FIGURES

FIG. 1

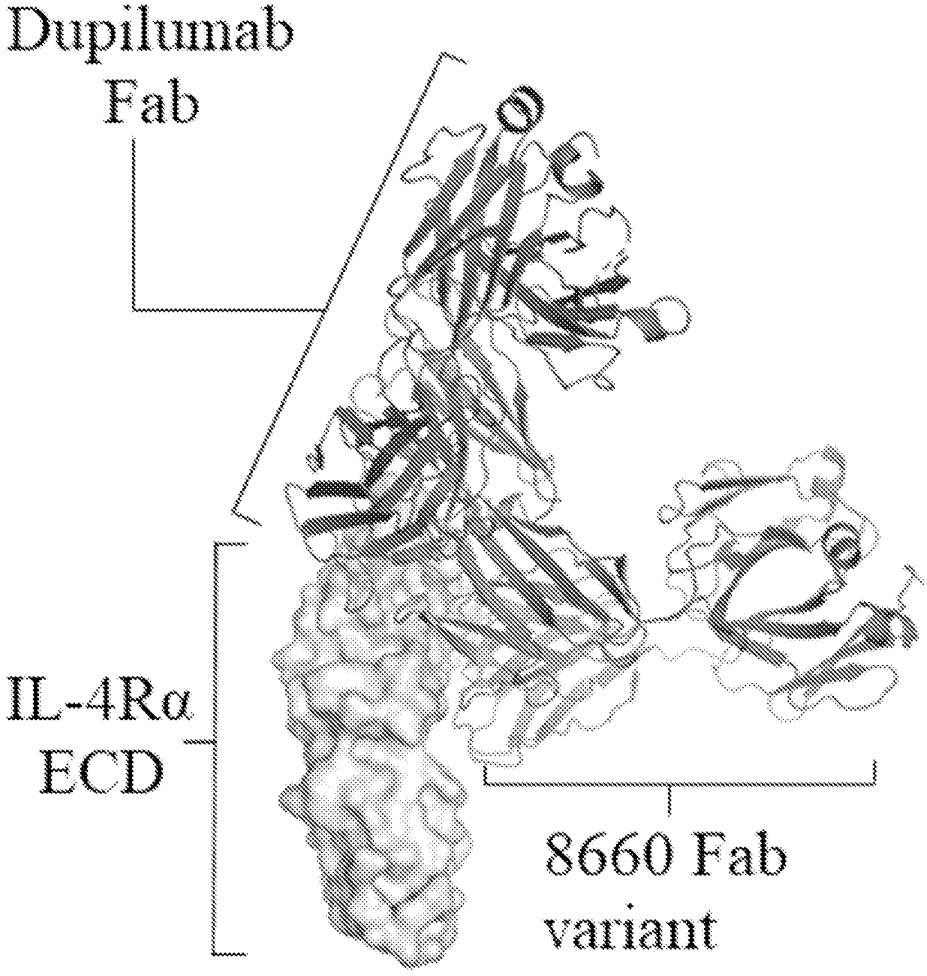


FIG. 2

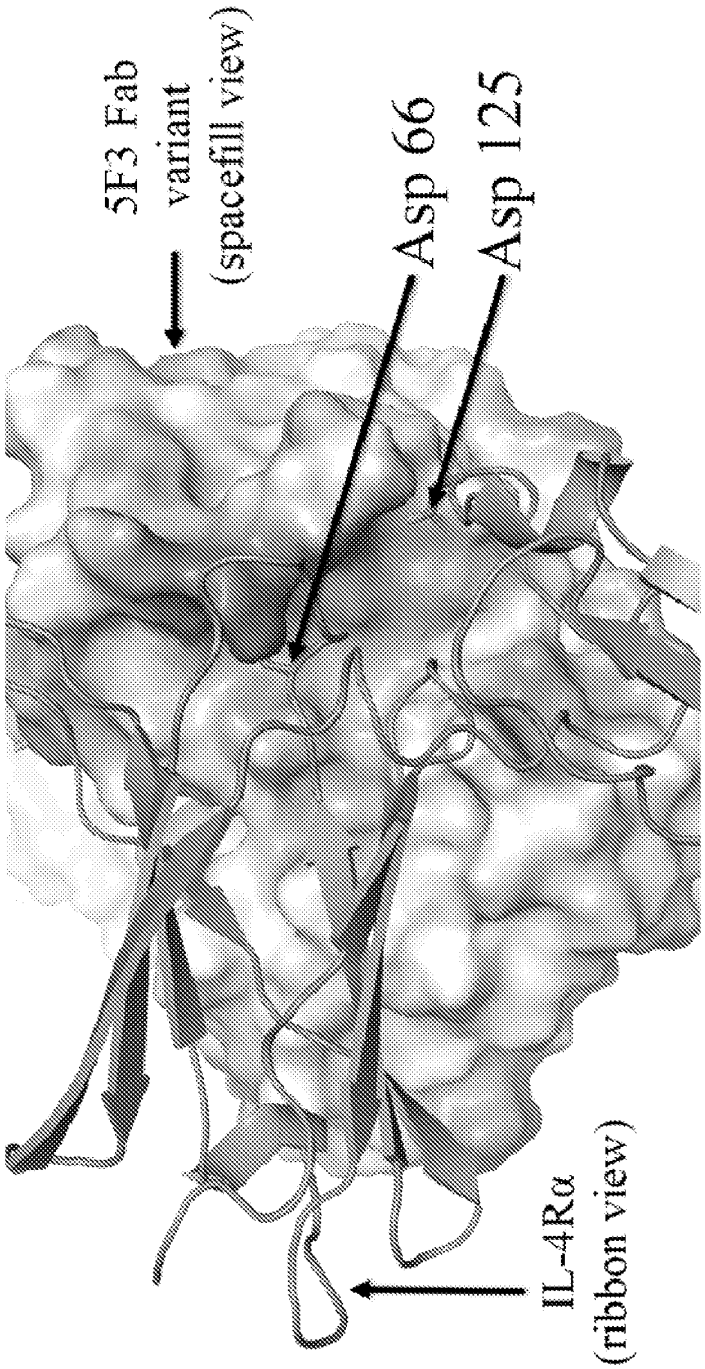

5F3 Fab
variant
(spacefill view)
Asp 66
Asp 125
IL-4Rα
(ribbon view)

