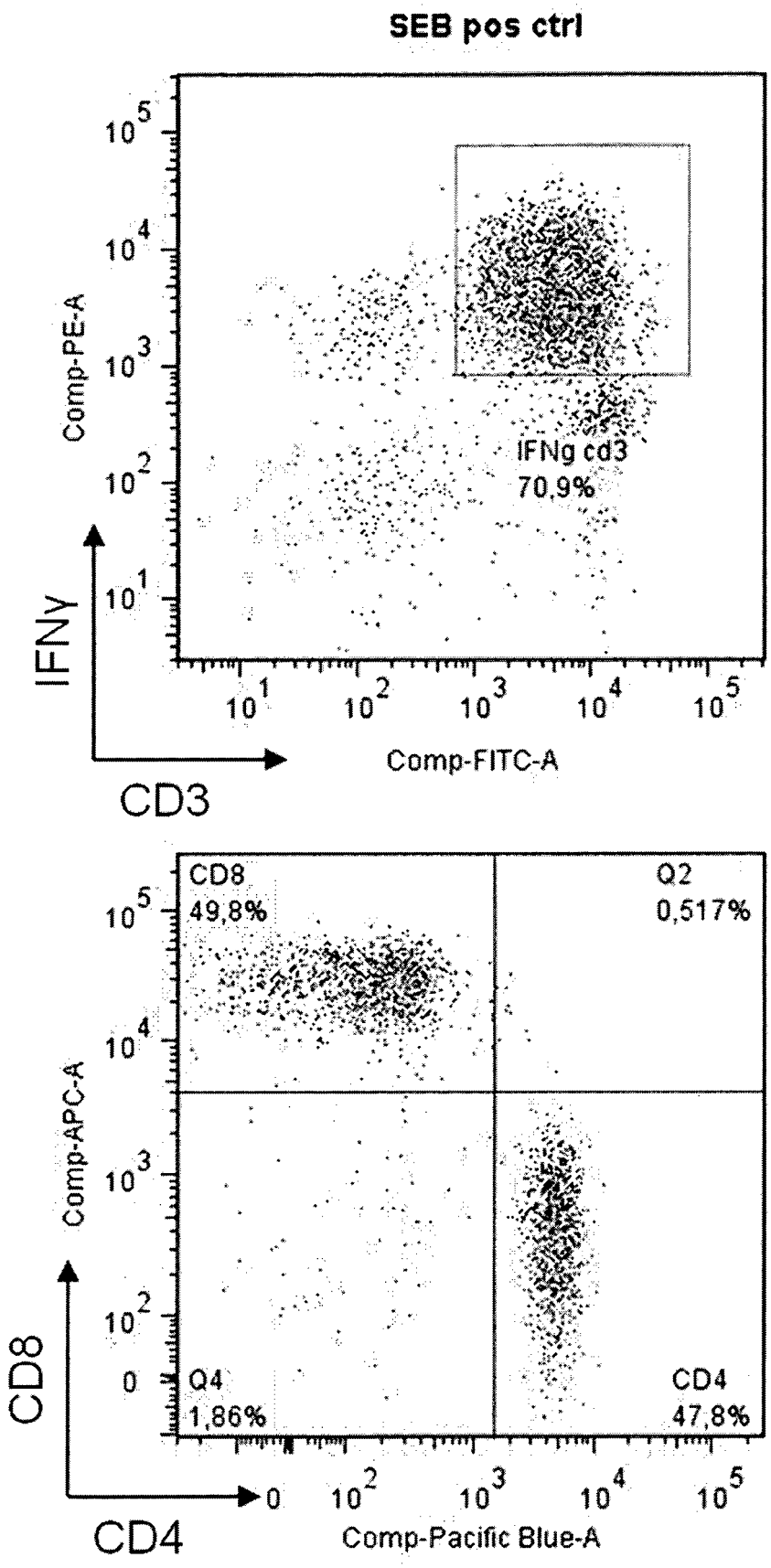

SEB pos ctrl
Comp-PE-A
IFNg cd3
70,9%
IFNγ
CD3
Comp-FITC-A
CD8
49,8%
Q2
0,517%
Comp-APC-A
Q4
1,86%
CD4
47,8%
CD8
CD4
Comp-Pacific Blue-A

Fig. 14 B(2)

