Figure 1

16H11 1 QVQLHQSGAELVKPGASVKISCKGSGYDFSNFWMNWVKQRPGKGLEWIGQIYPGDGEIKYNGKFKGKATLTADESSSTAYIHLSSL
2G12 1 QVQLQQPGAELVKPGASVKLSCKASGYTFTSYWMQWVKQRPGQGLEWIGEIDPSVSYTEYNQKFKGKATLTVDTSSSTAYMQLSSL
5D1 1 QVQLQQPGAELVKPGASVKMSCKASGYTFTSSWITWVKDRPGQGLEWIGDIYPGNGNTNYNEKFKSKATLTVDTSSNTVYMQLSSL
8A2 1 QVQLKESGPGLVAPSQSLSITCTVSGFSLTTYGVDWVRQFPGKGLEWLGVIWGGGNTNYNSALMSRLSISKDTSKSQVFLKMNSL
9D4 1 QVTLKESGPGILQPSQTLSLTCSFSGFSLSTFGMGVGWIRQPSGKGLEWLAHIWWDDDKYYHPALKSRLTISKDTSNNQVFLKIANV
13D2 1 DVQLQESGPGMVKPSQSLSLTCTVTGYSITSDYDWHWIRHFPGNKLEWMGYISYSGSTKYNPSLKSRISITHDTSKNHFFLKLNSV
5215-2 1 DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYVWTWIRQFPGNKLEWMGYITYSDSTNYNPSLKSRLSITRDTSKNQFFLQLSSV
5G10 1 EVKLEESGGGLVQPGGSMKVSCVASGFTFSNYWMNWVRQSPEKGLEWVAQIRLKSDNYATHYAESVKGRFTISRDDSKSSVYLQMNNL
9H11 1 EVQLQQSGPELVKPGASVKISCKASGYTFTDYYINWVKQSHGKSLEWIGDNNPNNGGASYNQSFKGKATMTVDQSSRTAYLELRSL
10E11 1 EVQLQQSGPELVKPGDSVKISCKASGYSSTGYFMNWVMQSHGKSLEWIGRIIPYNGDTFYNQKFKDKATLTVDKSSNTAHLELRSL
4B12 1 EVQLQQSGPELVKPGASVKIPCKASGYTFTDYNMDWVKQSHEKSLEWIGDIDPHNGVTLYNQKFKDKATLTIDKSSNTAYMELRSL
3F1 1 EFQLQQSGPEMVKPGASVKMSCKASGDSFTDYKINWVKQNNGKSLEWIGVINPDSGTTSYNQIFEGKATLTVDQSSSTAYMQVNRL
