CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCTGGCCCTCACCTGCGCTGTCTCT
GGTGGGTCCTTCACTGATCATTACTGGAGTTGGATCCGTCAGGCCCCAGGGAAGGGGCTGGAGTGGATTGGAGAA
ATCAATCATAGTGGAGTCACCAACTACAACCCGTCCCTCAAGAGTCGACTCACCATATCAGTAGACACGTCCAAG
AGCCAGTTCTCCCTGAGGCTGACCTCTGTGACCGCCGCGGACACGGCTCTGTACTACTGT GCGAAAACTGGCCTG
TATTATGATGACGTTTGGGGGACTTTTCGTCCACGGGGCGGGTTCGACTCC TGGGGCCAGGGAACCCTGGTCACC
GTCTCCTCA (SEQ ID NO: 1)

FIG. 1

Q V Q L Q Q W G A G L L K P S E T L A L T C A V S
G G S F T D H Y W S W I R Q A P G K G L E W I G E
I N H S G V T N Y N P S L K S R L T I S V D T S K
S Q F S L R L T S V T A A D T A L Y Y C A K T G L
Y Y D D V W G T F R P G G F D S W G Q G T L V T
V S S (SEQ ID NO: 2)

FIG. 2

GACATCGTGATGACCCAGTCTCCGGACTCCCTGGCTGTGTCTCTGGGCGAGAGGGCCACCATCAACTGCAAGTCC
AGCCAGAGTATTTTATATAGCTCCGACAATAAGAATTACTTAGCTTGGTACCAGCACAAGGCCAGGACAGCCTCCT
AAGCTCCTCTTTTACTGGGCATCTATCCGGGAATCCGGGTCCCTGACCGATTCAGTGGCGGCGGGTCTGGGACA
GATTTCACTCTCACCATCAGCAGTCTGCAGGCTGAAGATGTGGCAGTTTATTACTGTCAGCAATATTATAGTCCT
CCTTGCAGTTTGGCCAGGGGACCAAGCTGGAGATCCAA (SEQ ID NO: 10)

FIG. 3

D I V M T Q S P D S L A V S L G E R A T I N C K S
S Q S L L Y S S D N K N Y L A W Y Q H K P G Q P P
K L L F Y W A S I R E S G V P D R F S G S G T
D F T L T I S S L Q A E D V A V Y Y C Q Q Y Y S P
P C S F G Q G T K L E I Q (SEQ ID NO: 11)

FIG. 4

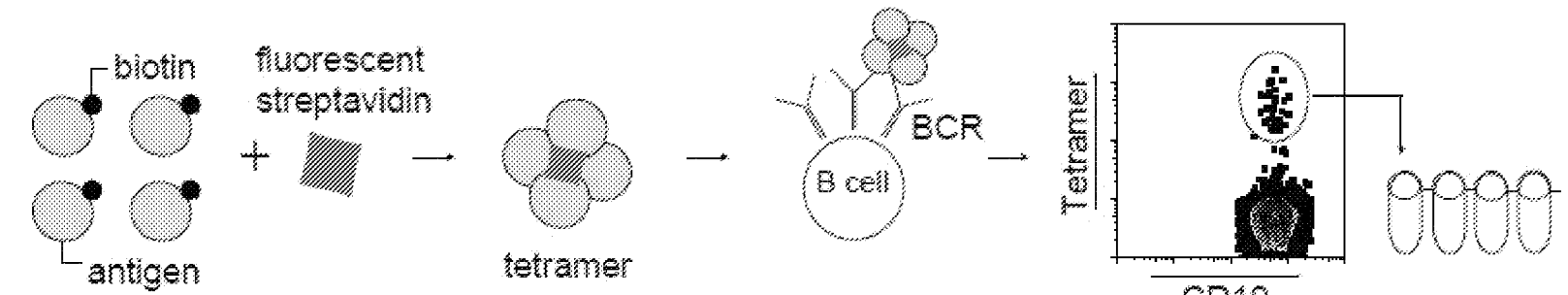


FIG. 5A

FIG. 5B

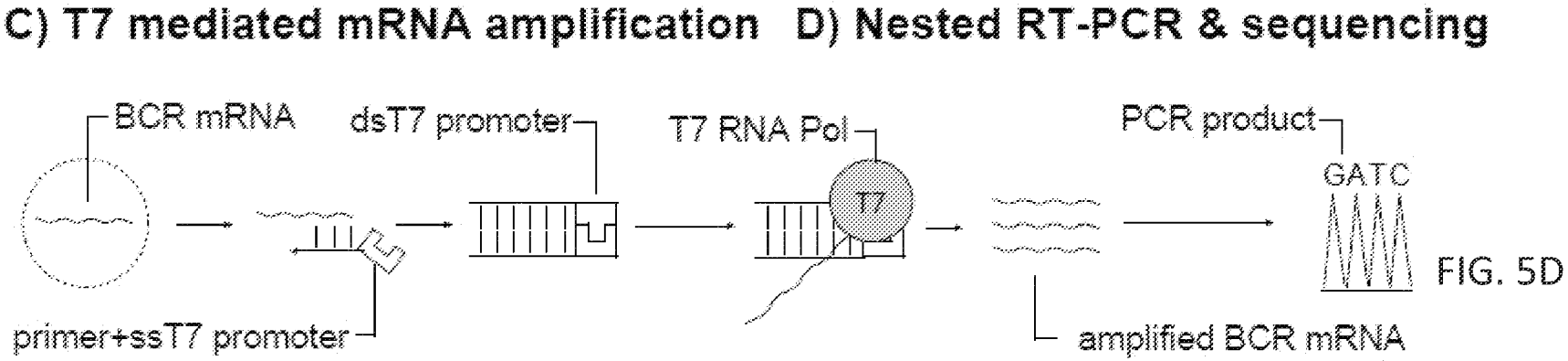


FIG. 5C

FIG. 5D

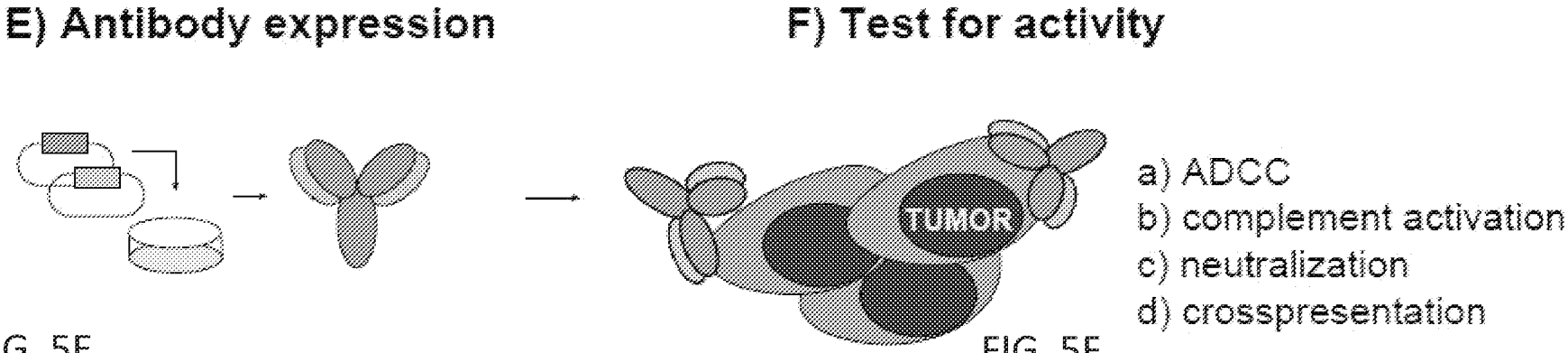


FIG. 5E

FIG. 5F

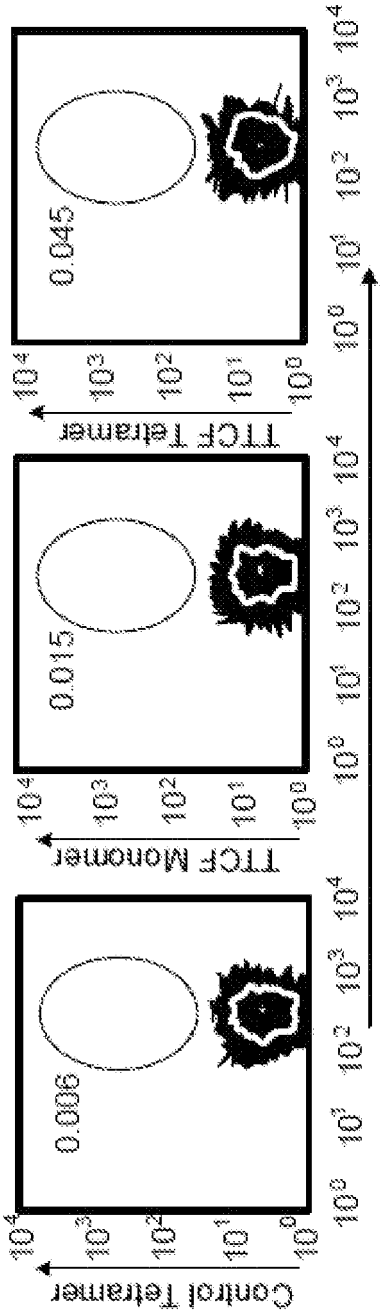


FIG. 6A

	Control Tet/ 10^5 B cells	TTCF Monomer/ 10^4 B cells	TTCF Tet/# 10^4 B cells	#Tet/#Mono Foldchange
Donor 1	3.98	2.53	18.41	7.3
Donor 2	15.03	38.64	117.18	3.1
Donor 3	4.14	48.92	77.55	1.6

FIG. 6B

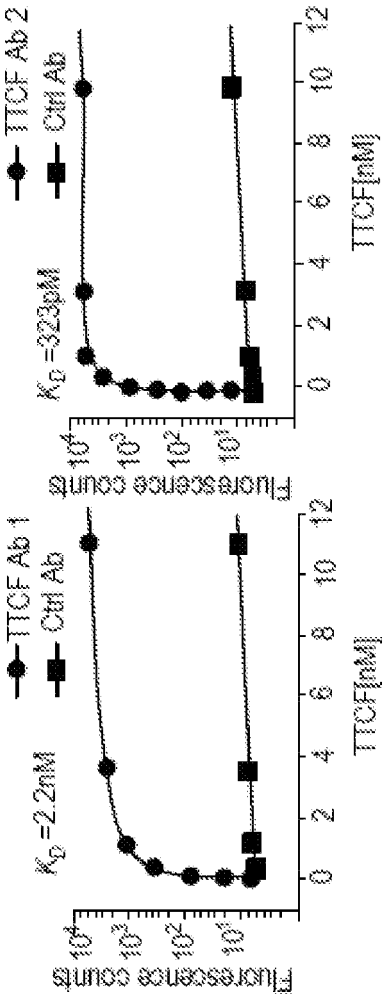

TTCF Ab 1
Ctrl Ab
K_D =2.2nM
TTCF Ab 2
Ctrl Ab
K_D =323pM
Fluorescence counts
TTCF[nM]

FIG. 7A

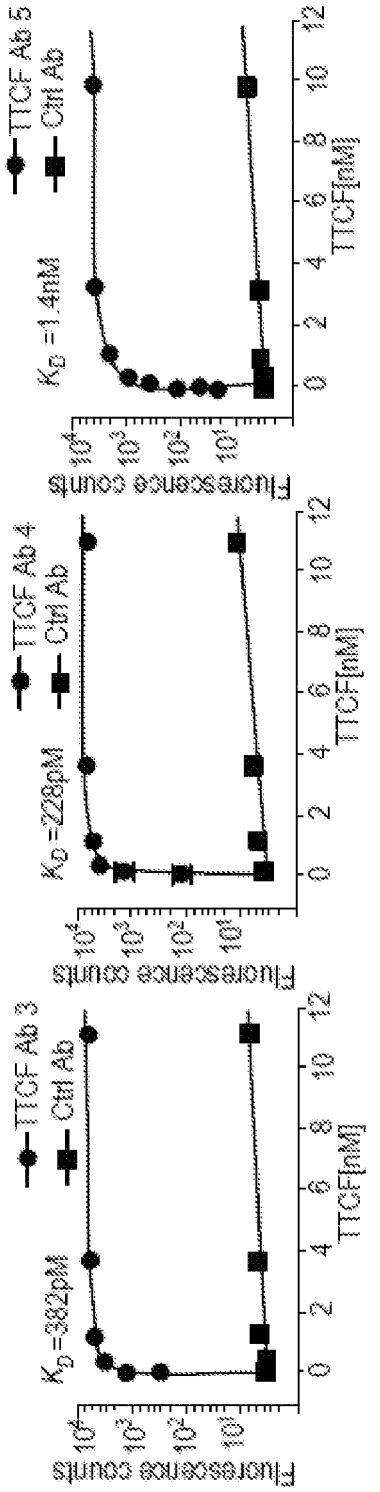

TTCF Ab 3
Ctrl Ab
K_D =382pM
TTCF Ab 4
Ctrl Ab
K_D =228pM
TTCF Ab 5
Ctrl Ab
K_D =1.4nM
Fluorescence counts
TTCF[nM]

FIG. 7B

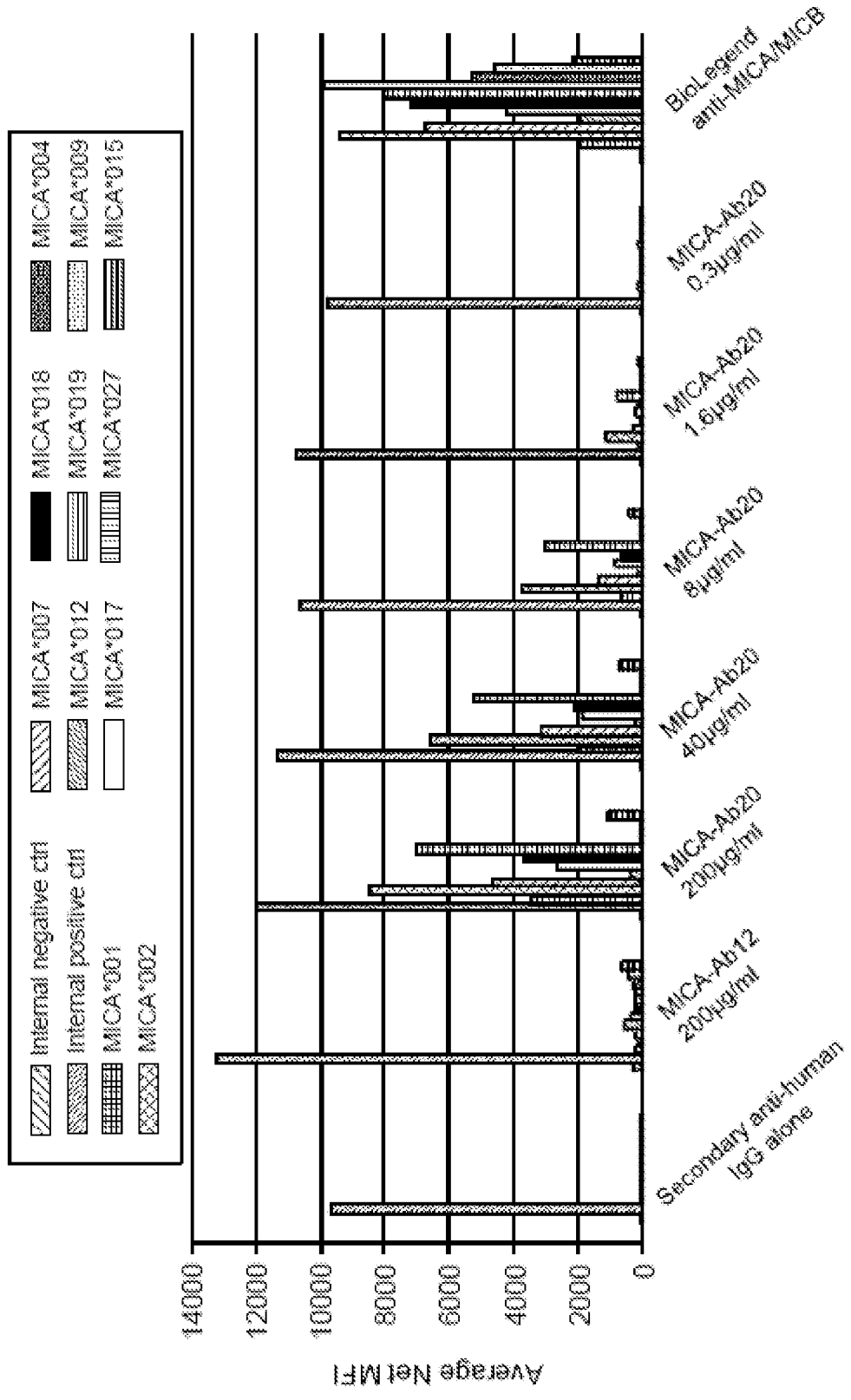

Internal negative ctrl
Internal positive ctrl
MICA*001
MICA*002
MICA*007
MICA*012
MICA*017
MICA*018
MICA*019
MICA*027
MICA*004
MICA*009
MICA*015
Average Net MFI
14000
12000
10000
8000
6000
4000
2000
0
Secondary anti-human IgG alone
MICA-Ab12 200µg/ml
MICA-Ab20 200µg/ml
MICA-Ab20 40µg/ml
MICA-Ab20 8µg/ml
MICA-Ab20 1.6µg/ml
MICA-Ab20 0.3µg/ml
BioLegend anti-MICA/MICB