FIG. 3A

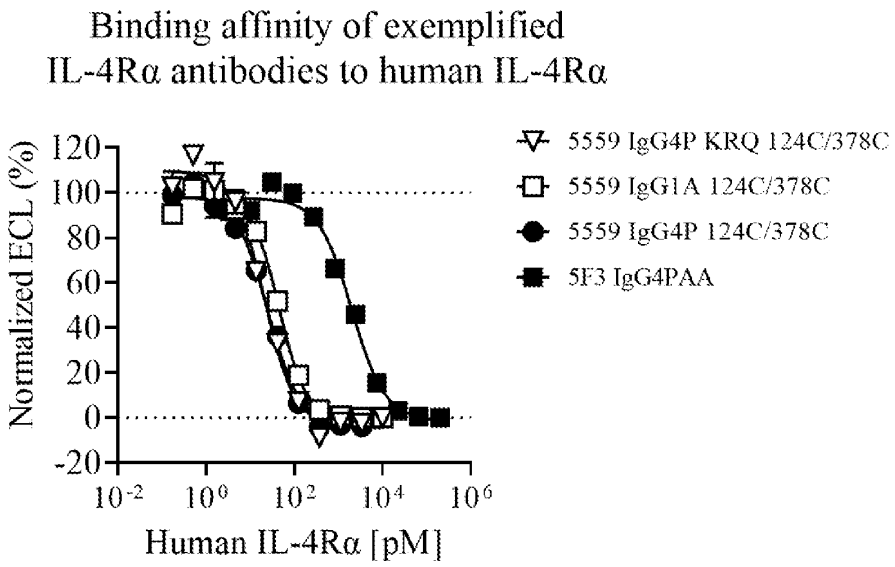

Binding affinity of exemplified
IL-4Rα antibodies to human IL-4Rα
Normalized ECL (%)
120
100
80
60
40
20
0
-20
10-2
100
102
104
106
Human IL-4Rα [pM]
5559 IgG4P KRQ 124C/378C
5559 IgG1A 124C/378C
5559 IgG4P 124C/378C
5F3 IgG4PAA

FIG. 3B

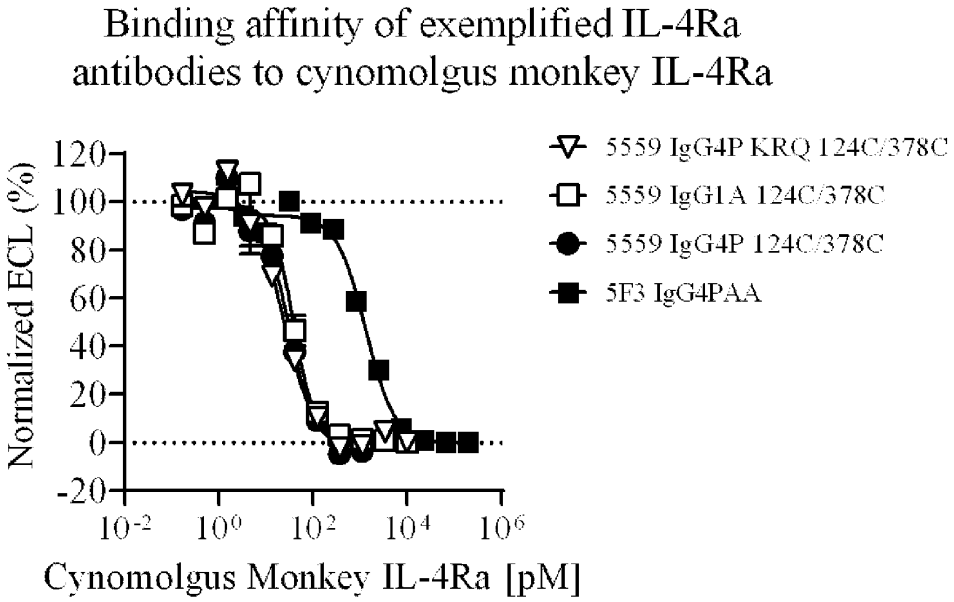

Binding affinity of exemplified IL-4Ra
antibodies to cynomolgus monkey IL-4Ra
Normalized ECL (%)
120
100
80
60
40
20
0
-20
10-2
100
102
104
106
Cynomolgus Monkey IL-4Ra [pM]
5559 IgG4P KRQ 124C/378C
5559 IgG1A 124C/378C
5559 IgG4P 124C/378C
5F3 IgG4PAA

FIG. 4A

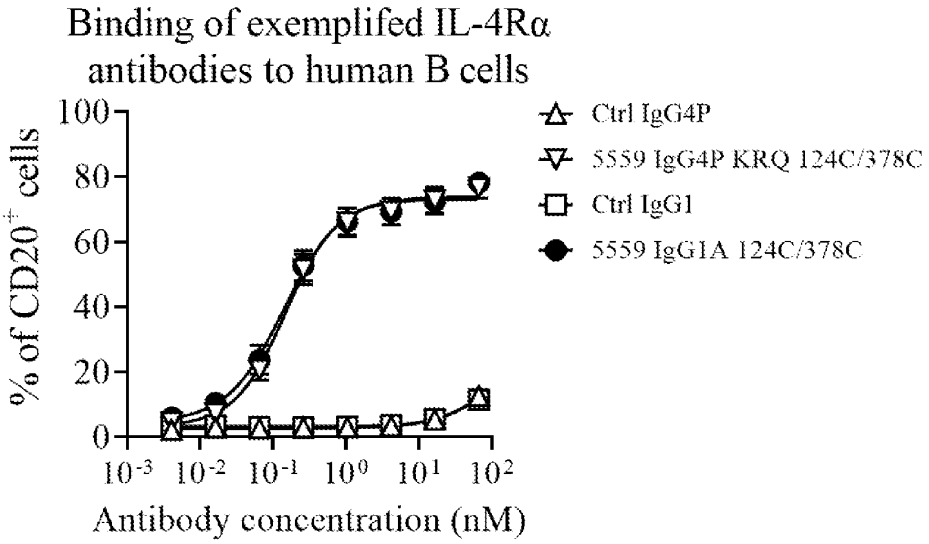

Binding of exemplifed IL-4Rα antibodies to human B cells
% of CD20+ cells
100
80
60
40
20
0
10-3 10-2 10-1 100 101 102
Antibody concentration (nM)
Ctrl IgG4P
5559 IgG4P KRQ 124C/378C
Ctrl IgG1
5559 IgG1A 124C/378C

