

MF nr.	Specificity:	Germline:	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
1337	TT	IGH1-08	EVQLVETGAEVKRPGASVKVSCRASDITFT	KYDIN	WVRQAPGGGLEWMG	WMSANTGNIGYAKQFG	RVITMDTSLINTAYMELSLTSGDTAVYFCAR	SSLFKETETAPYYHEALDV	WGQGTTLVTVSS
3125	HER3	IGH3-30	QVQLVDSGGVQPGSRIRLSCAASGFTFS	SYGMH	WVRQAPGGGLEWVA	VISTGSRNRYADSVRG	RFTISDRNSKNTIYLQMSNLRSEDVAVYYCAR	GSGRPSYNSWGFDY	WGQGTTLVTVSS
3176	HER3	IGH3-23	EQVQLLESGGIVQPGSLRLSCAASGFTFS	SYAMS	WVRQAPGGGLEWVS	AIISGGSGSTVYADSVRG	RFTISDRNSKNTIYLQMSNLRSEDVAVYYCAR	DWVYPPYWGFDY	WGQGTTLVTVSS
3178	HER3	IGH1-2	QVQLVQSGAEVKRPGASVKVSCRASGTYFT	GYNMH	WVRQAPGGGLEWMG	WINPNSGGTNYAQKFG	RVITMDTSLINTAYMELSLRSDDTAVYYCAR	DHGSRHFWSYWGFDY	WGQGTTLVTVSS
4863	HER3	IGH7-4-1	EVQLVQSGSEELKPKGASVKVSCRASGTYTSI	RYALN	WVRQAPGGGLEWLG	WINTNTGNPTVYARGFTG	RFVFSLDTSVSTAYLQISSLKAEEDTAVYYCAR	DTYDSTGYLWFDY	WGQGTTLVTVSS
3370	EGFR	IGH1-18	QVQLVQSGAEVKRPGASVKVSCRASGTYFT	SYGIS	WVRQAPGGGLEWMG	WISAYNGNTNYAQKFG	RVITMDTSLINTAYMELSLRSDDTAVYYCAR	DREWHWLDADF	WGQGTTLVTVSS
3755	EGFR	IGH7-4-1	QVQLVQSGSEELKPKGASVKVSCRASGTYFT	NYAMN	WVRQAPGGGLEWMG	WINANTGDPVYAGFTG	RFVFSLDTSVSTAYLQISSLKAEEDTAVYYCAR	BRFLBWLHFDY	WGQGTTLVTVSS
4280	EGFR	IGH1-24	QVQLVQSGAEVKRPGASVKVSCRVSGTYFT	ELSMH	WVRQAPGGGLEWMG	GFDPEYKGTTFEAGNFG	RVITMDTSLINTAYMELSLRSEDVAVYYCAT	EGYVETTTTYTNLFDS	WGQGTTLVTVSS
4289	EGFR	IGH7-4-1	QVQLVQSGSEELKPKGASVKVSCRVSGTYFT	DYAMT	WVRQAPGGGLEWMG	WITNTGDPVYAGFTG	RFVFSLDTSVSTAYLQISSLKAEEDTAVYYCAR	VYHWRGFEF	WGQGTTLVTVSS
5777	LGR4	IGH7-4-1	QVQLVQSGSEELKPKGASVKVSCRASGTYFT	NYVMN	WVRQAPGGGLEWMG	WINTNTGNPTVYAGFTG	RFVFSLDTSVSTAYLQISSLKAEEDTAVYYCAR	WELLDY	WGQGTTLVTVSS
5781	LGR4	IGH3-23	EVQLVDSGGIVQPGSLRLSCAASGFTFS	SYAMS	WVRQAPGGGLEWVS	VISGGGTYYADSVRG	RFTISDRNSKNTIYLQMSNLRSEDVAVYYCAR	GAGELDY	WGQGTTLVTVSS
5790	LGR5	IGH4-39	QVQLQESGPGIVKPSSETLSLTCTVSGSSTFS	SSSYWNG	WIRQPPGGGLEWIG	SFYYSNGNTYYNPSLKS	RVITISBDTSKNOFSLKLSSTVTAADTAVYYCAR	QTYSSWDGVLTYFDY	WGQGTTLVTVSS
5803	LGR5	IGH4-59	QVQLQESGPGIVKPSSETLSLTCTVSGSSTFS	TYTWS	WIRQPPGGGLEWIG	VYVYTGRTKYNPSLKS	RVITISVDTSKNOFSLNLSSTVTAADTAVYYCAR	GEIVVPAARDYYVMDV	WGQGTTLVTVSS