5215-13 1 EVQLQQSGAELVKPGASVKLSCTVSGFNFKDTYIHWVKQRPEQGLEWIGRIDPANGNTKYASKFQDKATITADTSSNTVYMQLSSL
5215-9 1 EVQLQQSGAELVKSGASVKLSCTASGFNIKDTYMHWVKQRPEKGLEWIGWIDPADGHTKYDPKFQGKATITADTSSNTAYLHLSSL
16H11 87 TSEDSAVYFCARDDYLRAMDYWGQGTSVTVSS (SEQ ID NO:1)
2G12 87 TSEDSAVYFCARWSKDYYGMDYWGQGTSVTVSS (SEQ ID NO:2)
5D1 87 TSEDSAVHYCARDGRGYFDYWGPGTTLTVSS (SEQ ID NO:3)
8A2 86 QTDDTAMYYCAKHKGTSHAMEYWGQGTSVTVSS (SEQ ID NO:4)
9D4 88 DTAETATFYCARVERGYPLDHWGQGTTLRVSS (SEQ ID NO:5)
13D2 87 TAEDTATYYCARENDFPGFWYFDVWGTGTTVTVSS (SEQ ID NO:6)
5215-2 87 TTEDTATYFCARSLTGNYFDYWGQGTTLTVSS (SEQ ID NO:7)
5G10 89 RAEDTGIYYCTEGDYDIFAYWGQGTLVTVSA (SEQ ID NO:8)
9H11 87 TSEDSAVYYCARPERYWYFDAWGTGTTVTVSS (SEQ ID NO:9)
10E11 87 TSEDSVVYYCAGPRIGGDYDGGSWLAYWGQGTLVTVSA (SEQ ID NO:10)
4B12 87 TSEDSAVYYCALTGSTYWGQGTLVTVSA (SEQ ID NO:11)
3F1 87 TSEDSAVYYCTTWDDYSFYAMDYWGQGTSVTVSS (SEQ ID NO:12)
5215-13 87 TSEDTAVYYCTRGWDGYYFDCWGQGTTLTVSS (SEQ ID NO:13)
5215-9 87 TSEDAAVYYCPRGGSSPYFDYWGQGTTLTVSS (SEQ ID NO:14)

Figure 2

16H11 1 QVQLHQSGAELVKPGASVKISCKGSGYDFSNFWMNWVKQRPGKGLEWIGQIYPGDGEIKYNGKFKGKATLTADESSSTAYIHLSSL
2G12 1 QVQLQQPGAELVKPGASVKLSCKASGYTFTSYWMQWVKQRPGQGLEWIGEIDPSVSYTEYNQKFKGKATLTVDTSSSTAYMQLSSL