FIG. 4B

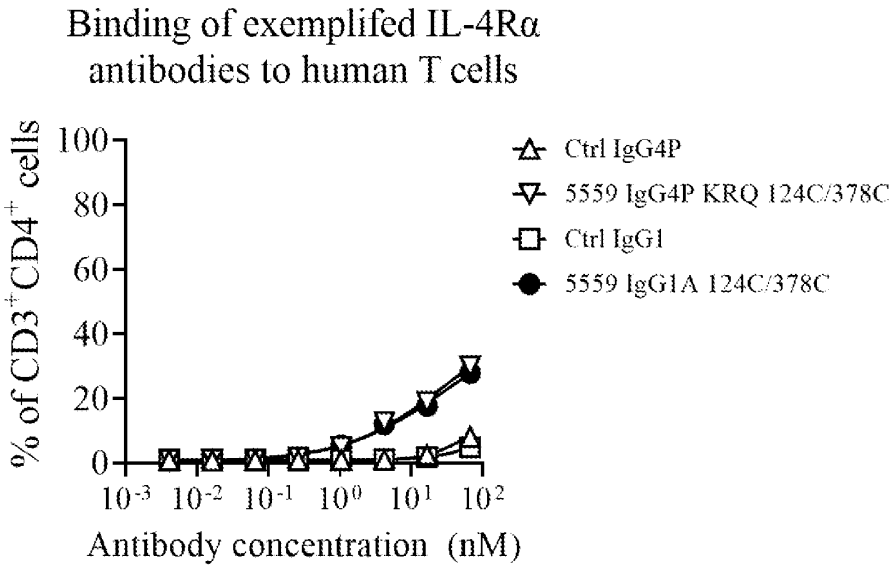

Binding of exemplifed IL-4Rα antibodies to human T cells
% of CD3+CD4+ cells
100
80
60
40
20
0
10-3 10-2 10-1 100 101 102
Antibody concentration (nM)
Ctrl IgG4P
5559 IgG4P KRQ 124C/378C
Ctrl IgG1
5559 IgG1A 124C/378C

FIG. 4C

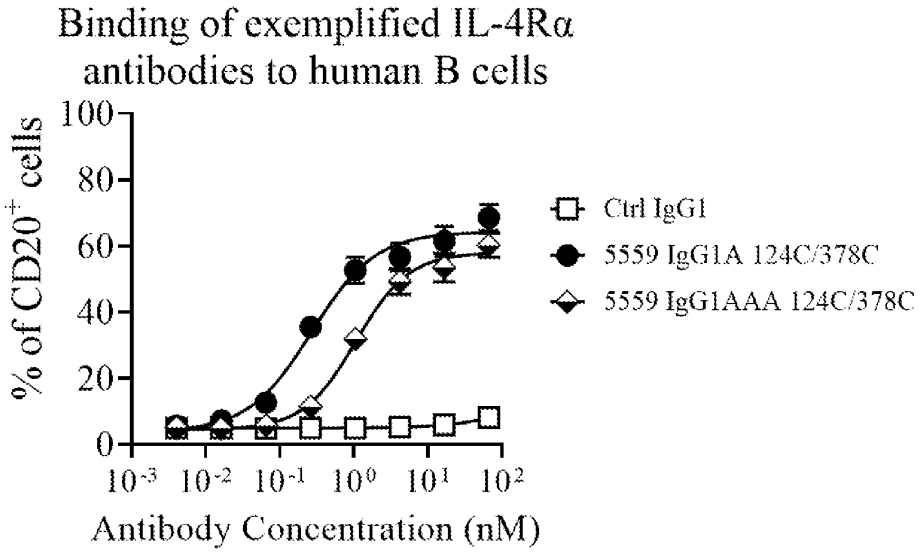

Binding of exemplified IL-4Rα antibodies to human B cells
% of CD20+ cells
100
80
60
40
20
0
10-3 10-2 10-1 100 101 102
Antibody Concentration (nM)
Ctrl IgG1
5559 IgG1A 124C/378C
5559 IgG1AAA 124C/378C

FIG. 5A

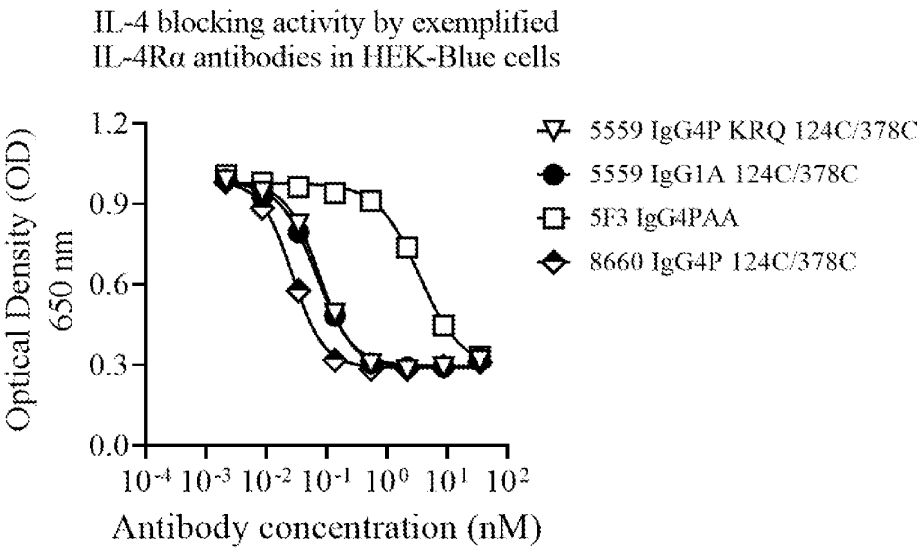

IL-4 blocking activity by exemplified
IL-4Rα antibodies in HEK-Blue cells
Optical Density (OD)
650 nm
1.2
0.9
0.6
0.3
0.0
10-4 10-3 10-2 10-1 100 101 102
Antibody concentration (nM)
5559 IgG4P KRQ 124C/378C
5559 IgG1A 124C/378C
5F3 IgG4PAA
8660 IgG4P 124C/378C