FIG. 8

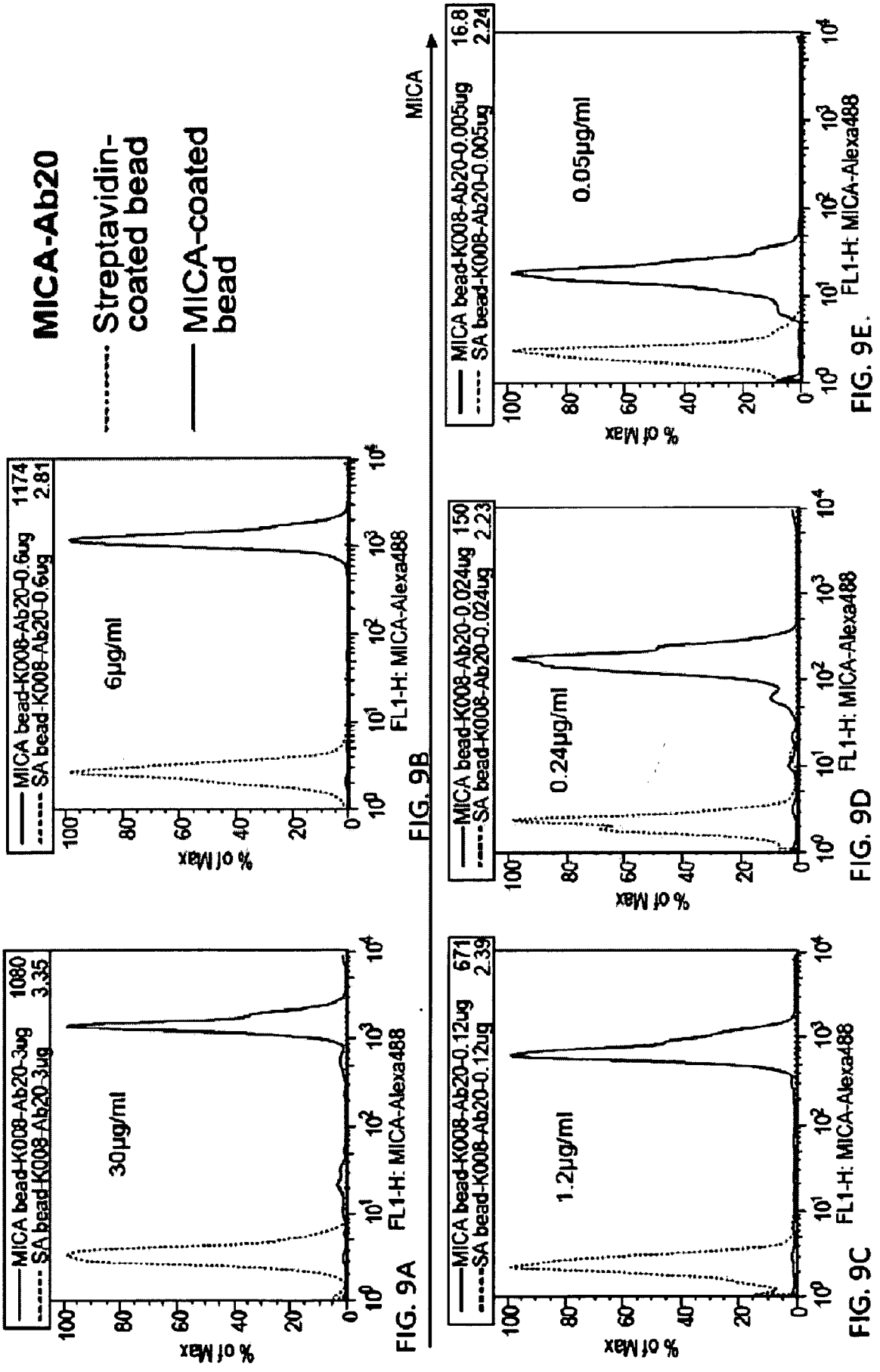


FIG. 9A FIG. 9B FIG. 9C FIG. 9D FIG. 9E

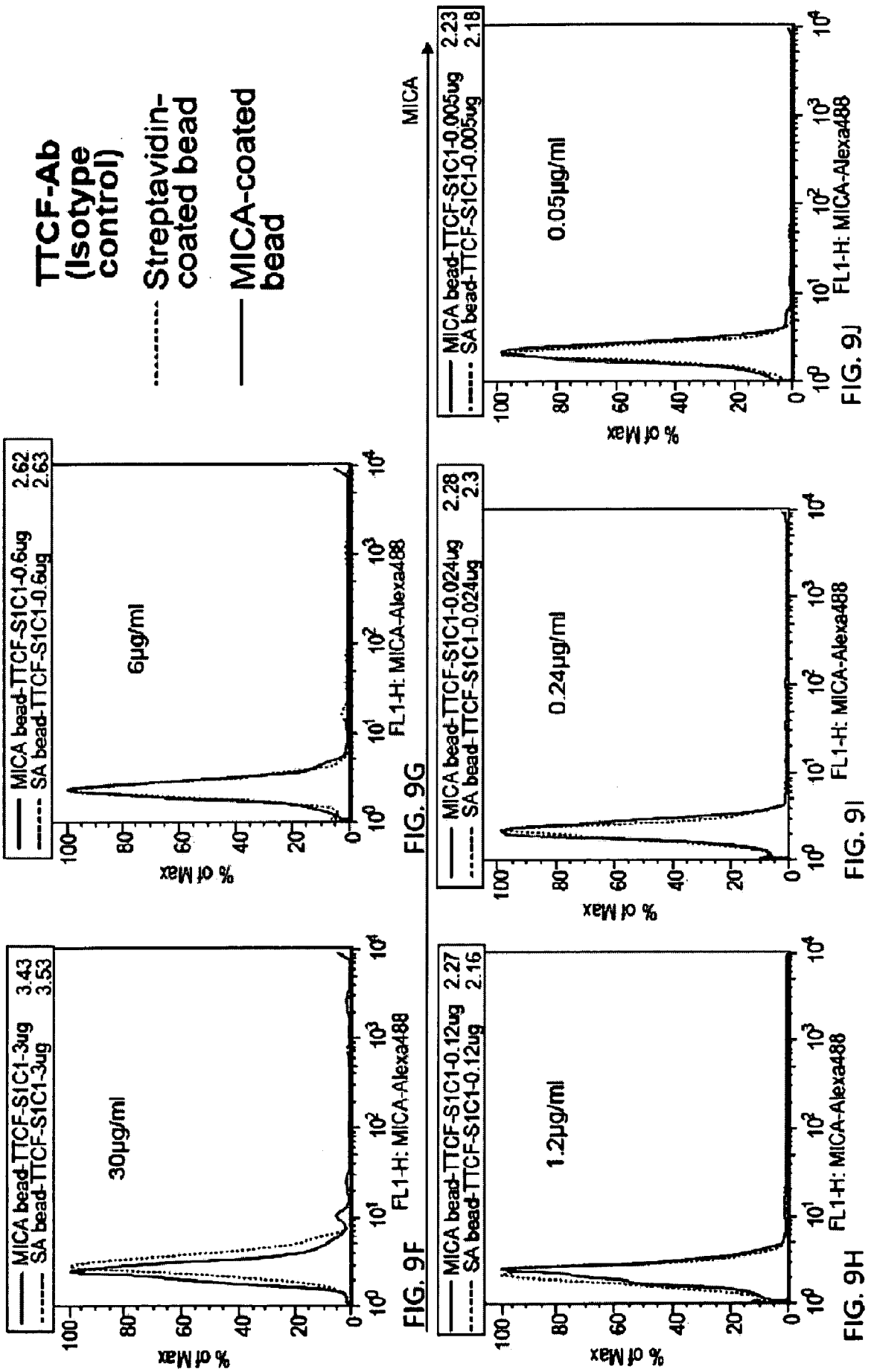


FIG. 9F FIG. 9G FIG. 9H FIG. 9I FIG. 9J

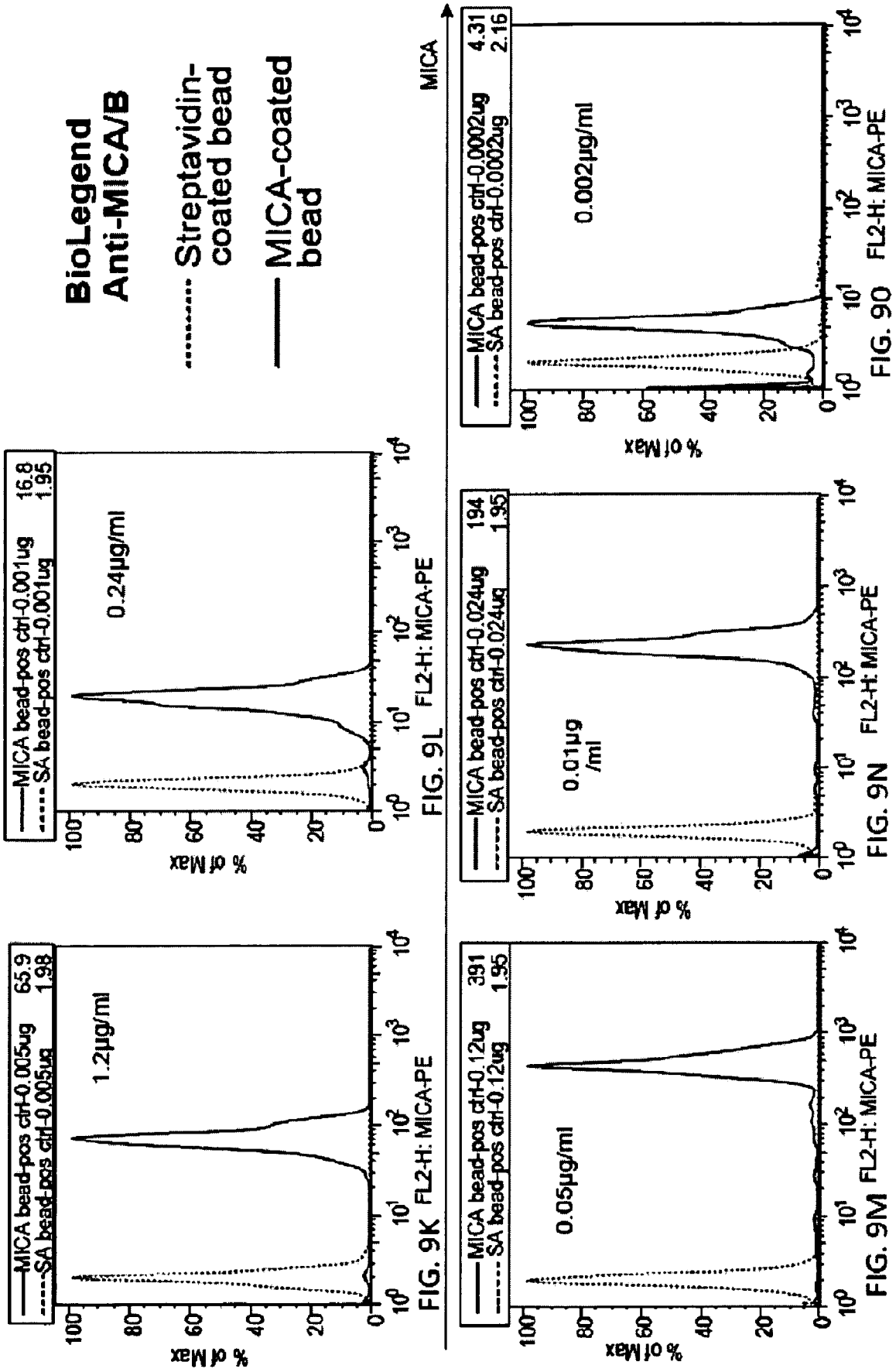


FIG. 9K FIG. 9L FIG. 9M FIG. 9N FIG. 9O

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGGAGCCTTCGGGGACCCTGTCCCT
CACCTGCACTGTGTCTGGTGGCTCCATCAGCAGGAGTAACTGGTGGAGTTGGGTCCGCC
AGCCCCCAGGGGAGGGGCTGGAATGGATTGGAGAAATCCATCACATTGGGAGGTCCAGC
TACAATCCGTCCCTCAAGAGTCGAGTCACCATGTCTGTAGACAAGTCCCAGAACCAGTT
CTCCCTGAGGCTGACCTCTGTGACCGCCGCGGACACGGCCGTGTATTACTGTGCGAAAA
ATGGCTACTACGCTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCG
(SEQ ID NO.76)

FIG. 10

QVQLQESGPGLVEPSGTLSLTCTVSGGSISRSNWWSWVRQPPGEGLEWIGEIHHIGRSS
YNPSLKSRVTMSVDKSQNQFSLRLTSVTAADTAVYYCAKNGYYAMDVWGQGTTVTVSS
(SEQ ID NO.77)

FIG. 11

GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCAC
CCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCGACTTCCTAGCCTGGTACCAGCAGA
AACCTGGCCAGGCTCCCCAGGCTCCTCATCTACGCTACATCCTTCAGGGCCACTGGCATC
TCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCTCTCACCATCAACAGACT
GGAACCTGAAGATTTTGCAGTGTATTACTGTCAGCACTATCGTAGTTCACCTCCGTGGT
ACACTTTTGCCCCAGGGGACCAAGCTGGACATGAGACGTACGGTGGCTGCACCATCTGTC
(SEQ ID NO. 78)

FIG. 12

EIVLTQSPGTLSLSPGERATLSCRASQSVSSDFLAWYQQKPGQAPRLLIYATSFRATGI
SDRFSGSGSGTDFSLTINRLEPEDFAVYYCQHYRSSPPWYTFAQGTKLDMRRTVAAPSV
(SEQ ID NO. 79)

FIG. 13

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGGGACCCTGTCCCTC ACCTGCGCTGTCTCT GGTGCCTCCATTACCAATGGT GCCTGGTGGAGTTGGGTCCGCCAG CCCCCAGGGAAGGGGCTGGAGTGGATTGGAGAA ATCTATCTTAATGGGAACACC AACTCC AACCCGTCCCTGAAGAGTCGAGTCATCATATCAGTGGACAAGTCCAAGAACCACTTCTCG CTGACCCTGAACTCTGTGACCGCCGCGGACACGGCCGTGTATTAC TGTGCGAAGAACGCT GCCTACAACCTTGAGTTCTGG GGCCAGGGAGCCCTGGTCACCGTCTCCTCA (SEQ ID NO: 95)

FIG. 14

QVQLQESGPGLVKPSGTLSLTCAVS GASITNGAW WSWVRQPPGKGLEWIGE IYLNGNT NS NPSLKSRVIISVDKSKNHFSLTLNSVTA ADTAVYY CAKNAAYNLEFW GQGALVTVSS (SEQ ID NO:96)

FIG. 15

GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACC

CTCTCCTGCAGGGCCAGTCAGACTGTTAGCAGCCCCTAC GTAGCCTGGTACCAGCAGAAA

CGTGGCCAGGCTCCCAGGCTCCTCATCTA TGGTGCATCC ACCAGGGCCACCGGCATCCCAG

ACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGC

CTGAAGATTTTGCAGTGTATTAC TGTCAGGCAGTATGATAGATCATACTATTACACTTT T

GGCCAGGGGACCAAGCTGGAGATCAAA (SEQ ID NO:97)

FIG. 16

EIVLTQSPGTLSLSPGERATLSCRAS QTVSSPYVAWYQQKRGQAPRLLIY GASTRATGIPDR

FSGSGSGTDFTLTISRLEPEDFAVYY CQQYDRSYYTF GQGTKLEIK (SEQ ID NO: 98)

FIG. 17

CAGGTGCAGCTGCAGGAGTCGGGCCC AGGACTGGTGAAGCCTTCGGAGAACCTGTCGCTC ACCTGCACTGTCTCTGATGCCTCCATGAGTGATTATCAC TGGAGCTGGATCCGGCAGGCC GCCGGGAAGGGACTGGAGTGGATTGGGCGT ATGTACAGCACTGGGAGTCCC TACTACAA ACCCTCCCTCAAAGGTCGGGTCACCATGTCAATAGACACGTCCAAGAACCAGTTCTCCCT GAAGCTGGCCTCTGTGACCGCCGCAGACACGGCCATCTATTAT TGTGCGAGCGGACAACA TATTGGTGGCTGGGTCCCCCCTGACTTCTGG GGCCAGGGAACCCTGGTCACCGTCTCCTC A (SEQ ID NO: 112)

FIG. 18

QVQLQESGPGLVKPSENLSLT CTVSDASMSDYHWSWIRQAAGKGLEWIGR MYSTGSPYY KPSLKGRVTMSIDTSKNQFSLKLASVTAADTAIYY CASGQHIGGWVPPDFWGQGTLVTVS S (SEQ ID NO:113)

FIG. 19

GATATTGTGATGACCCAGACTCCACTCTCCTCACCTGTCACCCTTGGACAGCCGGCCTCCA TCTCCTGCAGGTCTAGT GAAGGCCTCGTATATAGTGATGGAGACACCTAC TTGAGTTGGT TTCACCAGAGGCCAGGCCAGCCTCCAAGACTCCTGATTTAT AAAATTTCT AACCGGTTCT CTGGGGTCCCCGACAGATTCAGTGGCAGTGGGGCAGGCACAGATTTCACACTGAAAATCA GCAGGGTGGAGGCTGAGGATGTCGGGGTTTATTAC TGCATGCAAGCTACACATTTTCCGT GGACGTTCGGCCAGGGGACCAAAGTGGAAGTCAAACGT (SEQ ID NO: 114)

FIG. 20

DIVMTQTPLSSPVTLGQPASISCRSS EGLVYSDGDTYLSWFHQRPGQPPRLLIY KIS NRFSG VPDRFSGSGAGTDFTLKISRVEAEDVGVYY CMQATHFPWTF GQGTKVEVKR (SEQ ID NO: 115)

FIG. 21

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGG TACAGCCTGGGGGGTCCCTGAGACTC TCCTGTGCAGCCTCTGGATTCACCTTTAGTTCATATGGC TTGACCTGGATACGCCAGGCT CCGGGGAAGGGCCTGGAGTGGGTCTCAAGT ATCAGTGGCAGTGGCAATAACACA TACTA CGCAGACTCTGTGAAGGGCCGGTTCACCATCTCCAGAGACAAAGTCAAGAAGACACTATA TCTACAAATGGACAGCCTGACAGTCGGAGACACGGCCGTCTATTAC TGCTTAGGAGTCGG TCAGGGCCACGGAATTCCGGTCATCGTCTCCT CA (SEQ ID NO. 130)

FIG. 22

EVQLLESGGGLVQPGGSLRLSC AASGFTFSSYG LTWIRQAPGKGLEWVSS ISGSGNNTYYA DSVKGRFTISRDKVKKTLYLQMDSLTVGDTAVYY CLGVGQGHGIPVIVSS (SEQ ID NO. 131)

FIG. 23

GATATTGTGATGACCCAGACTCCACTCTCCTCACCTGTCACCCTTGGACAGCC GGCCTCCA
TCTCCTGCAGGTCTAGT CAGAGCCTCGTACACCGTGATGGAAACACCTAC TTGAGTTGGT
TTCTGCAGAGGCCAGGCCAGGCTCCAAGACTCCTAATTTAT CGGATTTCT AACCGGTTCT
CTGGGGTCCCAGACAGATTCAGTGGCAGTGGGGCAGGGACGGATTTCACACTGAAAATC
AGCAGGGTGGAAGCTGAGGATGTCGGCGTTTACTAC TGCATGCAAGCTACACAAATCCCC
AACACTTTT GGCCAGGGGACCAAGCTGGAGATCAAG (SEQ ID NO. 132)

FIG. 24

DVVMTQSPLSLPVTLGQPASISCRSS QSLVHSDGNTY LNWFHQRPGQSPRRLIY KVS KR
DSGVPDRFSGSGSGSDFTLKISRVEAEDVGIYY CMQGTHWPTF GQGTKVEIKRTVAA
(SEQ ID NO. 133)

