Figure 1:

Heatmap	38-27-A11	Urelumab	Utomilumab
38-27-A11	0%	0%	52%
Urelumab	0%	0%	41%
Utomilumab	17%	21%	0%

Binding level normalized to theroretical R_{max} [%]

Figure 2:

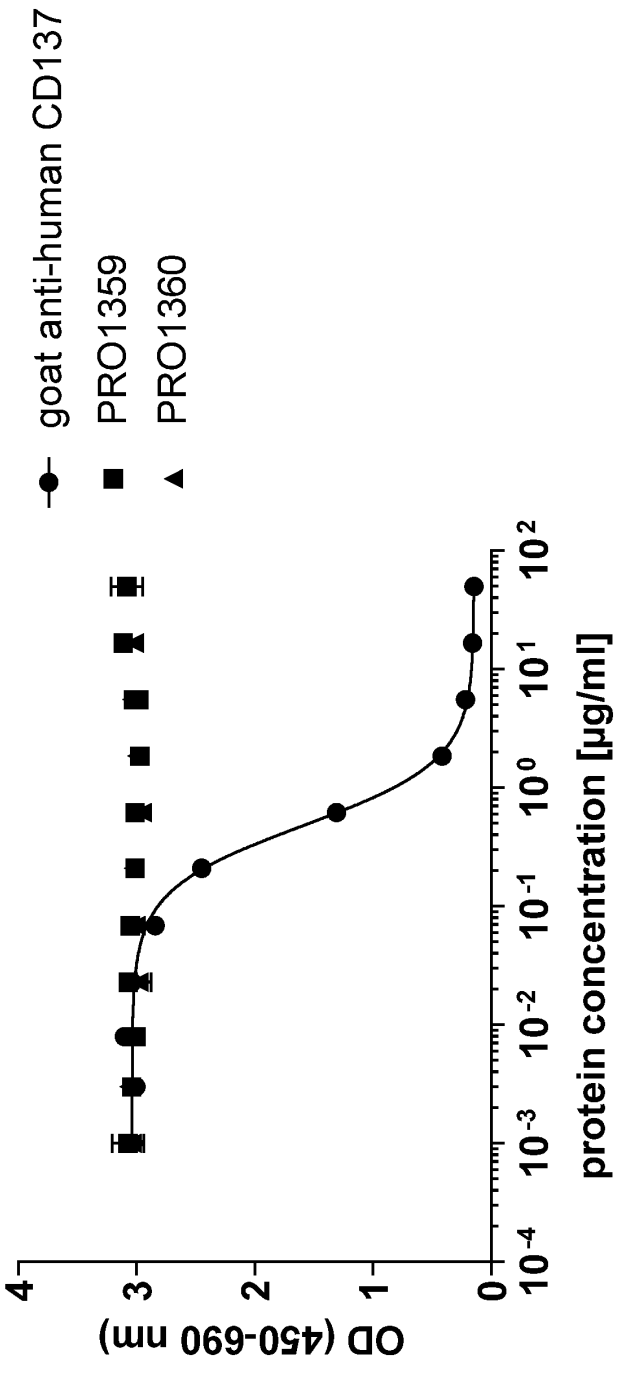

goat anti-human CD137
PRO1359
PRO1360
OD (450-690 nm)
protein concentration [µg/ml]
0
1
2
3
4
10-4
10-3
10-2
10-1
100
101
102

Figure 3:

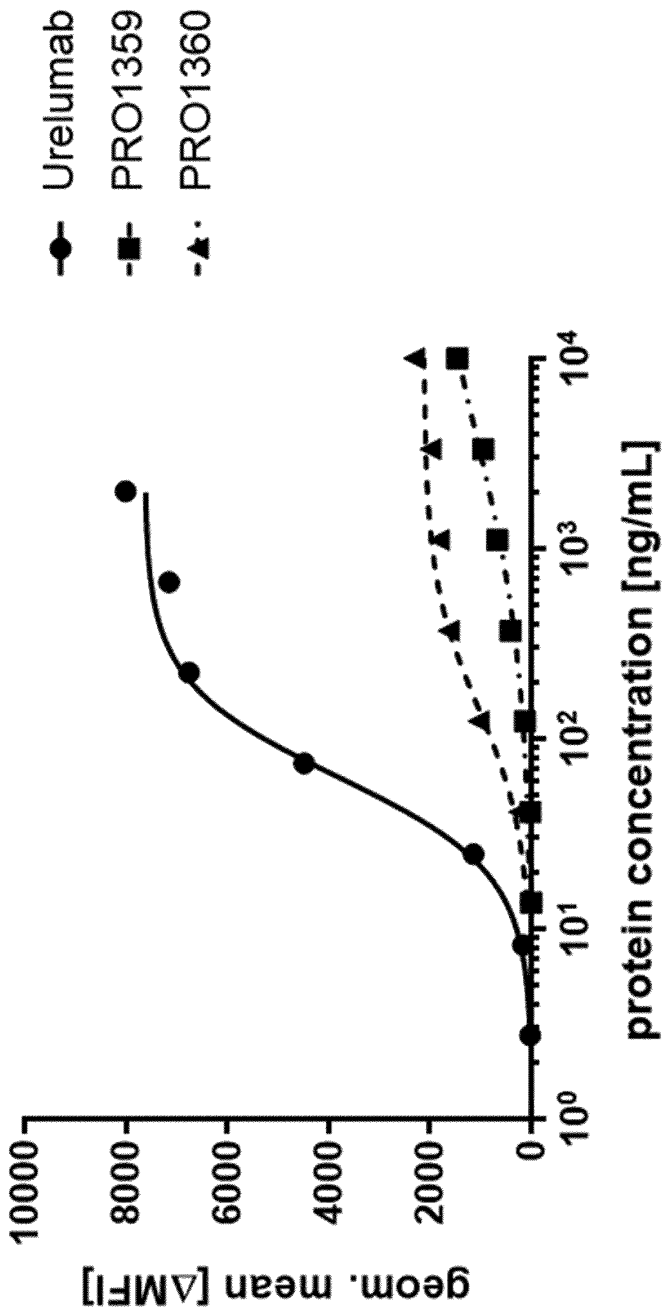
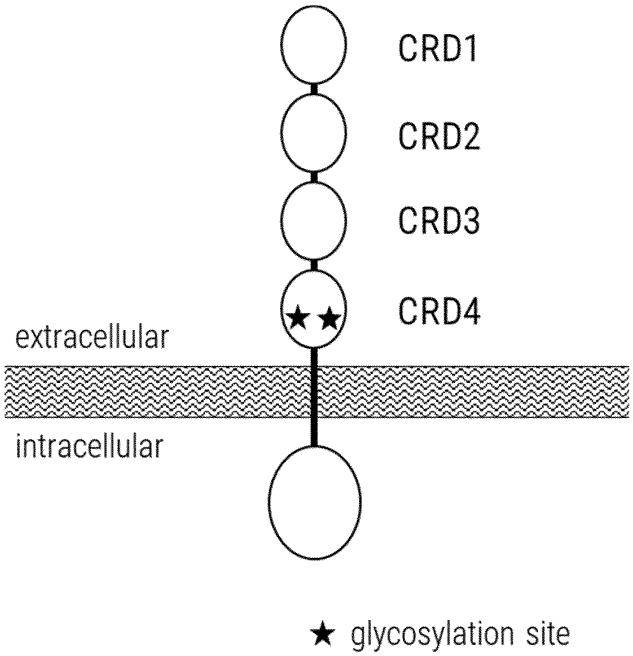

Urelumab
PRO1359
PRO1360
geom. mean [ΔMFI]
10000
8000
6000
4000
2000
0
10^0
10^1
10^2
10^3
10^4
protein concentration [ng/mL]

Figure 4 (A):


CRD1
CRD2
CRD3
CRD4
extracellular
intracellular
★ glycosylation site

(B)

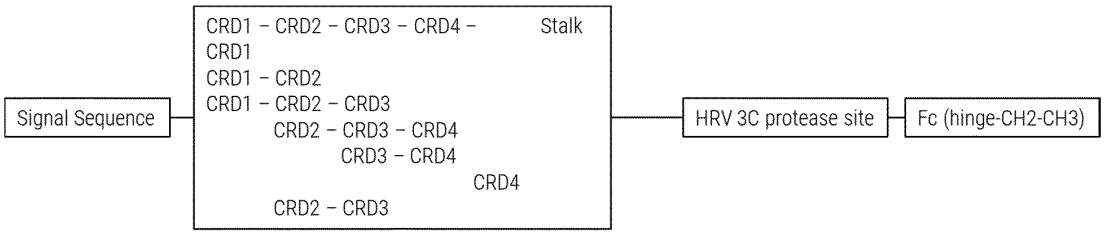

Signal Sequence
CRD1 – CRD2 – CRD3 – CRD4 –
CRD1
CRD1 – CRD2
CRD1 – CRD2 – CRD3
CRD2 – CRD3 – CRD4
CRD3 – CRD4
CRD4
CRD2 – CRD3
Stalk
HRV 3C protease site
Fc (hinge-CH2-CH3)

