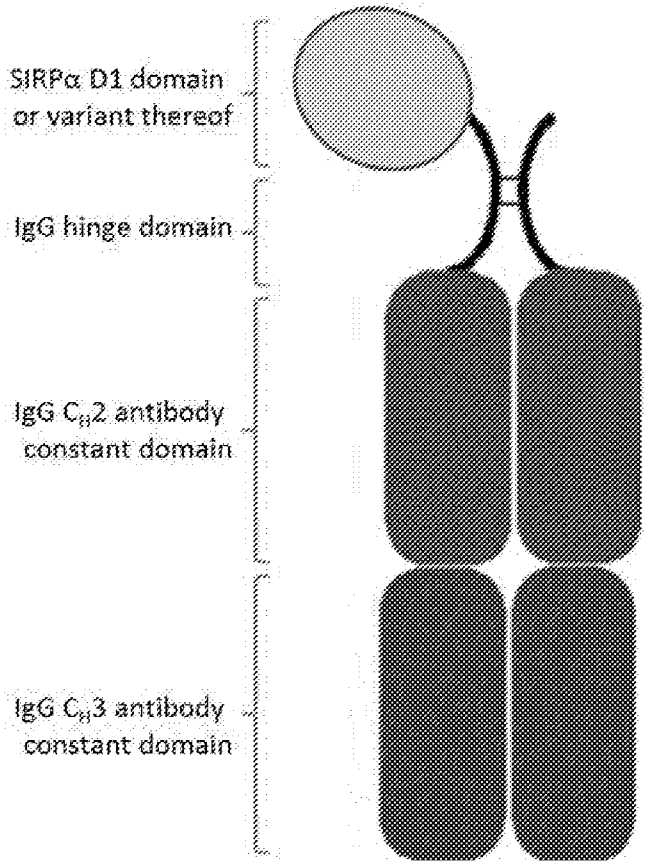
SIRPα D1 domain
or variant thereof
IgG hinge domain
IgG C_H2 antibody
constant domain
IgG C_H3 antibody
constant domain

FIG. 1

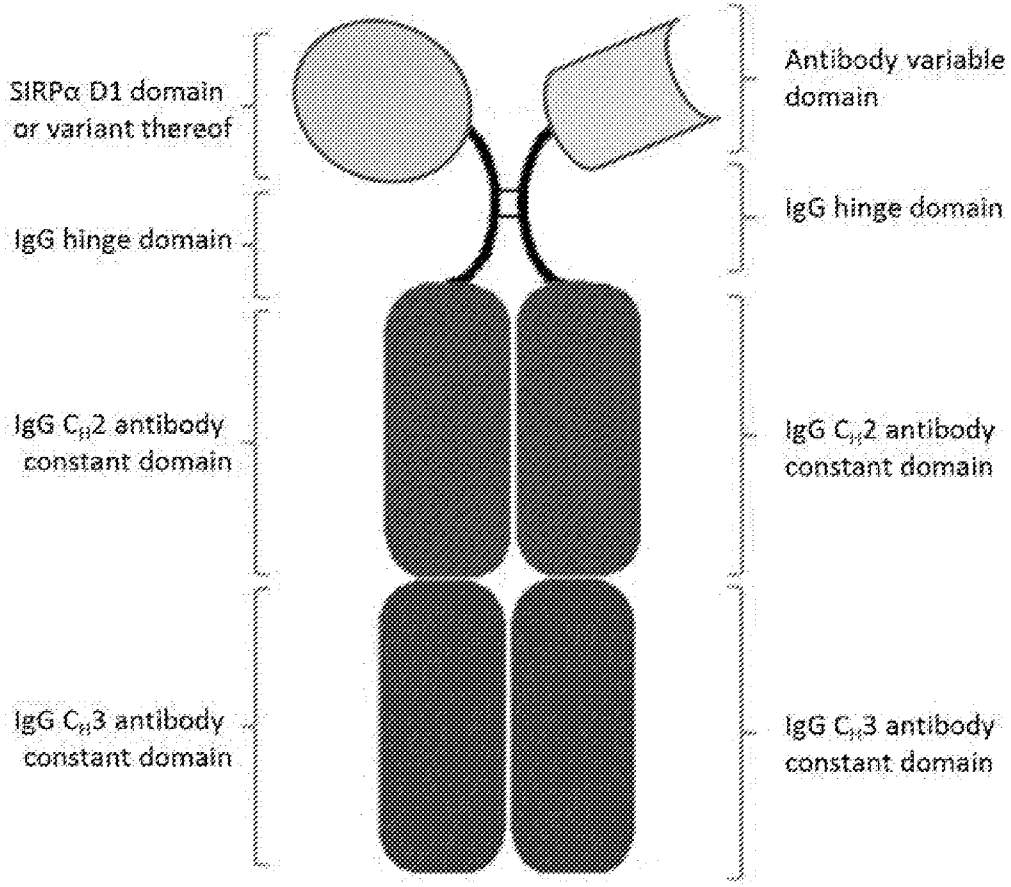
SIRPα D1 domain or variant thereof
IgG hinge domain
IgG C_H2 antibody constant domain
IgG C_H3 antibody constant domain
Antibody variable domain
IgG hinge domain
IgG C_H2 antibody constant domain
IgG C_H3 antibody constant domain

FIG. 2

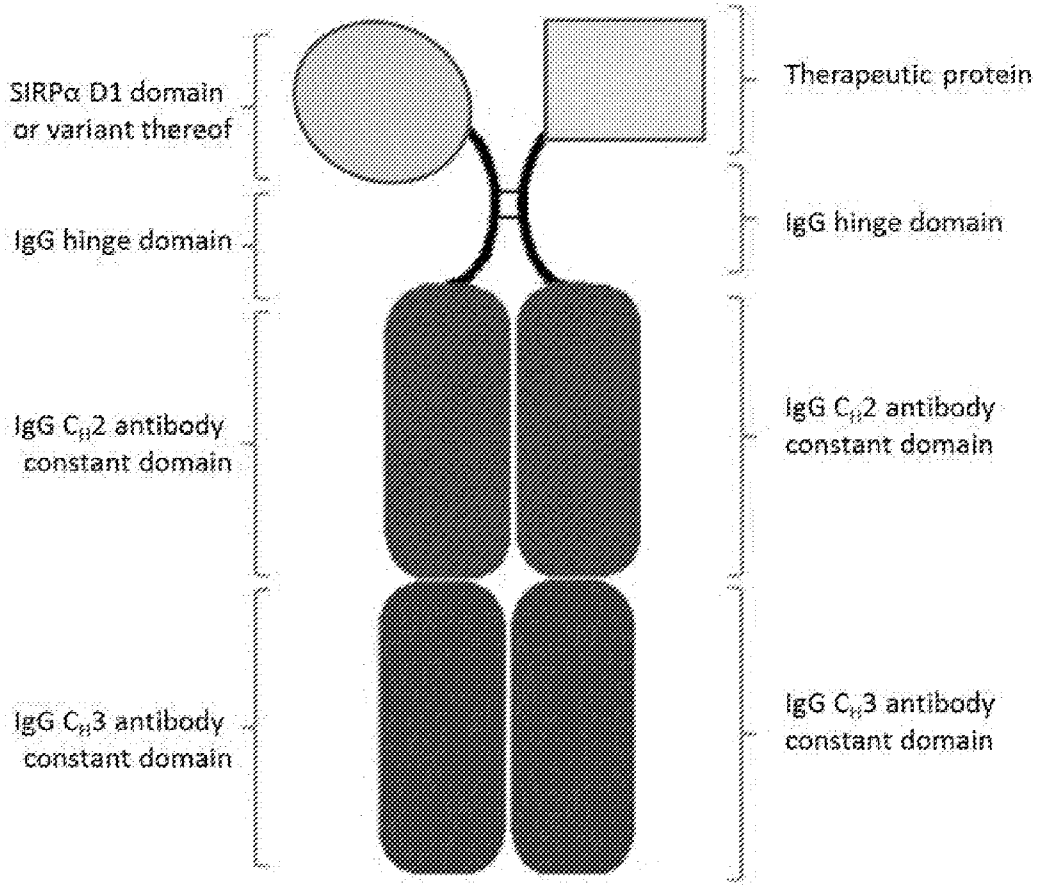
SIRPα D1 domain or variant thereof
IgG hinge domain
IgG C_H2 antibody constant domain
IgG C_H3 antibody constant domain
Therapeutic protein
IgG hinge domain
IgG C_H2 antibody constant domain
IgG C_H3 antibody constant domain