FIG. 5B

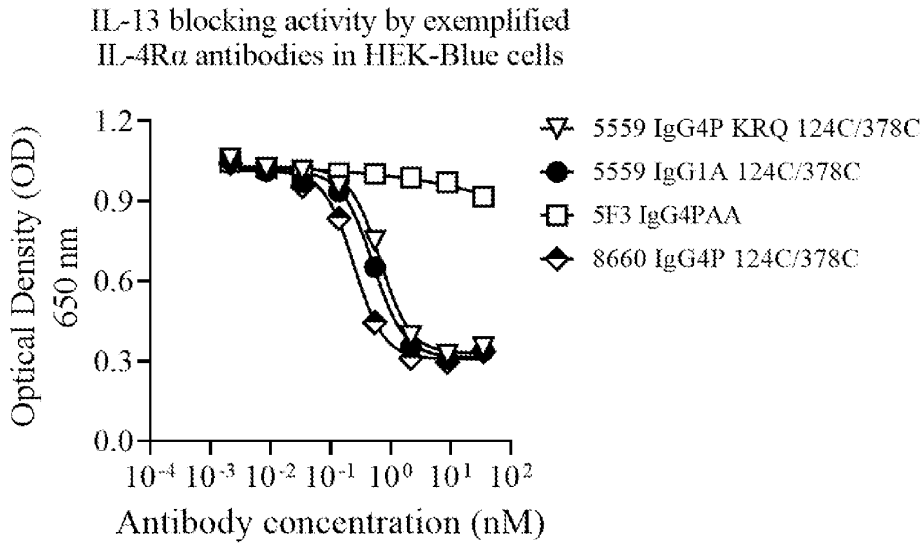

IL-13 blocking activity by exemplified
IL-4Rα antibodies in HEK-Blue cells
Optical Density (OD)
650 nm
1.2
0.9
0.6
0.3
0.0
10-4 10-3 10-2 10-1 100 101 102
Antibody concentration (nM)
5559 IgG4P KRQ 124C/378C
5559 IgG1A 124C/378C
5F3 IgG4PAA
8660 IgG4P 124C/378C

FIG. 6A

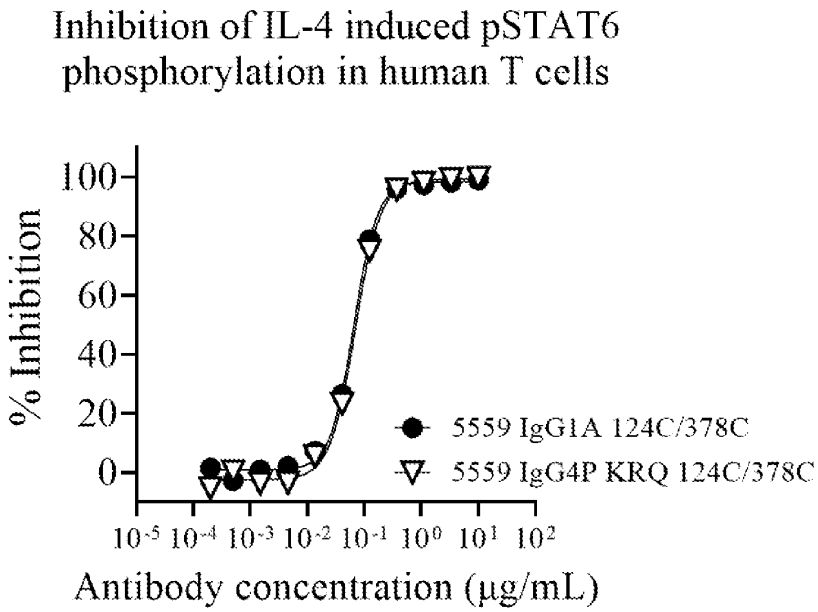

Inhibition of IL-4 induced pSTAT6 phosphorylation in human T cells
% Inhibition
100
80
60
40
20
0
5559 IgG1A 124C/378C
5559 IgG4P KRQ 124C/378C
10-5 10-4 10-3 10-2 10-1 100 101 102
Antibody concentration (µg/mL)

FIG. 6B

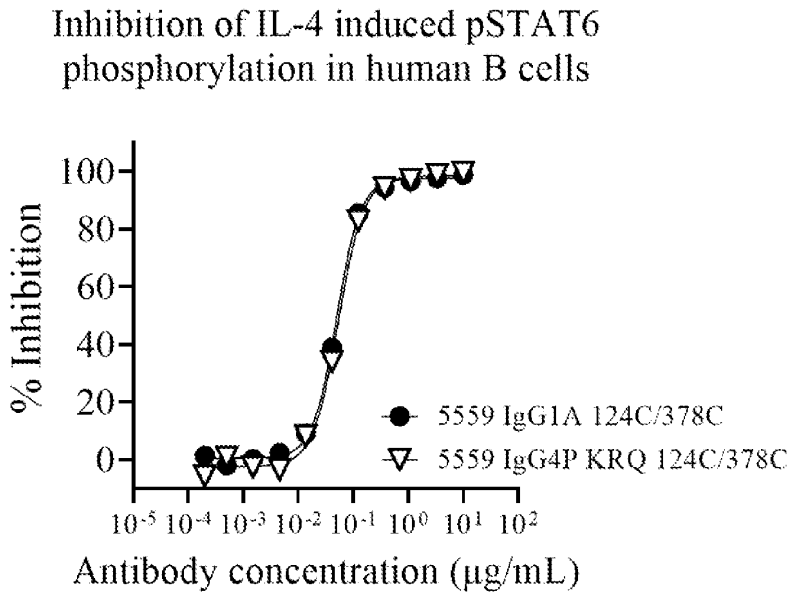

Inhibition of IL-4 induced pSTAT6 phosphorylation in human B cells
% Inhibition
100
80
60
40
20
0
5559 IgG1A 124C/378C
5559 IgG4P KRQ 124C/378C
10-5 10-4 10-3 10-2 10-1 100 101 102
Antibody concentration (µg/mL)