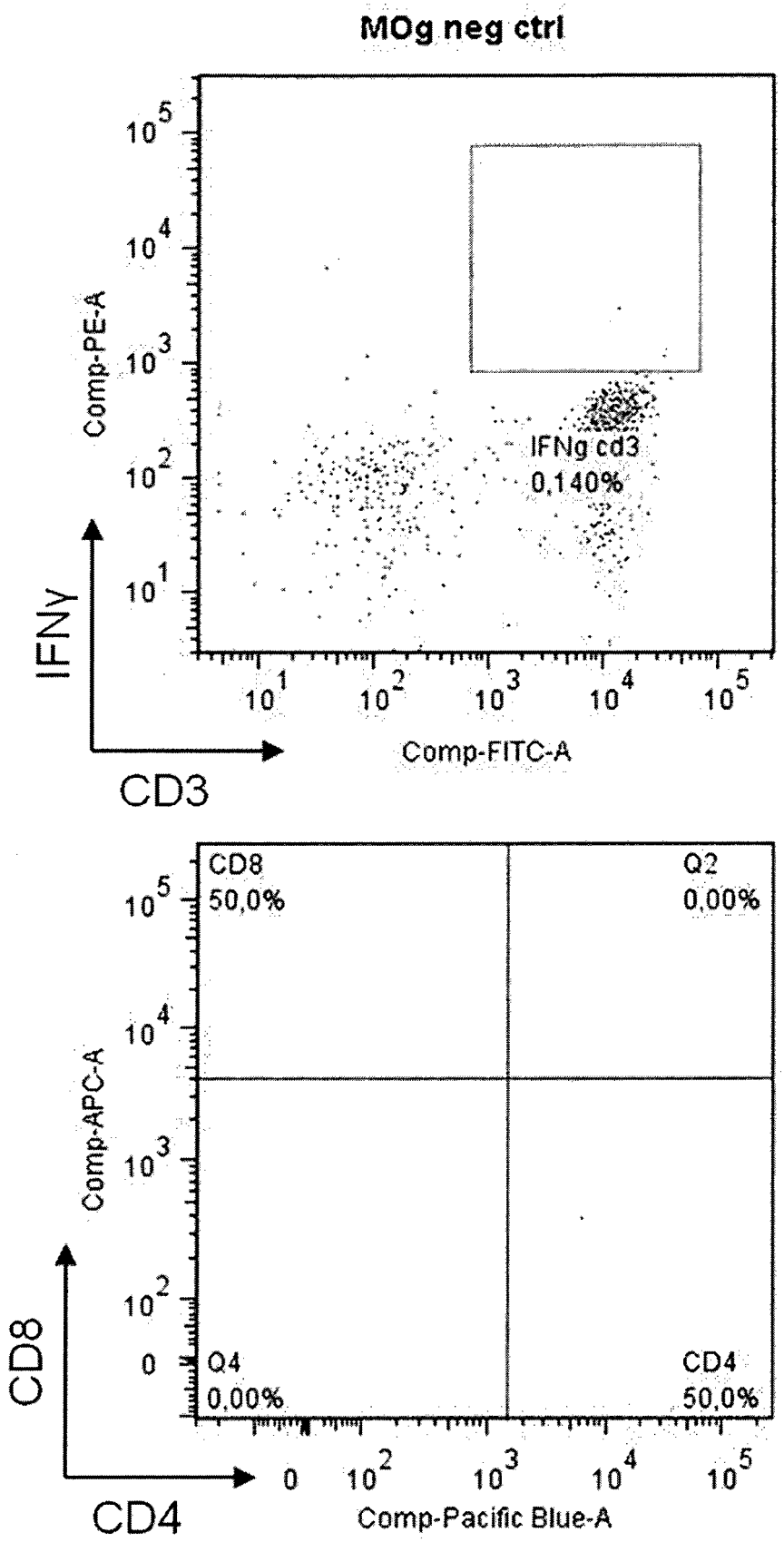

MOg neg ctrl
Comp-PE-A
IFNg cd3
0,140%
IFNγ
CD3
Comp-FITC-A
CD8
50,0%
Q2
0,00%
Comp-APC-A
Q4
0,00%
CD4
50,0%
CD8
CD4
Comp-Pacific Blue-A

Fig. 14 B(3)