FIG. 3

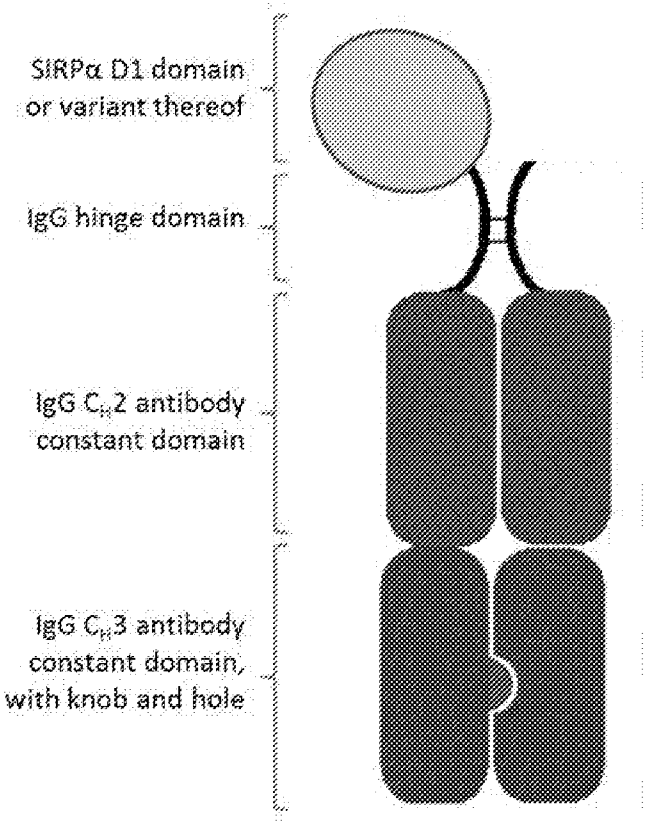
SIRPα D1 domain
or variant thereof
IgG hinge domain
IgG C_H2 antibody
constant domain
IgG C_H3 antibody
constant domain,
with knob and hole

FIG. 4A

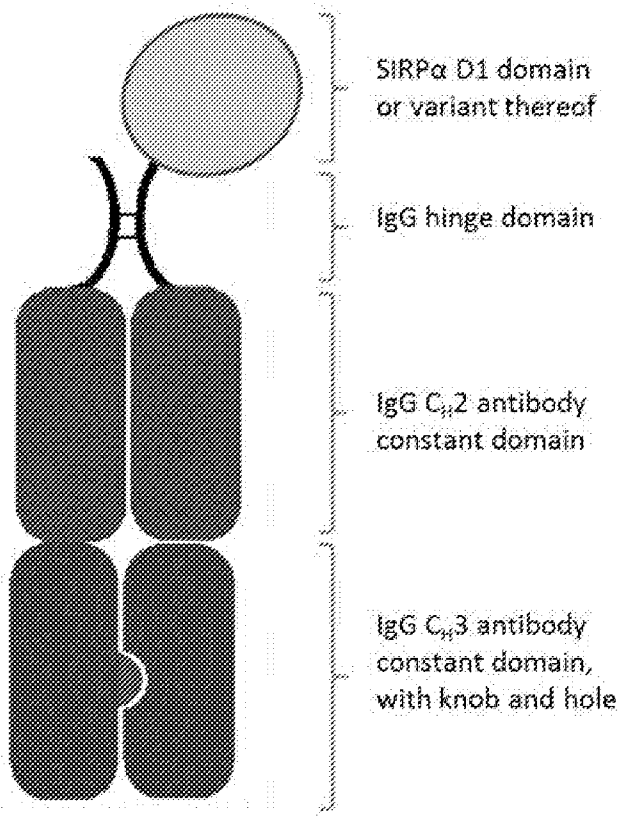
SIRPα D1 domain
or variant thereof
IgG hinge domain
IgG C_H2 antibody
constant domain
IgG C_H3 antibody
constant domain,
with knob and hole

FIG. 4B

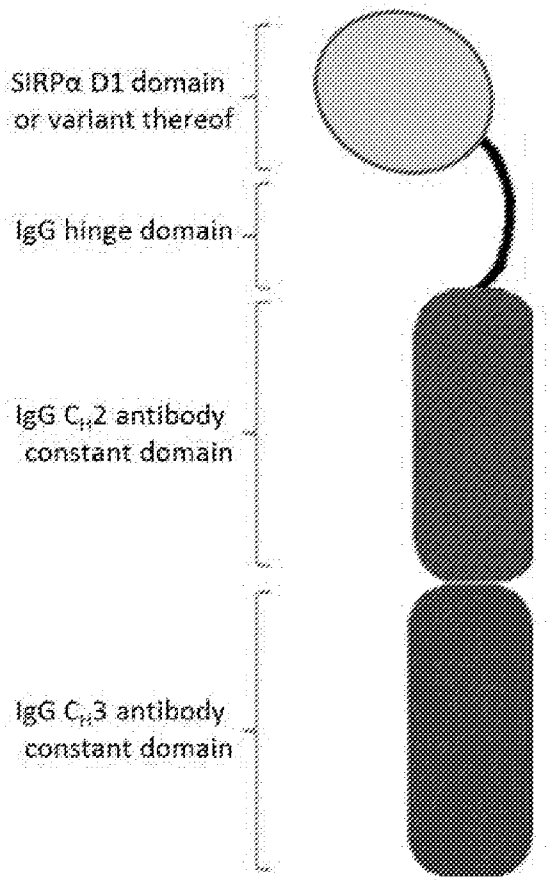
SIRPα D1 domain
or variant thereof
IgG hinge domain
IgG C_H2 antibody
constant domain
IgG C_H3 antibody
constant domain