5805	LGR5	IGH5-51	EVQLVQSGAEVKRPGESLKIACTGSGFTFS	SHWIG	WIRQPPGGGLEWMG	VYIPGDSDTTRYSPSTFG	QVTVSADKSLINTAYLQMSNLRSEDVAVYYCAR	PNSGSPRYFEF	WGQGTTLVTVSS
5808	LGR5	IGH4-39	QVQLQESGPGIVKPSSETLSLTCTVSGSSTFS	SSSYWNG	WIRQPPGGGLEWIG	SFYYSNGNTYYNPSLKS	RVITISVDTSKNOFSLKLSSTVTAADTAVYYCAR	QEVYYGSGSPSYFDY	WGQGTTLVTVSS
5809	LGR5	IGH5-51	EVQLVQSGAEVKRPGESLKISCRGSDSTFS	SHWIA	WIRQPPGGGLEWMG	VYIPGDSDTTRYSPSTFG	QVTVSADKSLINTAYLQMSNLRSEDVAVYYCAR	HWELLIGPEFY	WGQGTTLVTVSS
5814	LGR5	IGH1-69	EVQLVQSGAEVKRPGSIVKYSCKASGTSFT	NDALIS	WVRQTPGGGLEWMG	SIIIFILDTTHAQKFG	RVITITADKSTNTAYMELNSLRSDDTAVYYCAR	EHIAARQDYFDY	WGQGTTLVTVSS
5816	LGR5	IGH7-4-1	EVQLVQSGSKLKKPGASVKVSCRASGTYFT	SYTMN	WVRQAPGGGLEWMG	WINTDGTDPVYAGFTG	RFVFSLDTSVSTAFIQLINSLRSEDVAVYYCAR	GCDDSTCYRYSYGYEDY	WGQGTTLVTVSS
5817	LGR5	IGH1-69	QVQLVQSGAEVKRPGSIVKYSCKVSGTFT	SYALIS	WVRQAPGGGLEWMG	GIIIFIDTRNYAQKFG	RVITITADLSTSTAYMELNSLRSEDVAVYYCAR	GSGEGWDFP	WGQGTTLVTVSS
5818	LGR5	IGH1-69	EVQLVQSGTEVVRKPGSSIVKYSCKASGTSFT	NYALIS	WVRQAPGGGLEWMG	SIIIFILDTTHAQKFG	RVITITADKSNNTTAYMELNSLRSDDTAVYYCAR	EYIAARLDYFDS	WGQGTTLVTVSS
5832	RNF43	IGH3-13	EVQLVDSGGIVQPGSLRLSCVVSSTFTFS	XYDMH	WVRQVTKGGLEWVS	AICTAGATYYPGSVKG	RFVFSRENKNSIYLQMSNLRAGDTAVYYCAR	DRGYSGYDAYYFE	WGQGTTLVTVSS
5836	RNF43	IGH4-39	QVQLQESGPGIVKPSSETLSLTCTVSGSSTFS	SSSYWNG	WIRQPPGGGLEWIG	NIIYRPGTYNPSLKS	RVITISVDTSKNOFSLTSSVTAADTAVYYCAR	BGSDYGDYVGAADI	WDQGTMTVTVSS
5839	RNF43	IGH3-13	EVQLVQSGGIVQPGSLRLSCAASGFTFS	XYDMH	WVRQVTKGGLEWVS	TIGATGTPYYSDSVKG	RFVFSRQNAKNSIYLQINSLRAGDTAVYYCVR	DRGYIGYDSYVFDN	WGQGTTLVTVSS
5850	ZNF3	IGH7-4-1	QVQLVQSGSEELKPKGASVKVSCRASGTYFT	RYPMN	WVRQAPGGGLEWMG	WINTNTGNPTVYAGFTG	RFVFSLDTSVSTAFIQLISSLKAEEDTAVYYCAR	BRTNFYDAEDI	WGQGTMTVTVSS
5853	ZNF3	IGH7-4-1	QVQLVQSGSEELKPKGASVKVSCRASGTYFT	SYAMD	WVRQAPGGGLEWMG	WINTNTGNPTVYAGFTG	RFVFSLDTSVSTAYLQISSLKAEEDTAVYYCAR	BRHGYFEAFDI	WGQGTMTVTVSS
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5887	ZNF3	IGH7-4-1	QVQLVQSGSEELKPKGASVKVSCRASGTYFT	RYAMN	WVRQAPGGGLEWMG	WINTNTGNPTVYAGFTG	RFVFSLDTSVSTAYLQISSLKAEEDTAVYYCAR	DRGYNNWNGAADI	WGQGTMTVTVSS
5888	ZNF3	IGH7-4-1	QVQLVQSGSEELKPKGSKVSKASGTYFT	RYAMN	WVRQAPGGGLEWMG	WINTNTGNPTVYAGFTG	RFVFSLDTSVSTAYLQISSLKAEEDTAVYYCAR	RSGSYDYFDY	WGQGTTLVTVSS