FIG. 25

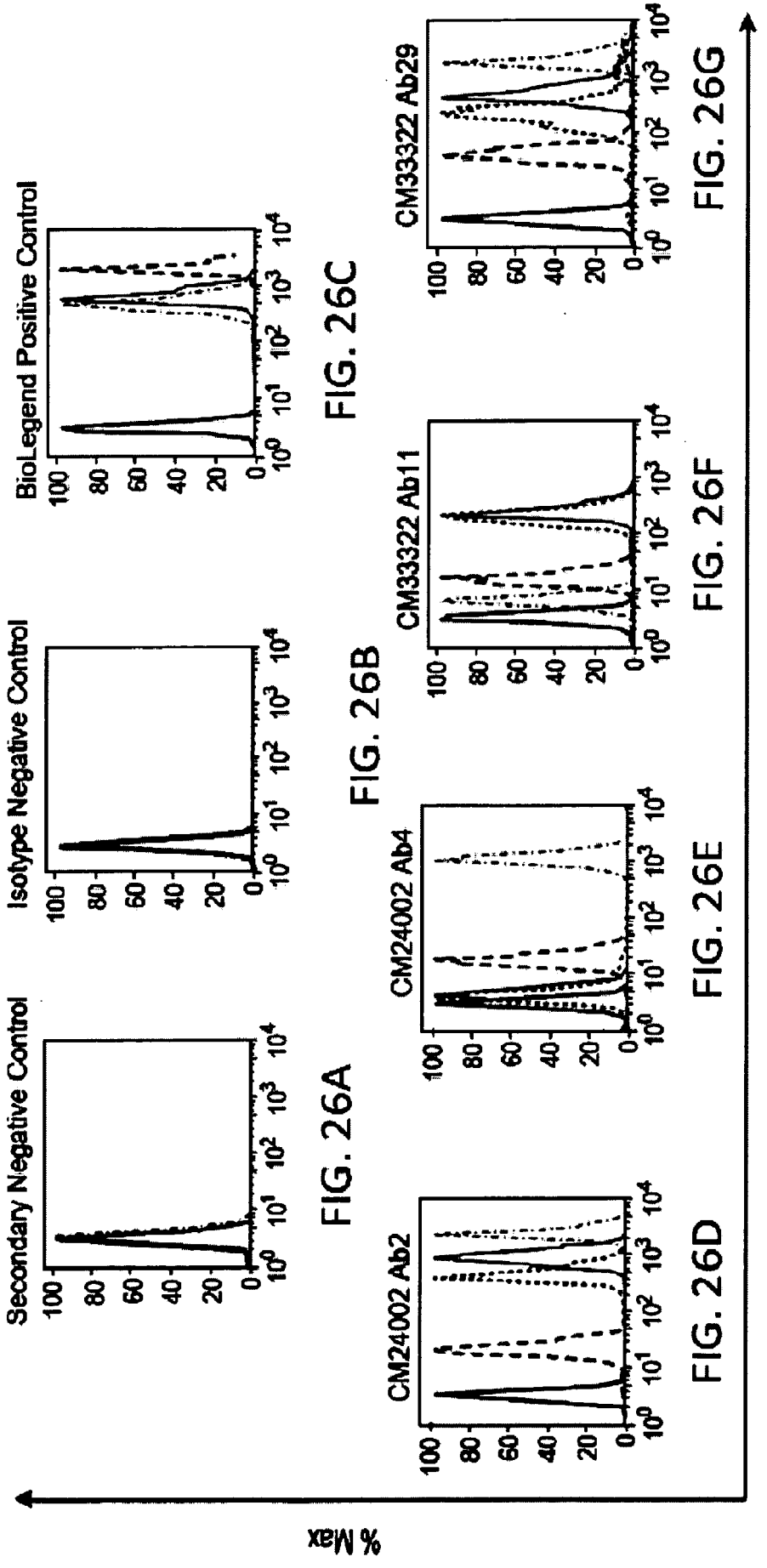


FIG. 26A FIG. 26B FIG. 26C FIG. 26D FIG. 26E FIG. 26F FIG. 26G

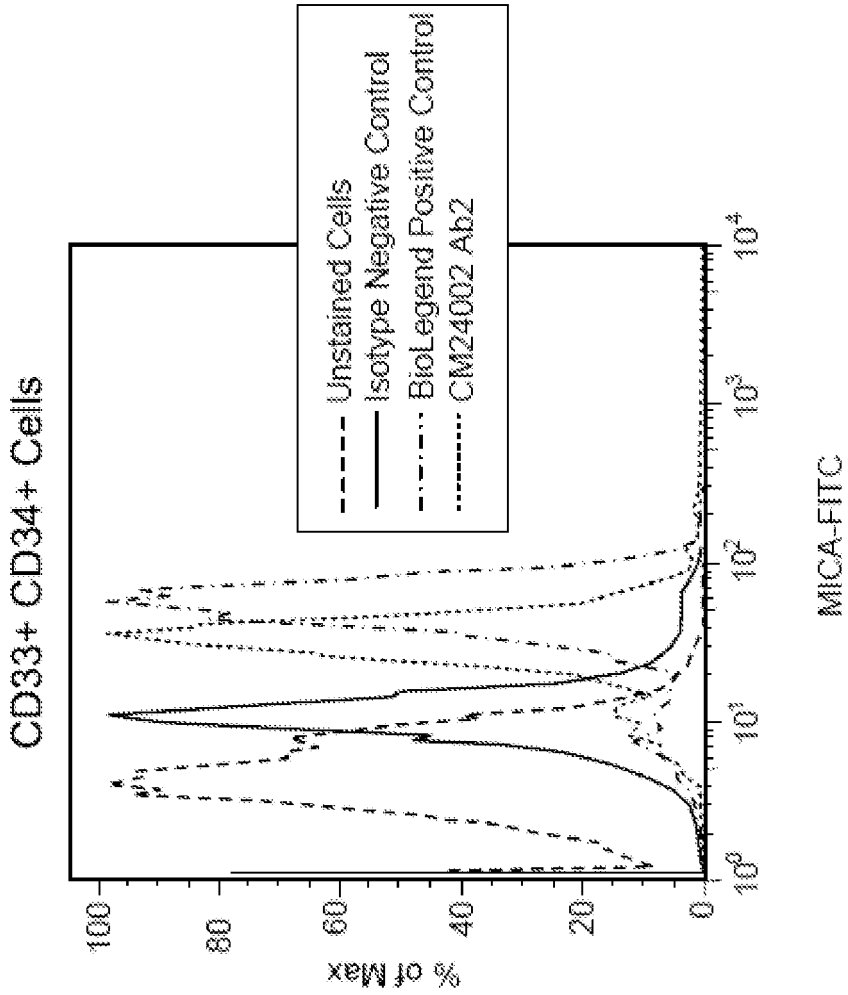

CD33+ CD34+ Cells
Unstained Cells
Isotype Negative Control
BioLegend Positive Control
CM24002 Ab2
% of Max
MICA-FITC
0
20
40
60
80
100
10^0
10^1
10^2
10^3
10^4

FIG. 27

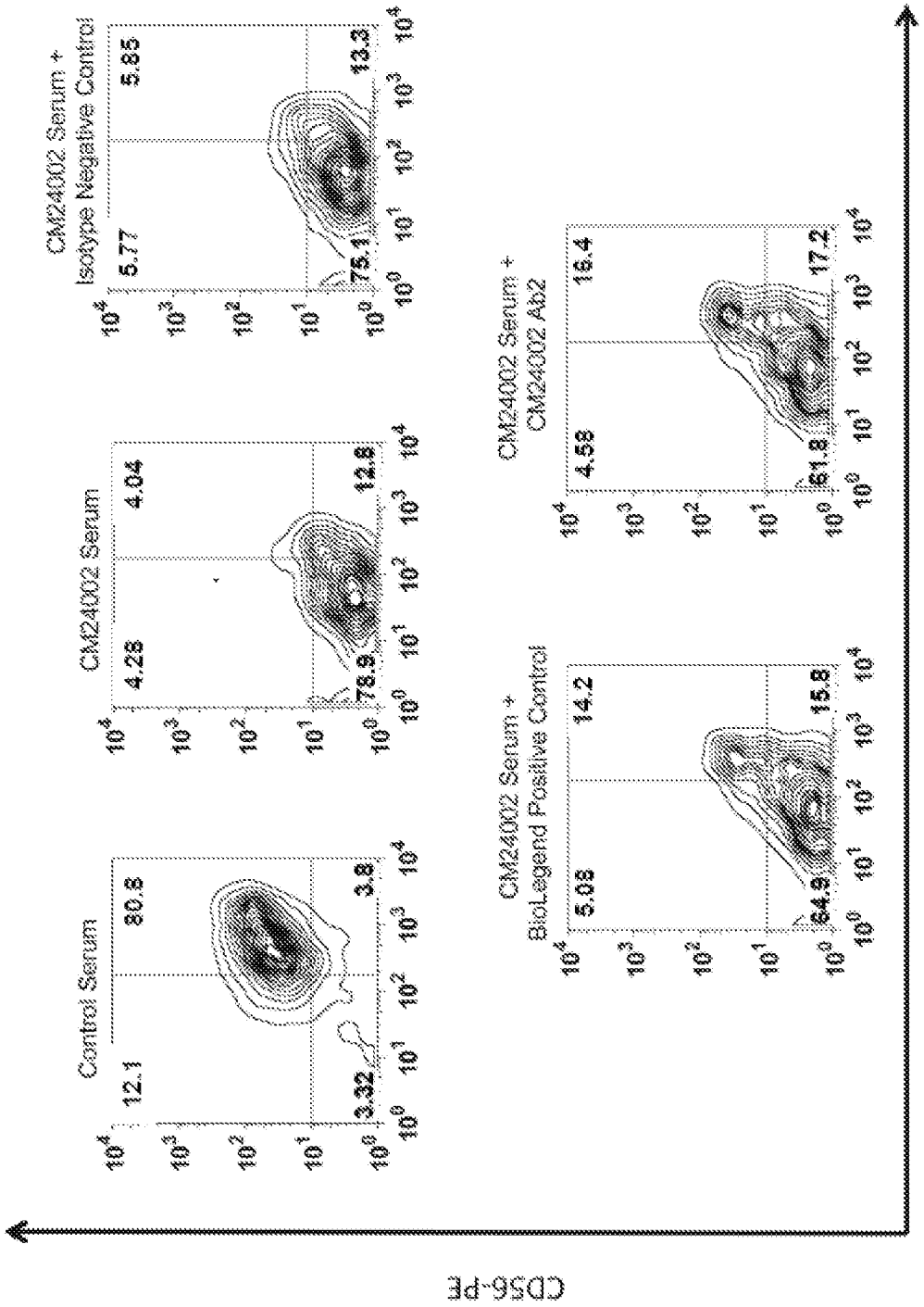

Control Serum
12.1
80.8
3.32
3.8
CM24002 Serum
4.28
4.04
78.9
12.8
CM24002 Serum +
Isotype Negative Control
5.77
5.85
75.1
13.3
CM24002 Serum +
BioLegend Positive Control
5.08
14.2
64.9
15.8
CM24002 Serum +
CM24002 Ab2
4.58
16.4
61.8
17.2
CD56-PE
NKG2D-APC

FIG. 28

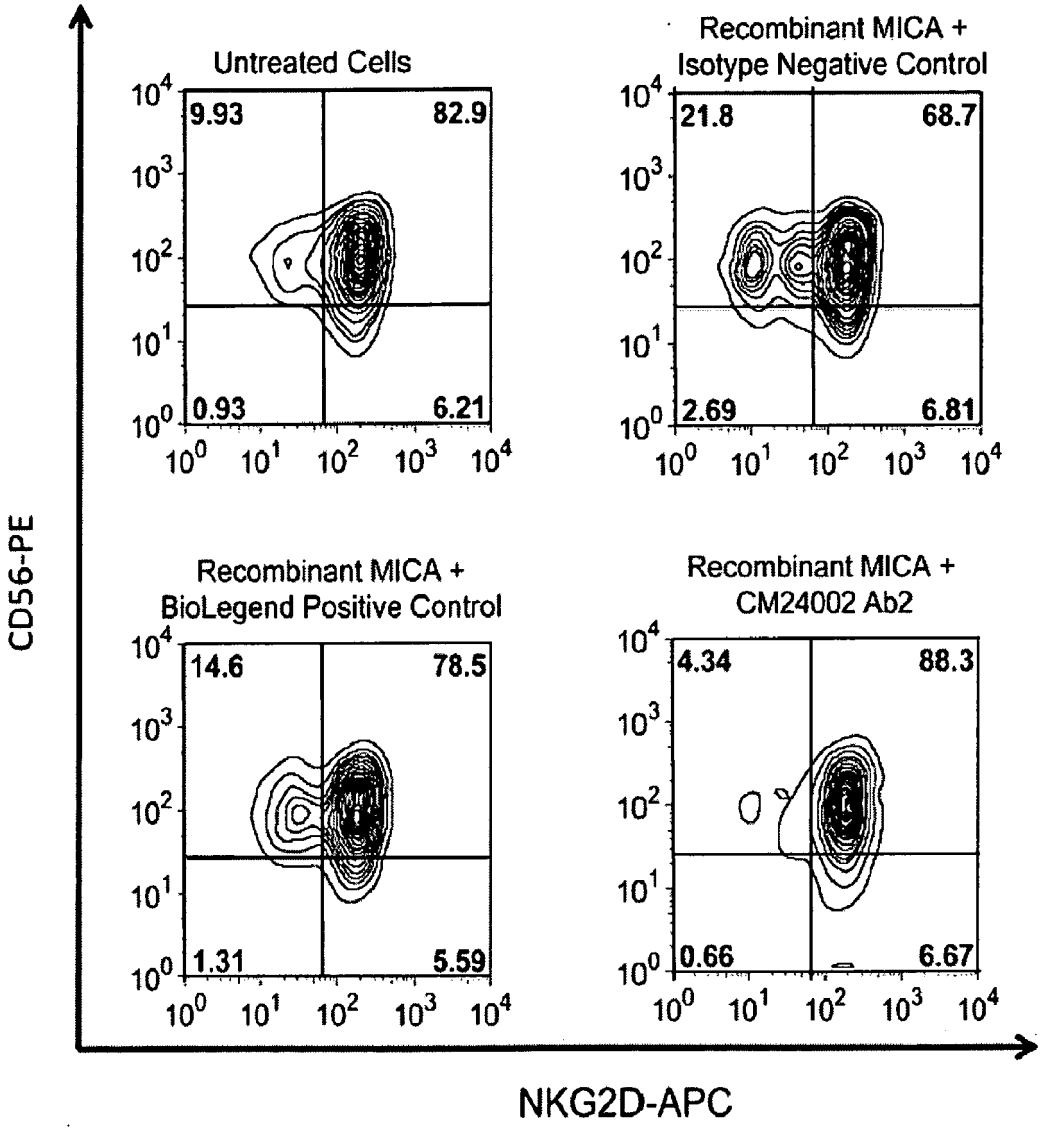

Untreated Cells
9.93
82.9
0.93
6.21
Recombinant MICA +
Isotype Negative Control
21.8
68.7
2.69
6.81
Recombinant MICA +
BioLegend Positive Control
14.6
78.5
1.31
5.59
Recombinant MICA +
CM24002 Ab2
4.34
88.3
0.66
6.67
CD56-PE
NKG2D-APC

FIG. 29

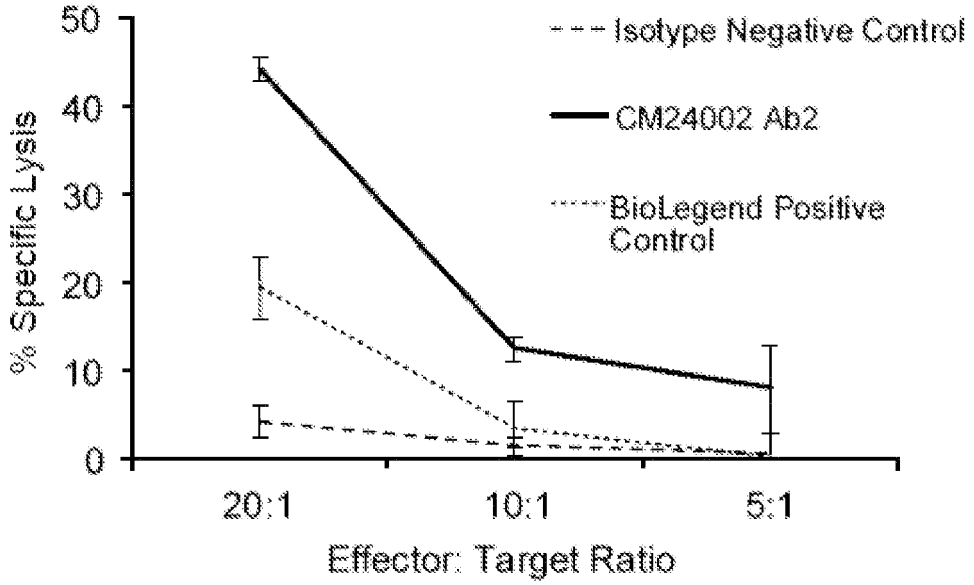

50
40
30
20
10
0
% Specific Lysis
Isotype Negative Control
CM24002 Ab2
BioLegend Positive Control
20:1
10:1
5:1
Effector: Target Ratio

FIG. 30

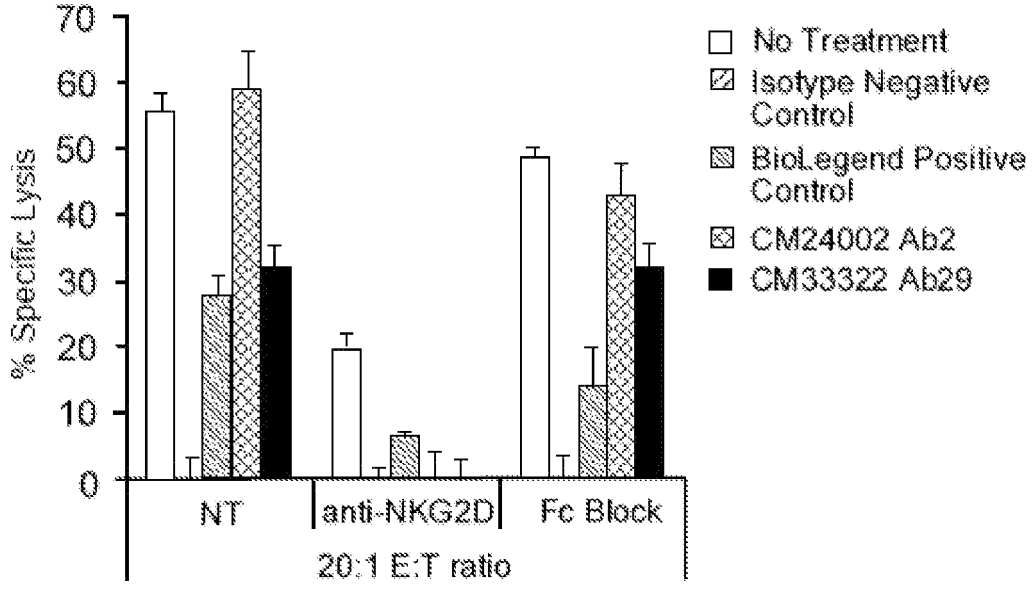

70
60
50
40
30
20
10
0
% Specific Lysis
No Treatment
Isotype Negative Control
BioLegend Positive Control
CM24002 Ab2
CM33322 Ab29
NT
anti-NKG2D
Fc Block
20:1 E:T ratio

FIG. 31

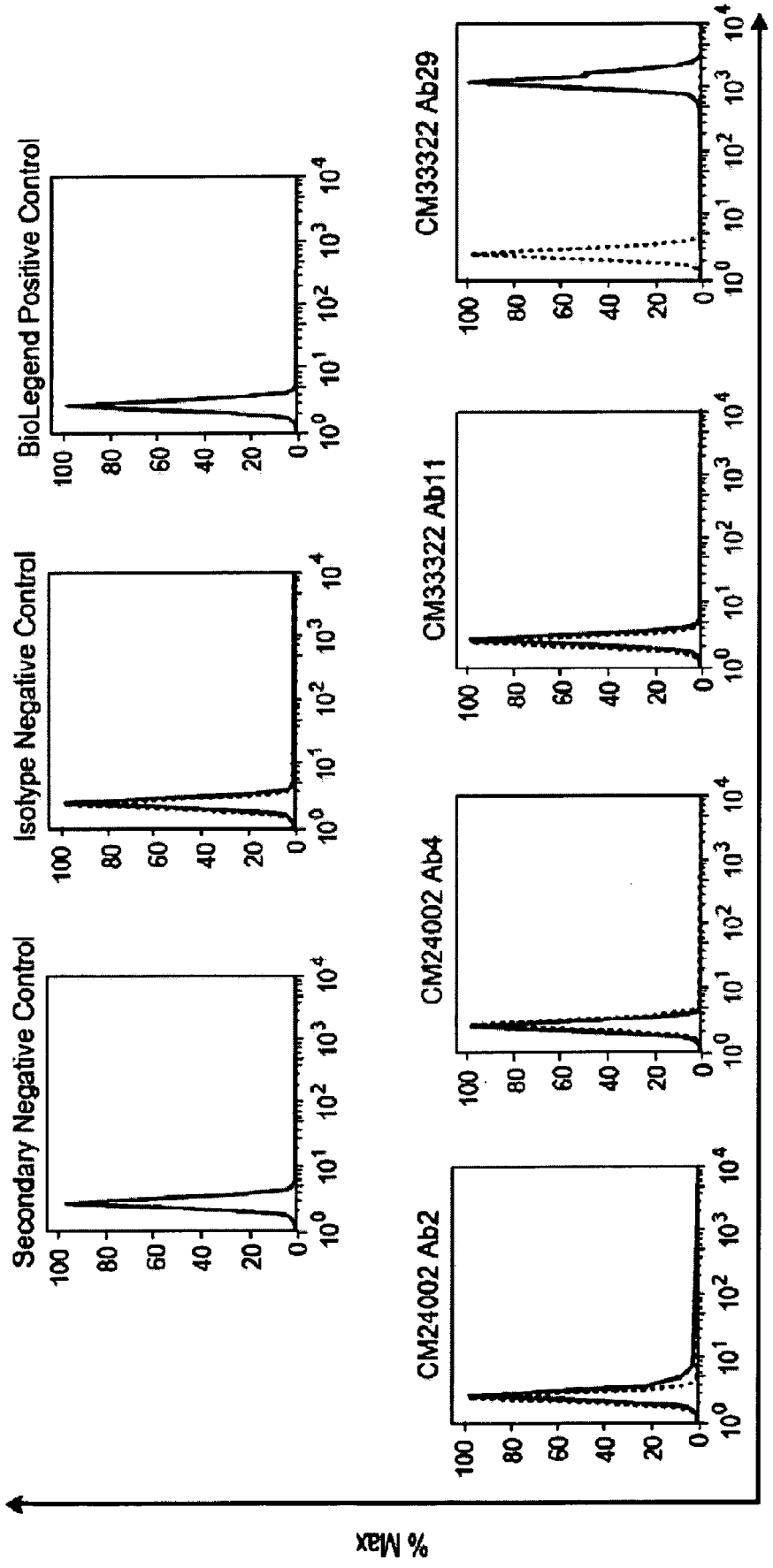

Secondary Negative Control
Isotype Negative Control
BioLegend Positive Control
CM24002 Ab2
CM24002 Ab4
CM33322 Ab11
CM33322 Ab29
% Max
Streptavidin Negative Control
MICA α3 Domain
MICA-α3 DOMAIN-FITC