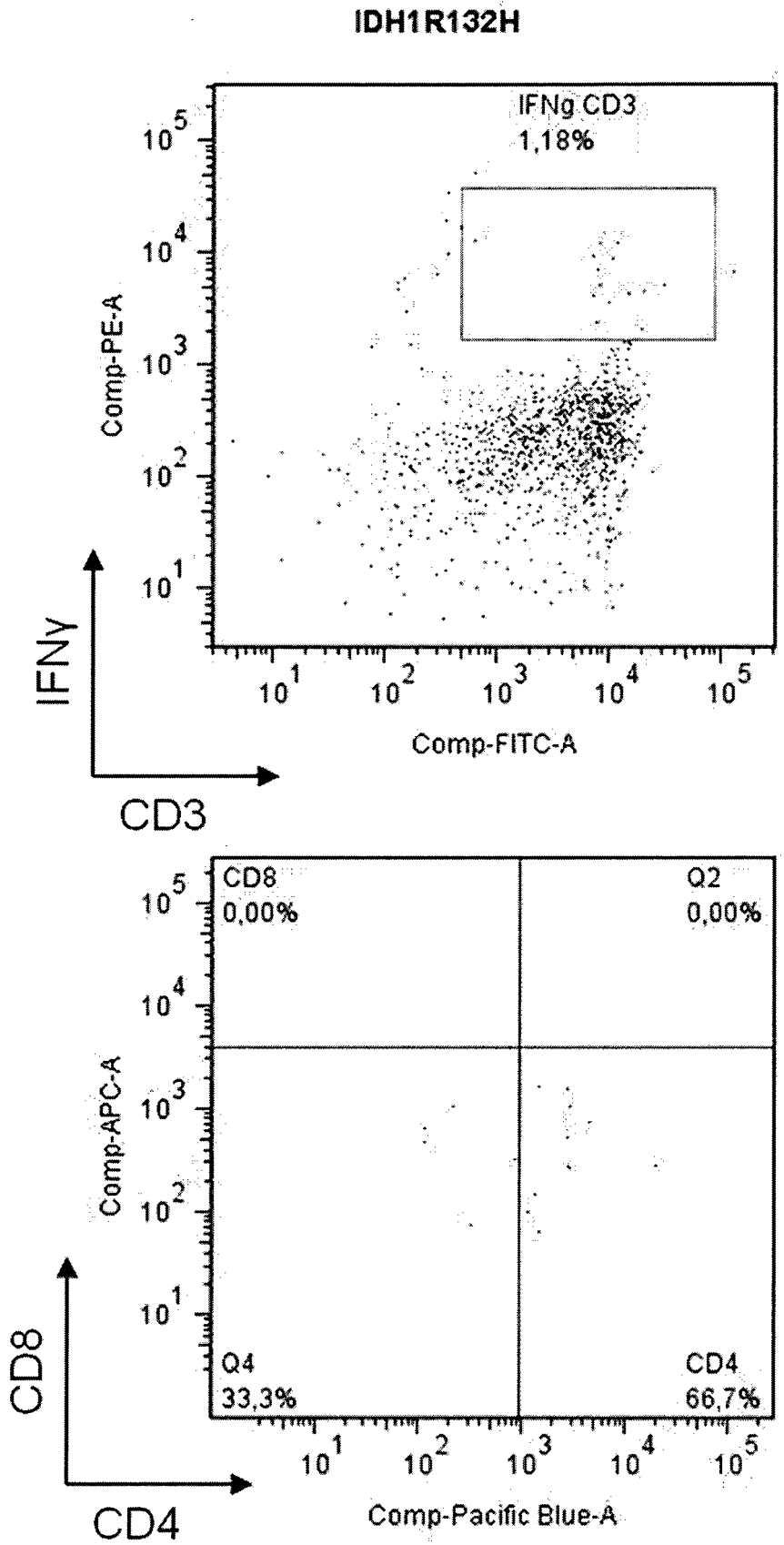

IDH1R132H
IFNg CD3
1,18%
Comp-PE-A
IFNγ
CD3
Comp-FITC-A
CD8
0,00%
Q2
0,00%
Q4
33,3%
CD4
66,7%
Comp-APC-A
CD8
CD4
Comp-Pacific Blue-A

Fig. 14 C(1)

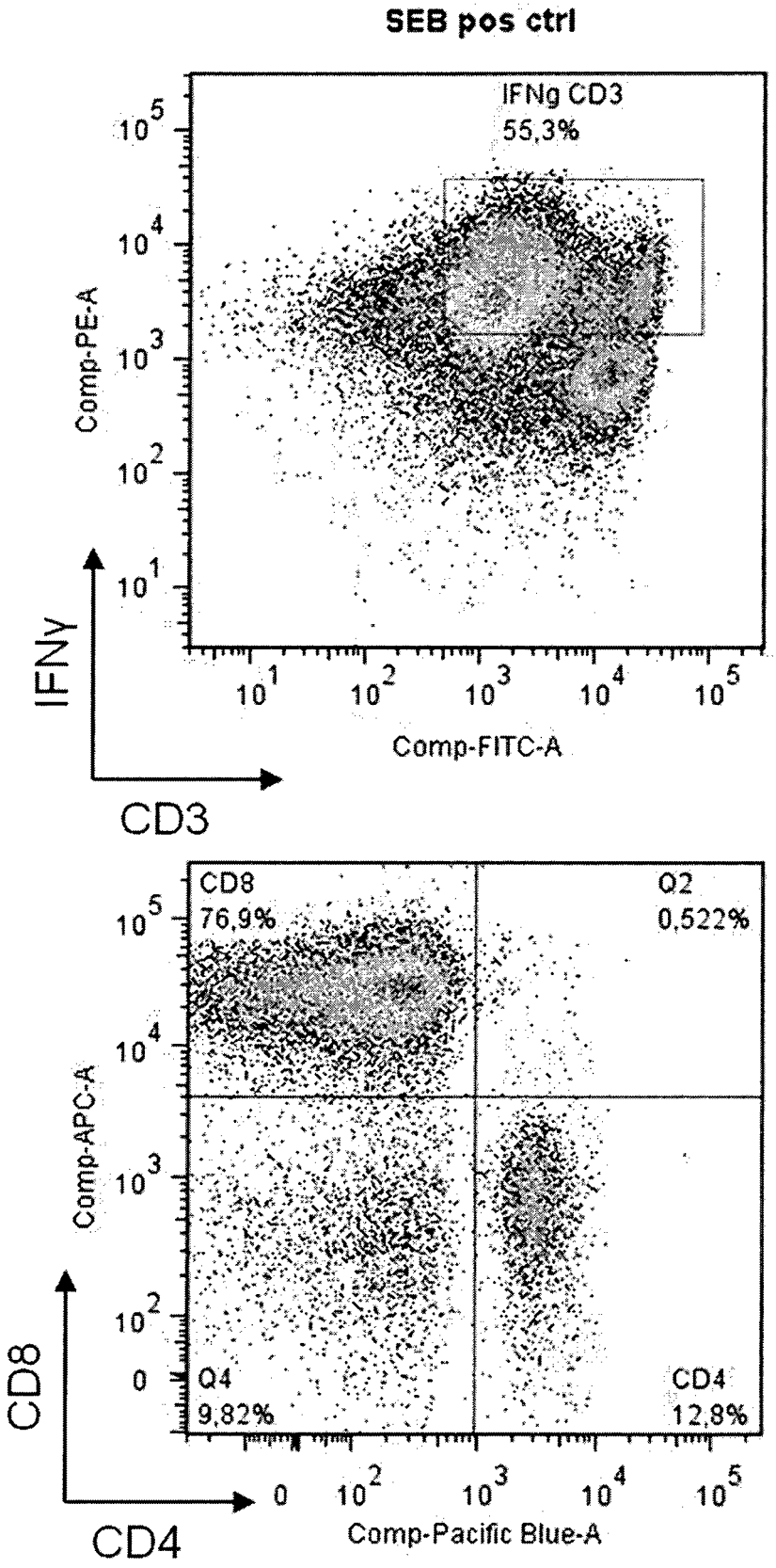

SEB pos ctrl
IFNg CD3
55,3%
Comp-PE-A
IFNγ
Comp-FITC-A
CD3
CD8
76,9%
Q2
0,522%
Q4
9,82%
CD4
12,8%
Comp-APC-A
CD8
Comp-Pacific Blue-A
CD4

Fig. 14 C(2)