FIG. 5A

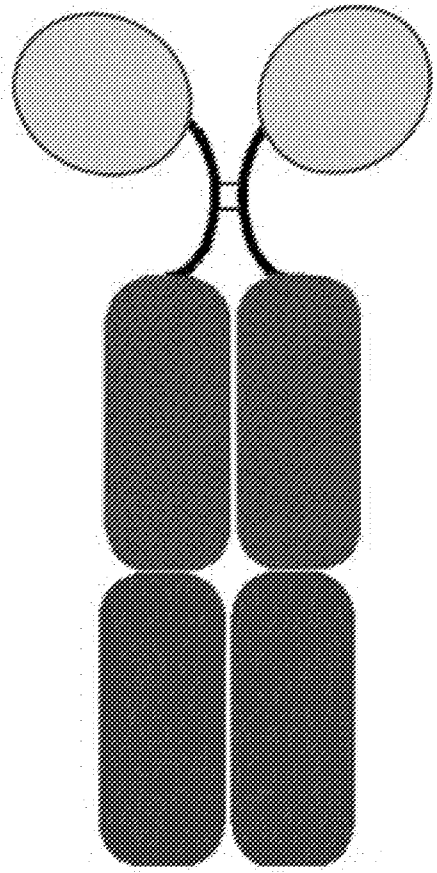

FIG. 5B

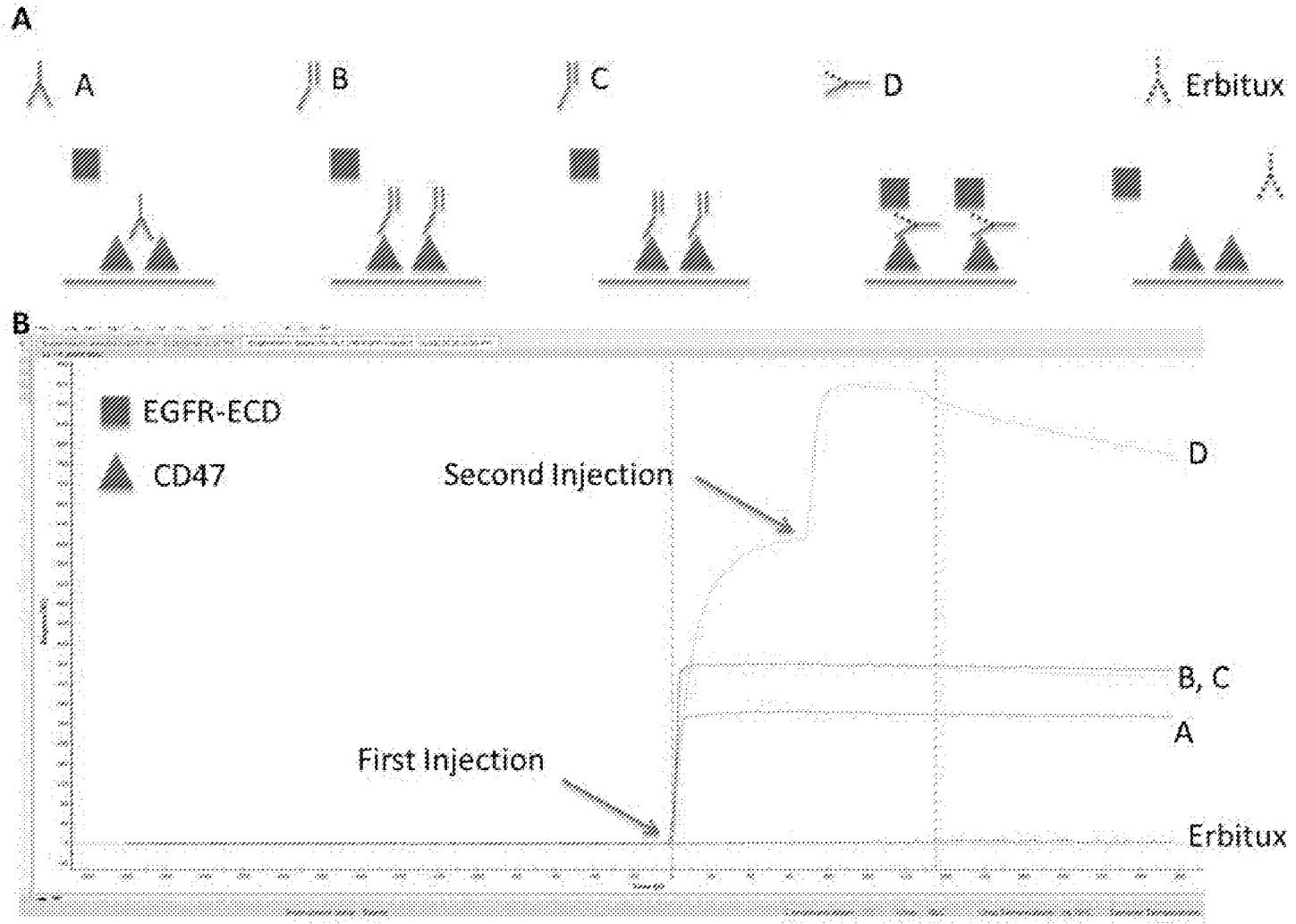
A
A
B
C
D
Erbitux
B
EGFR-ECD
CD47
Second Injection
First Injection
D
B, C
A
Erbitux

FIG. 6

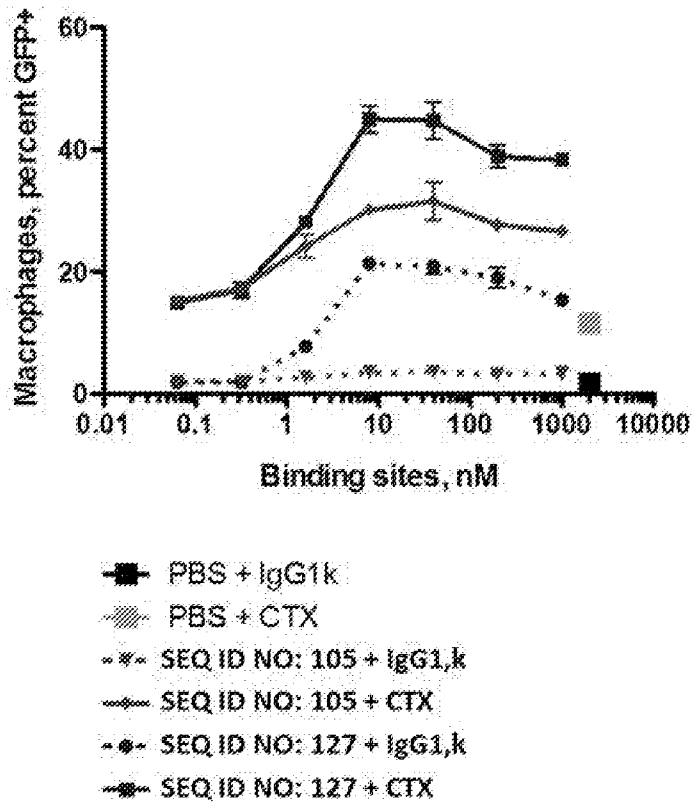
Macrophages, percent GFP+
60
40
20
0
0.01
0.1
1
10
100
1000
10000
Binding sites, nM
PBS + IgG1k
PBS + CTX
SEQ ID NO: 105 + IgG1,k
SEQ ID NO: 105 + CTX
SEQ ID NO: 127 + IgG1,k
SEQ ID NO: 127 + CTX

FIG. 7

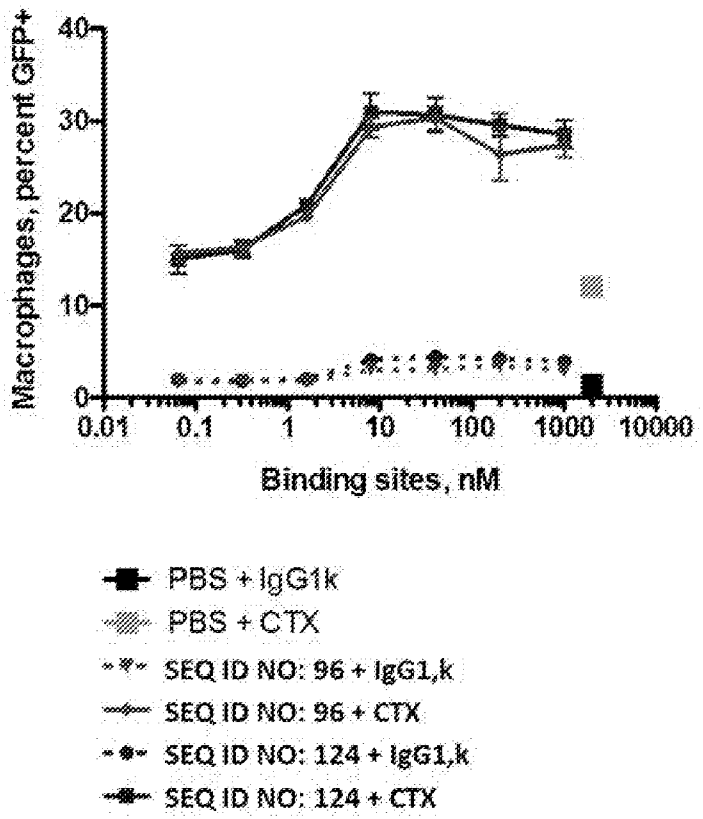
Macrophages, percent GFP+
40
30
20
10
0
0.01
0.1
1
10
100
1000
10000
Binding sites, nM
PBS + IgG1k
PBS + CTX
SEQ ID NO: 96 + IgG1,k
SEQ ID NO: 96 + CTX
SEQ ID NO: 124 + IgG1,k
SEQ ID NO: 124 + CTX