5D1 1 QVQLQQPGAELVKPGASVKMSCKASGYTFTSSWITWVKDRPGQGLEWIGDIYPGNGNTNYNEKFKSKATLTVDTSSNTVYMQLSSL
8A2 1 QVQLKESGPGLVAPSQSLSITCTVSGFSLTTYGVDWVRQFPGKGLEWLGVIWGGGNTNYNSALMSRLSISKDTSKSQVFLKMNSL
9D4 1 QVTLKESGPGILQPSQTLSLTCSFSGFSLSTFGMGVGWIRQPSGKGLEWLAHIWWDDDKYYHPALKSRLTISKDTSNNQVFLKIANV
13D2 1 DVQLQESGPGMVKPSQSLSLTCTVTGYSITSDYDWHWIRHFPGNKLEWMGYISYSGSTKYNPSLKSRISITHDTSKNHFFLKLNSV
5215-2 1 DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYVWTWIRQFPGNKLEWMGYITYSDSTNYNPSLKSRLSITRDTSKNQFFLQLSSV
5G10 1 EVKLEESGGGLVQPGGSMKVSCVASGFTFSNYWMNWVRQSPEKGLEWVAQIRLKSDNYATHYAESVKGRFTISRDDSKSSVYLQMNNL
9H11 1 EVQLQQSGPELVKPGASVKISCKASGYTFTDYYINWVKQSHGKSLEWIGDNNPNNGGASYNQSFKGKATMTVDQSSRTAYLELRSL
10E11 1 EVQLQQSGPELVKPGDSVKISCKASGYSSTGYFMNWVMQSHGKSLEWIGRIIPYNGDTFYNQKFKDKATLTVDKSSNTAHLELRSL
4B12 1 EVQLQQSGPELVKPGASVKIPCKASGYTFTDYNMDWVKQSHEKSLEWIGDIDPHNGVTLYNQKFKDKATLTIDKSSNTAYMELRSL
3F1 1 EFQLQQSGPEMVKPGASVKMSCKASGDSFTDYKINWVKQNNGKSLEWIGVINPDSGTTSYNQIFEGKATLTVDQSSSTAYMQVNRL
5215-13 1 EVQLQQSGAELVKPGASVKLSCTVSGFNFKDTYIHWVKQRPEQGLEWIGRIDPANGNTKYASKFQDKATITADTSSNTVYMQLSSL
5215-9 1 EVQLQQSGAELVKSGASVKLSCTASGFNIKDTYMHWVKQRPEKGLEWIGWIDPADGHTKYDPKFQGKATITADTSSNTAYLHLSSL
16H11 87 TSEDSAVYFCARDDYLRAMDYWGQGTSVTVSS (SEQ ID NO:1)