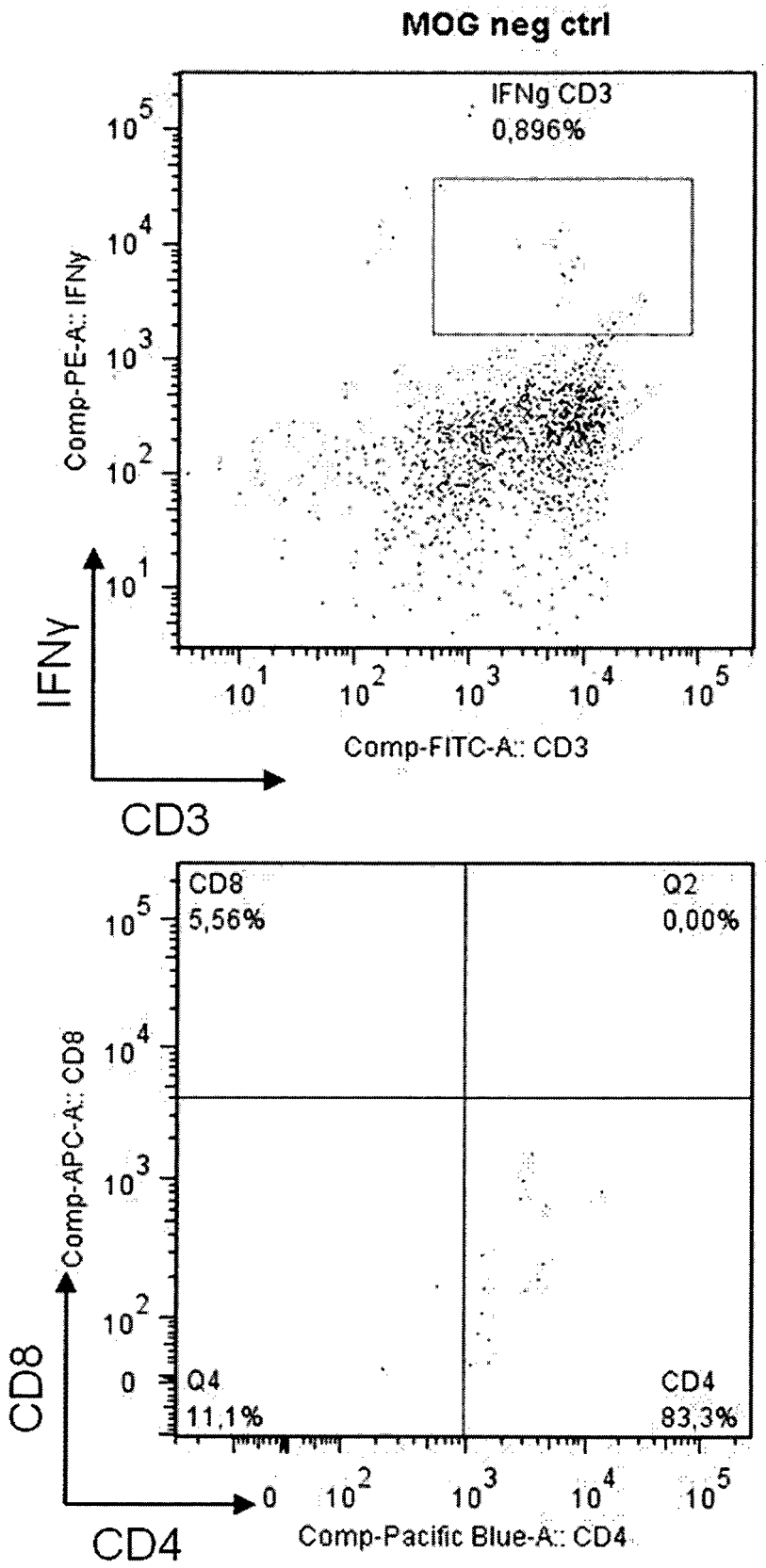

MOG neg ctrl
IFNg CD3
0,896%
Comp-PE-A:: IFNγ
IFNγ
Comp-FITC-A:: CD3
CD3
CD8
5,56%
Q2
0,00%
Q4
11,1%
CD4
83,3%
Comp-APC-A:: CD8
CD8
Comp-Pacific Blue-A:: CD4
CD4

Fig. 14 C(3)