FIG. 6C

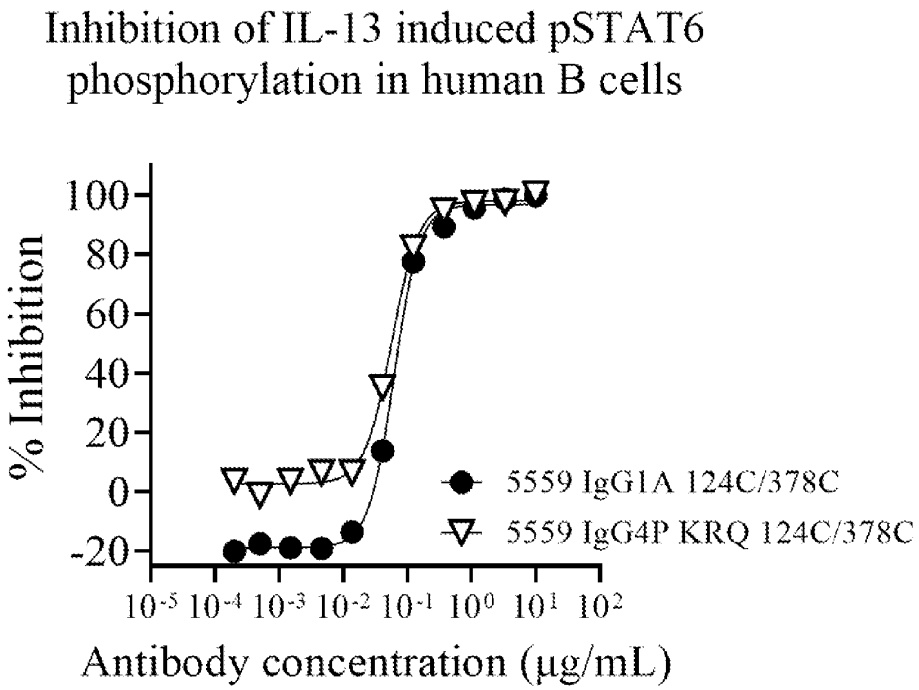

Inhibition of IL-13 induced pSTAT6 phosphorylation in human B cells
% Inhibition
100
80
60
40
20
0
-20
10-5 10-4 10-3 10-2 10-1 100 101 102
Antibody concentration (µg/mL)
5559 IgG1A 124C/378C
5559 IgG4P KRQ 124C/378C

FIG. 7

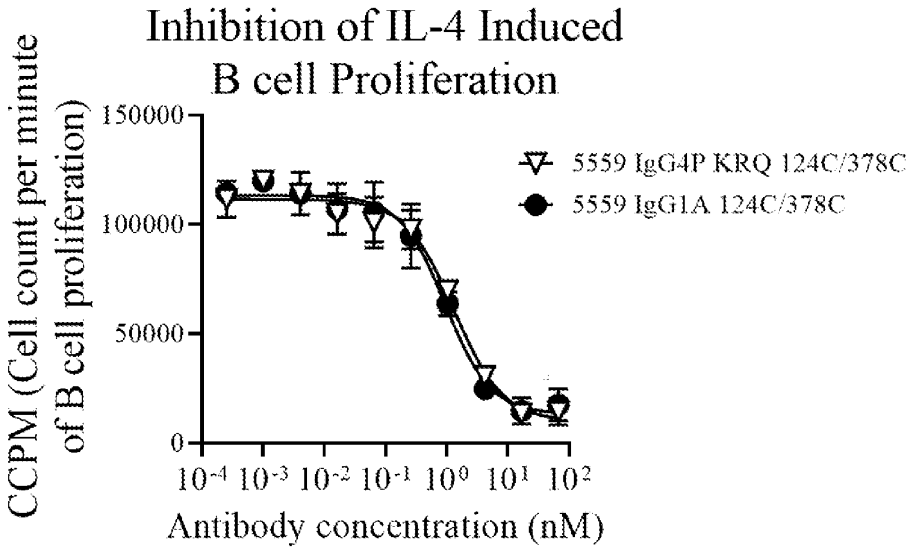

Inhibition of IL-4 Induced
B cell Proliferation
CCPM (Cell count per minute of B cell proliferation)
150000
100000
50000
0
10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Antibody concentration (nM)
5559 IgG4P KRQ 124C/378C
5559 IgG1A 124C/378C

FIG. 8A

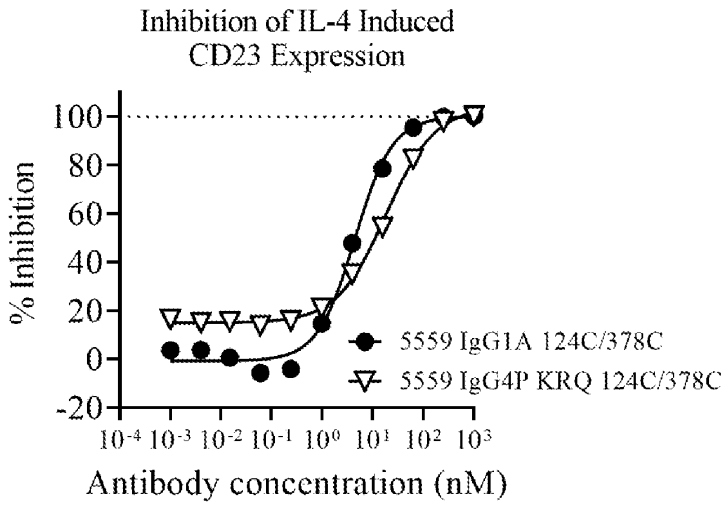

Inhibition of IL-4 Induced
CD23 Expression
% Inhibition
100
80
60
40
20
0
-20
10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3}
Antibody concentration (nM)
5559 IgG1A 124C/378C
5559 IgG4P KRQ 124C/378C

FIG. 8B

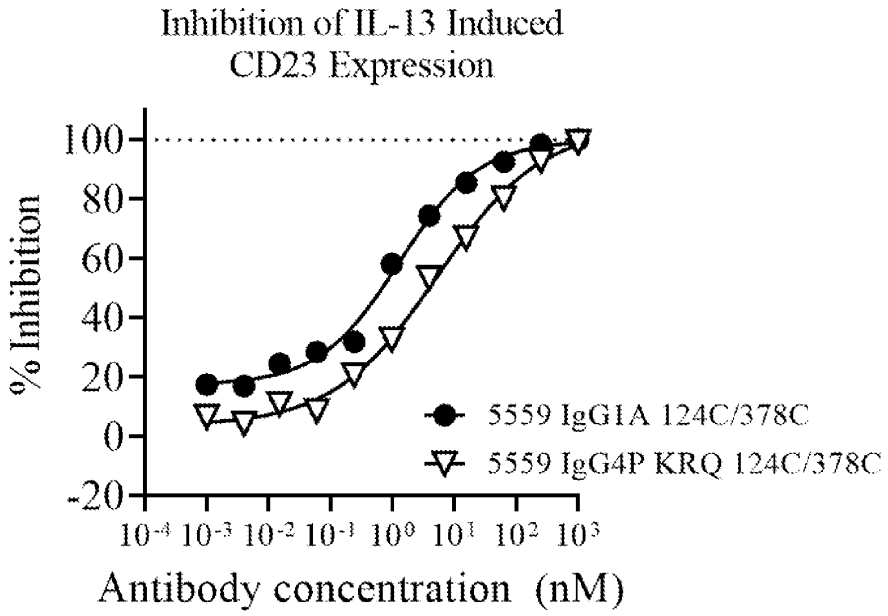

Inhibition of IL-13 Induced
CD23 Expression
% Inhibition
100
80
60
40
20
0
-20
10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3}
Antibody concentration (nM)
5559 IgG1A 124C/378C
5559 IgG4P KRQ 124C/378C