FIG. 32

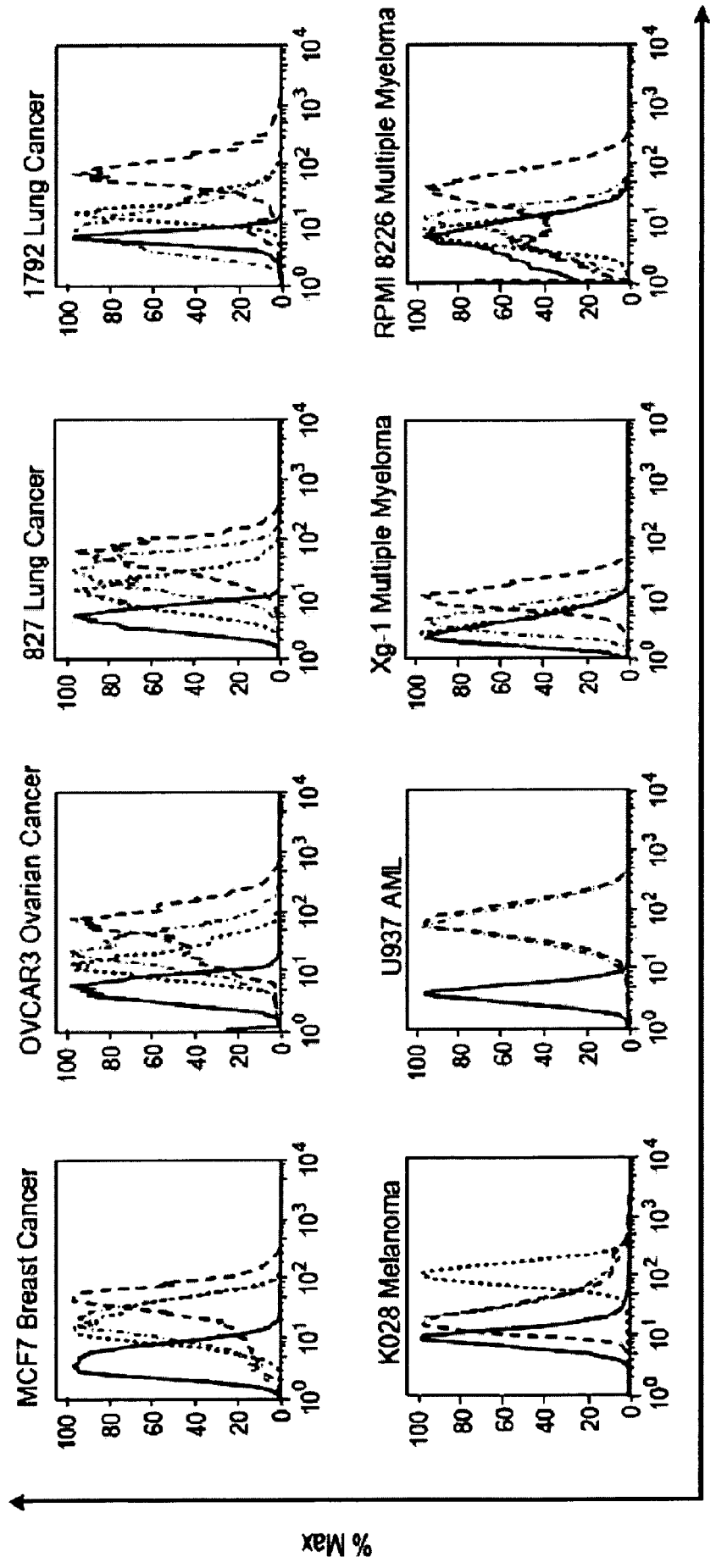

MCF7 Breast Cancer
OVCAR3 Ovarian Cancer
827 Lung Cancer
1792 Lung Cancer
K028 Melanoma
U937 AML
Xg-1 Multiple Myeloma
RPMI 8226 Multiple Myeloma
% Max
MICA-FITC
Unstained Cells
Isotype Negative Control
BioLegend Positive Control
CM24002 Ab2
CM33322 Ab29

FIG. 33

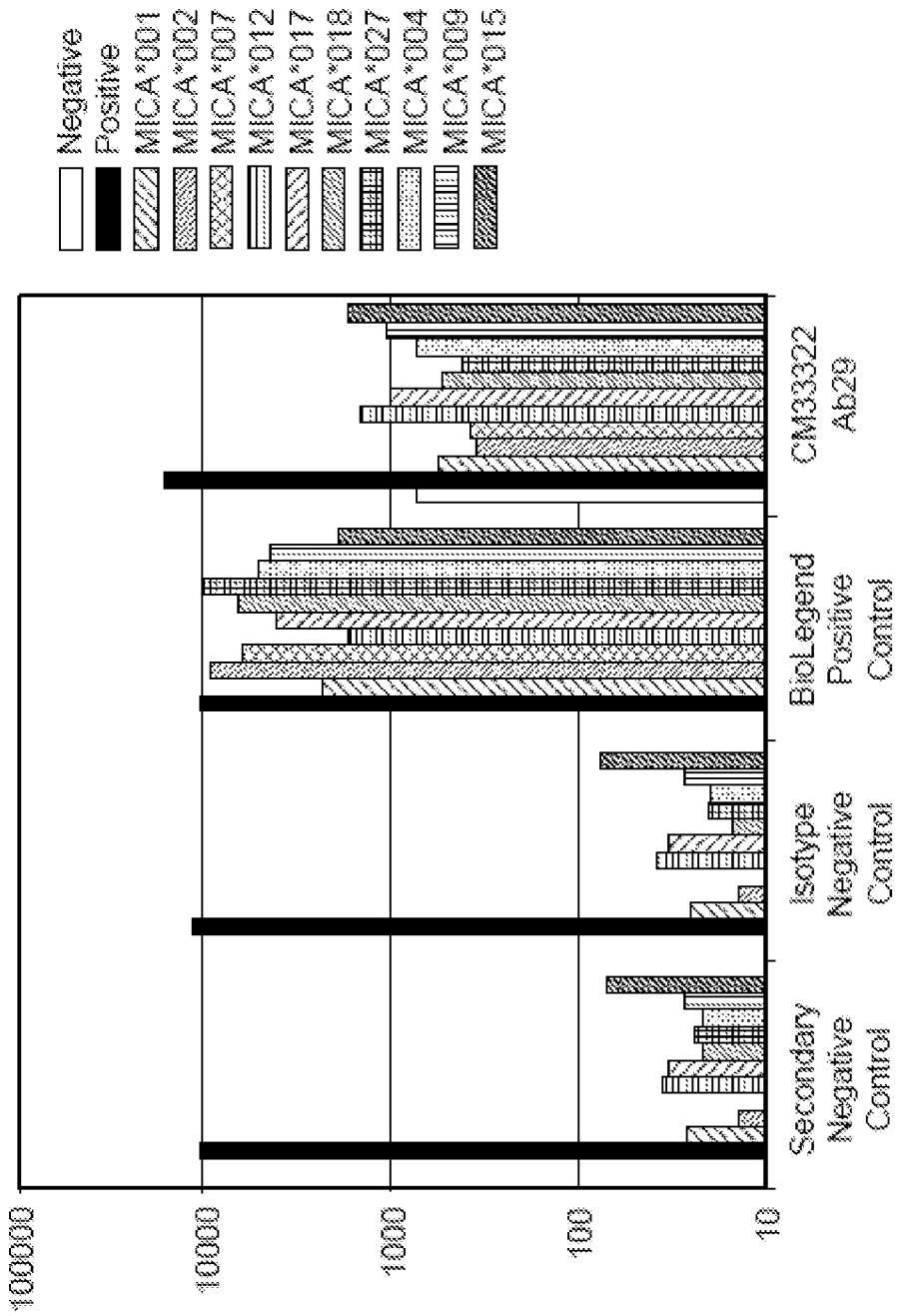

Negative
Positive
MICA*001
MICA*002
MICA*007
MICA*012
MICA*017
MICA*018
MICA*027
MICA*004
MICA*009
MICA*015
100000
10000
1000
100
10
Secondary Negative Control
Isotype Negative Control
BioLegend Positive Control
CM33322 Ab29

FIG. 34

FIG. 35

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTG
GTGAGGCCTTCGGGGACCCTGTCCCTCACTTGCG
CTGTGTCTGGTGGCTCCATCGACTATAGTAATTGGT
GGGGTTGGGTCCGCCAAGTCCCAGGAAAGGGGC
TGGAGTGGATTGGCGAAGTCTATCATACTGGGGC
CACTCATTACAACCCGTCCCTCGAGCGTCGATGCA
TCATTTCAGTGGACAAGTCTAATAACCAGGTCTCC
CTCCAATTGACTTCTGTGACCGCCGCAGACTCGGC
CATCTATTATTGTGCGAGAGAGAGGGGCACGCATT
GTGATGGAAACCGCTGTTATTATGTTTTCTTTGACC
ATTGGGGCCAGGGAATCCCGGTCACCGTCTCCTC
A (SEQ ID NO:149)

FIG. 36

QVQLQESGPGLVRPSGTLSLTCAVSGGSIDYSNWW
GWVRQVPGKGLEWIGEVYHTGATHYNPSLERRCII
SVDKSNNQVSLQLTSVTAADSAIYYCARERGTHCDG
NRCYYVFFDHWGQGIPVTVSS (SEQ ID NO:150)

FIG. 37

GATATTGTGATGACCCAGACTCCACTGTCCTCACC
TGTCACCCTTGGACAACCGGCCTCCATCTCCTGCA
GGTCTAGTGAAAGCCTCGTACATTGGGATGGAAC
CACGTACTTGAGTTGGTTTCACCAGAGGCCAGGC
CAGCCTCCAAGACTCCTAATTTATAAGGTTTCTAAC
CGCTTCTCTGGGGTCCCAGACAGATTCAGTGGCA
GTGGGGCAGGGACAGATTTCACACTGAAAATCAG
CAGGGTGGAAGCTGACGATGTCGGCATTTATTATT
GCATGCAAGCTACACAGTTTCCTCGGACGTTCGG
CCAAGGGACGAAGGTGGAAATCAAACGTAC (SEQ
ID NO:151)

FIG. 38

DIVMTQTPLSSPVTLGQPASISCRSSESLVHWDGTT
YLSWFHQRPGQPPRLLIYKVSNRFSGVPDRFSGSG
AGTDFTLKISRVEADDVGIYYCMQATQFPRTFGQG
TKVEIKR (SEQ ID NO:152)

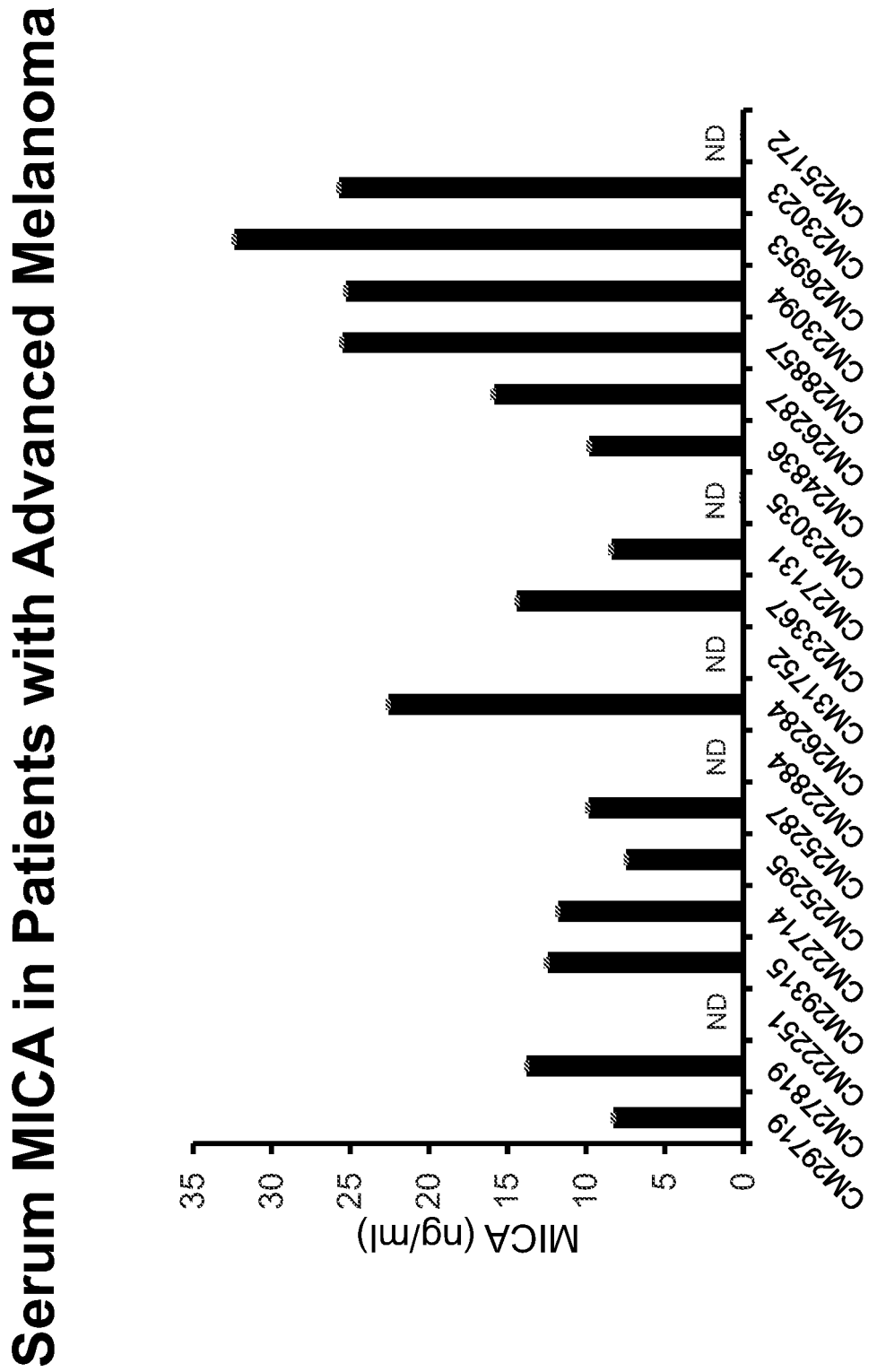

Serum MICA in Patients with Advanced Melanoma
MICA (ng/ml)
0
5
10
15
20
25
30
35
ND
ND
ND
ND
CM297-19
CM27819
CM22251
CM29315
CM22714
CM25295
CM25287
CM22884
CM26284
CM31752
CM23367
CM27131
CM23035
CM24836
CM26287
CM28857
CM23094
CM26953
CM23023
CM25172

FIG. 39

FIG. 40

Patient #	Soluble MICA (ng/ml)	Control Serum	Melanoma Serum	Melanoma Serum + Isotype	Melanoma Serum + CM24002 Ab2	Melanoma Serum + CM33322 Ab29	Melanoma Serum + CM33322 Ab4
CM28857	25.49	63.2	41.8	39.8	**57.5**	62	53.3
CM26953	32.36	61.3	52.9	48.3	**62.1**	66	55.7
CM26284	22.54	76.4	50	50	62.5	71.4	63.6
CM23023	25.69	60.4	28.9	29.7	46.4	44.9	48.3
CM23094	25.27	72.8	50	48.4	**68.9**	75.4	64.2
CM29315	12.42	59.5	38.6	36.4	50	60	**54.3**
CM22714	11.76	62.7	51.5	49.1	**59.7**	**70.8**	71.1
CM23367	14.39	63.9	47.1	53.3	**67.9**	68.1	**67.7**
CM24836	9.8	69.8	54.5	58.1	**67.2**	75.6	**70.2**
CM27819	13.76	59.3	44.2	45.8	57	52.4	**56.9**
CM25287	9.84	60.8	46.7	47.2	63.3	**61**	**58.5**
CM25295	7.43	60.1	46.7	47.2	**60.1**	60.6	**58.8**
CM26287	15.84	67.6	56.7	51.7	74.3	**72.6**	**72.3**
CM27131	8.37	72.3	57.1	62.8	**73.2**	**75.4**	75.6
CM29719	8.25	64	53.4	56.7	68.9	**66.9**	**65.4**