2G12 87 TSEDSAVYFCARWSKDYYGMDYWGQGTSVTVSS (SEQ ID NO:2)
5D1 87 TSEDSAVHYCARDGRGYFDYWGPGTTLTVSS (SEQ ID NO:3)
8A2 86 QTDDTAMYYCAKHKGTSHAMEYWGQGTSVTVSS (SEQ ID NO:4)
9D4 88 DTAETATFYCARVERGYPLDHWGQGTTLRVSS (SEQ ID NO:5)
13D2 87 TAEDTATYYCARENDFPGFWYFDVWGTGTTVTVSS (SEQ ID NO:6)
5215-2 87 TTEDTATYFCARSLTGNYFDYWGQGTTLTVSS (SEQ ID NO:7)
5G10 89 RAEDTGIYYCTEGDYDIFAYWGQGTLVTVSA (SEQ ID NO:8)
9H11 87 TSEDSAVYYCARPERYWYFDAWGTGTTVTVSS (SEQ ID NO:9)
10E11 87 TSEDSVVYYCAGPRIGGDYDGGSWLAYWGQGTLVTVSA (SEQ ID NO:10)
4B12 87 TSEDSAVYYCALTGSTYWGQGTLVTVSA (SEQ ID NO:11)
3F1 87 TSEDSAVYYCTTWDDYSFYAMDYWGQGTSVTVSS (SEQ ID NO:12)
5215-13 87 TSEDTAVYYCTRGWDGYYFDCWGQGTTLTVSS (SEQ ID NO:13)
5215-9 87 TSEDAAVYYCPRGGSSPYFDYWGQGTTLTVSS (SEQ ID NO:14)

Figure 3

```
16H11        1 DIQMTQSPASLSASVGETVTITCRASGNIHNYLAWFQQKQGKSPHFLVYSAKALADGVPSRFSGSGSGTQYSLK
9D4          1 DIVLTQSPASLAVSLGQRATISCRASQSVSSSSYSYMHWYQQKPGQPPKLLIKYASNLKSGVPARFSGSGSGTDFTLT
SL2          1 VIVLTQSPASLEVSLGQRATISCRASQTVRISSYSYMNWYQQKPGQPPKLLIKYASNLESGVPARFSGSGSGTDFTLN
SL13         1 DIVLTQSPASLVVSLGLRATISCRASQSVSTSSHSYLHWYQQKPGQPPKLLIKYASNLASGVPARFSGSGSGADFTLN