FIG. 8

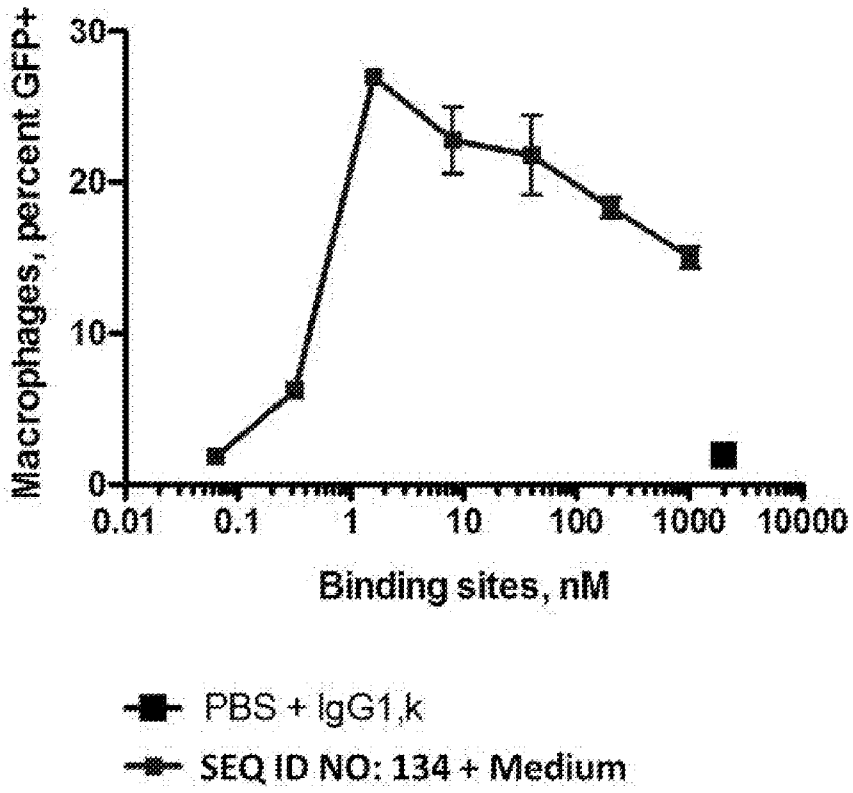
Macrophages, percent GFP+
30
20
10
0
0.01
0.1
1
10
100
1000
10000
Binding sites, nM
PBS + IgG1,k
SEQ ID NO: 134 + Medium

FIG. 9

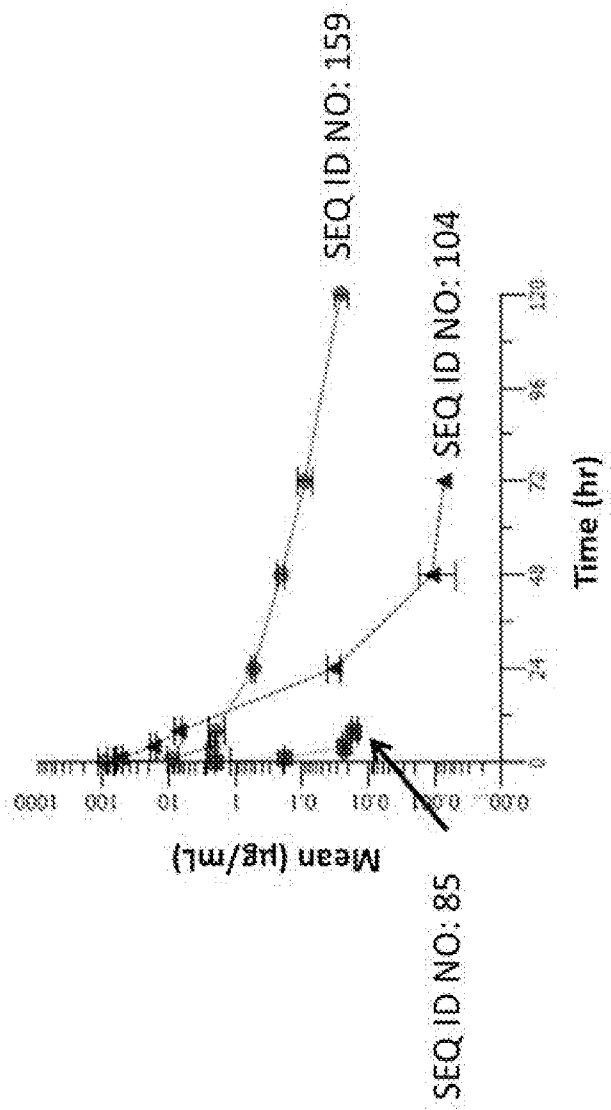
SEQ ID NO: 159
SEQ ID NO: 104
SEQ ID NO: 85
Mean (µg/mL)
Time (hr)
1000
100
10
1
0.1
0.01
0.001
0
24
48
72
96
120

FIG. 10

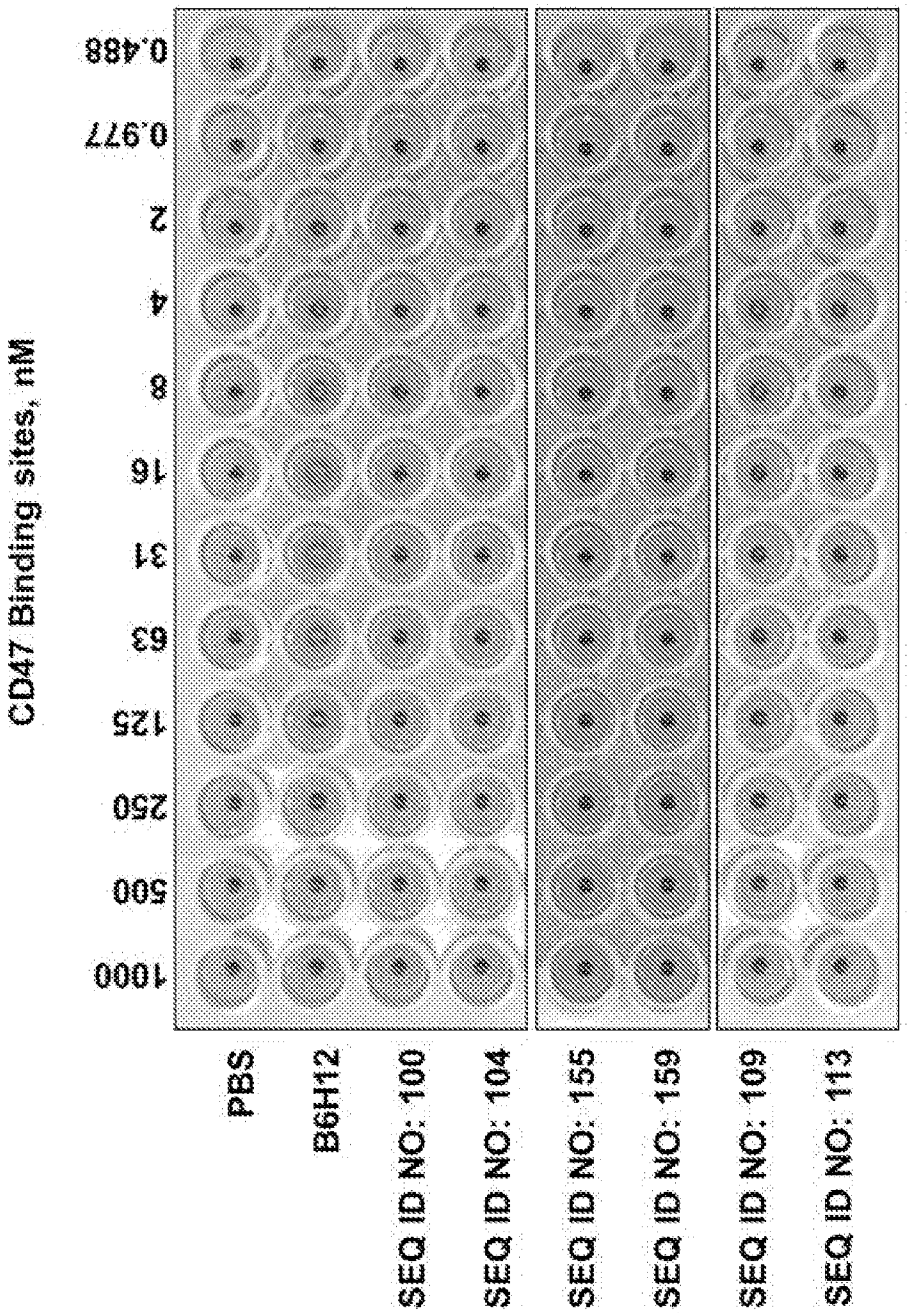
CD47 Binding sites, nM
1000
500
250
125
63
31
16
8
4
2
0.977
0.488
PBS
B6H12
SEQ ID NO: 100
SEQ ID NO: 104
SEQ ID NO: 155
SEQ ID NO: 159
SEQ ID NO: 109
SEQ ID NO: 113