FIG. 9

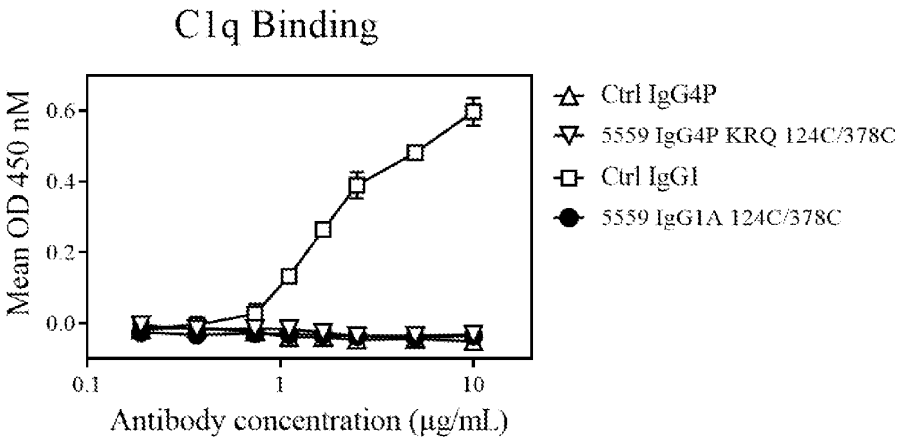

C1q Binding
Mean OD 450 nM
0.6
0.4
0.2
0.0
0.1
1
10
Antibody concentration (µg/mL)
Ctrl IgG4P
5559 IgG4P KRQ 124C/378C
Ctrl IgG1
5559 IgG1A 124C/378C

FIG. 10A

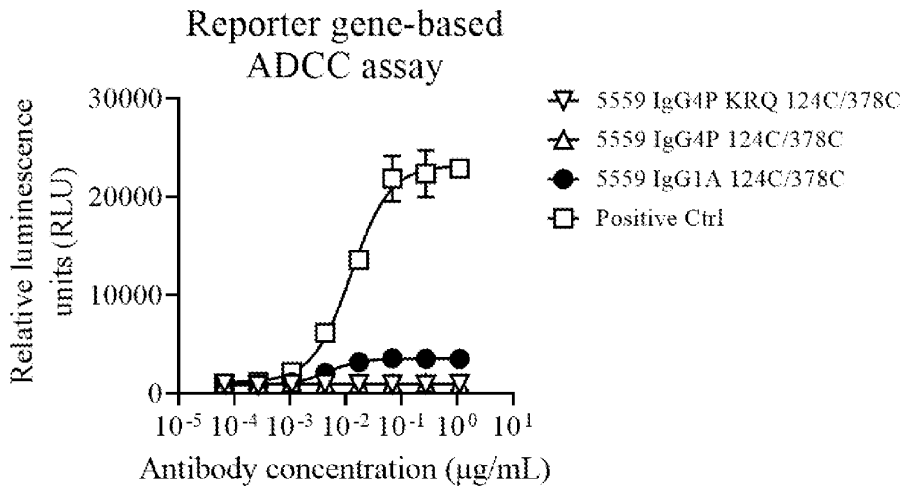


FIG. 10B

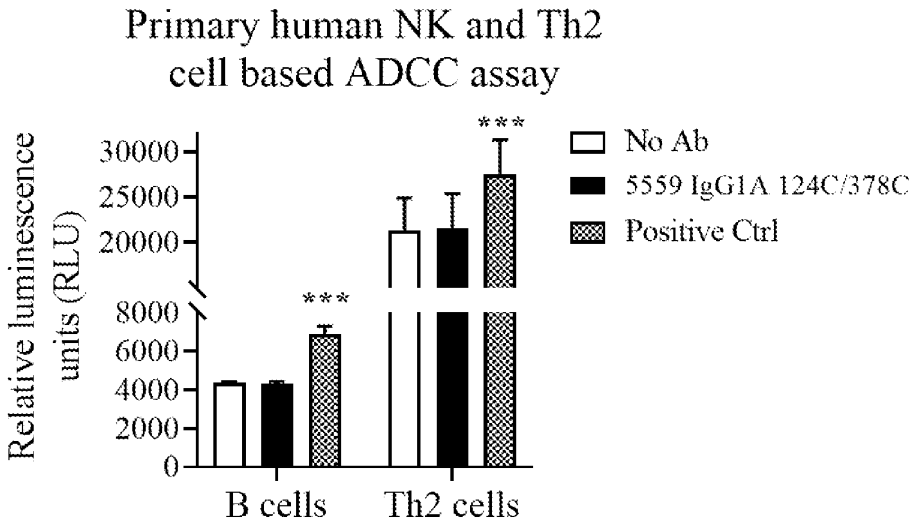


FIG. 11

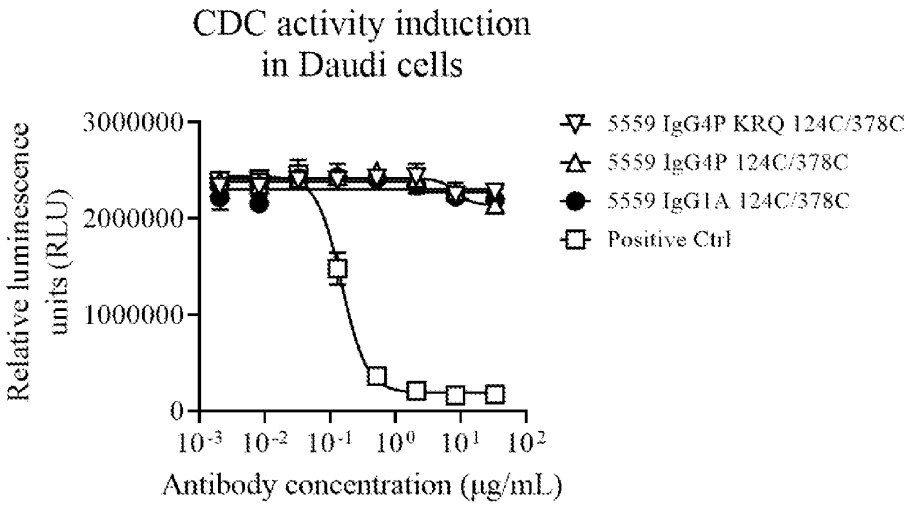

CDC activity induction
in Daudi cells
Relative luminescence units (RLU)
3000000
2000000
1000000
0
10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Antibody concentration (µg/mL)
5559 IgG4P KRQ 124C/378C
5559 IgG4P 124C/378C
5559 IgG1A 124C/378C
Positive Ctrl