Figure 2

MF1337:

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MF5862:

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gttctggatacagctttaccacctactggatcggctgggtgcgccagatgcccggaaggcctggagtg
gatgggaatcatctatcctggtgactctgataccagatacagccgtccttccaaggccaggtcaccatc
tcagccgacaagtccatcagcacccgctacctgcagttgagcagcctgaaggcctcggaacccgcatgt
attactgtgcgagacgggggtcttagtatggttcgggtgagcgcttttgatgtctggggccaaggaaacct
ggtcacctctccagt

MF5882:

caggtgcagctggtgcaatctgggtctgagttgaagaagcctggggcctcagtgaagggtttcctgcaagg
cttctggatacacccttcactagatatgctatgaattgggtgcgacaggccctggacaagggttgagtg
gatgggatggatcaacaccaaactgggaacccaacgtatgccagggttcacaggacgggtttgtcttc
tccttggacacctctgtcagcacggcataatctgcagatcagcagcctaaaggctgaggacactgccgtgt
attactgtgcgagagatcgtgggagctactatgatgcttttgatatctggggccaagggaacaatggtcac
cgtctccagt

MF5884:

gaggtgcagctggtgcagctctgggtctgaattgaagaagcctggggcctcagtgaagggtttcctgcaagg
cttctggatacacccttcactaagtatgctatgaattgggtgcgacaggccctggacaagggttgagtg
gatgggatggatcaacaccaacactgggaacccaacgtatgccagggttcacaggacgggtttgtcttc
tccttggacacctctgtccgcacggcataatctgcagatcagcagcctaaaggctgaggacactgccgtgt
attactgtgcgagaaaaggggggagctactacgactggttcgacccctggggccagggaacctggtcac
cgtctccagt

MF5887:

caggtgcagctggtgcagctctgggtctgagttgaagaagcctggggcctcagtgaagggtttcctgcaagg
cttctggatacacccttcactcgctatgctatgaattgggtgcgacaggccctggacaagggttgagtg
gatgggatggatcaacaccaacactgggaacccaacgtatgccagggttcacaggacgggtttgtcttc
tccttggacacctctgtcagcacggcataatctgcagatcagcagcctgaaggctgaggacactgccgtgt
attactgtgcgagagataagggtataactggaactacatgggtgcttttgatatctggggccaagggaac
cacggtcacgtctccagt