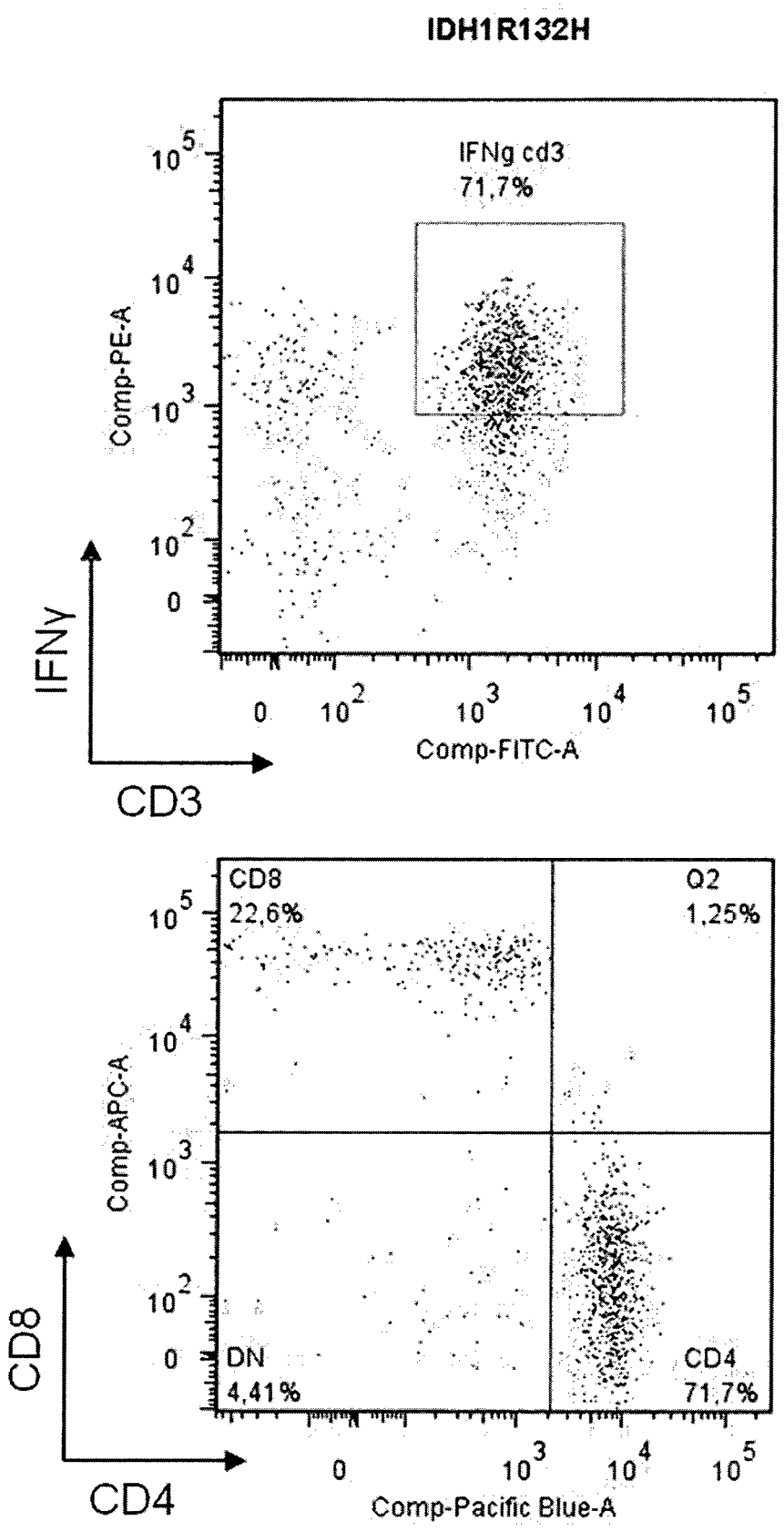

IDH1R132H
IFNg cd3
71,7%
Comp-PE-A
IFNγ
CD3
Comp-FITC-A
CD8
22,6%
Q2
1,25%
DN
4,41%
CD4
71,7%
Comp-APC-A
CD8
CD4
Comp-Pacific Blue-A

Fig. 15 A(1)

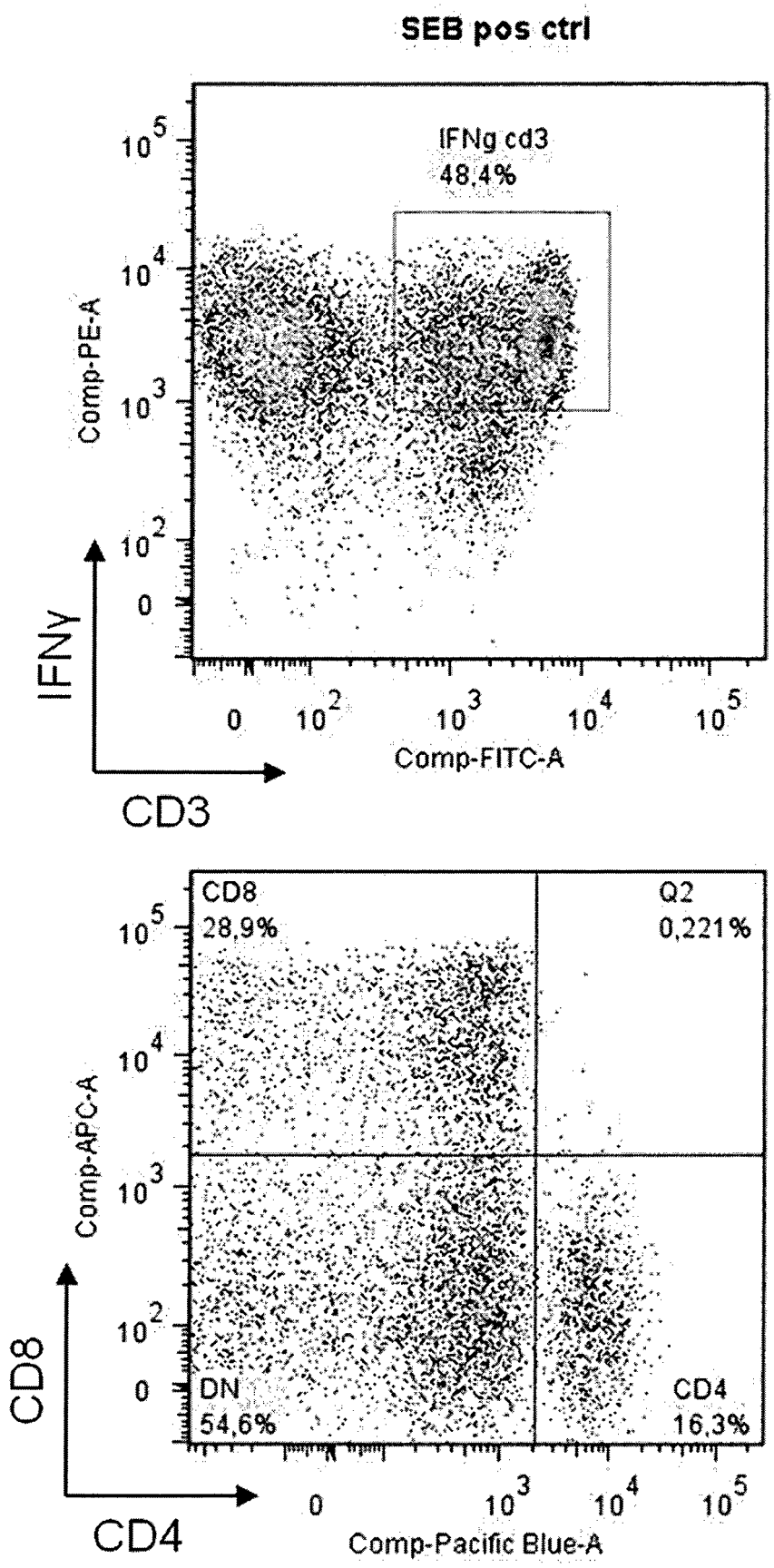

SEB pos ctrl
IFNg cd3
48,4%
Comp-PE-A
IFNγ
CD3
Comp-FITC-A
CD8
28,9%
Q2
0,221%
DN
54,6%
CD4
16,3%
Comp-APC-A
CD8
CD4
Comp-Pacific Blue-A