Fig. 12A

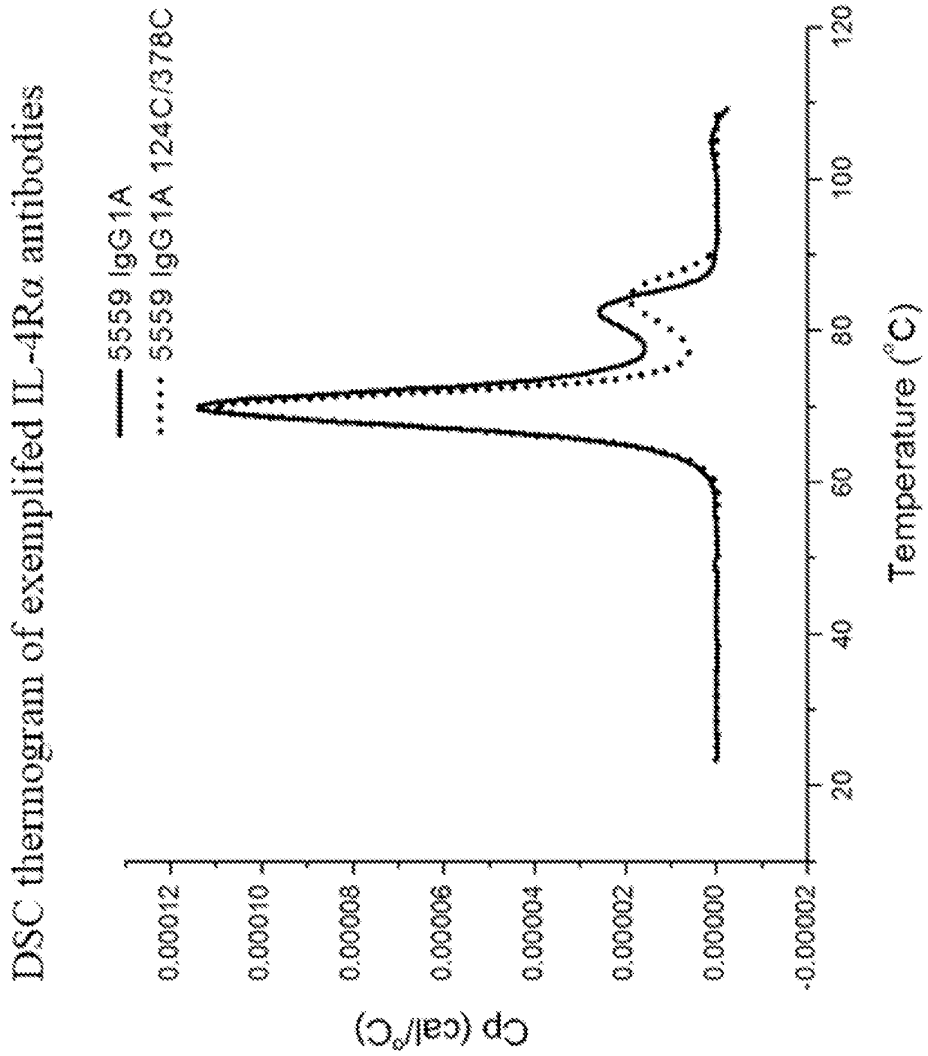

DSC thermogram of exemplified IL-4Rα antibodies
5559 IgG1A
5559 IgG1A 124C/378C
Cp (cal/°C)
0.00012
0.00010
0.00008
0.00006
0.00004
0.00002
0.00000
-0.00002
20
40
60
80
100
120
Temperature (°C)

FIG. 12B

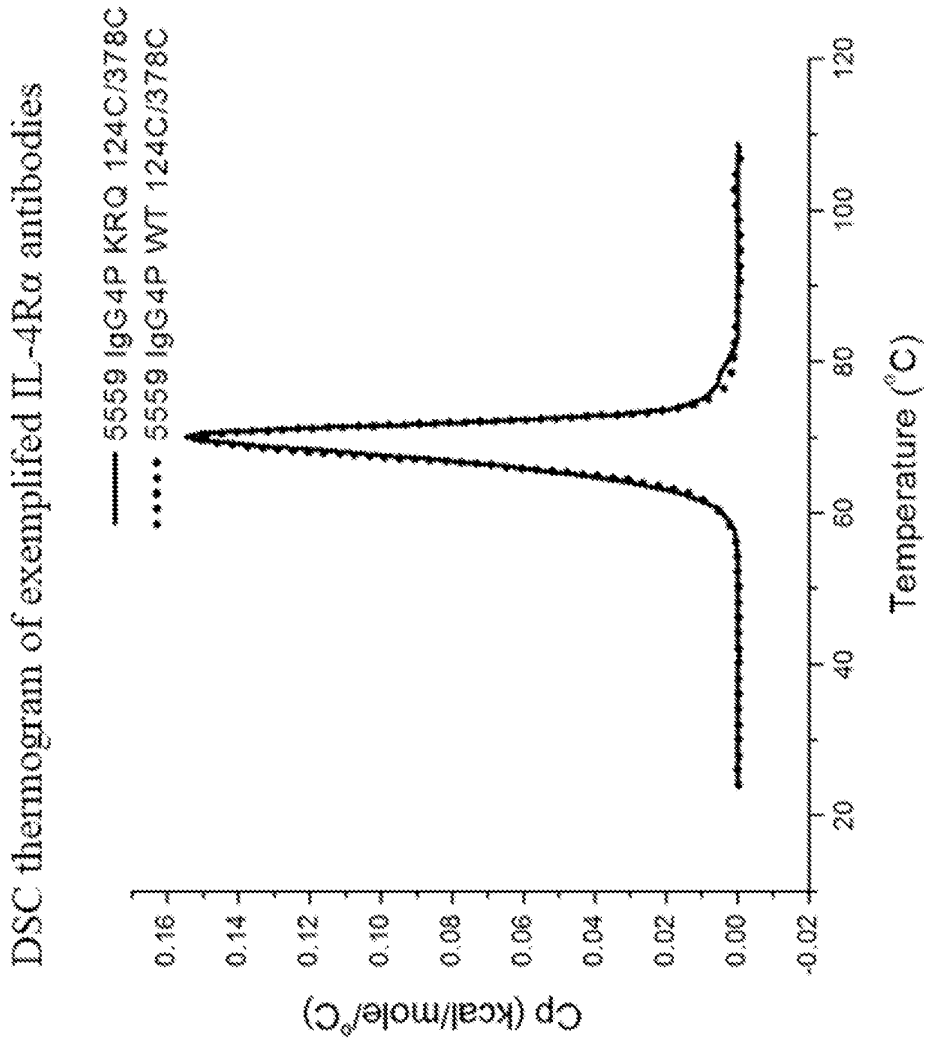

DSC thermogram of exemplified IL-4Rα antibodies
5559 IgG4P KRQ 124C/378C
5559 IgG4P WT 124C/378C
Cp (kcal/mole/°C)
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
-0.02
20
40
60
80
100
120
Temperature (°C)