MF5888:

caggtgcagctggtgcagctctgggtctgagttgaagaagcccgggggtcaatgaagggtttcctgcaagg
cttctggatacacccttcactagatatgctatgaattgggtgcgacaggccctggacaagggttgagtg
gatgggatggatcaacaccaacactgggaacccaacgtatgccagggttcacaggacgggtttgtcttc
tccttggacacctctgtcagcacggcataatctgcagatcagcagcctaaaggctgaggacactgccgtct
attattgtgcgagacggagtgaggagctactacgactactttgactactggggccagggaacctggtcac
cgtctccagt

Figure 3

Common Light Chain amino acid (A.A.) sequence

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQ
PEDFATYYCQSYSTPPTFGQGTKVEIK
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA
DYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Annotated sequence:

VL:

gacatccagatgacccagtcctccatcctccctgtctgcatctgtaggagacagagtcacc
D I Q M T Q S P S S L S A S V G D R V T
atcacttgccgggcaagtcagagcatttagcagctacttaaattggatcagcagaaacca
I T C R A S Q S I S S Y L N W Y Q Q K P
gggaaagcccctaagctcctgatctatgctgcatccagtttgcaaagtgggtcccatca
G K A P K L L I Y A A S S L Q S G V P S
aggttcagtggcagtggtatctgggacagatttcactctcaccatcagcagtcctgcaacct
R F S G S G S G T D F T L T I S S L Q P
gaagattttgcaacttactactgtcaacagagttacagtaccctccaacggttcggccaa
E D F A T Y Y C Q Q S Y S T P P T F G Q
gggaccaaggtggagatcaaa
G T K V E I K

CL:

cgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatct
R T V A A P S V F I F P P S D E Q L K S
ggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacag
G T A S V V C L L N N F Y P R E A K V Q
tggaaggtggataacgccctccaatcgggtaactcccaggagagtggtcacagagcaggac
W K V D N A L Q S G N S Q E S V T E Q D
agcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgag
S K D S T Y S L S S T L T L S K A D Y E
aaacacaaagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaag
K H K V Y A C E V T H Q G L S S P V T K
agcttcaacaggggagagtgtag
S F N R G E C -

Figure 4

VH: dependent on the MF (target): Figures 1 and 2.

CH1:

gctagcaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctggg
A S T K G P S V F P L A P S S K S T S G
ggcacagcgccctgggctgcctgggtcaaggactacttccccgaaccggtgacgggtgtcg
G T A A L G C L V K D Y F P E P V T V S
tggaactcagggccctgaccagcggtgcacaccttcccggtgtcctacagtcctca
W N S G A L T S G V H T F P A V L Q S S
ggactctactccctcagcagcgctgcgtgaccgtgccctccagcagcttgggcacccagacc
G L Y S L S S V V T V P S S S L G T Q T
tacatctgcaacgtgaatcacaagcccagcaacaccaaggtggacaagagagtt
Y I C N V N H K P S N T K V D K R V

Hinge:

gagcccaaattctgtgacaaaactcacacatgccaccgtgccc
E P K S C D K T H T C P P C P

CH2:

gcacctgaactcctggggggaccgtcagtccttcttccccccaaaacccaaggacacc
A P E L L G G P S V F L F P P K P K D T
ctcatgatctcccggaacctgaggtcacatgcgtggtggtggacgtgagccacgaagac
L M I S R T P E V T C V V V D V S H E D
cctgaggtcaagttcaactggtacgtggacggcggtggaggtgcataatgccaagacaaag
P E V K F N W Y V D G V E V H N A K T K
ccgcgaggagcagtagacaacagcacgtaccgtgtggtcagcgtcctcaccgtcctgcac
P R E E Q Y N S T Y R V V S V L T V L H
caggactgggtgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagcc
Q D W L N G K E Y K C K V S N K A L P A
cccatcgagaaaaccatctccaaagccaaa
P I E K T I S K A K