FIG. 41

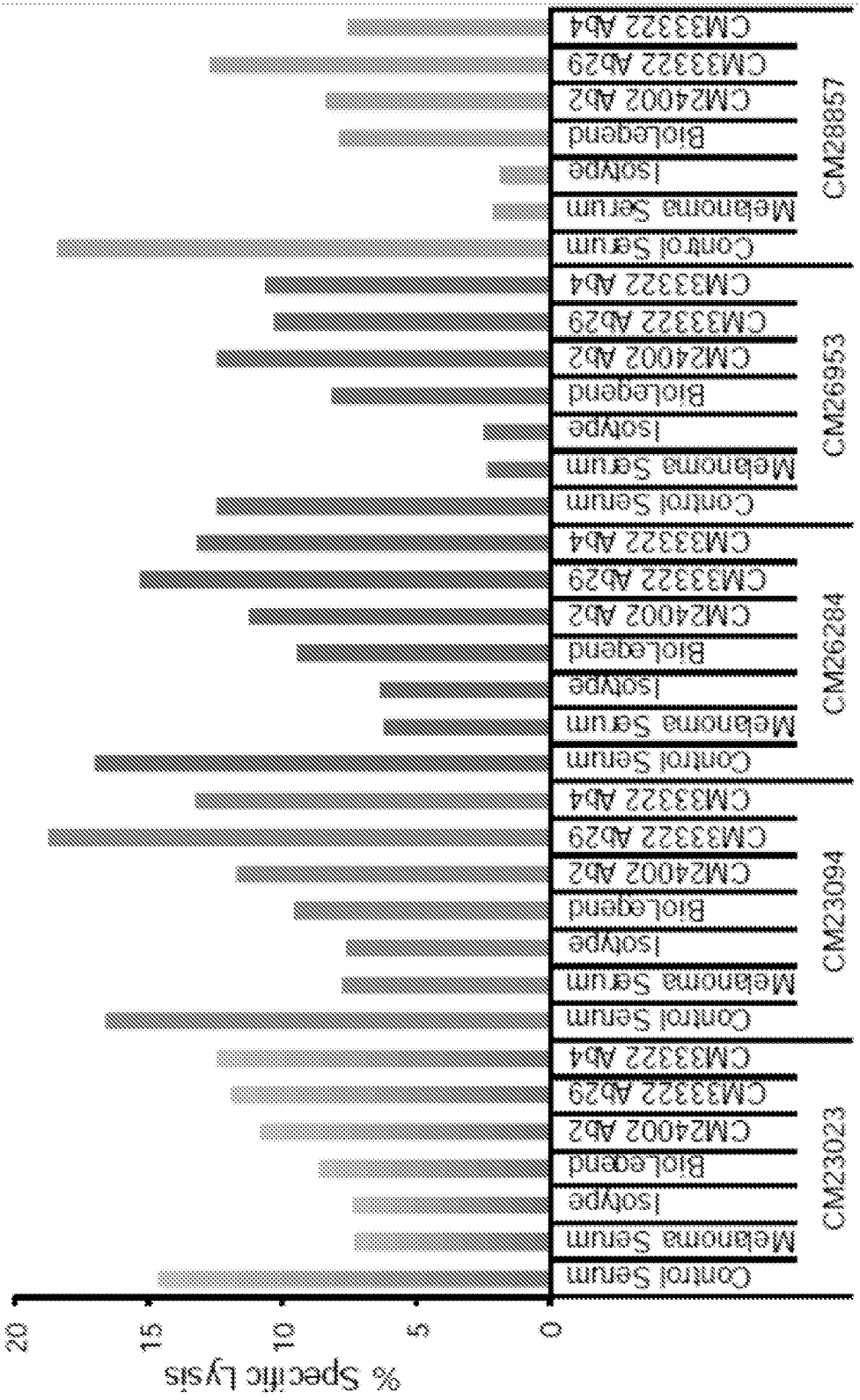

% Specific Lysis
20
15
10
5
0
Control Serum
Melanoma Serum
Isotype
Biolegend
CM24002 Ab2
CM33322 Ab29
CM33322 Ab4
CM23023
Control Serum
Melanoma Serum
Isotype
Biolegend
CM24002 Ab2
CM33322 Ab29
CM33322 Ab4
CM23094
Control Serum
Melanoma Serum
Isotype
Biolegend
CM24002 Ab2
CM33322 Ab29
CM33322 Ab4
CM26284
Control Serum
Melanoma Serum
Isotype
Biolegend
CM24002 Ab2
CM33322 Ab29
CM33322 Ab4
CM26953
Control Serum
Melanoma Serum
Isotype
Biolegend
CM24002 Ab2
CM33322 Ab29
CM33322 Ab4
CM28857

FIG. 42

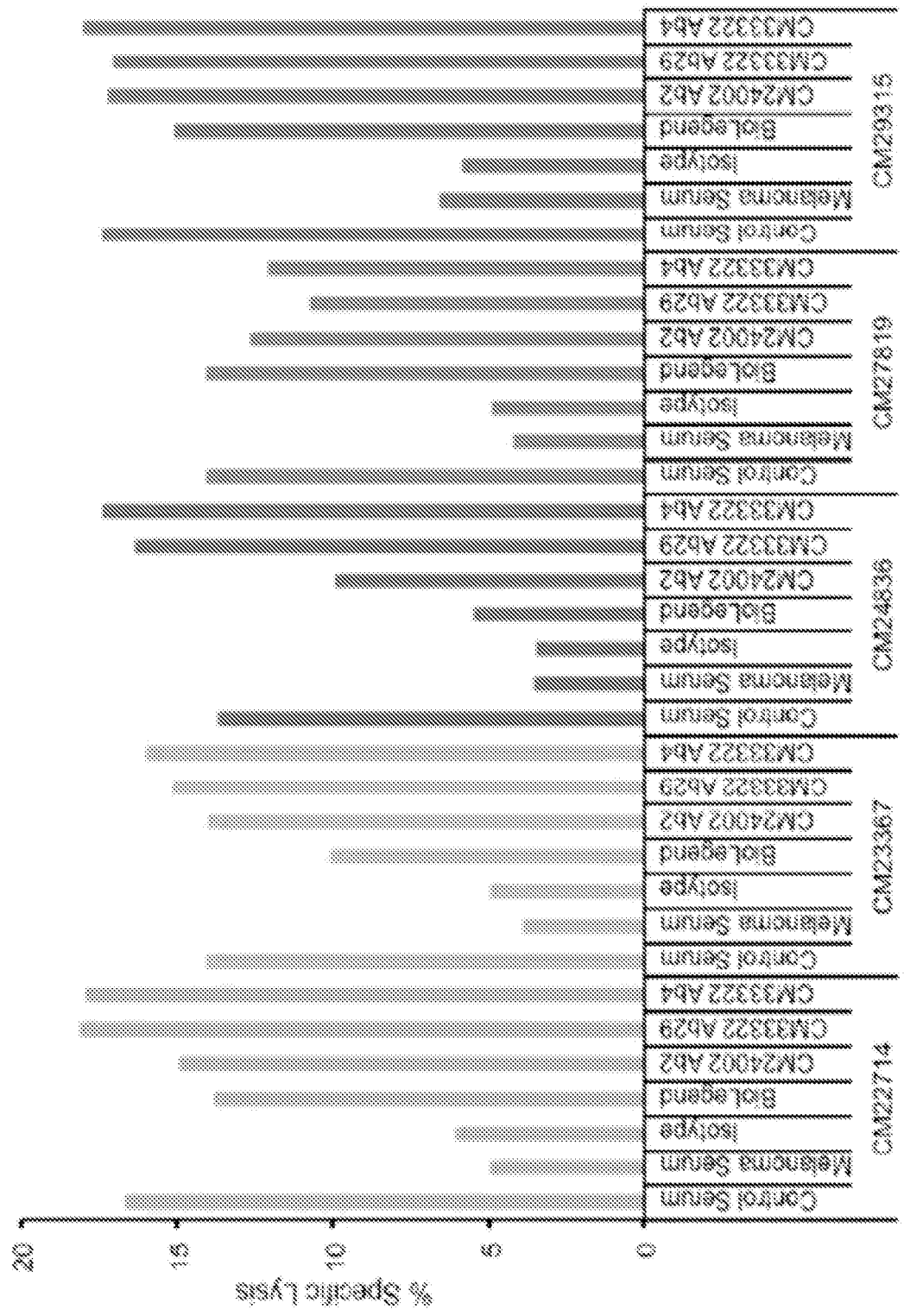

% Specific Lysis
0
20
40
60
80
Control Serum
Melanoma Serum
Isotype
BsLegend
CM24002 Ab2
CM33322 Ab29
CM33322 Ab4
CM22714
CM23367
CM24836
CM27819
CM29316

FIG. 43

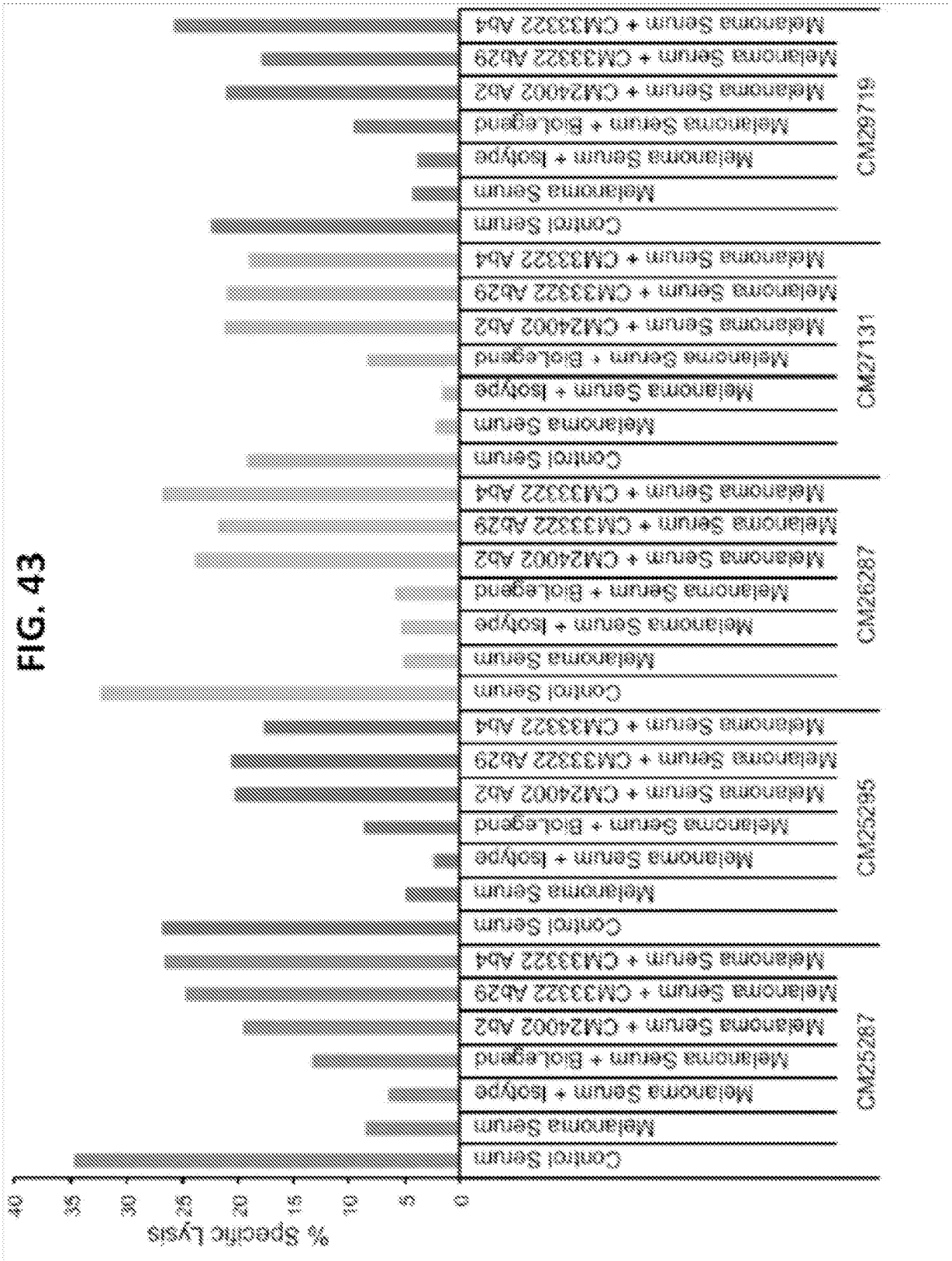
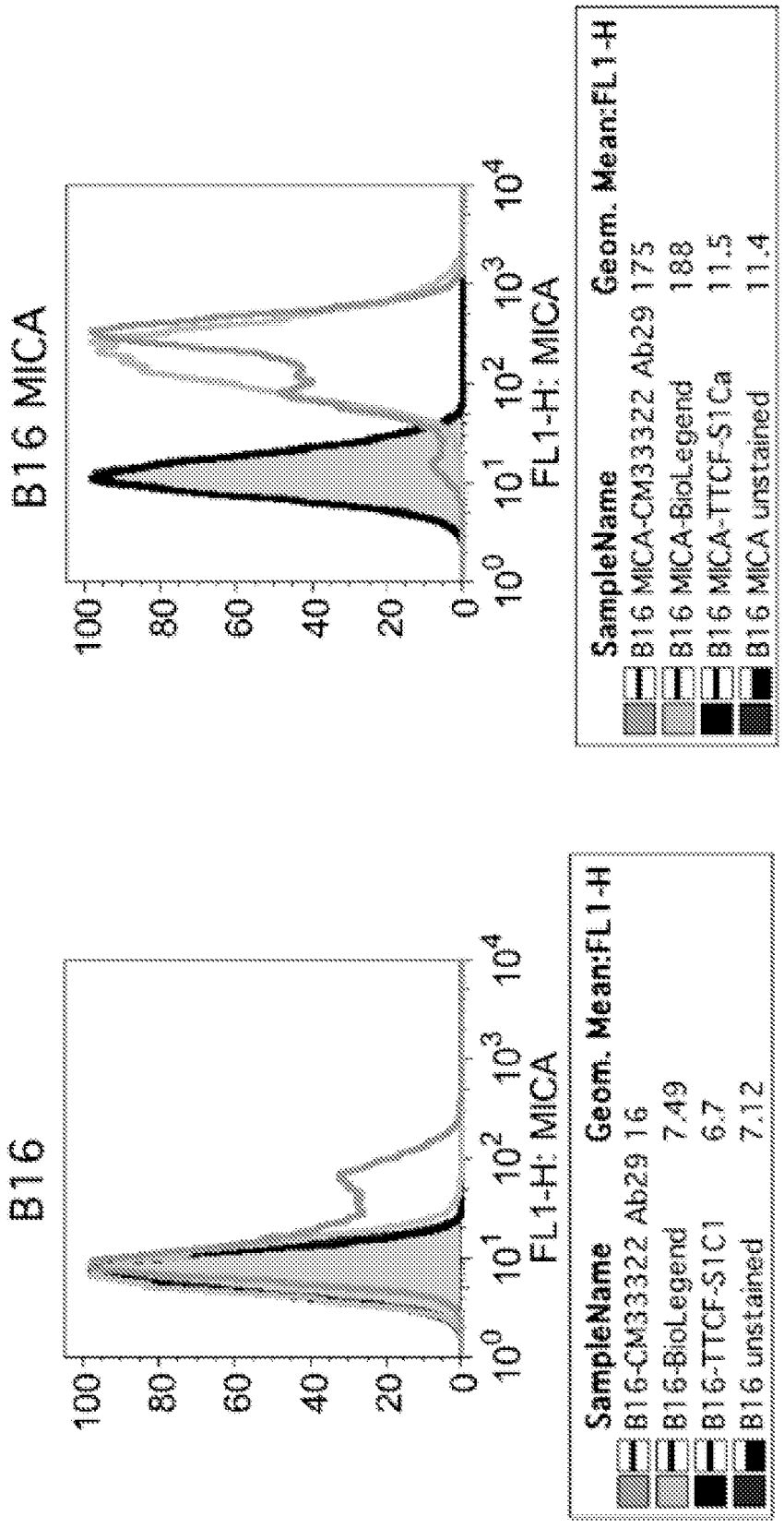

% Specific Lysis
40
35
30
25
20
15
10
5
0
CM252287
CM252295
CM262287
CM271131
CM297119
Control Serum
Melanoma Serum
Melanoma Serum + Isotype
Melanoma Serum + Biolegend
Melanoma Serum + CM24002 Ab2
Melanoma Serum + CM33322 Ab29
Melanoma Serum + CM33322 Ab4

FIG. 44


B16
B16 MICA
100
80
60
40
20
0
10^0 10^1 10^2 10^3 10^4
FL1-H: MICA
SampleName Geom. Mean:FL1-H
B16-CM33322 Ab29 16
B16-BioLegend 7.49
B16-TTCF-S1C1 6.7
B16 unstained 7.12
SampleName Geom. Mean:FL1-H
B16 MICA-CM33322 Ab29 173
B16 MICA-BioLegend 188
B16 MICA-TTCF-S1Ca 11.5
B16 MICA unstained 11.4

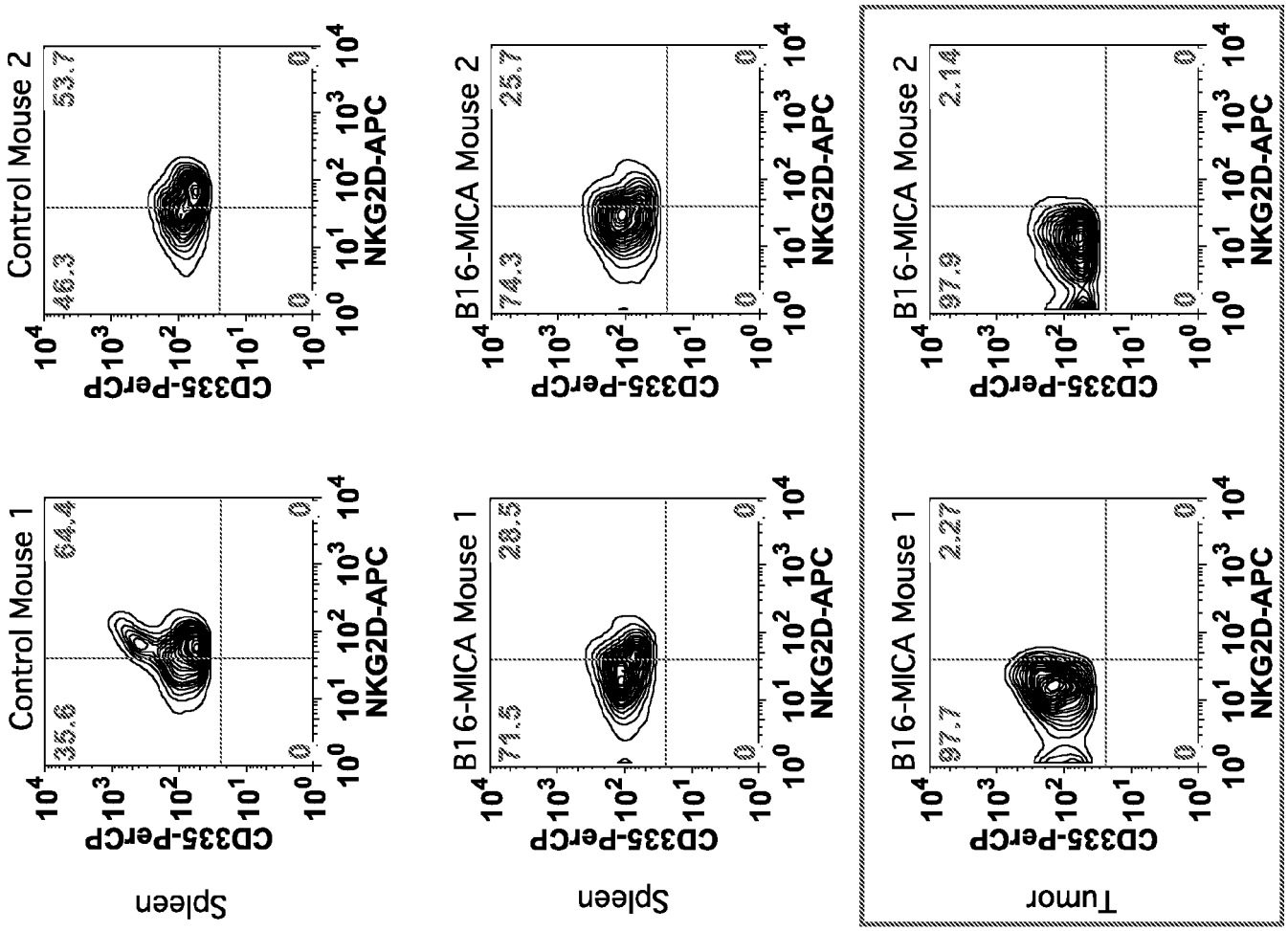

Control Mouse 2
Control Mouse 1
B16-MICA Mouse 2
B16-MICA Mouse 1
Spleen
Spleen
Tumor
CD335-PerCP
NKG2D-APC
46.3
53.7
35.6
64.4
74.3
25.7
71.5
28.5
97.9
2.14
97.7
2.27
0
10^0 10^1 10^2 10^3 10^4