SL9          1 DIVLTQSPASLTISLGQRATISCRASQSVSTSTYSYIHWYQQKPGQPPKLLIKYASNLASGVPARFSGSGSGTDFSLS
8A2          1 QIVLTQSPAIMSASPGEKVTMTCSASSRVIFMYWYQQKPGSSPRLLIYDTSNLASGVPVRFSGGGSGTSYSLT
2G12         1 DIVLTQSHKFMSTSVGDRVTITCKASQDVSTAVAWYQQKPGQSPKLLIYWTSTRHTGVPDRFTGSGSGTDHTLT
10E11        1 DIVMTQSQKFMSTTVGDRVSITCKASQNVGTAVAWYQQKPGHSPKLLIYSASNRYTGVPDRFTGSGYGTDFTLT
4B12         1 DIVMTQSQKFMSTSVGDRVSVTCKASQNVGTNVAWYQQKPGQSPKAVIYSASYRNSGVPDRFTGSGSGTDFTLT
13D2         1 DIVMSQSPSSQVVSVGEKVTVTCTSSQSLLYGTNQKNYLAWYQQKPGQSPKLLIYWASIRESGVPDRFTGSGSGTDFTLT
3F1          1 DVLMTQTPLSLPVSLGDQASISCRSSQNIVHSNGNTYLEWFLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLK
5D1          1 DIQMTQTTSSLSASLGDRVTIICRASQDISNFLNWYQQKPDGTVKLLMYDTSILQSGVPSRFSGRGSGADYSLT
5G10         1 DIQMTQTTSSLSASLGDRVTISCSASQGITNYLNWYQQKPDGTVKLLIYYTSILHSGVPSRFSGSGSGTDYSLT
9H11         1 DIVLTQSPVTLSVTPGDSVSLSCRASQSIRNNLHWYQQKSHESPRLLINYASQSISGIPSRFSGSGSGTDFILS

16H11       75 INSLQPEDFGTYYCQHFWSSPYTFGGGTKLEIK (SEQ ID NO:15)
9D4         79 IHPVEEEDTATYYCQHSWEIPPTFGGGTKLEIK (SEQ ID NO:19)
SL2         79 IHPVEEEDTATYYCQHSWKIPTFGGGTKLEIK (SEQ ID NO:20)
SL13        79 IHPVEEEDTATYYCQHSWEIPYTFGGGTKLEIK (SEQ ID NO:21)