FIG. 11

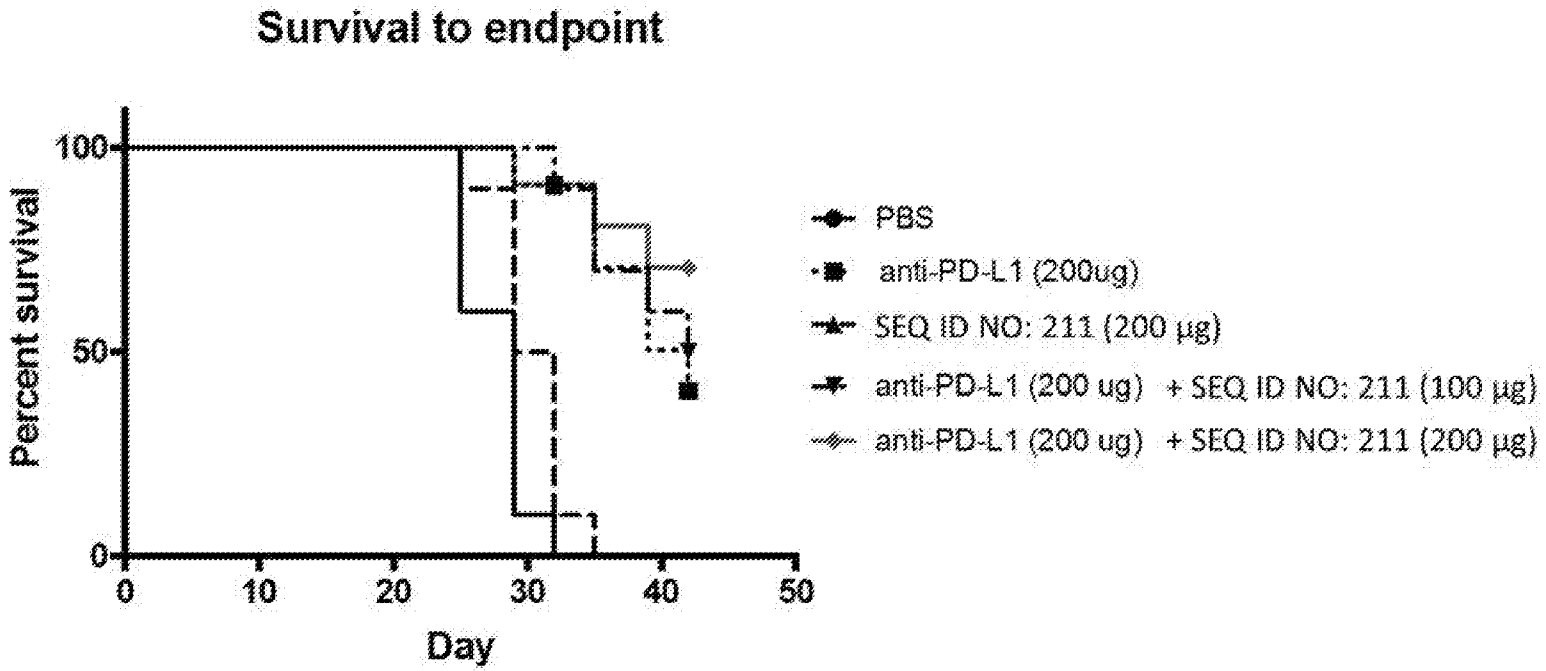
Survival to endpoint
Percent survival
100
50
0
0
10
20
30
40
50
Day
PBS
anti-PD-L1 (200ug)
SEQ ID NO: 211 (200 µg)
anti-PD-L1 (200 ug) + SEQ ID NO: 211 (100 µg)
anti-PD-L1 (200 ug) + SEQ ID NO: 211 (200 µg)

FIG. 12

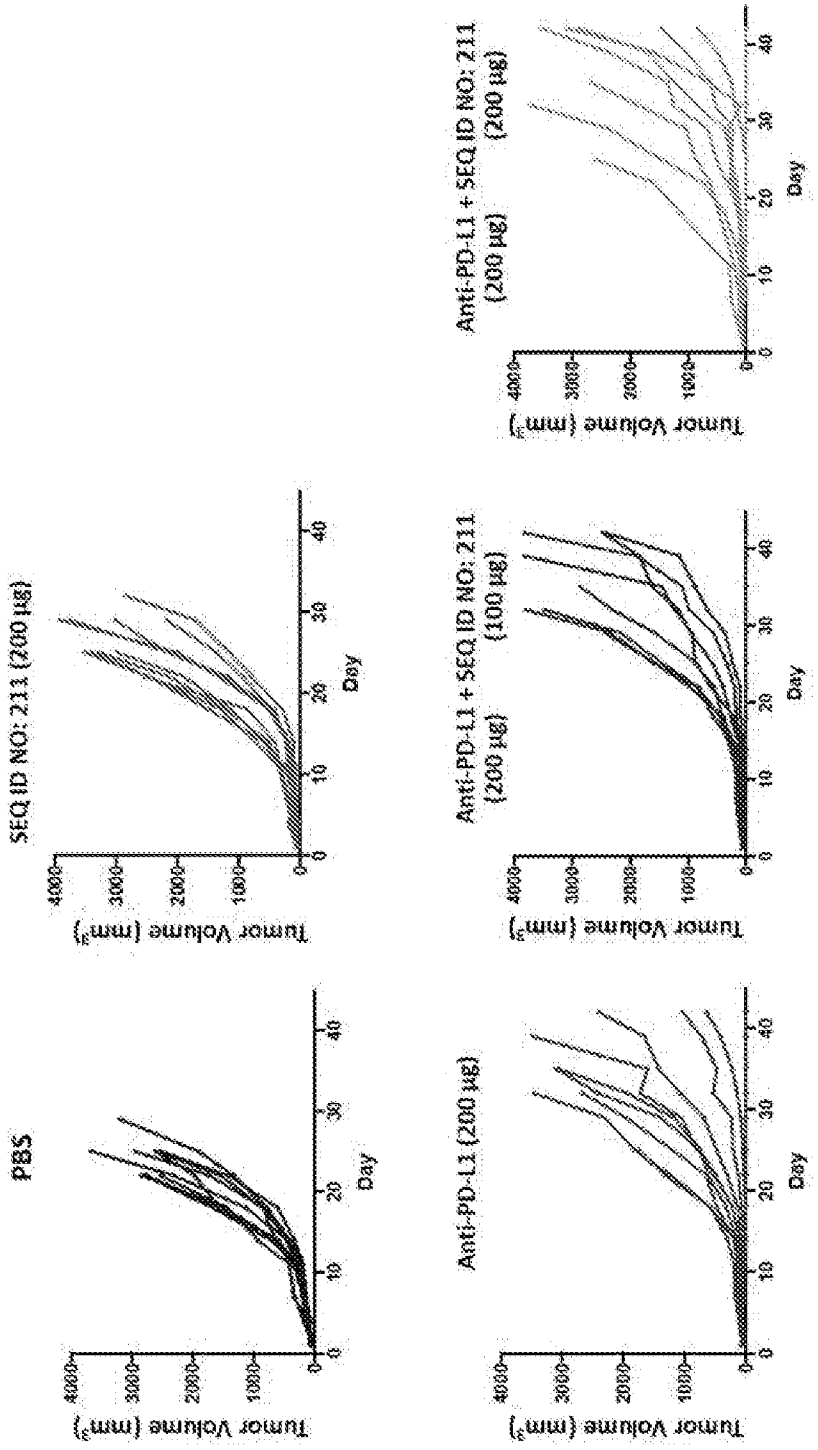
PBS
SEQ ID NO: 211 (200 μg)
Anti-PD-L1 + SEQ ID NO: 211 (200 μg) (200 μg)
Anti-PD-L1 (200 μg)
Anti-PD-L1 + SEQ ID NO: 211 (200 μg) (100 μg)
Tumor Volume (mm³)
Day
0
1000
2000
3000
4000
10
20
30
40