Figure 5:

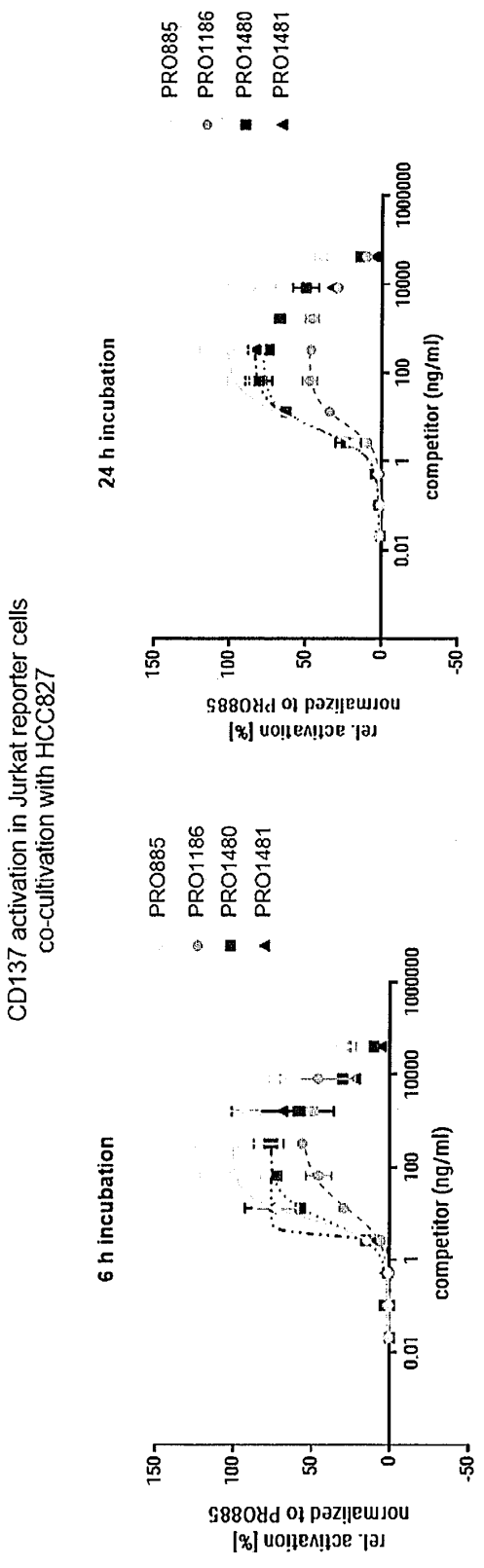

CD137 activation in Jurkat reporter cells
co-cultivation with HCC827
6 h incubation
24 h incubation
PRO885
PRO1186
PRO1480
PRO1481
rel. activation [%]
normalized to PRO885
competitor (ng/ml)
150
100
50
0
-50
0.01
1
100
10000
1000000

Figure 6:

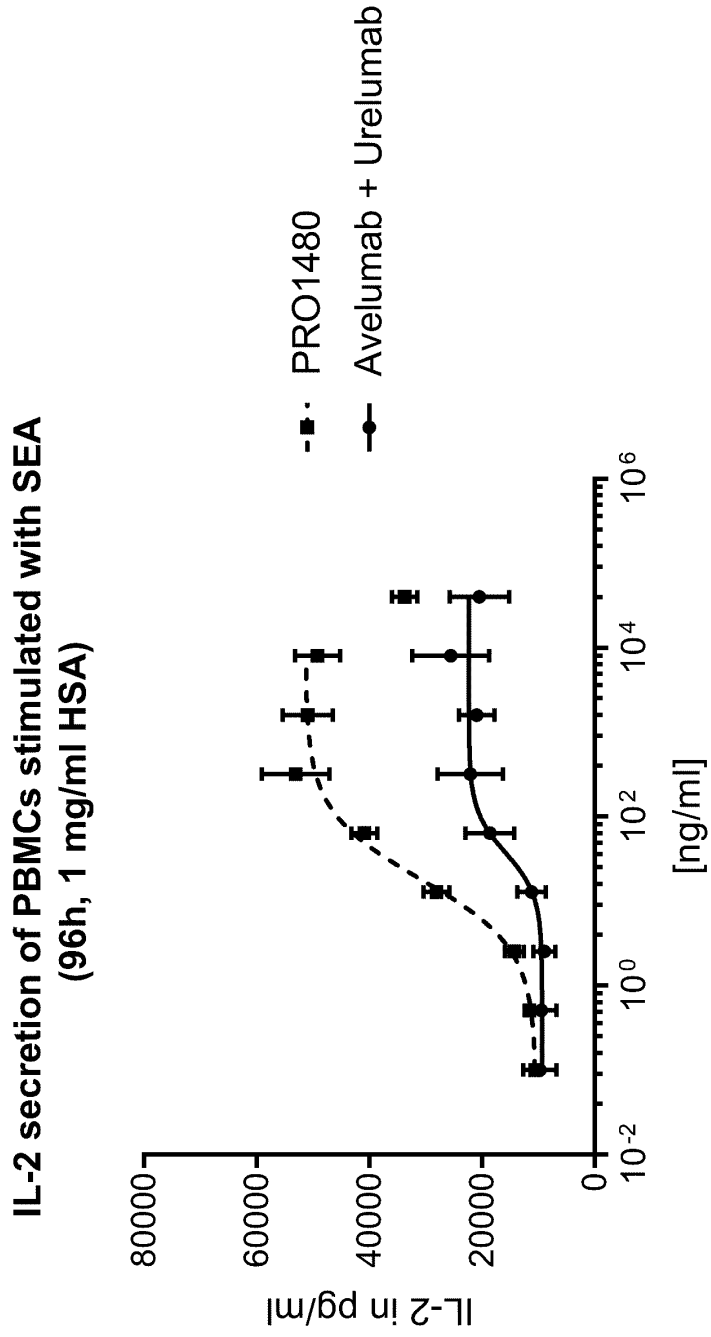

IL-2 secretion of PBMCs stimulated with SEA
(96h, 1 mg/ml HSA)
PRO1480
Avelumab + Urelumab
IL-2 in pg/ml
80000
60000
40000
20000
0
10-2
100
102
104
106
[ng/ml]

Figure 7:

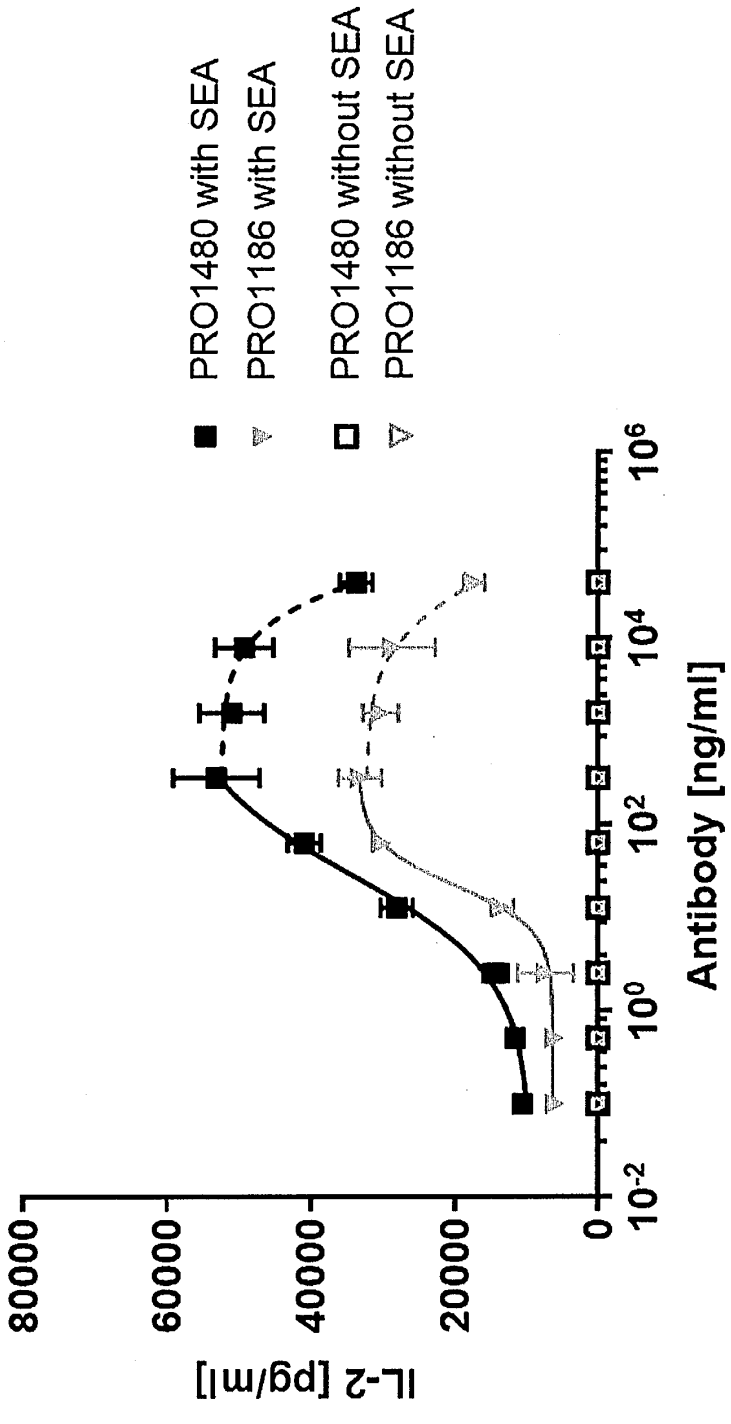

PRO1480 with SEA
PRO1186 with SEA
PRO1480 without SEA
PRO1186 without SEA
IL-2 [pg/ml]
80000
60000
40000
20000
0
10-2
100
102
104
106
Antibody [ng/ml]

Figure 8:

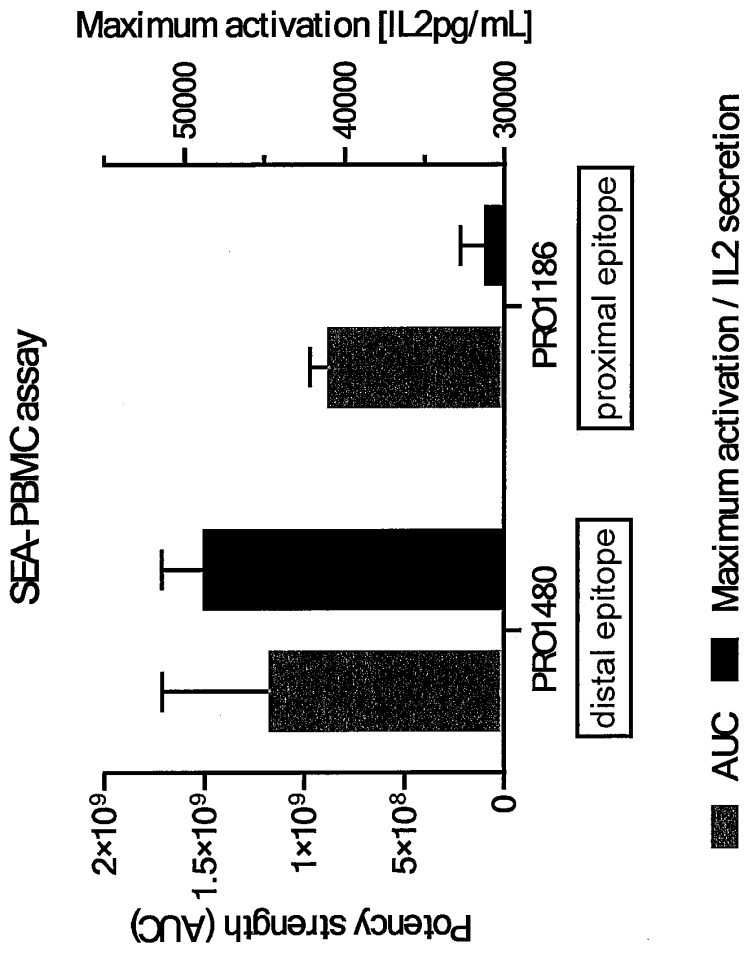
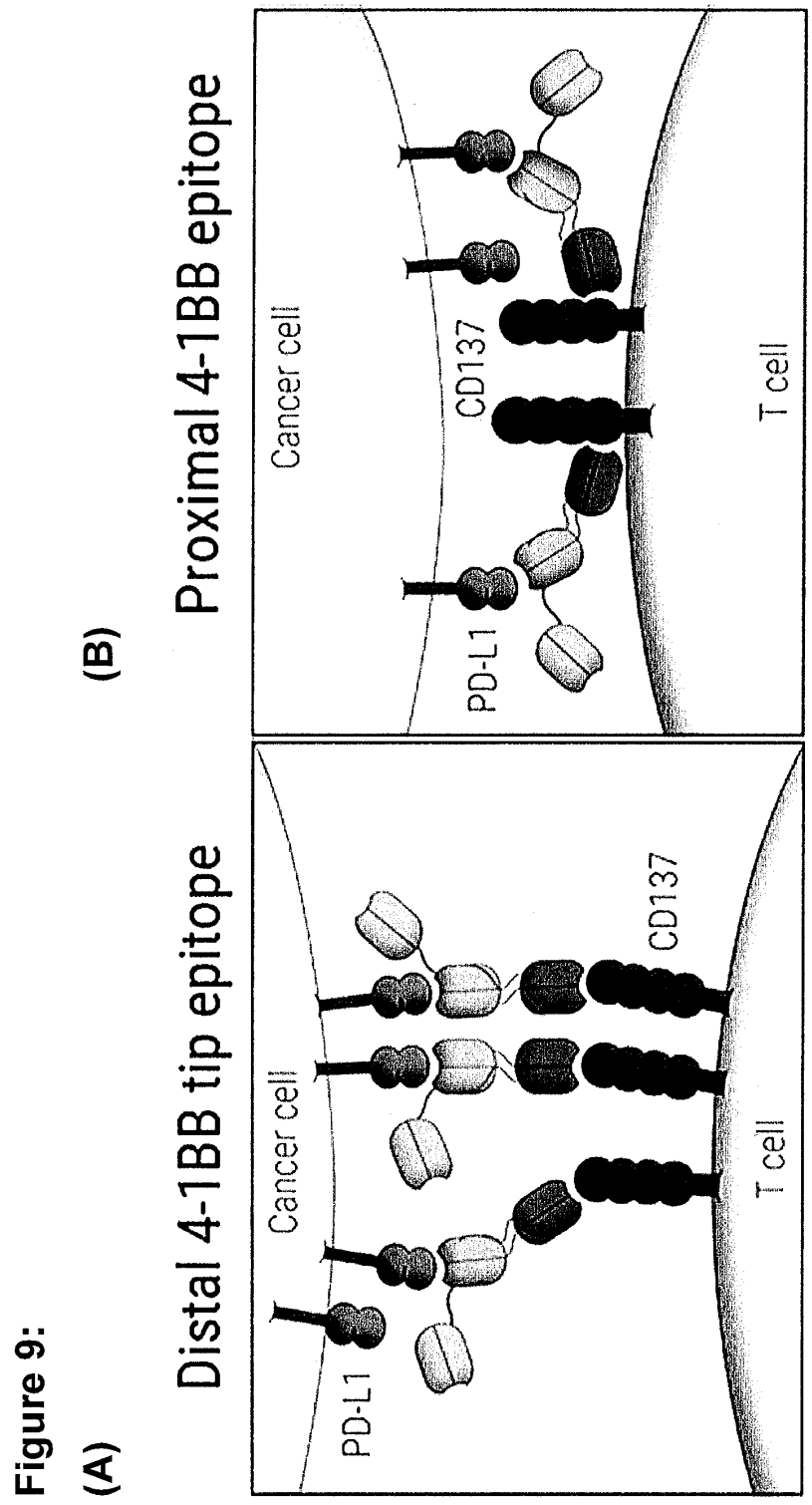

SEA-PBMC assay
Potency strength (AUC)
2×10^9
1.5×10^9
1×10^9
5×10^8
0
Maximum activation [IL2pg/mL]
50000
40000
30000
PRO1480
PRO1186
distal epitope
proximal epitope
AUC
Maximum activation / IL2 secretion

Figure 9:


(A)
Distal 4-1BB tip epitope
Cancer cell
PD-L1
CD137
T cell
(B)
Proximal 4-1BB epitope
Cancer cell
CD137
PD-L1
T cell