SL9         79 IHPMEEEDTATYYCQHSWKIPFTFGSGTKLEIK (SEQ ID NO:22)
8A2         74 ISRMEAEDAATYYCQQWSSYPPTFGAGTKLELK (SEQ ID NO:18)
2G12        75 ISSVQAEDLALYYCHQQYSTPPTFGGGTKLEIK (SEQ ID NO:16)
10E11       75 ISNMQSEDLADYFCQQYNSYPLTFGAGTKLELK (SEQ ID NO:23)
4B12        75 ISNVQSEDLTEYFCQQYNNYPYTFGGGTKLEIK (SEQ ID NO:25)
13D2        81 ISSVKAEDLAVYYCQQYYSYPLTFGAGTKLELK (SEQ ID NO:28)
3F1         80 ISRVEAEDLGVYYCFQGSHIPWTFGGGTKLEIK (SEQ ID NO:24)
5D1         75 INNLEQEDLATYFCQQGKTLPYTFGGGTKLEIK (SEQ ID NO:17)
5G10        75 ISNLEPEDIATYYCQQYSKPPYTFGGGTKLEIK (SEQ ID NO:26)
9H11        75 INSVETEDFGMYFCQQSNNWPRTFGGGTLLQIKR (SEQ ID NO:27)
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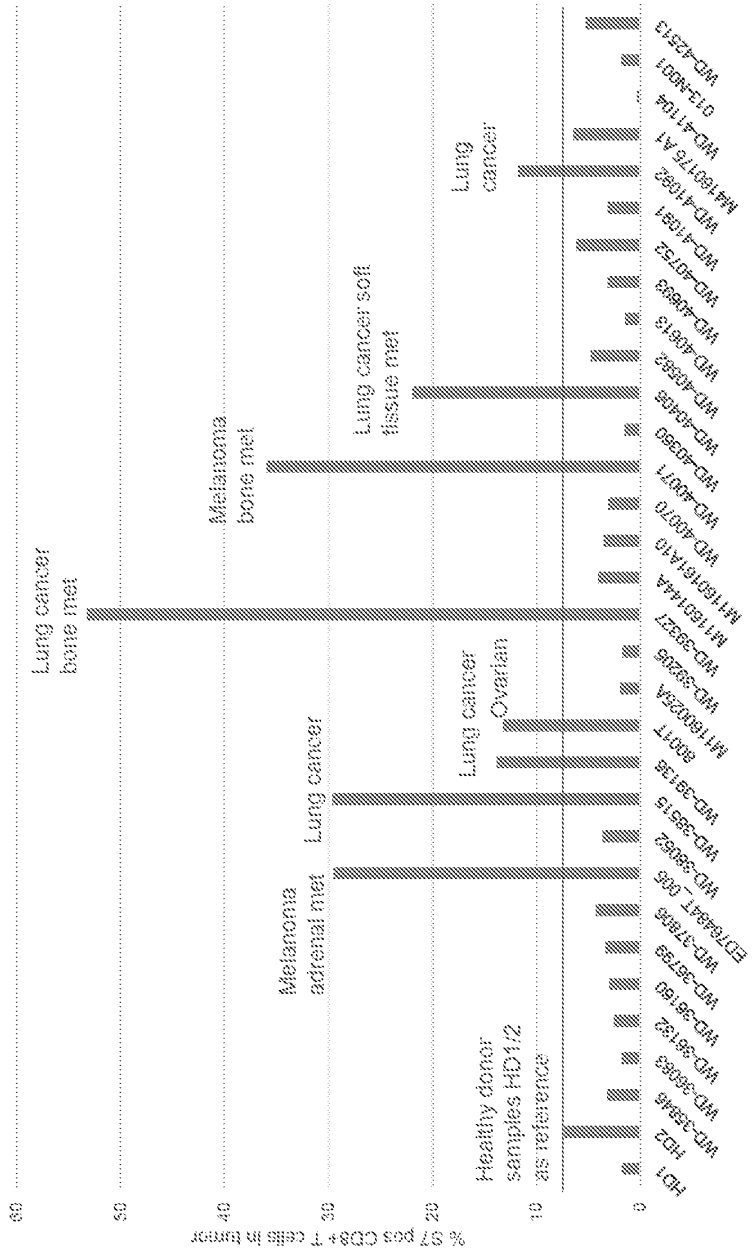
Figure 4


% ST pos CD8+ T cells in tumor
60
50
40
30
20
10
0
Lung cancer bone met
Melanoma bone met
Lung cancer soft tissue met
Lung cancer
Lung cancer Ovarian
Lung cancer
Melanoma adrenal met
Healthy donor samples HD1/2 as reference
HD1
HD2
WD-35846
WD-36082
WD-36132
WD-36160
WD-36759
WD-37806
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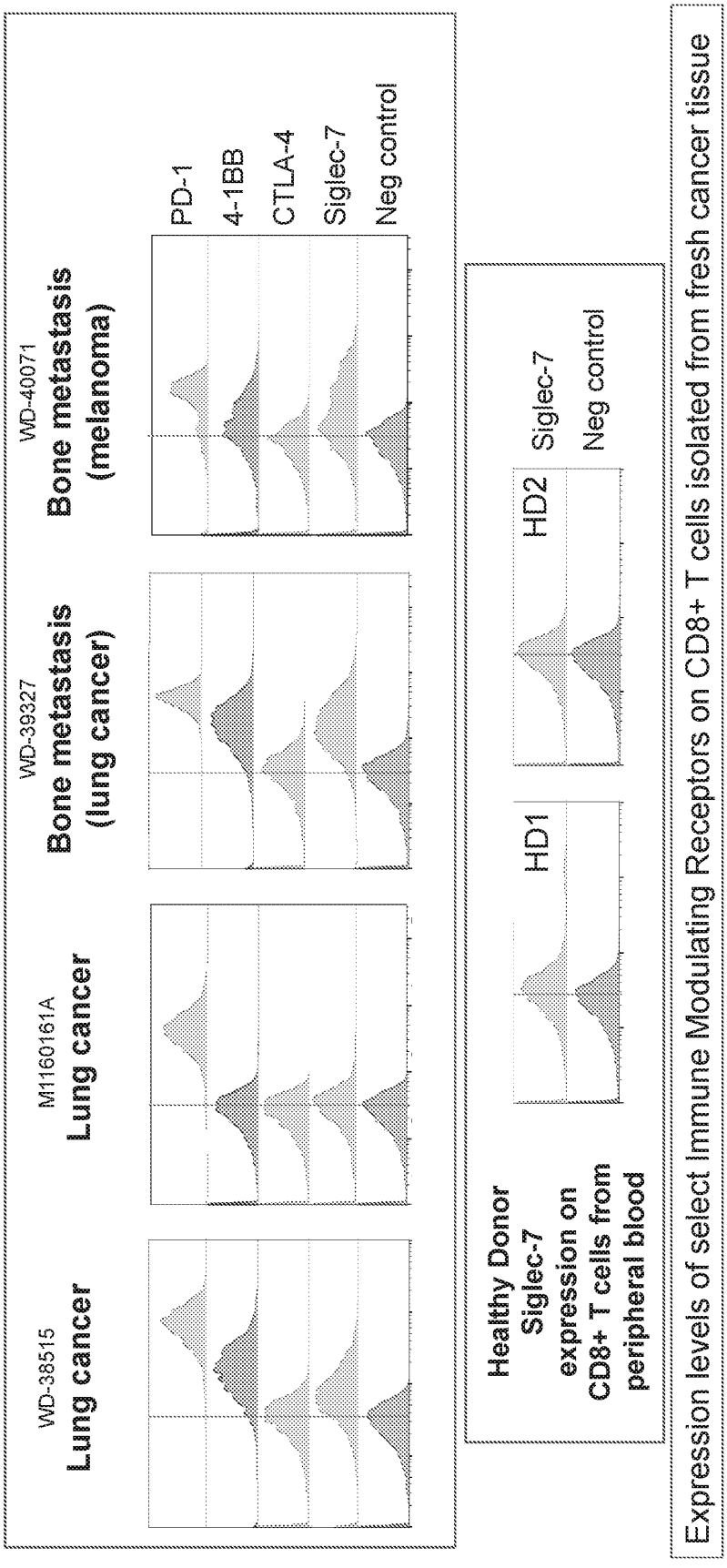
013-N001
WD-42513

Figure 5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Lung cancer