Fig. 15 A(2)

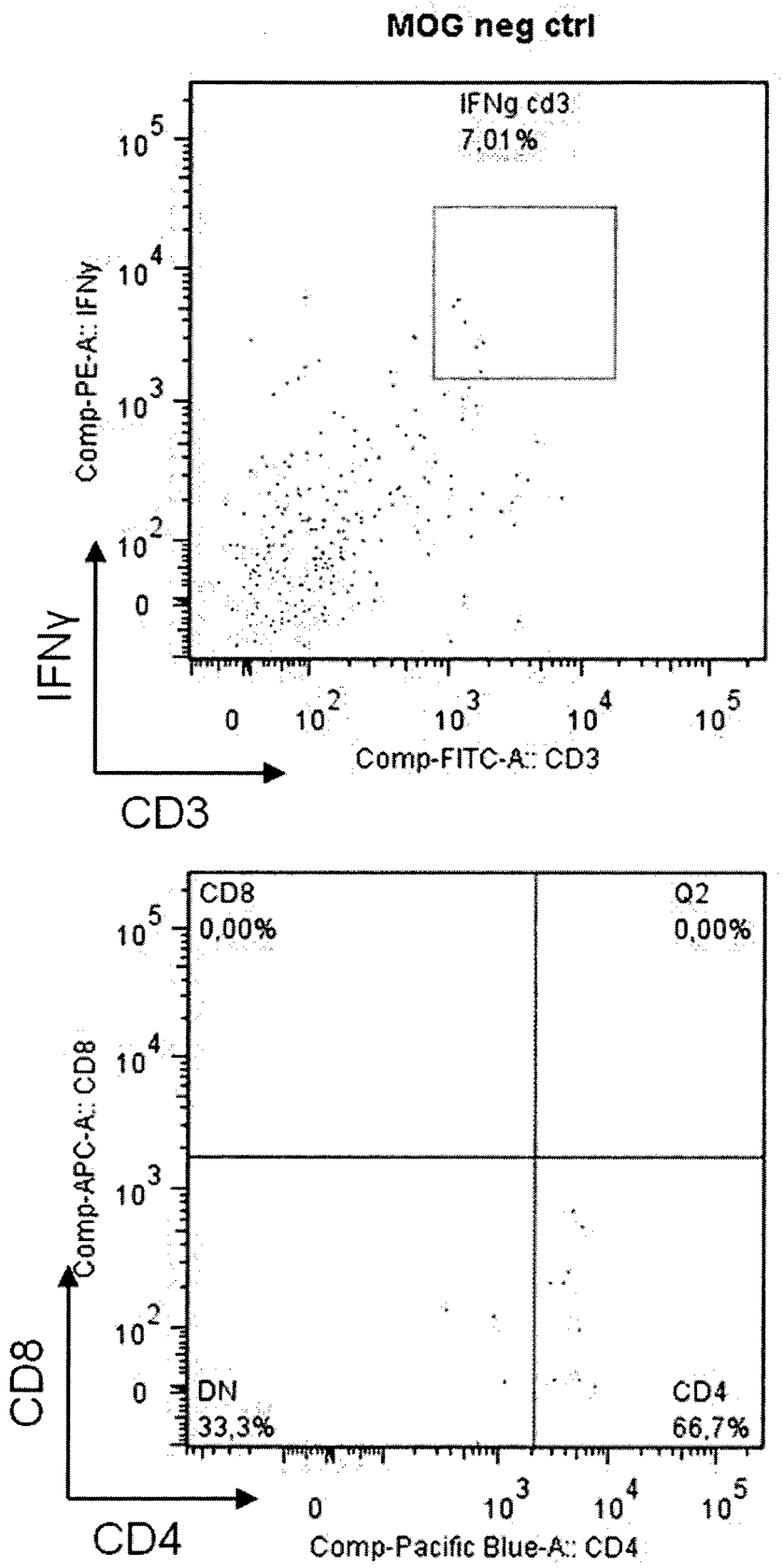

MOG neg ctrl
IFNg cd3
7,01%
Comp-PE-A:: IFNγ
IFNγ
CD3
Comp-FITC-A:: CD3
CD8
0,00%
Q2
0,00%
DN
33,3%
CD4
66,7%
Comp-APC-A:: CD8
CD8
CD4
Comp-Pacific Blue-A:: CD4

Fig. 15 A(3)