CH3: KK of DEKK

gggcagccccgagaaccacaggtgtacaccaagcccccatcccgaggagatgaccaag
G Q P R E P Q V Y T K P P S R E E M T K
aaccaggtcagcctgaagtgcctgggtcaaaggcttctatcccagcgacatcgccgtggag
N Q V S L K C L V K G F Y P S D I A V E
tgaggagcaatgggcagccggagaacaactacaagaccacgcctcccggtgctggactcc
W E S N G Q P E N N Y K T T P P V L D S
gacggctccttcttctctatagcaagctcaccgtggacaagagcaggtggcagcagggg
D G S F F L Y S K L T V D K S R W Q Q G
aacgtcttctcatgctccgtgatgcatgaggctctgcacaaccactacacgcagaagagc
N V F S C S V M H E A L H N H Y T Q K S
ctctccctgtctccgggttga
L S L S P G -

CH3: DE of DEKK

gggcagccccgagaaccacaggtgtacaccgaccccccatcccgggaggagatgaccaag
G Q P R E P Q V Y T D P P S R E E M T K
aaccaggtcagcctgacctgcgaggtcaaaggcttctatcccagcgacatcgccgtggag
N Q V S L T C E V K G F Y P S D I A V E
tgggagagcaatgggcagccgggagaacaactacaagaccacgcctcccgtgctggactcc
W E S N G Q P E N N Y K T T P P V L D S
gacggctccttcttctctatagcaagctcacccgtggacaagagcaggtggcagcagggg
D G S F F L Y S K L T V D K S R W Q Q G
aacgtcttctcatgctccgtgatgcatgaggctctgcacaaccactacacgcagaagagc
N V F S C S V M H E A L H N H Y T Q K S
ctctccctgtctccgggttga
L S L S P G -