FIG. 13

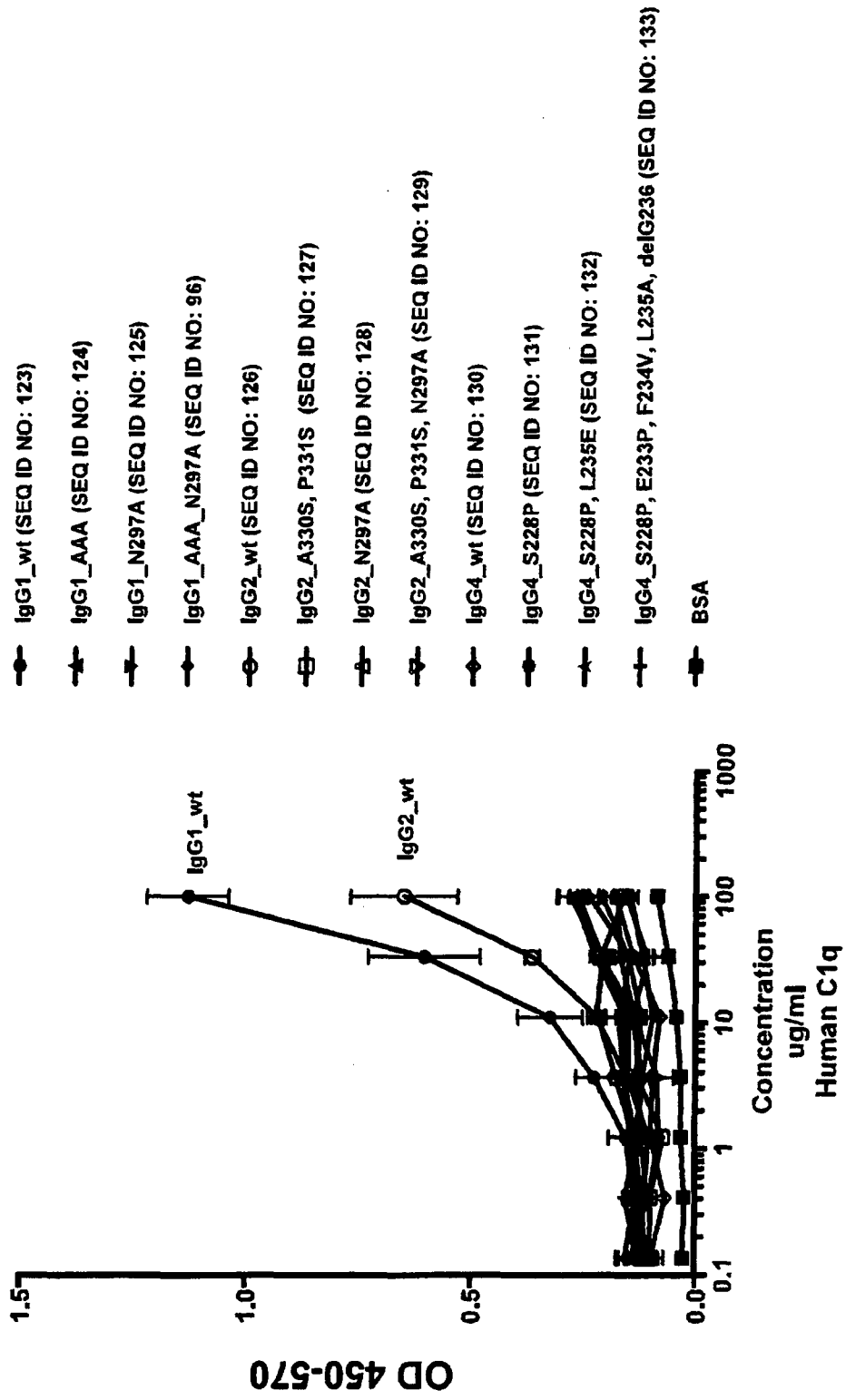
IgG1_wt (SEQ ID NO: 123)
IgG1_AAA (SEQ ID NO: 124)
IgG1_N297A (SEQ ID NO: 125)
IgG1_AAA_N297A (SEQ ID NO: 96)
IgG2_wt (SEQ ID NO: 126)
IgG2_A330S, P331S (SEQ ID NO: 127)
IgG2_N297A (SEQ ID NO: 128)
IgG2_A330S, P331S, N297A (SEQ ID NO: 129)
IgG4_wt (SEQ ID NO: 130)
IgG4_S228P (SEQ ID NO: 131)
IgG4_S228P, L235E (SEQ ID NO: 132)
IgG4_S228P, E233P, F234V, L235A, delG236 (SEQ ID NO: 133)
BSA
IgG1_wt
IgG2_wt
OD 450-570
1.5
1.0
0.5
0.0
0.1
1
10
100
1000
Concentration
ug/ml
Human C1q

FIG. 14

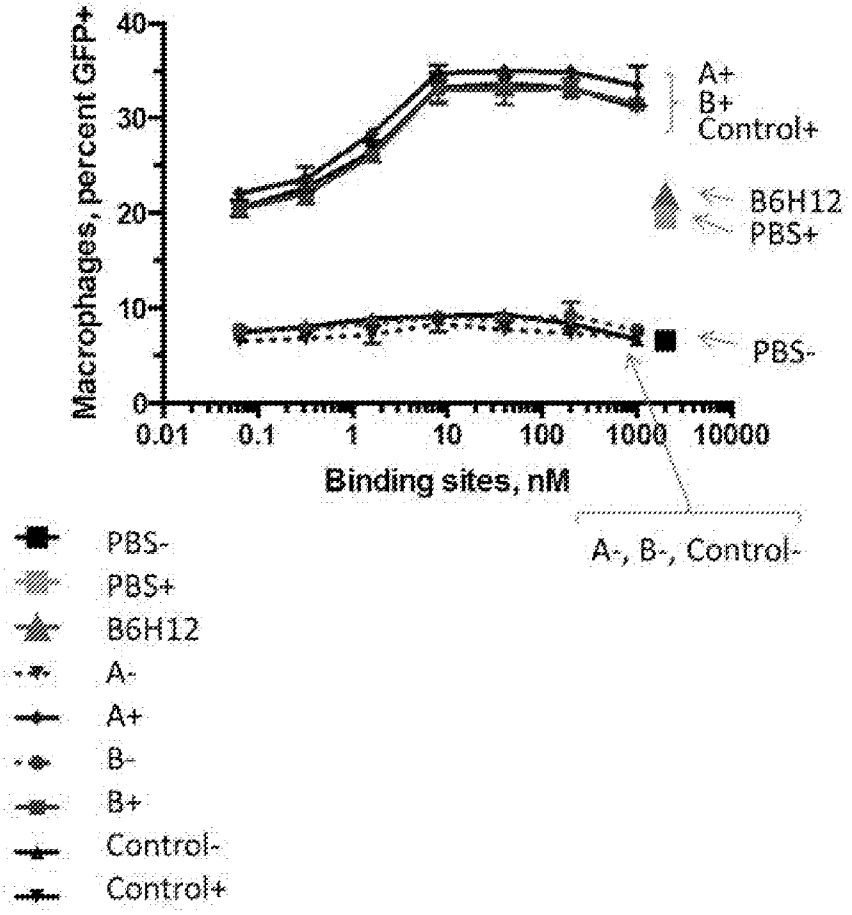
Macrophages, percent GFP+
40
30
20
10
0
0.01
0.1
1
10
100
1000
10000
Binding sites, nM
A+
B+
Control+
B6H12
PBS+
PBS-
A-, B-, Control-
PBS-
PBS+
B6H12
A-
A+
B-
B+
Control-
Control+