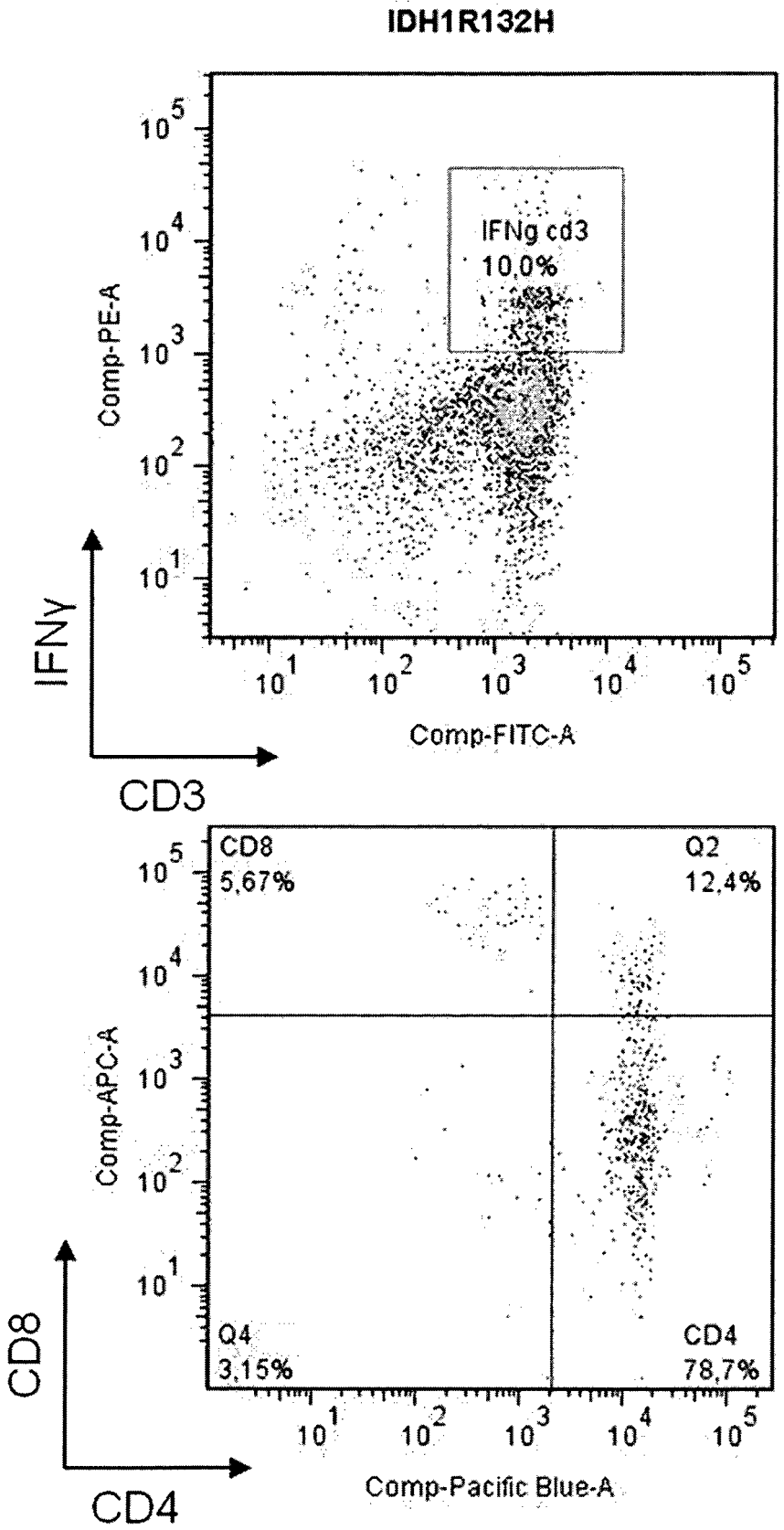

IDH1R132H
IFNg cd3
10,0%
Comp-PE-A
IFNγ
Comp-FITC-A
CD3
CD8
5,67%
Q2
12,4%
Q4
3,15%
CD4
78,7%
Comp-APC-A
CD8
Comp-Pacific Blue-A
CD4

Fig. 15 B(1)