M1160161A
Lung cancer
WD-39327
Bone metastasis
(lung cancer)
WD-40071
Bone metastasis
(melanoma)
PD-1
4-1BB
CTLA-4
Siglec-7
Neg control
Healthy Donor
Siglec-7
expression on
CD8+ T cells from
peripheral blood
HD1
HD2
Siglec-7
Neg control
Expression levels of select Immune Modulating Receptors on CD8+ T cells isolated from fresh cancer tissue

Figure 6

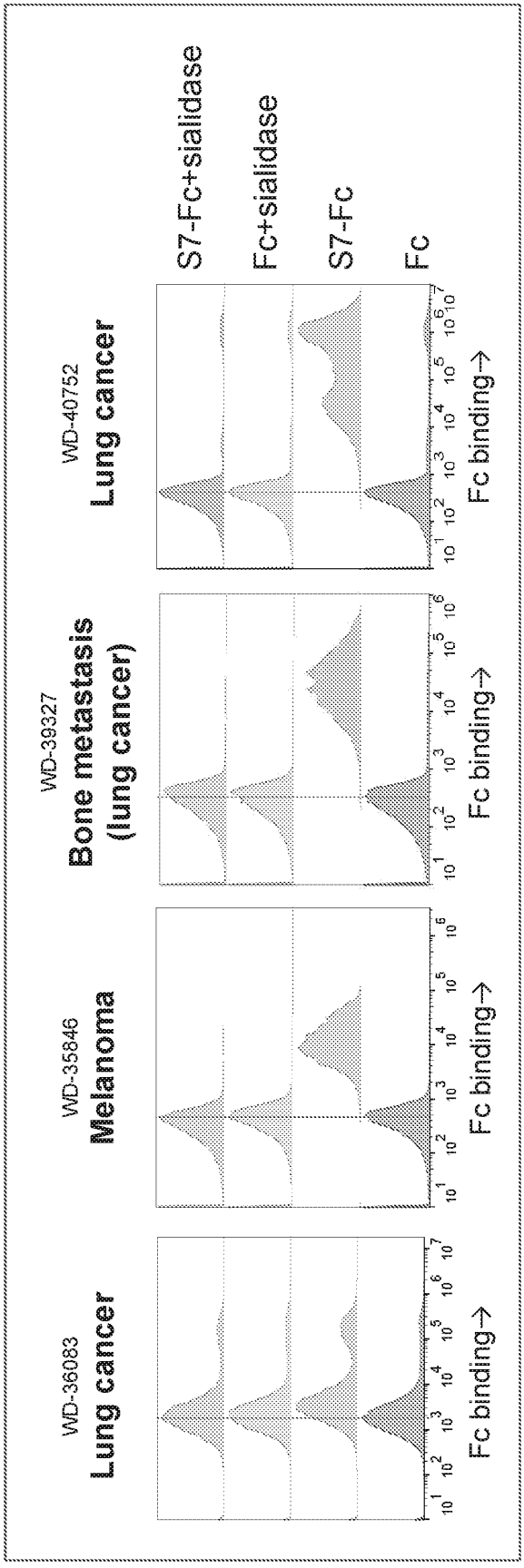
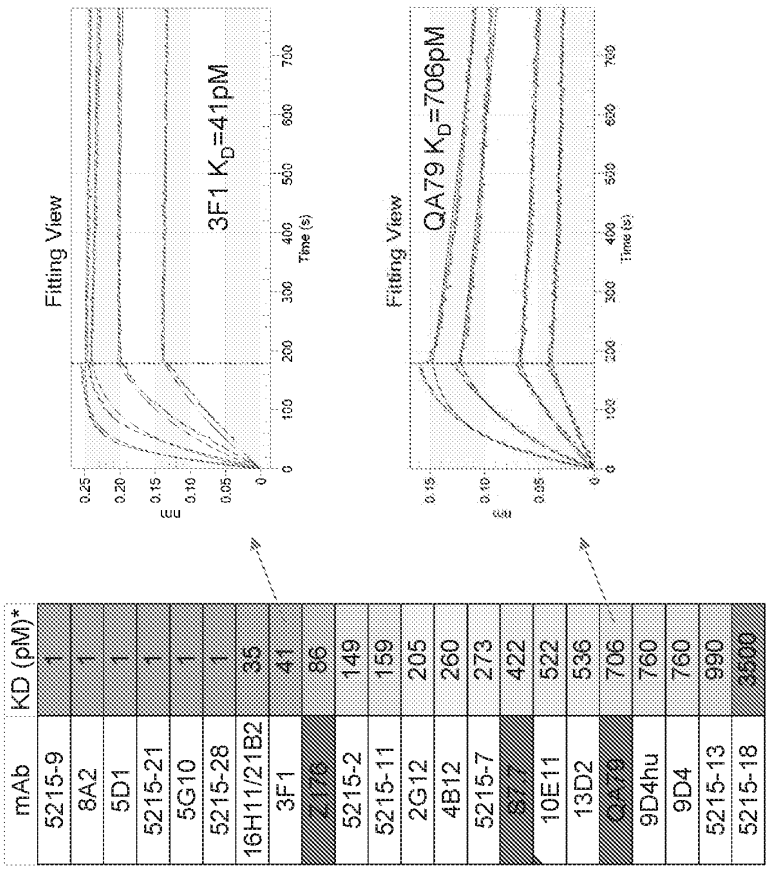
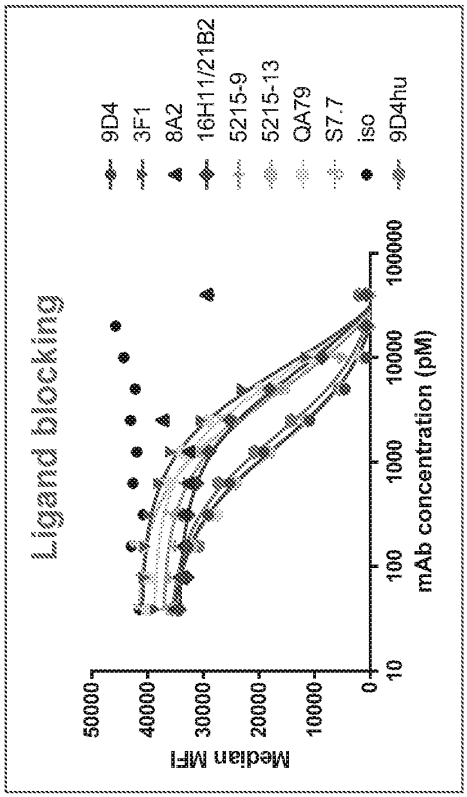

WD-36083
Lung cancer
WD-35846
Melanoma
WD-39327
Bone metastasis
(lung cancer)
WD-40752
Lung cancer
S7-Fc+sialidase
Fc+sialidase
S7-Fc
Fc
Fc binding→
Fc binding→
Fc binding→

Figure 7



mAb	KD (pM)*
5215-9	1
8A2	1
5D1	1
5215-21	1
5G10	1
5215-28	1
16H11/21B2	35
3F1	41
Z16	86
5215-2	149
5215-11	159
2G12	205
4B12	260
5215-7	273
5F7	422
10E11	522
13D2	536
QA79	706
9D4hu	760
9D4	760
5215-13	990
5215-18	3300

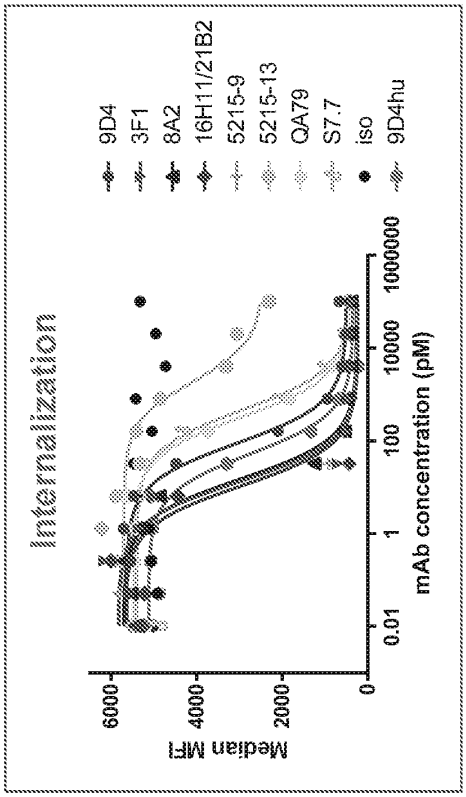
Figure 8



mAb	blocking IC50 (pM)
5215-18	543
5215-13	1324
9D4	1412
5215-7	1546
9D4hu	1760
5215-11	3050
5G10	3068
5215-28	3508
5215-21	3824
5215-2	4119
S7.7	4259
5215-9	5334
10E11	6232
16H11/21B2	7418
QA79	7492
3F1	8498
13D2	11893