FIG. 45

FIG. 46

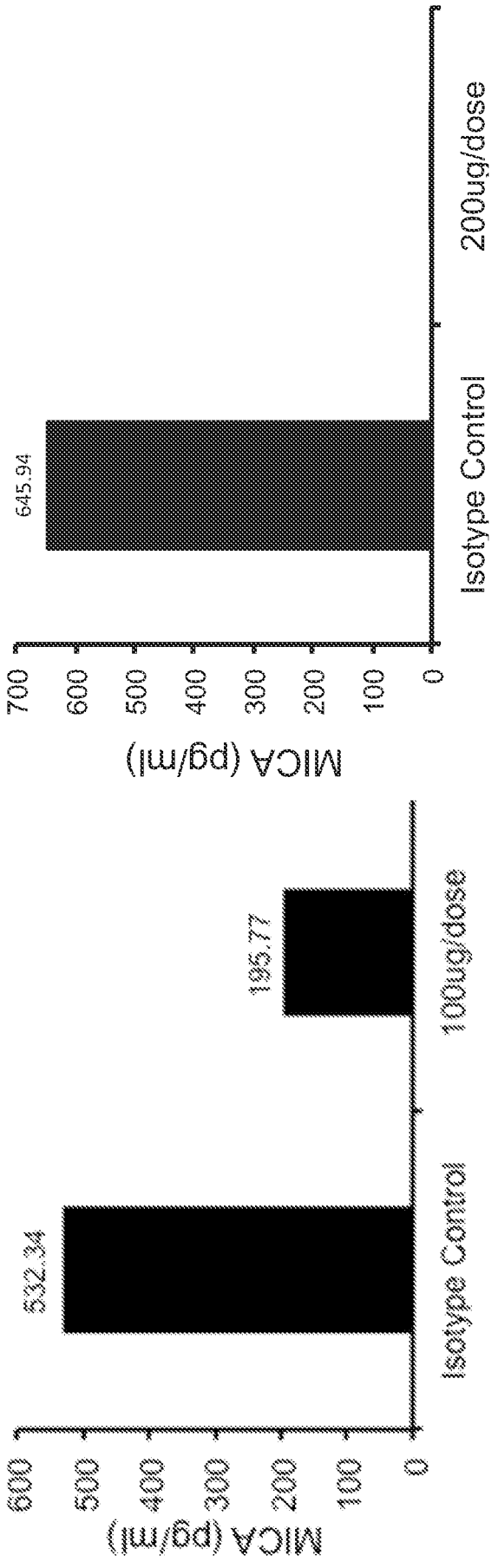

MICA (pg/ml)
600
500
400
300
200
100
0
532.34
195.77
Isotype Control
100ug/dose
MICA (pg/ml)
700
600
500
400
300
200
100
0
645.94
Isotype Control
200ug/dose

FIG. 47

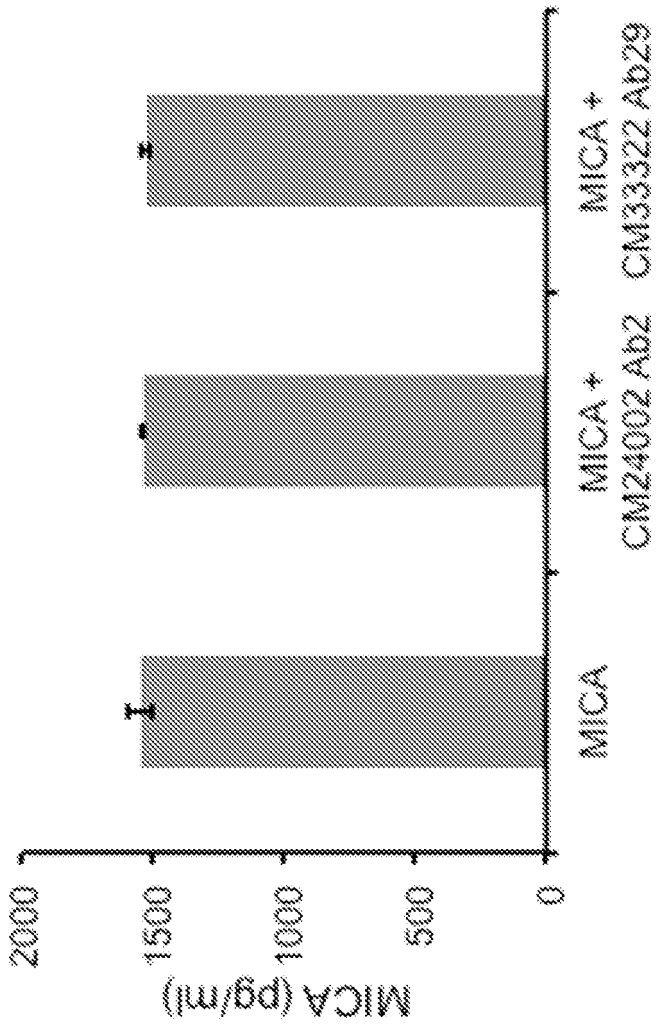

MICA (pg/ml)
2000
1500
1000
500
0
1
2
3
MICA
MICA + CM24002 Ab2
MICA + CM33322 Ab29

FIG. 48

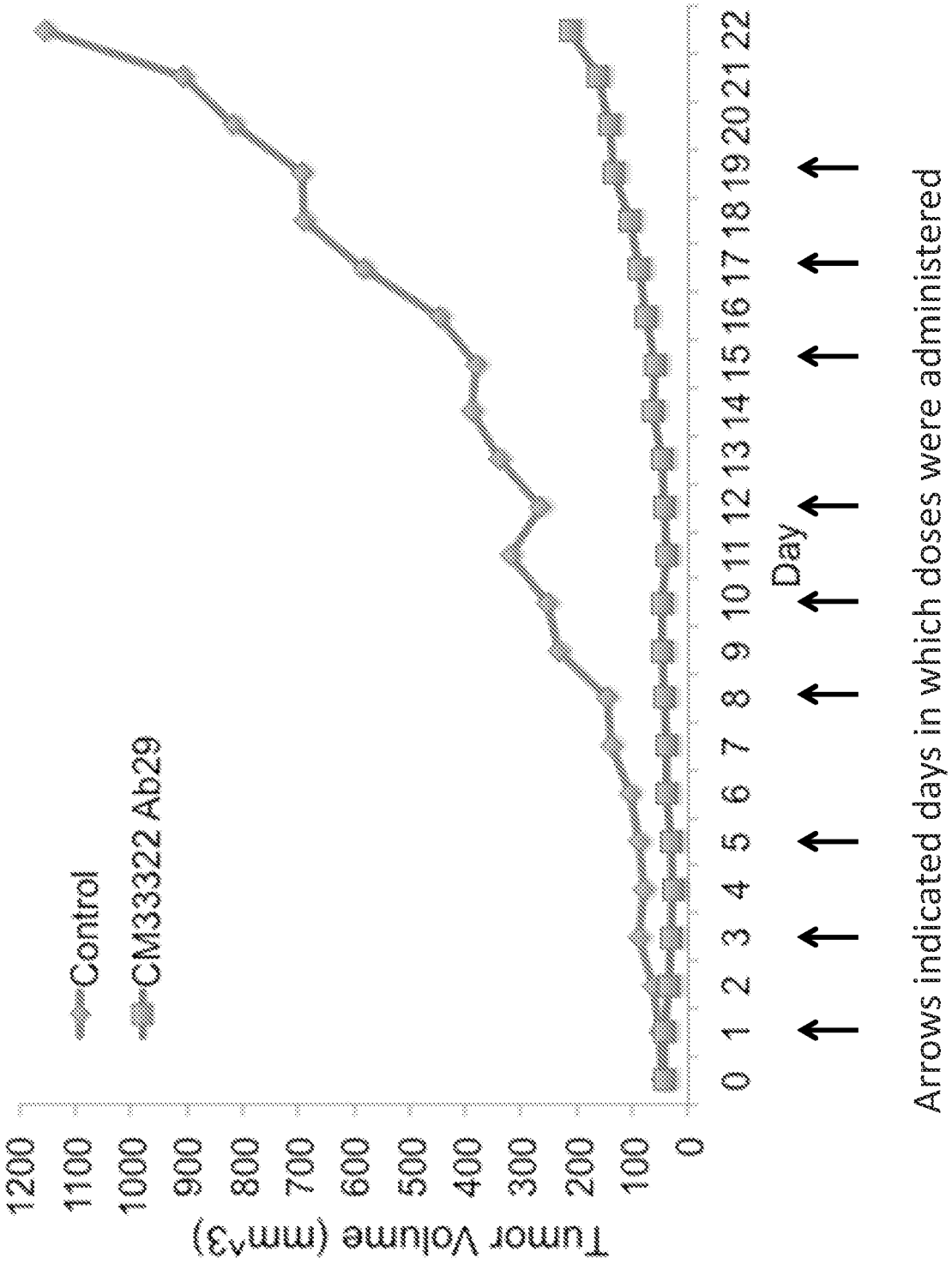
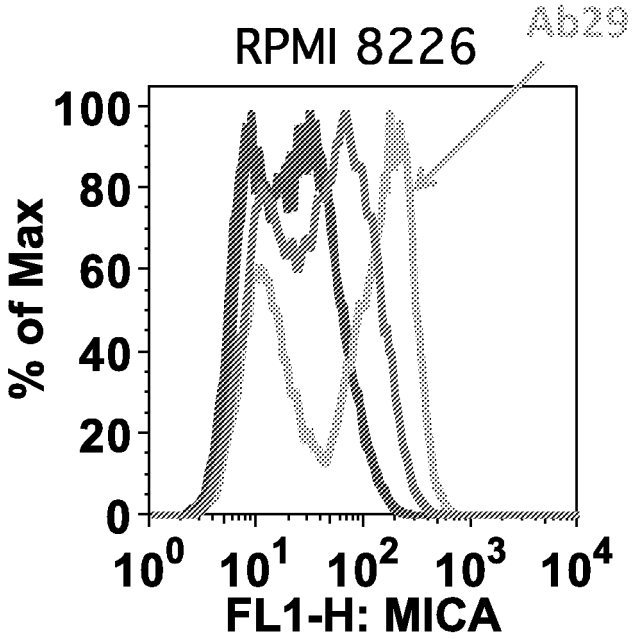
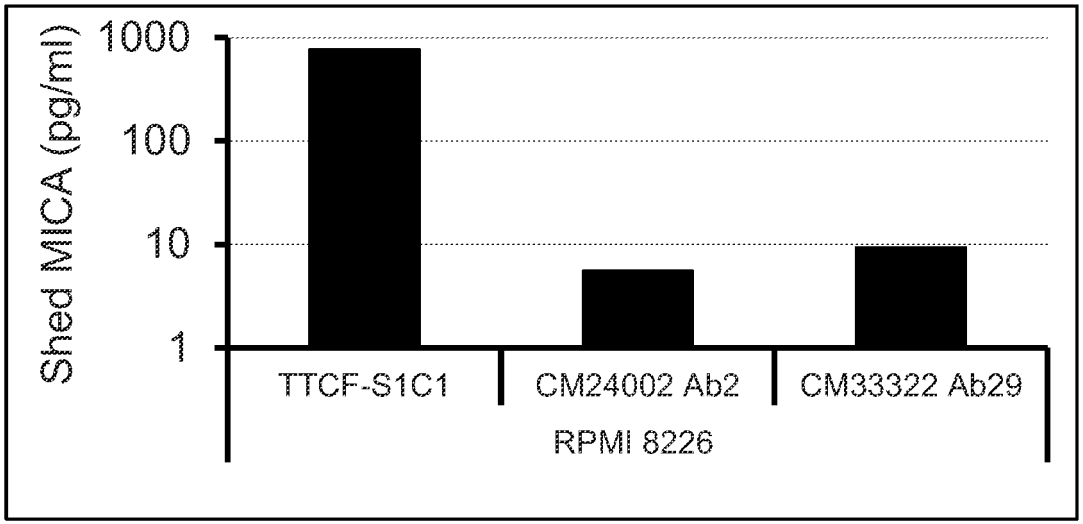

Tumor Volume (mm^3)
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
Control
CM33322 Ab29
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Day
Arrows indicated days in which doses were administered

FIG. 49





RPMI-8226 cells were cultured in the presence of 10ug/ml isotype control antibody, CM33322 Ab29, or CM24002 Ab2. After 48hrs, cells were washed, and MICA surface expression was determined by flow cytometry.

FIG. 50

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTG
AAGAAGCCTGGGTCCTCGGTGAGANTCTCCTGCA
GGGCCTCTGGAGGCTCCTCCACCACCTATGCTTTC
NACTGGGTGCGTCAGGCCCCTGGCCAAGGGCTT
GAGTGGATGGGAGGCATCGTCCCCATCTTTGGTA
CATTGAAATACGCACAGAAGTTCCAAGACAGAGT
CACACTTACCGCGGATAAGTCCACGGGCACAGCC
TACATGGAACTGAACAGCCTGAGATTAGACGACA
CGGCCGTCTATTATTGTGCGAGAGCGATACAATTG
GAAGGACGCCCCTTTGACCACTGGGGCCAGGGA
ACCCAGGTCACCGTCTCCGCA (SEQ ID NO:167)

FIG. 51

QVQLVQSGAEVKKPGSSVRXSCRASGGSSTTYAFX
WVRQAPGQGLEWMGGIVPIFGTLKYAQKFQDRV
TLTADKSTGTAYMELNSLRLDDTAVYYCARAIQLEGR
PFDHWGQGTQVTVSA (SEQ ID NO:168)

FIG. 52

GACATCCAGTTGACCCAGTCTCCATCCTTCCTGTCT
GCATCTGTTGGAGACAGAGTCACCATCACTTGCC
GGGCCAGTCAGGGCATTACCAGTTATTTAGCCTG
GTATCAGCAAAAACCAGGGAAAGCCCCTAAGCTC
CTGATCTATGCTGCATCCGCTTTGCAAAGTGGGGT
CCCATCAAGATTCAGCGGCCGTGGATCTGGGACA
GAGTTCACTCTCACAATCAGCAGCCTGCAGCCT
GAAGATTTTGCAACTTATTACTGTCAACAGGTGAA
TAGGGGTGCCGCGATCACCTTCGGCCACGGGACA
CGGCTGGACATTAAACGT (SEQ ID NO:169)

FIG. 53

DIQLTQSPSFLSASVGDRVTITCRASQGITSYLAWYQ
QKPGKAPKLLIYAASALQSGVPSRFSGRGSGTEFTLTI
SSLQPEDFATYYCQQVNRGAAITFGHGTRLDIKR
(SEQ ID NO:170)

FIG. 54

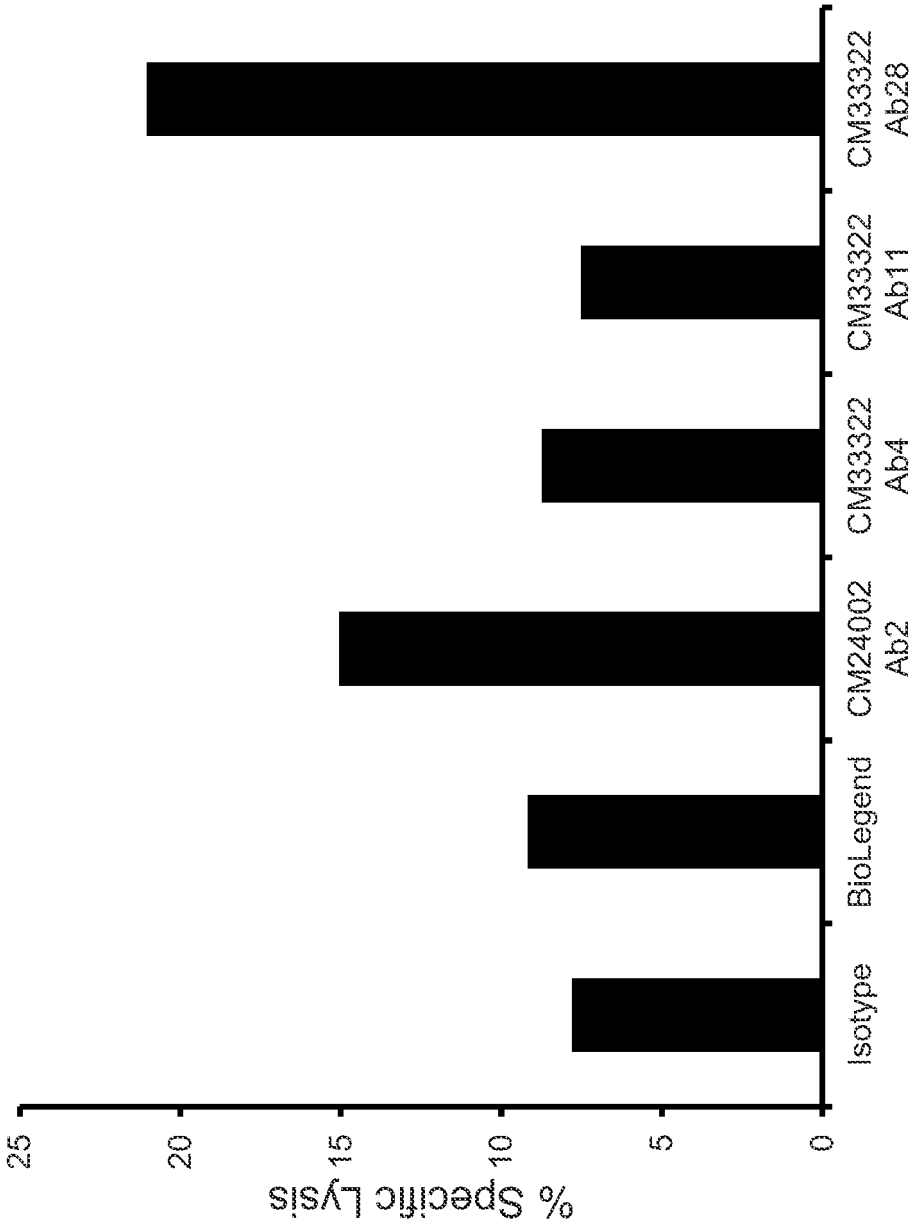

% Specific Lysis
0
5
10
15
20
25
Isotype
BioLegend
CM24002 Ab2
CM33322 Ab4
CM33322 Ab11
CM33322 Ab28

FIG. 55

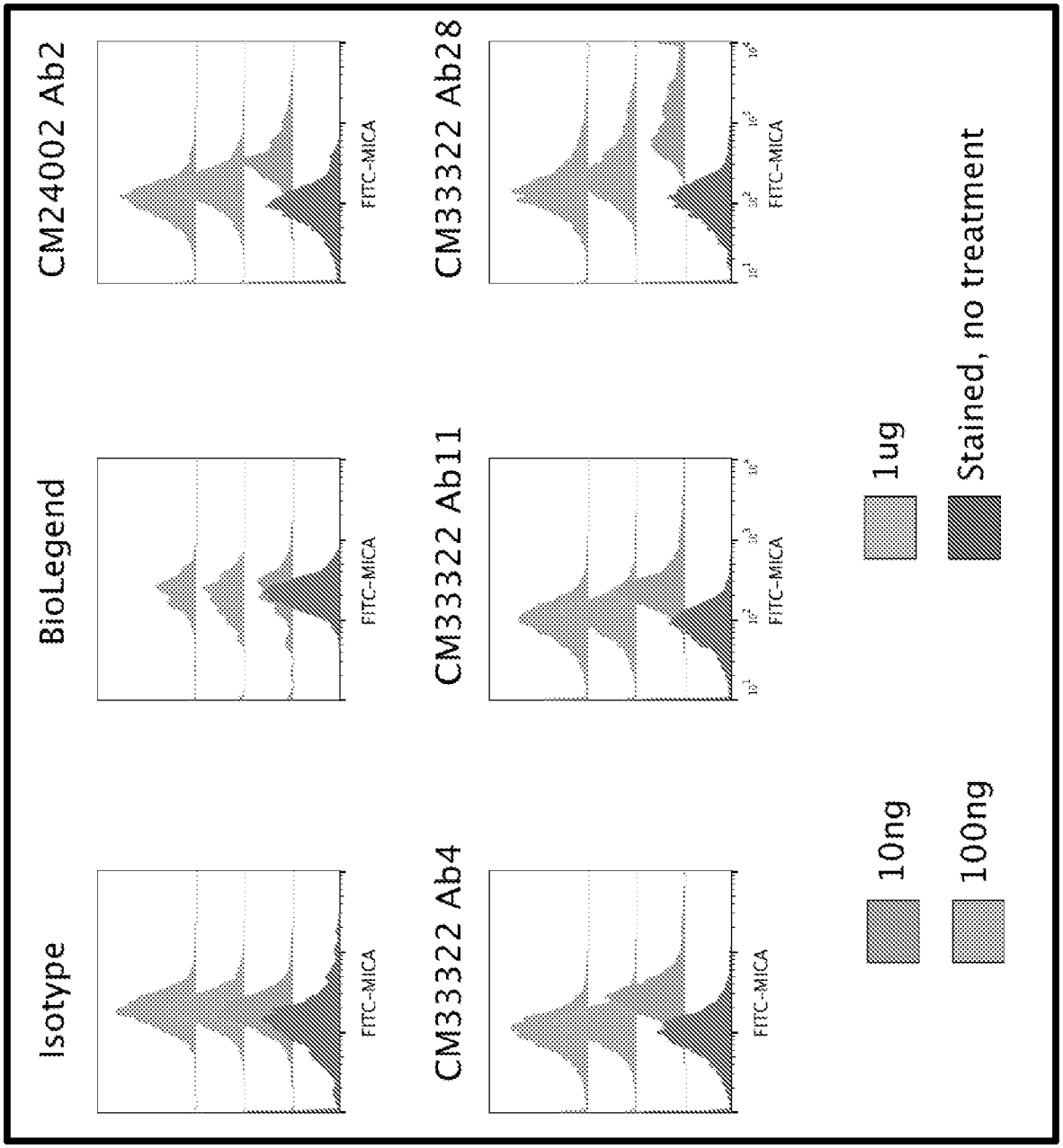

Isotype
BioLegend
CM24002 Ab2
CM33322 Ab4
CM33322 Ab11
CM33322 Ab28
FITC-MICA
10ng
100ng
1ug
Stained, no treatment