FIG. 15

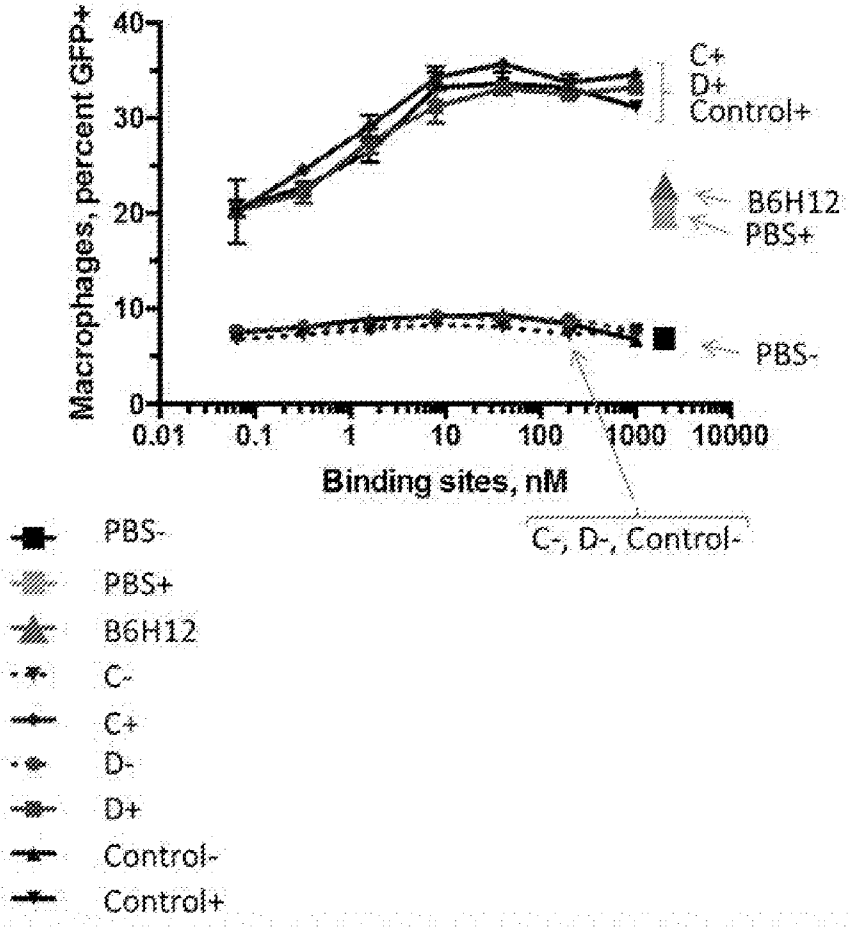
Macrophages, percent GFP+
40
30
20
10
0
0.01
0.1
1
10
100
1000
10000
Binding sites, nM
C+
D+
Control+
B6H12
PBS+
PBS-
C-, D-, Control-
PBS-
PBS+
B6H12
C-
C+
D-
D+
Control-
Control+

FIG. 16

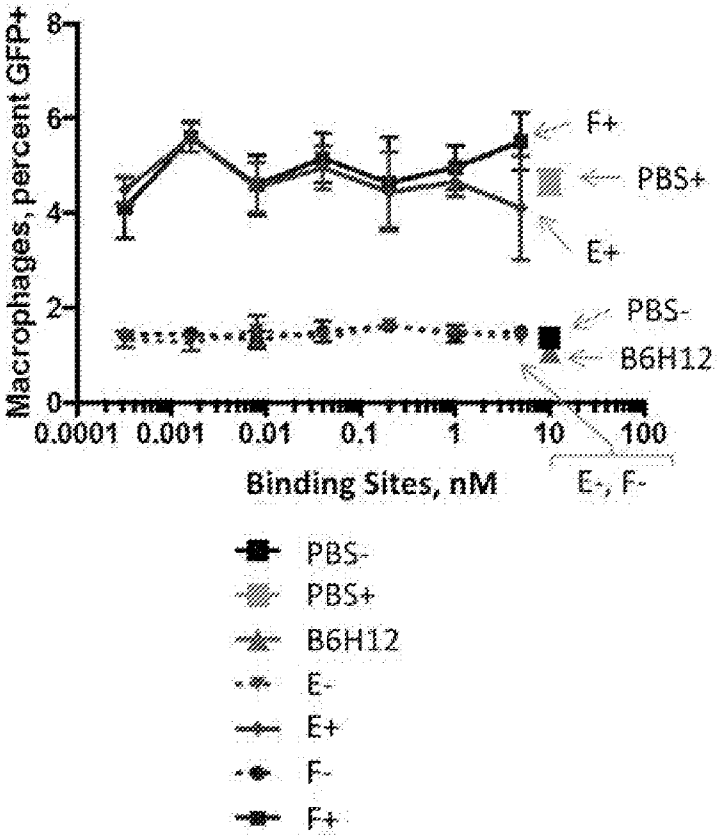
Macrophages, percent GFP+
8
6
4
2
0
0.0001
0.001
0.01
0.1
1
10
100
Binding Sites, nM
F+
PBS+
E+
PBS-
B6H12
E-, F-
PBS-
PBS+
B6H12
E-
E+
F-
F+

FIG. 17

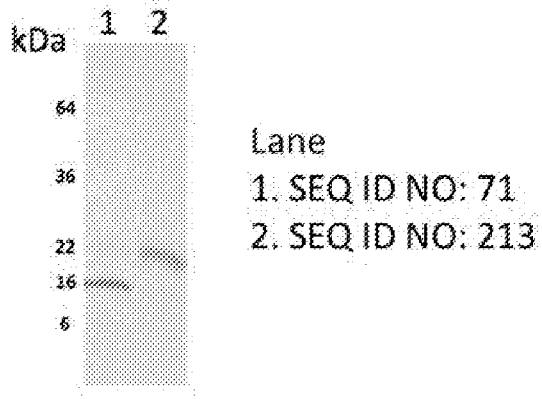

FIG. 18

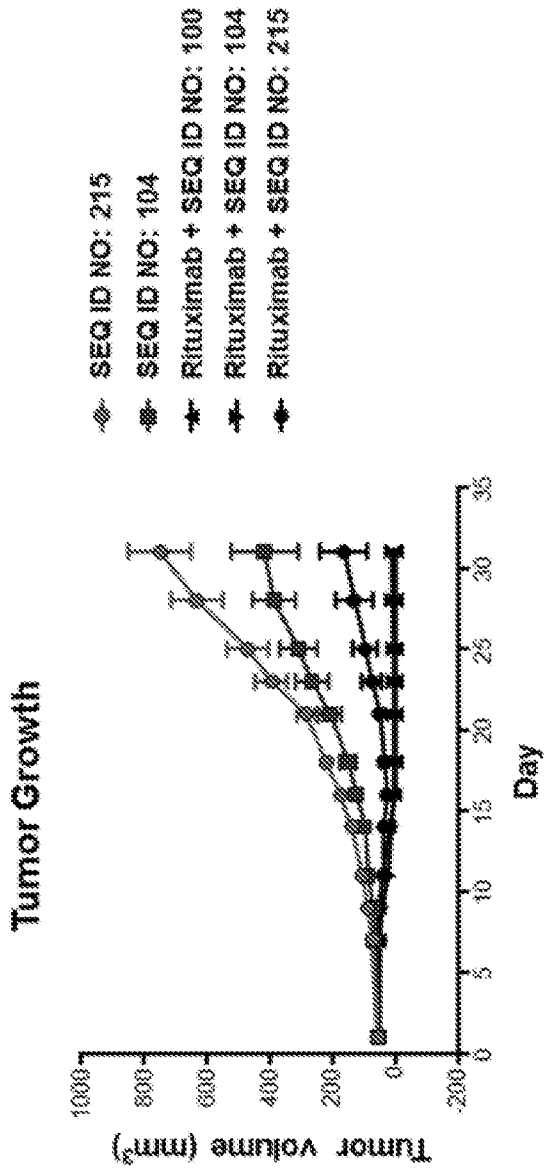
Tumor Growth
SEQ ID NO: 215
SEQ ID NO: 104
Rituximab + SEQ ID NO: 100
Rituximab + SEQ ID NO: 104
Rituximab + SEQ ID NO: 215
Tumor volume (mm³)
1000
800
600
400
200
0
-200
0
5
10
15
20
25
30
35
Day