FIG. 13

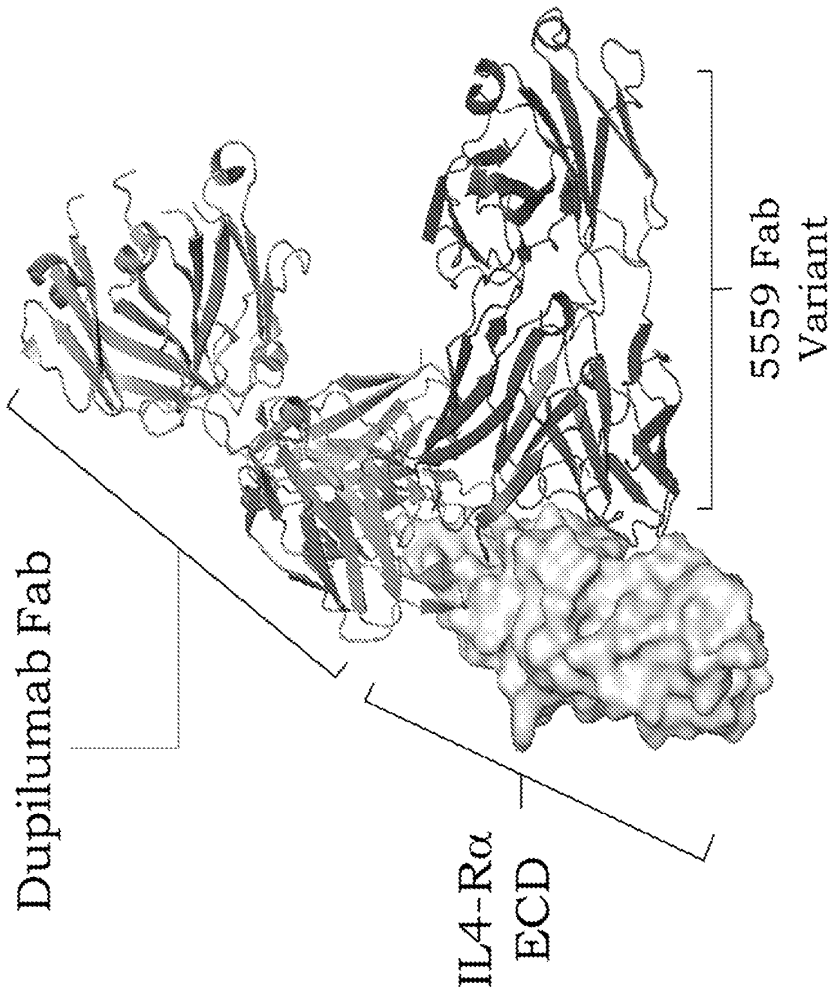
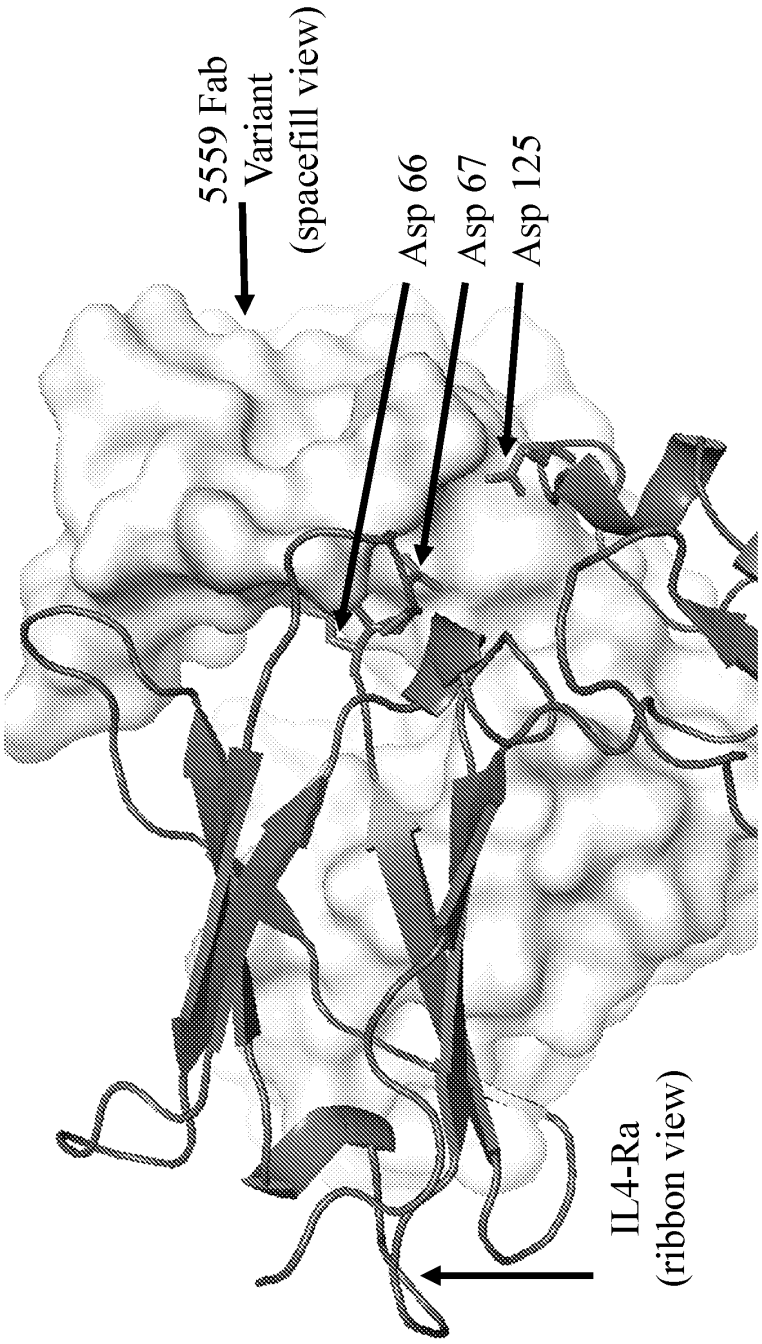


FIG. 14


5559 Fab
Variant
(spacefill view)
Asp 66
Asp 67
Asp 125
IL4-Ra
(ribbon view)