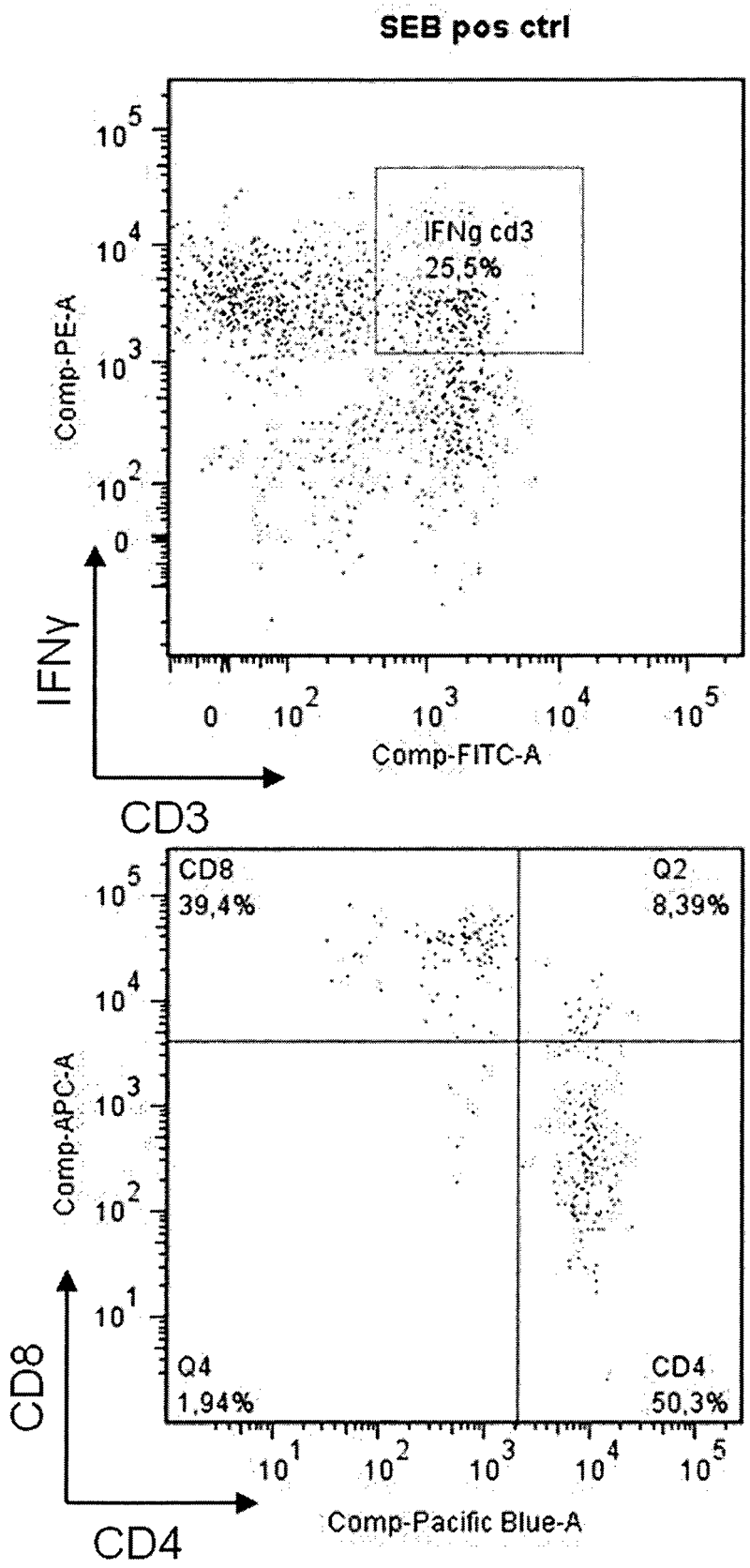

SEB pos ctrl
IFNg cd3
25,5%
Comp-PE-A
IFNγ
Comp-FITC-A
CD3
CD8
39,4%
Q2
8,39%
Q4
1,94%
CD4
50,3%
Comp-APC-A
CD8
Comp-Pacific Blue-A
CD4

Fig. 15 B(2)

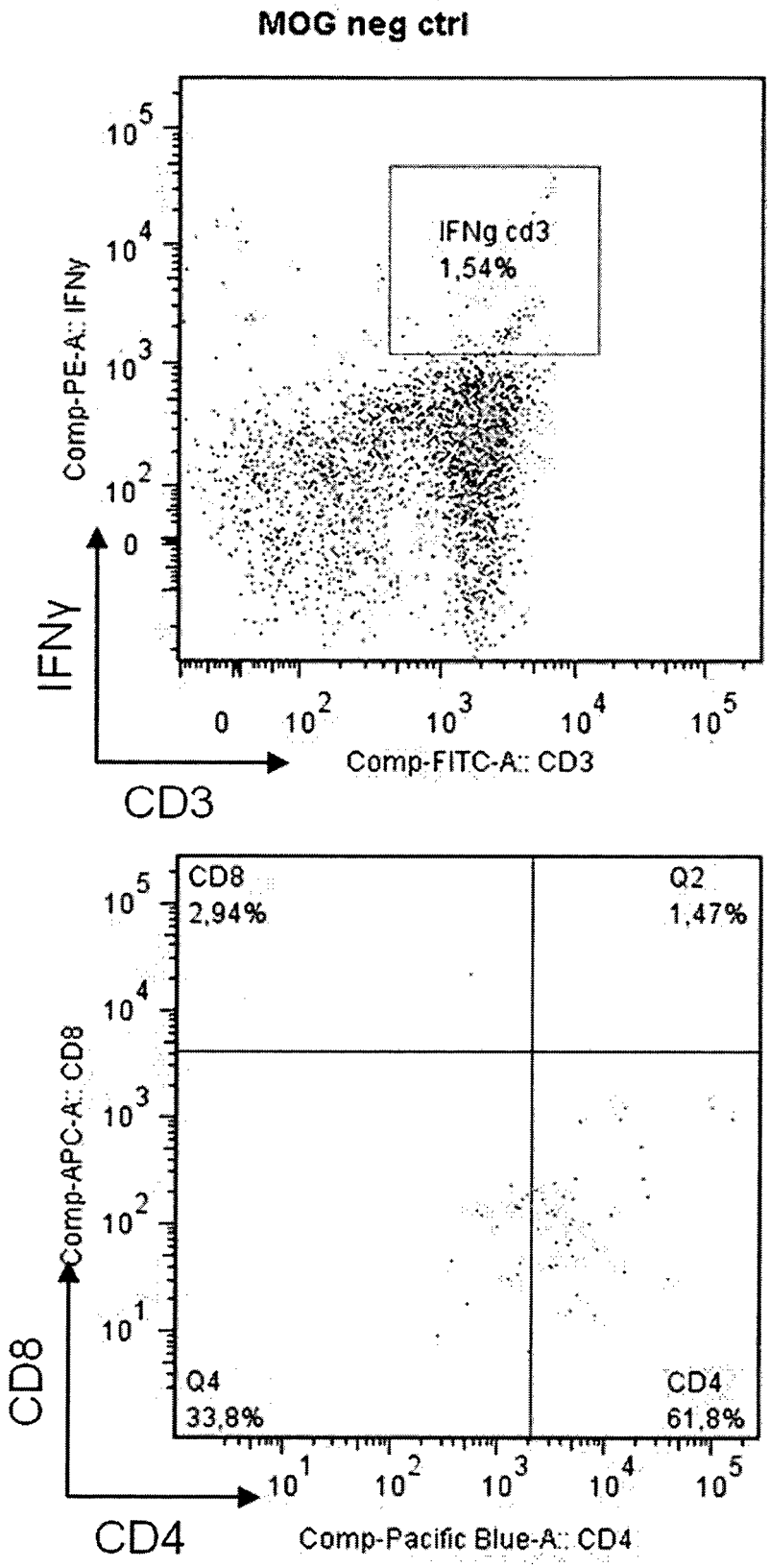

MOG neg ctrl
IFNg cd3
1,54%
Comp-PE-A:: IFNy
IFNγ
Comp-FITC-A:: CD3
CD3
CD8
2,94%
Q2
1,47%
Q4
33,8%
CD4
61,8%
Comp-APC-A:: CD8
CD8
CD4
Comp-Pacific Blue-A:: CD4

Fig. 15 B(3)