Figure 5

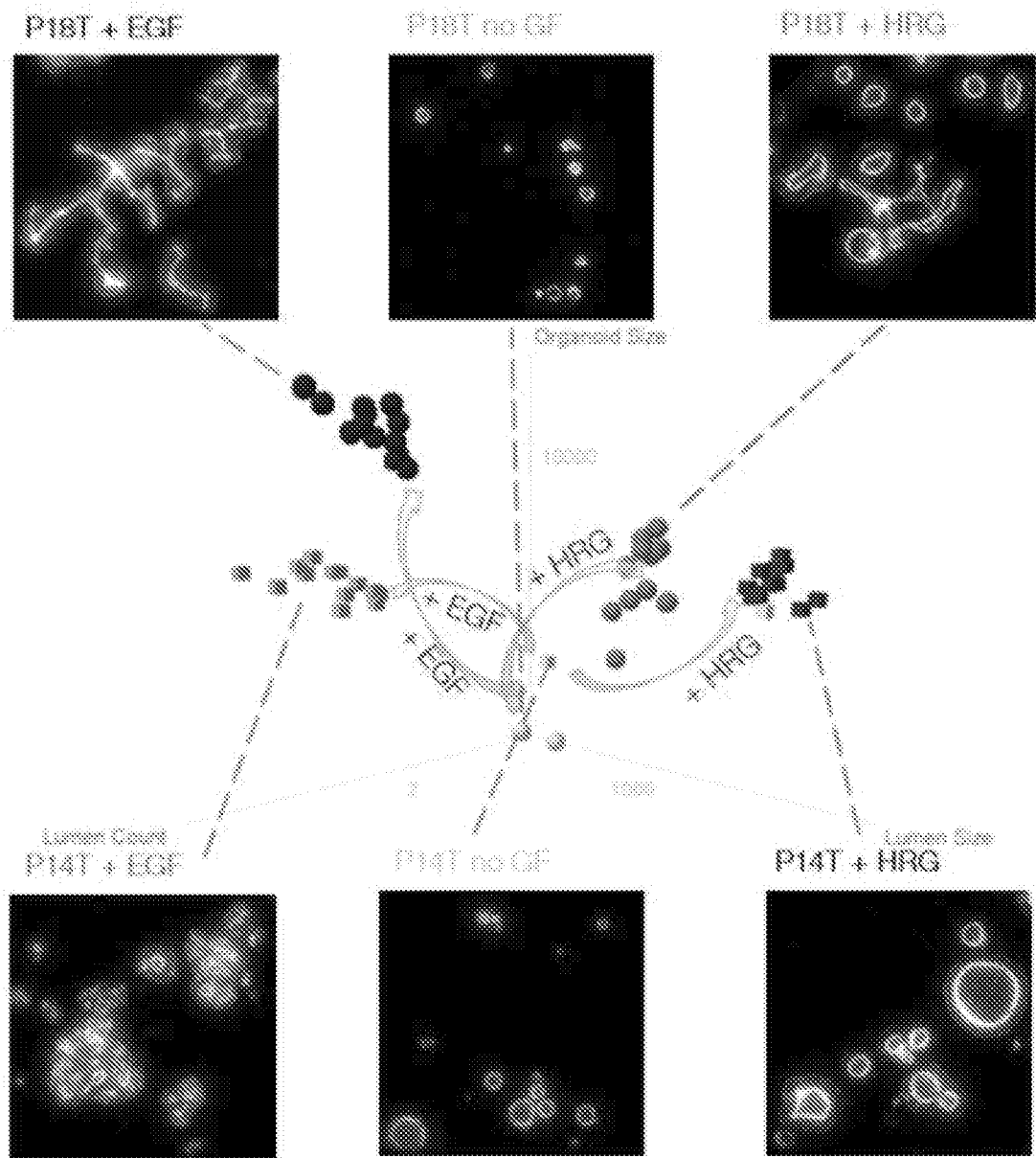


Figure 6