FIG. 56

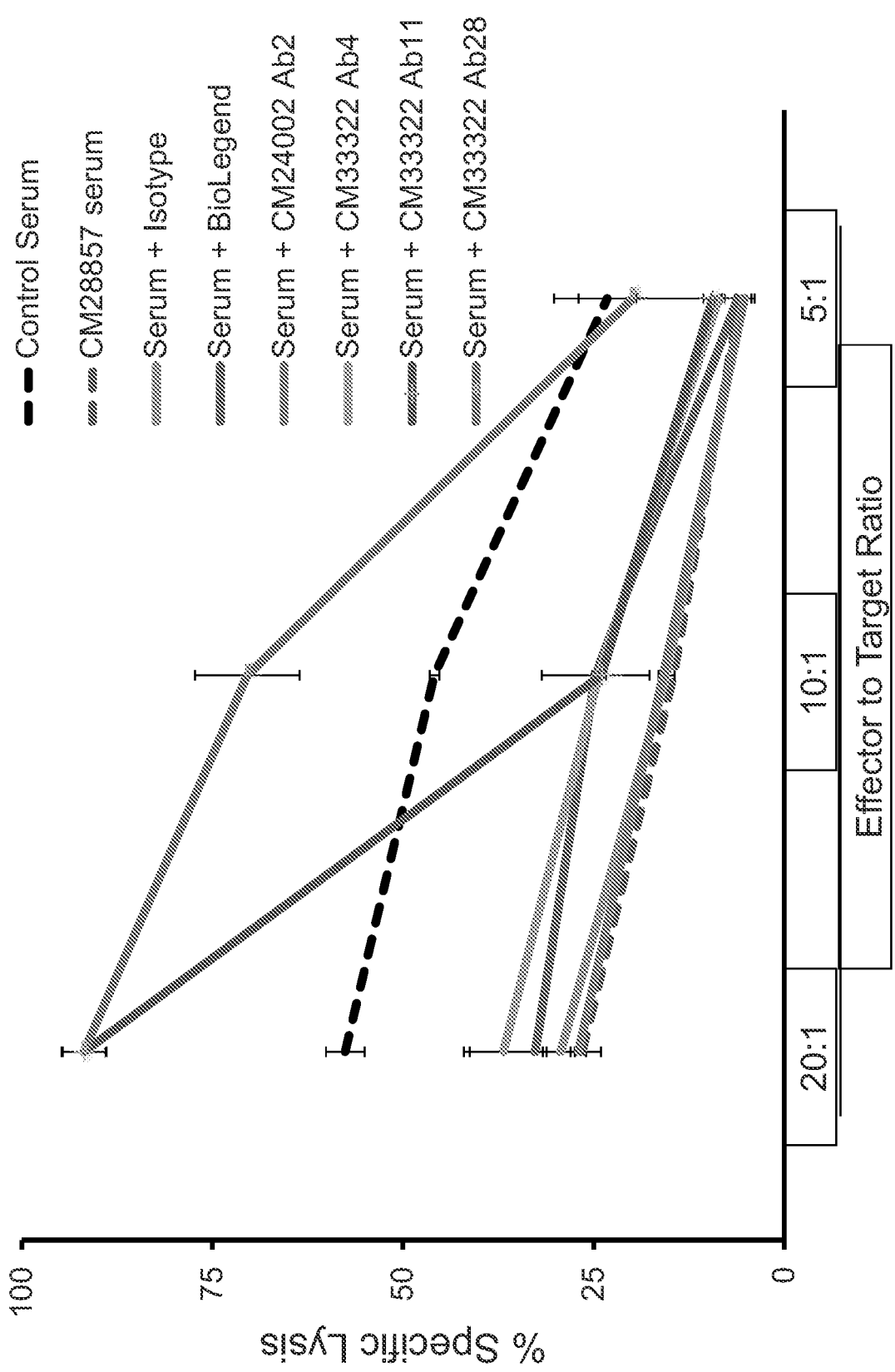
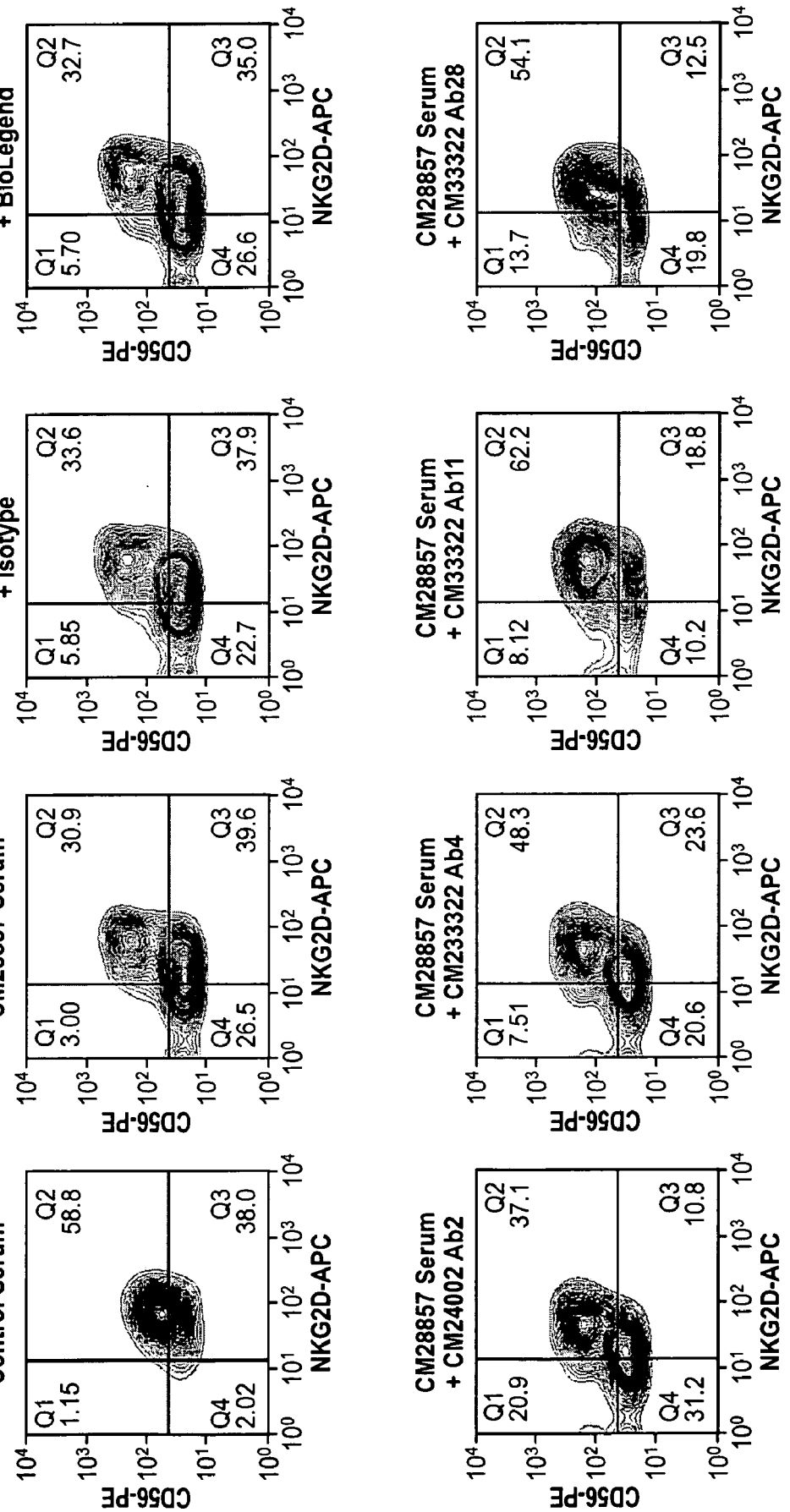

Control Serum
CM28857 serum
Serum + Isotype
Serum + BioLegend
Serum + CM24002 Ab2
Serum + CM33322 Ab4
Serum + CM33322 Ab11
Serum + CM33322 Ab28
% Specific Lysis
100
75
50
25
0
20:1
10:1
5:1
Effector to Target Ratio

FIG. 57



1:10 dilution of the CM28857 serum
All antibodies tested at 10 ug/ml

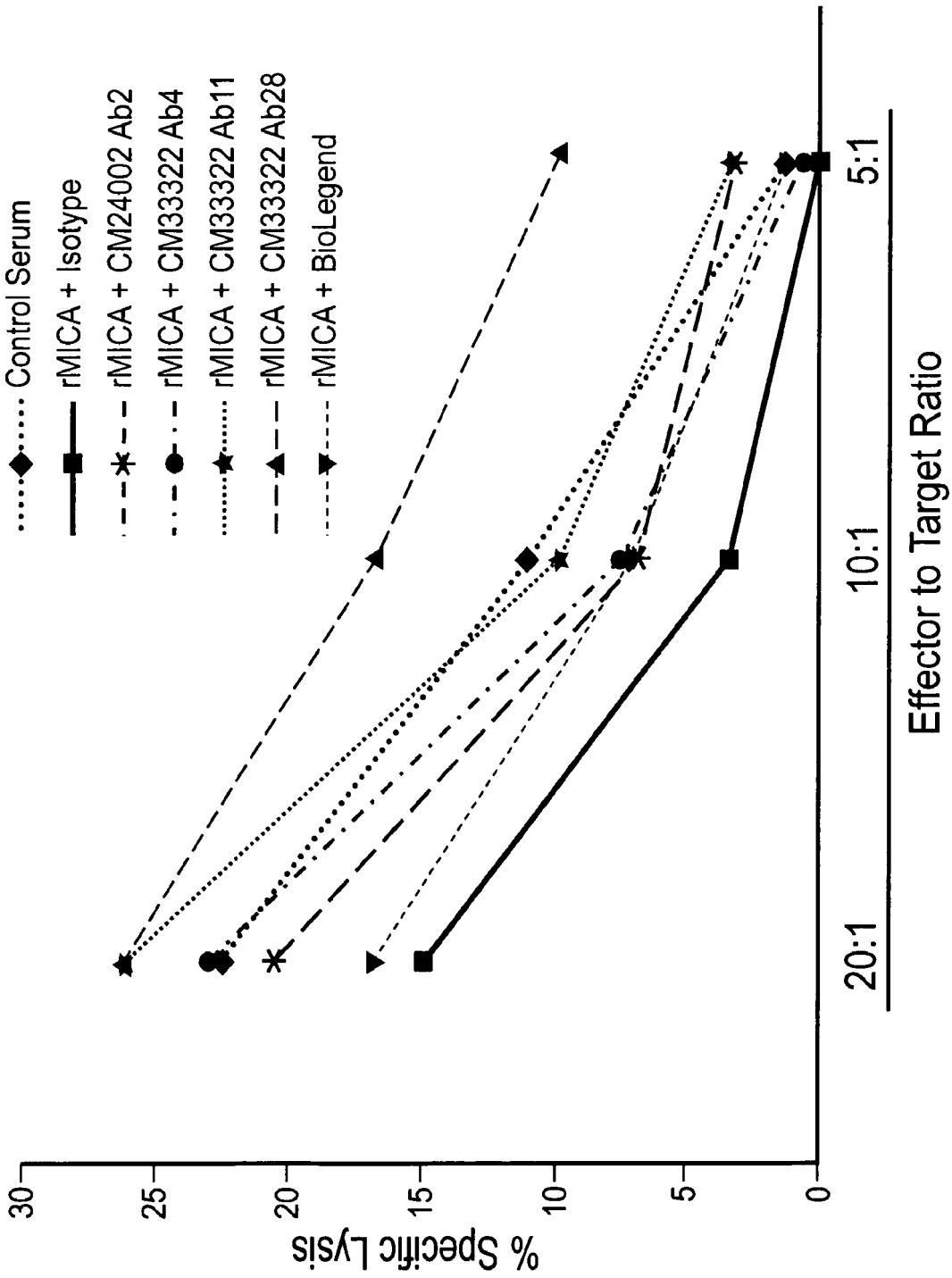
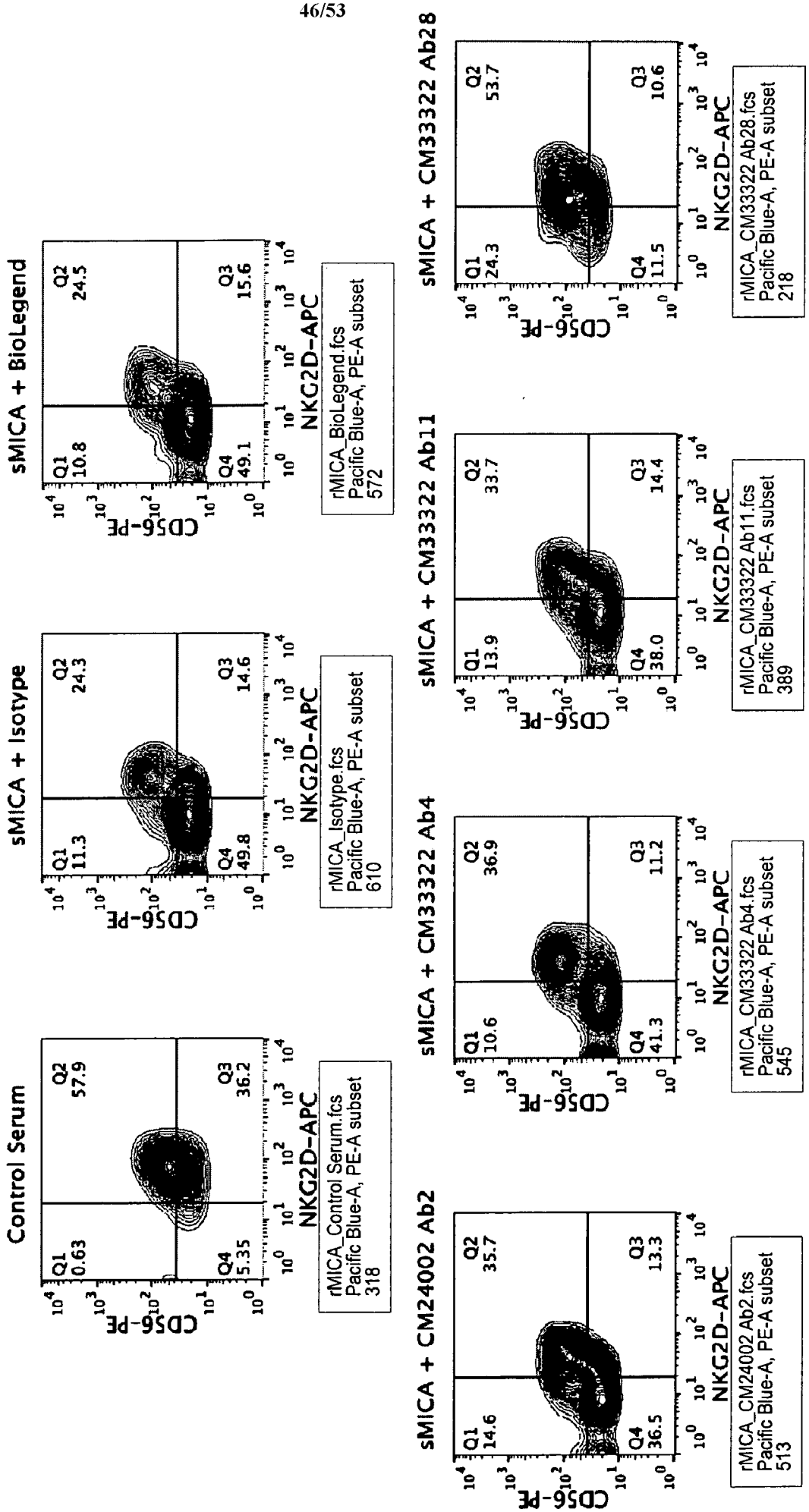

Control Serum
rMICA + Isotype
rMICA + CM24002 Ab2
rMICA + CM33322 Ab4
rMICA + CM33322 Ab11
rMICA + CM33322 Ab28
rMICA + BioLegend
% Specific Lysis
0
5
10
15
20
25
30
20:1
10:1
5:1
Effector to Target Ratio

FIG. 58

FIG. 59


Control Serum
Q1 0.63
Q2 57.9
Q4 5.35
Q3 36.2
rMICA_Control Serum.fcs
Pacific Blue-A, PE-A subset
318
sMICA + Isotype
Q1 11.3
Q2 24.3
Q4 49.8
Q3 14.6
rMICA_Isotype.fcs
Pacific Blue-A, PE-A subset
610
sMICA + BioLegend
Q1 10.8
Q2 24.5
Q4 49.1
Q3 15.6
rMICA_BioLegend.fcs
Pacific Blue-A, PE-A subset
572
sMICA + CM24002 Ab2
Q1 14.6
Q2 35.7
Q4 36.5
Q3 13.3
rMICA_CM24002 Ab2.fcs
Pacific Blue-A, PE-A subset
513
sMICA + CM33322 Ab4
Q1 10.6
Q2 36.9
Q4 41.3
Q3 11.2
rMICA_CM33322 Ab4.fcs
Pacific Blue-A, PE-A subset
545
sMICA + CM33322 Ab11
Q1 13.9
Q2 33.7
Q4 38.0
Q3 14.4
rMICA_CM33322 Ab11.fcs
Pacific Blue-A, PE-A subset
389
sMICA + CM33322 Ab28
Q1 24.3
Q2 53.7
Q4 11.5
Q3 10.6
rMICA_CM33322 Ab28.fcs
Pacific Blue-A, PE-A subset
218
CD56-PE
NKG2D-APC