FIG. 19A

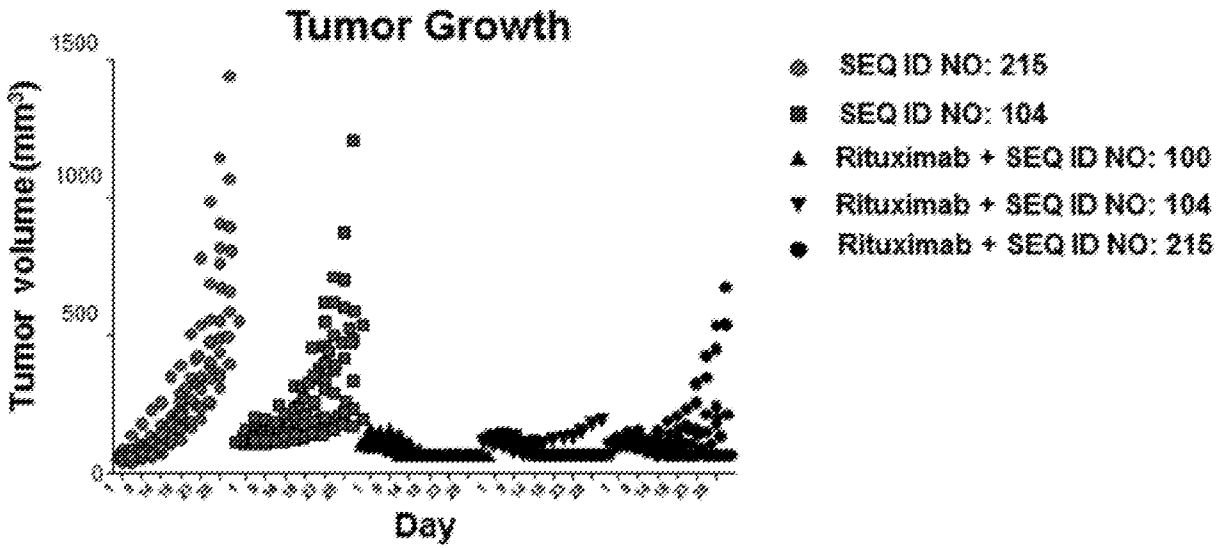
Tumor Growth
Tumor volume (mm3)
1500
1000
500
0
Day
SEQ ID NO: 215
SEQ ID NO: 104
Rituximab + SEQ ID NO: 100
Rituximab + SEQ ID NO: 104
Rituximab + SEQ ID NO: 215

FIG. 19B

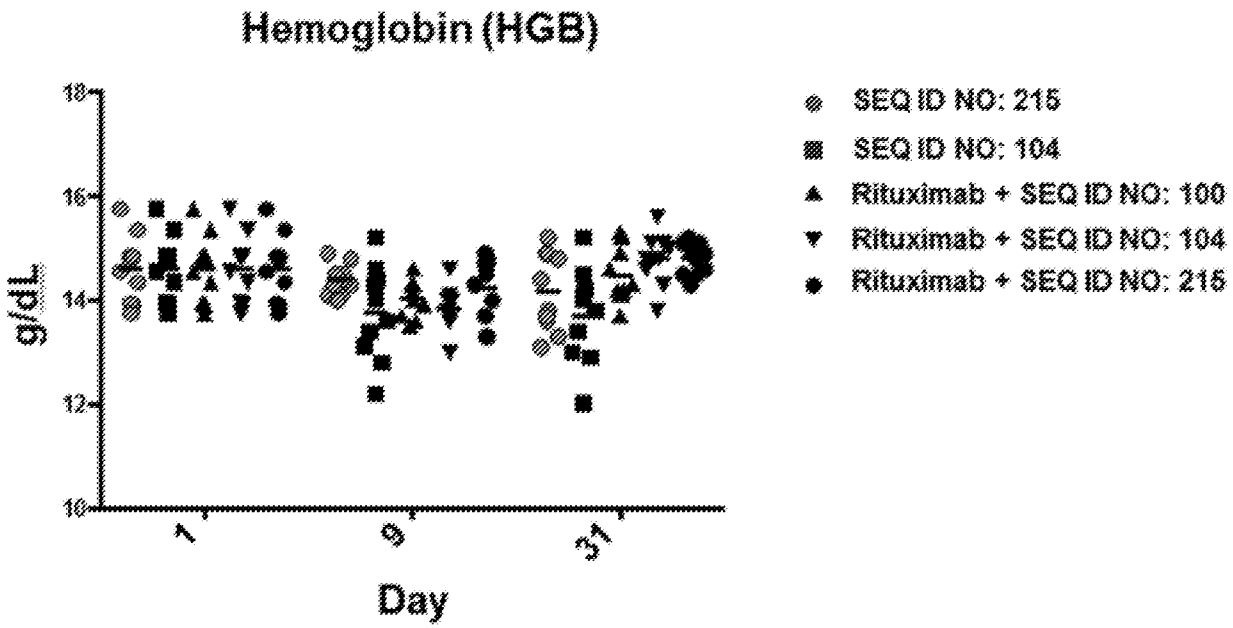
Hemoglobin (HGB)
g/dL
18
16
14
12
10
1
9
31
Day
SEQ ID NO: 215
SEQ ID NO: 104
Rituximab + SEQ ID NO: 100
Rituximab + SEQ ID NO: 104
Rituximab + SEQ ID NO: 215

FIG. 19C

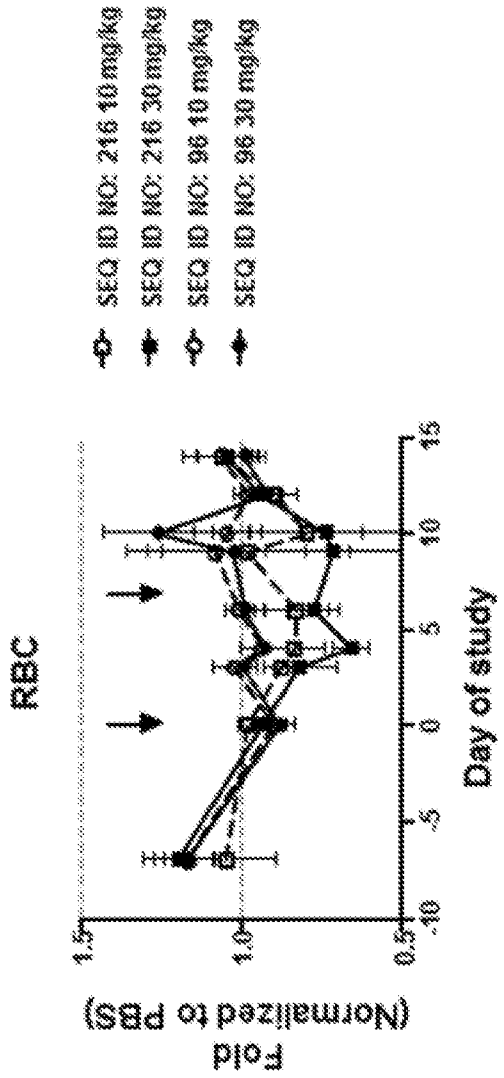
RBC
SEQ ID NO: 216 10 mg/kg
SEQ ID NO: 216 30 mg/kg
SEQ ID NO: 96 10 mg/kg
SEQ ID NO: 96 30 mg/kg
Fold (Normalized to PBS)
1.5
1.0
0.5
-10
-5
0
5
10
15
Day of study

FIG. 20