2G12	19841
Z176	13000000
8A2	DNB
5D1	DNB
4B12	DNB

DNB=does not block

Figure 9



mAb	Internalization IC50 (pM)
16H11/21B2	10.58
5215-9	12.77
3F1	12.97
8A2	14.9
5215-2	16.87
13D2	17.52
5D1	20.65
5215-21	22.88
10E11	49.26
9D4hu	52.55
2G12	67.29
iso	76.65
9D4	87.51
5215-11	122.8
5G10	206
5215-28	228.1
QA79	325.8
5215-7	374.3
S7.7	468.9
5215-13	1888
5215-18	14120

Figure 10

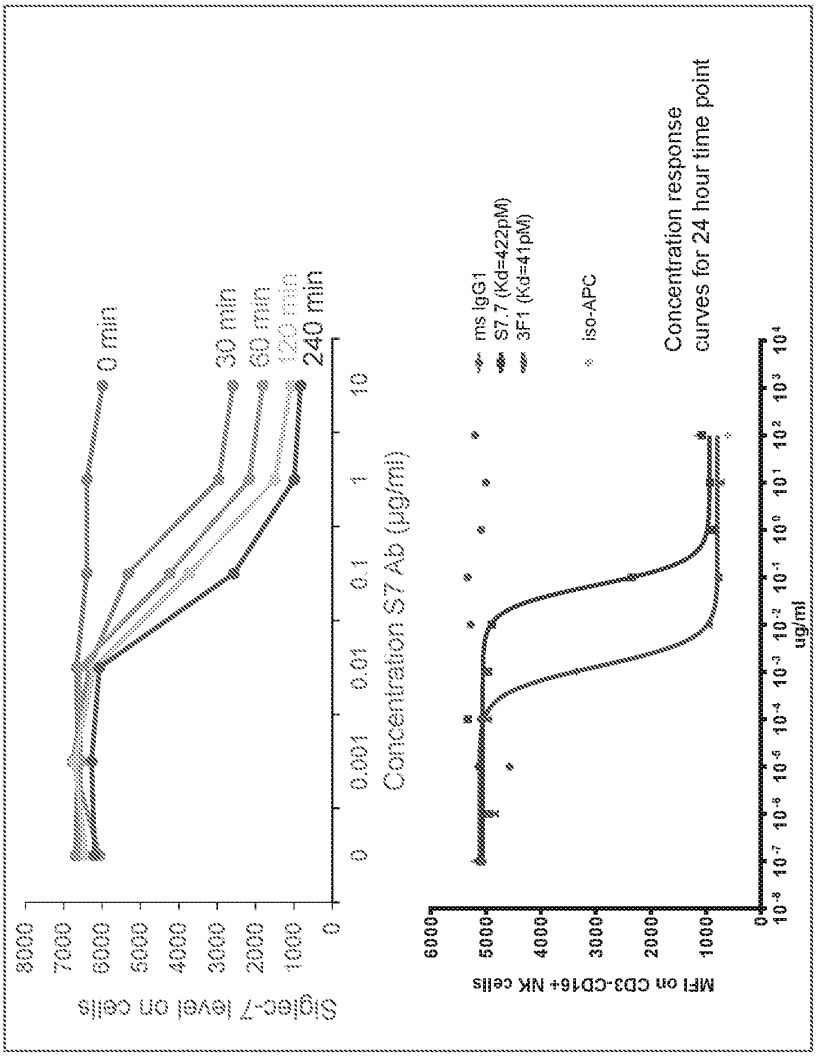
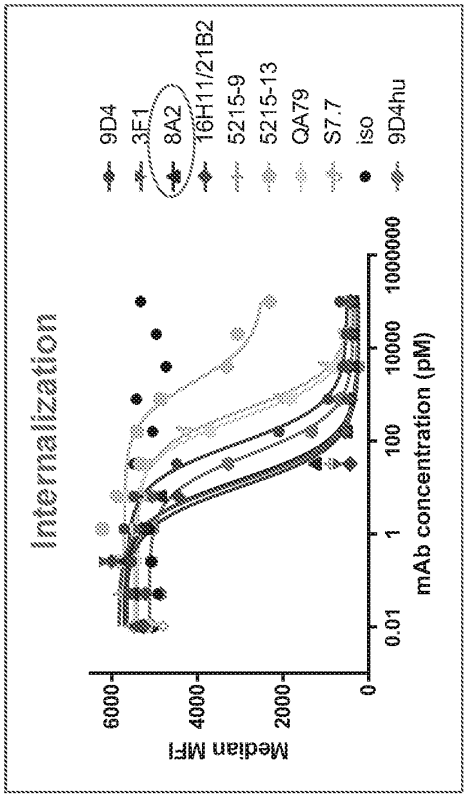
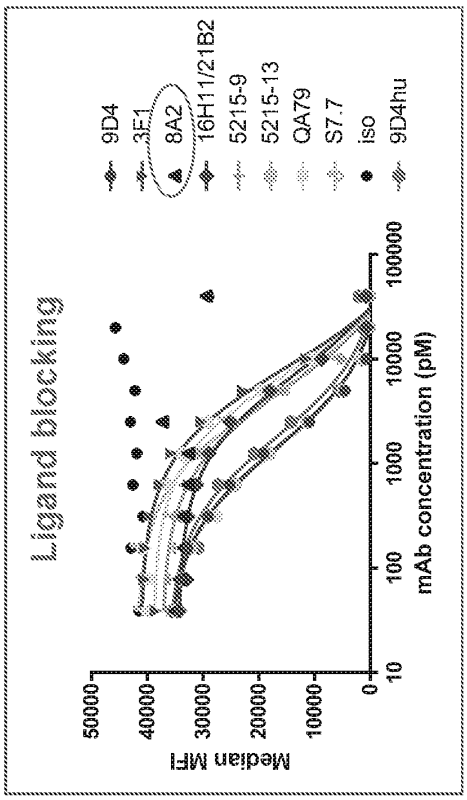

Cancer cell
Strongly inhibited activation
S7 internalization
Cancer cell
No inhibition
Siglec-7 level on cells
0 min
30 min
60 min
120 min
240 min
Concentration S7 Ab (µg/ml)
MFI on CD3-CD16+ NK cells
ms IgG1
S7.7 (Kd=422pM)
3F1 (Kd=41pM)
iso-APC
Concentration response curves for 24 hour time point
ug/ml

Figure 11


Internalization
Median MFI
6000
4000
2000
0
0.01
1
100
10000
1000000
mAb concentration (pM)
9D4
3E1
8A2
16H11/21B2
5215-9
5215-13
QA79
S7.7
iso
9D4hu


Ligand blocking
Median MFI
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40000
30000
20000
10000
0
10
100
1000
10000
100000
mAb concentration (pM)
9D4
3E1
8A2
16H11/21B2
5215-9
5215-13
QA79
S7.7
iso
9D4hu