Epitope of CN33322 Ab29

HSLRYNLTVLSWDGSVQSGFLAEVHLDGQPFLRYDR
QKCRAKPQGQWAEDVLGNKTWDRETRDLTGNGKD
LRMTLAHIKDQKEGLHSLQEIRVCEIHEDNSTRSSQH
FYYDGELFLSQNVETEEWTVPQSSRAQTLAMNVRN
FLKEDAMKTKTHYHAMHADCLQELRRYLESSVVLR
RTVPPMVNVTRSEASEGNITVTCRASSFYPRNITLTW
RQDGVSLSHDTQQWGDVLPDGNGTYQTWVATRIC
QGEEQRFTCYMEHSGNHSTHPVPSGKVLVLQSHWQ
TFHVSAVAAAAAAIFVIIIFYVRCCKKKTSAAEGPELV
SLQVLDQHPVGTSDHRDATQLGFQPLMSALGSTGST
EGA

FIG. 60A

Epitope of CM33322 Ab4

FIG. 60B

HSLRYNLTVLSWDGSVQSGFLAEVHLDGQPFLRYDRQKCRAKPQGQWAEDVLGNKTWDRETRDLTGNGKDLRM
TLAHIKDQKEGLHSLQEIRVCEIHEDNSTRSSQHFYYDGELFLSQNVETEEWTVPQSSRAQTLAMNVRNFLKEDAM
KTKTHYHAMHADCLQELRRYLESSVVLRRTVPPMVNVTRSEASEGNITVTCRASSFYPRNITLTWRQDGVSLSHDT
QQWGDVLPDGNGTYQTWVATRICQGEEQRFTCYMEHSGNHSTHPVPSGKVLVLQSHWQTFHVSAVAAAAAAIF
VIIIFYVRCCKKKTSAAEGPELVSLQVLDQHPVGTSDHRDATQLGFQPLMSALGSTGSTEGA

Epitope of CM33322 Ab11

FIG. 60C

HSLRYNLTVLSWDGSVQSGFLAEVHLDGQPFLRYDRQKCRAKPQGQWAEDVLGNKTWDRETRDLTGNGKDLR
MTLAHIKDQKEGLHSLQEIRVCEIHEDNSTRSSQHFYYDGELFLSQNVETEEWTVPQSSRAQTLAMNVRNFLKED
AMKTKTHYHAMHADCLQELRRYLESSVVLRRTVPPMVNVTRSEASEGNITVTCRASSFYPRNITLTWRQDGVSLS
HDTQQWGDVLPDGNGTYQTWVATRICQGEEQRFTCYMEHSGNHSTHPVPSGKVLVLQSHWQTFHVSAVAAAA
AAIFVIIIFYVRCCKKKTSAAEGPELVSLQVLDQHPVGTSDHRDATQLGFQPLMSALGSTGSTEGA

Epitope of CM33322 Ab28

FIG. 60D

HSLRYNLTVLSWDGSVQSGFLAEVHLDGQPFLRYDRQKCRAKPQGQWAEDVLGNKTWDRETRDLTGNGKDLR
MTLAHIKDQKEGLHSLQEIRVCEIHEDNSTRSSQHFYYDGELFLSQNVETEEWTVPQSSRAQTLAMNVRNFLKED
AMKTKTHYHAMHADCLQELRRYLESSVVLRRTVPPMVNVTRSEASEGNITVTCRASSFYPRNITLTWRQDGVSLS
HDTQQWGDVLPDGNGTYQTWVATRICQGEEQRFTCYMEHSGNHSTHPVPSGKVLVLQSHWQTFHVSAVAAAA
AAIFVIIIFYVRCCKKKTSAAEGPELVSLQVLDQHPVGTSDHRDATQLGFQPLMSALGSTGSTEGA


ERp5 binding site
Ab28 epitope
CM33322 Ab4
CM33322 Ab29
ERp5 binding site

FIG. 61

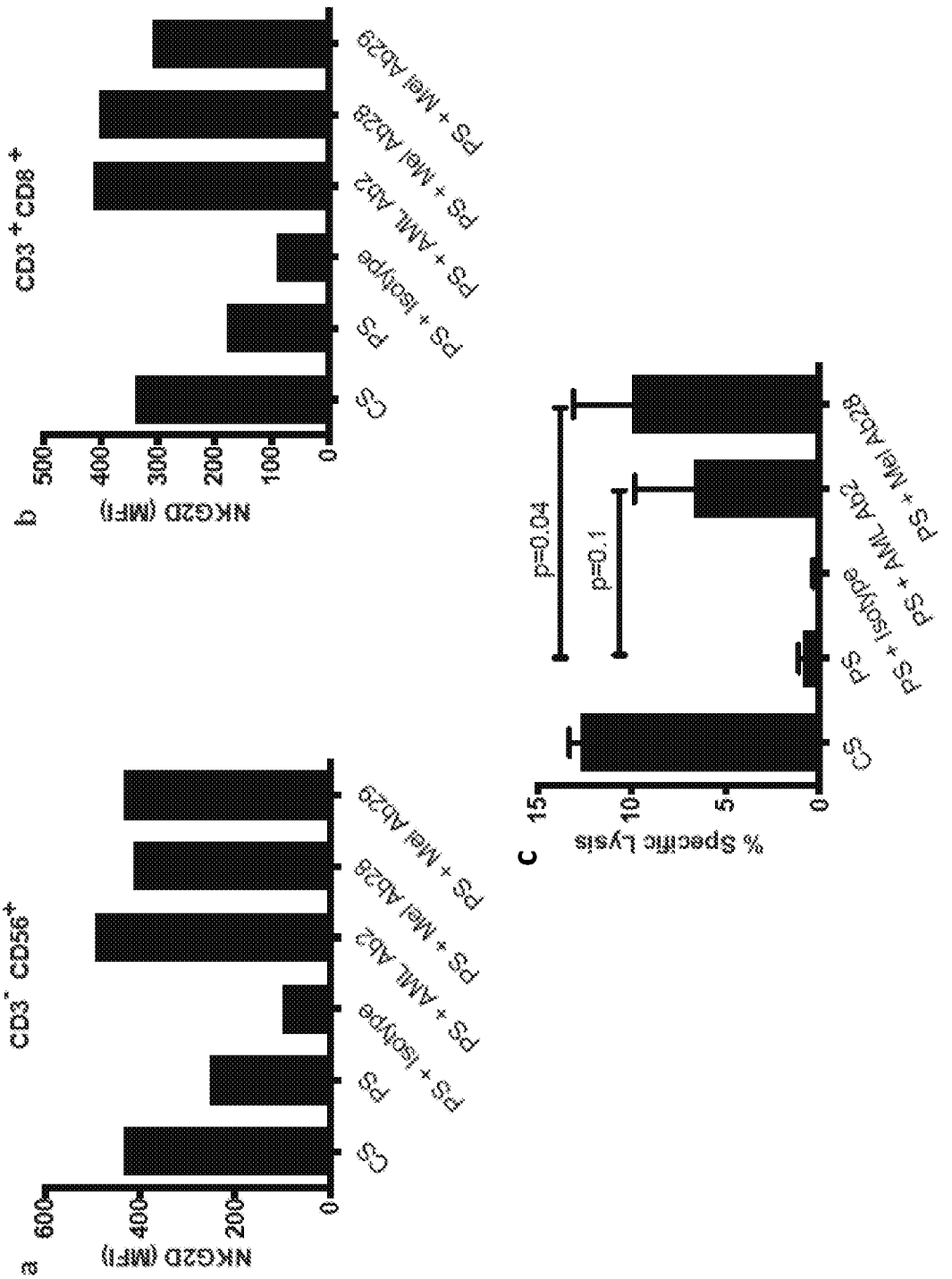

a
NKG2D (MFI)
600
400
200
0
CD3+ CD56+
CS
PS
PS + Isotype
PS + AML Ab2
PS + Mel Ab28
PS + Mel Ab29
b
NKG2D (MFI)
500
400
300
200
100
0
CD3+ CD8+
CS
PS
PS + Isotype
PS + AML Ab2
PS + Mel Ab28
PS + Mel Ab29
c
% Specific Lysis
15
10
5
0
p=0.04
p=0.1
CS
PS
PS + Isotype
PS + AML Ab2
PS + Mel Ab28

FIG. 62

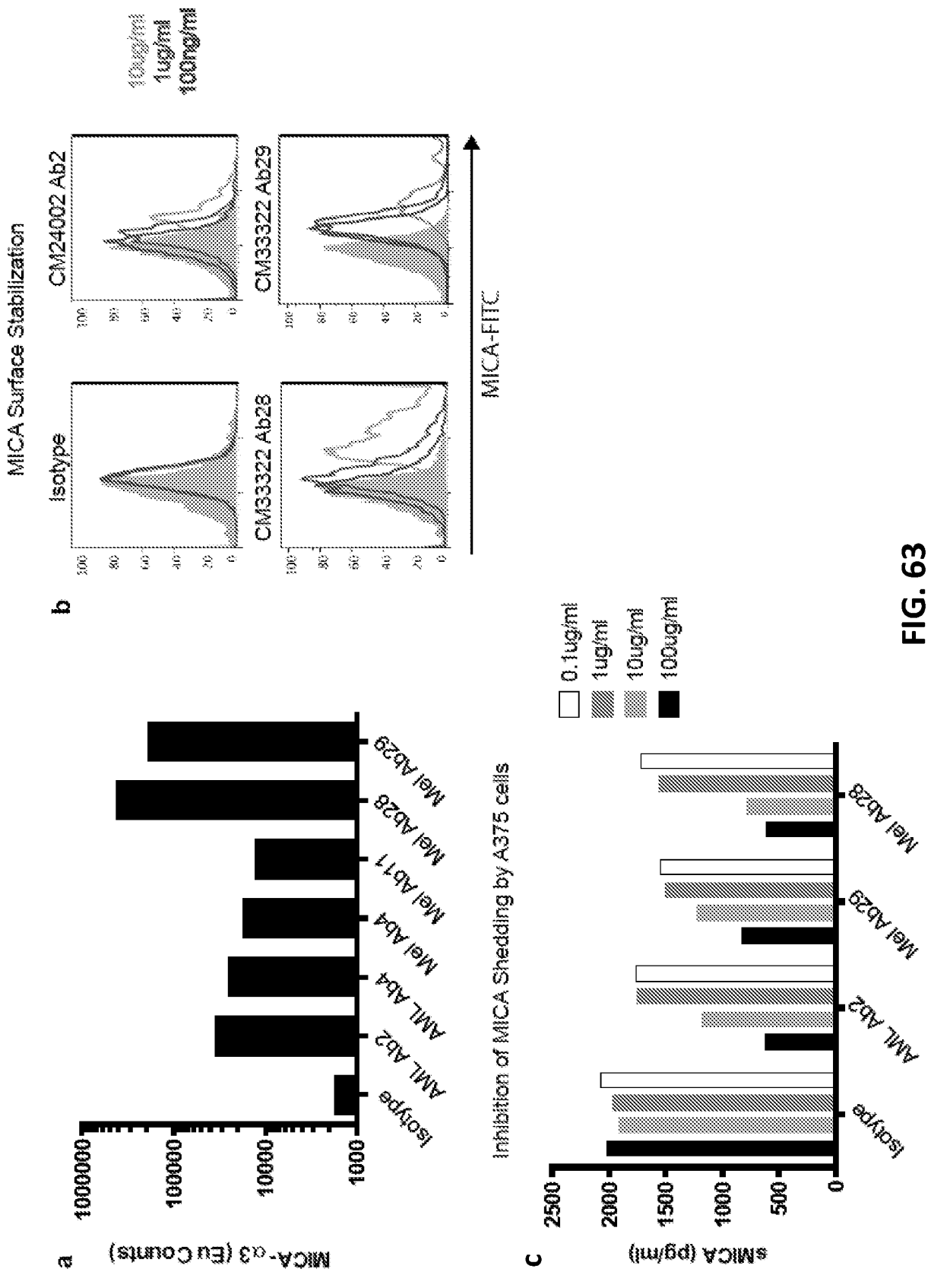

a
MICA-α3 (Eu Counts)
1000000
100000
10000
1000
Isotype
AML Ab2
AML Ab4
Mel Ab4
Mel Ab11
Mel Ab28
Mel Ab29
b
MICA Surface Stabilization
Isotype
CM24002 Ab2
CM33322 Ab28
CM33322 Ab29
10ug/ml
1ug/ml
100ng/ml
MICA-FITC
c
Inhibition of MICA Shedding by A375 cells
0.1ug/ml
1ug/ml
10ug/ml
100ug/ml
sMICA (pg/ml)
2500
2000
1500
1000
500
0
Isotype
AML Ab2
Mel Ab29
Mel Ab28

FIG. 63

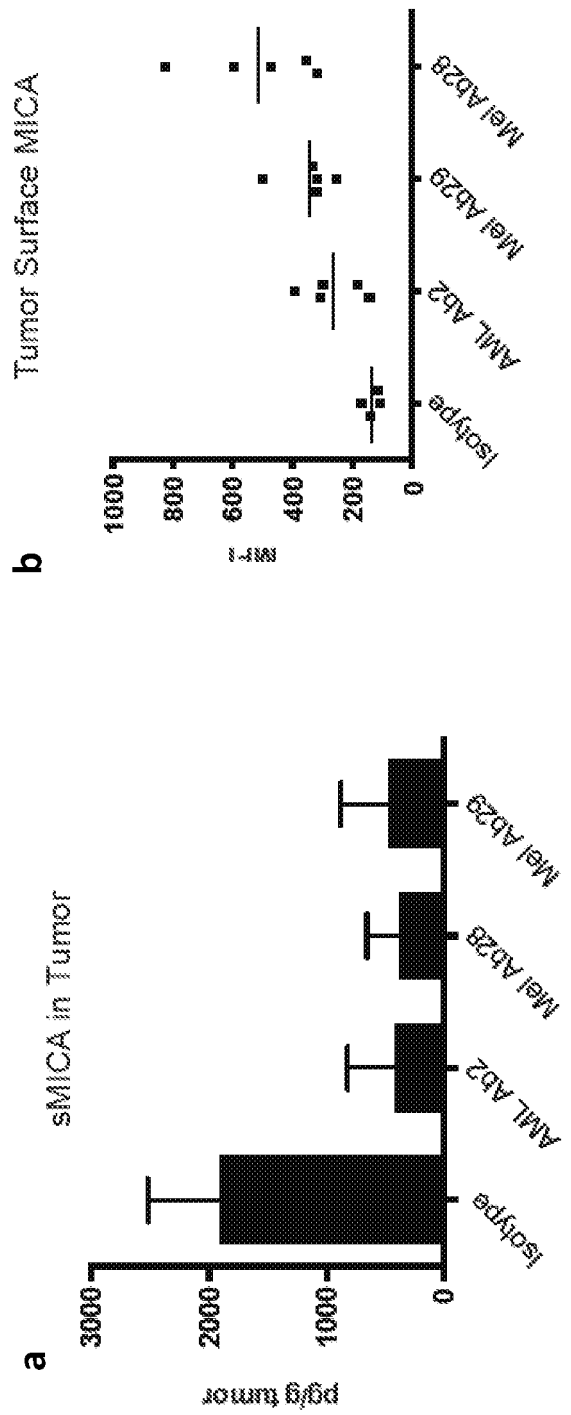

a
sMICA in Tumor
pg/g tumor
3000
2000
1000
0
Isotype
AML Ab2
Mel Ab28
Mel Ab29
b
Tumor Surface MICA
MFI
1000
800
600
400
200
0
Isotype
AML Ab2
Mel Ab29
Mel Ab28

FIG. 64

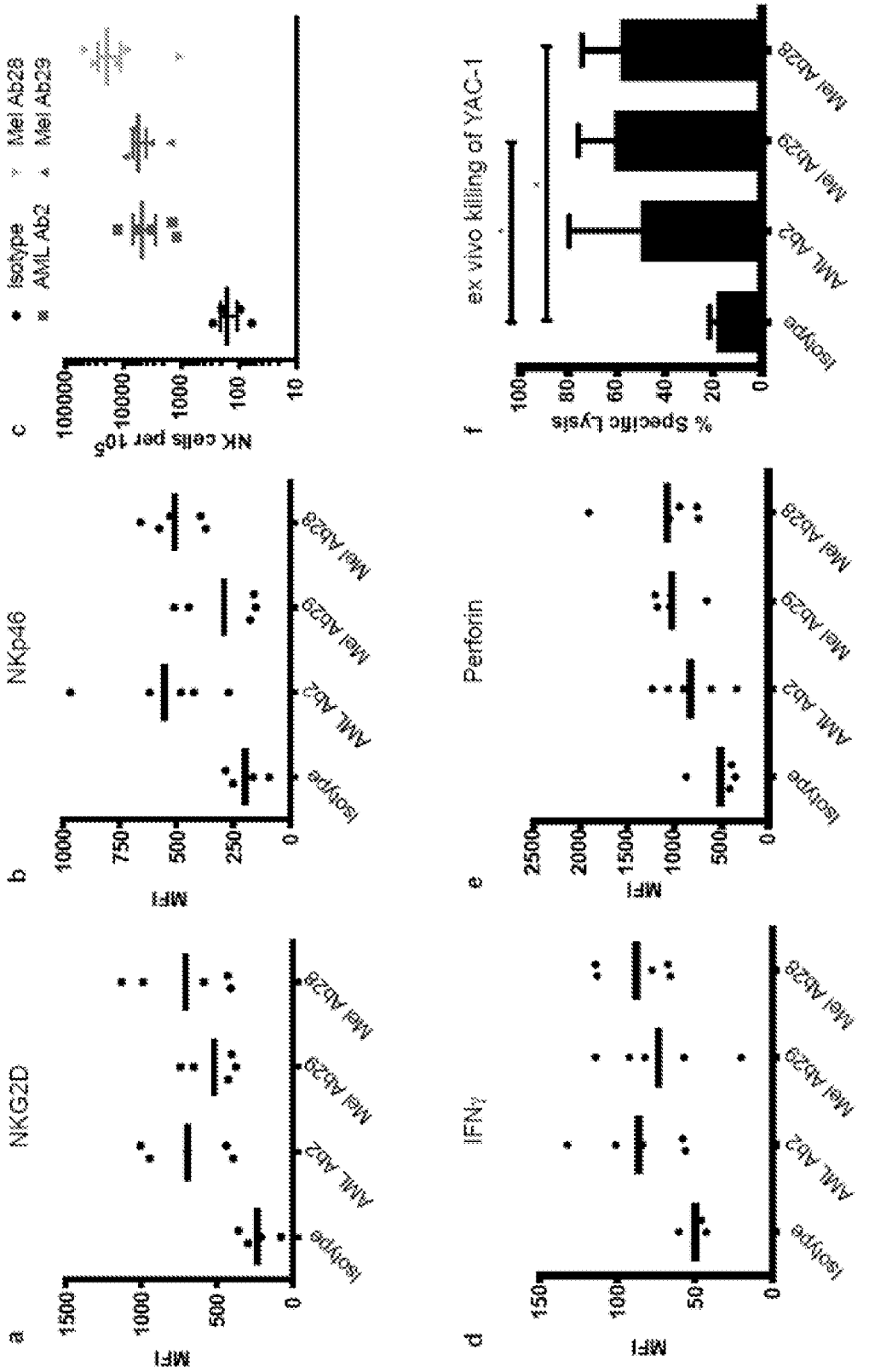

a
NKG2D
MFI
1500
1000
500
0
Isotype
AML Ab2
Mel Ab29
Mel Ab28
b
NKp46
MFI
1000
750
500
250
0
Isotype
AML Ab2
Mel Ab29
Mel Ab28
c
Isotype
AML Ab2
Mel Ab28
Mel Ab29
NK cells per 10^5
100000
10000
1000
100
10
d
IFNγ
MFI
150
100
50
0
Isotype
AML Ab2
Mel Ab29
Mel Ab28
e
Perforin
MFI
2500
2000
1500
1000
500
0
Isotype
AML Ab2
Mel Ab29
Mel Ab28
f
ex vivo killing of YAC-1
% Specific Lysis
100
80
60
40
20
0
Isotype
AML Ab2
Mel Ab29
Mel Ab28

FIG. 65