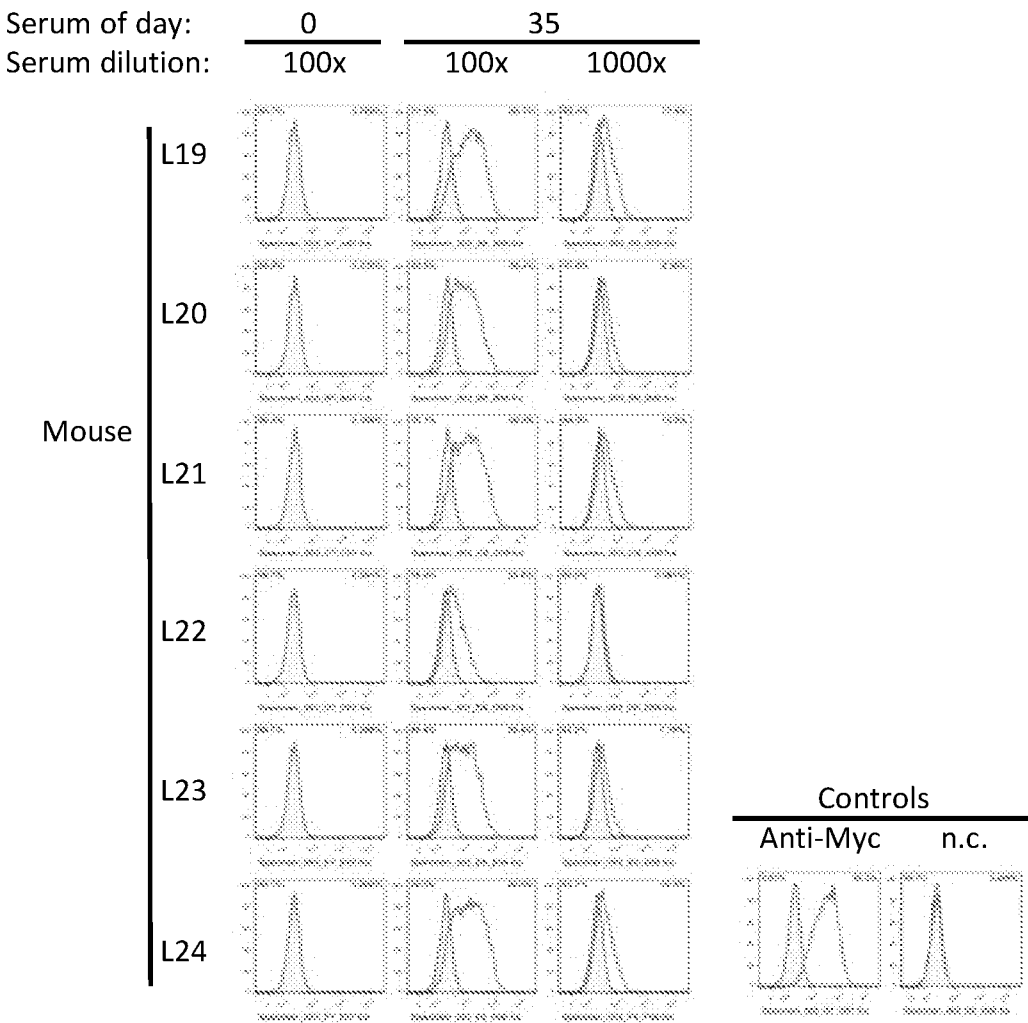
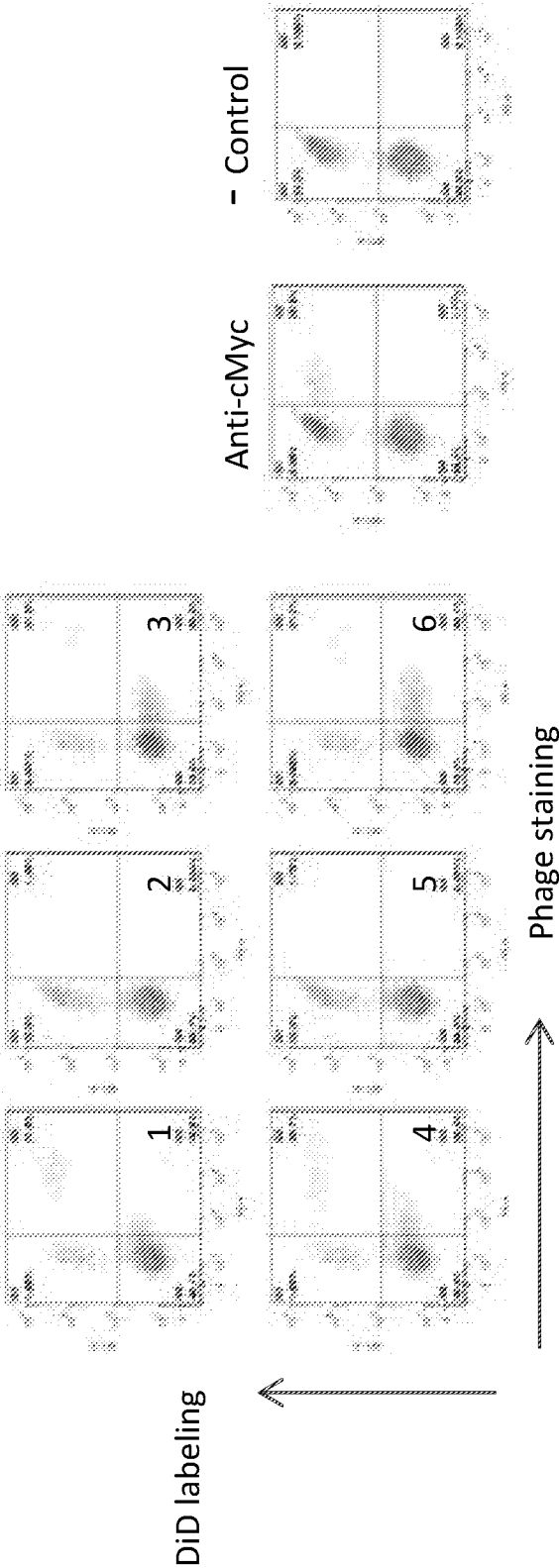


Figure 7



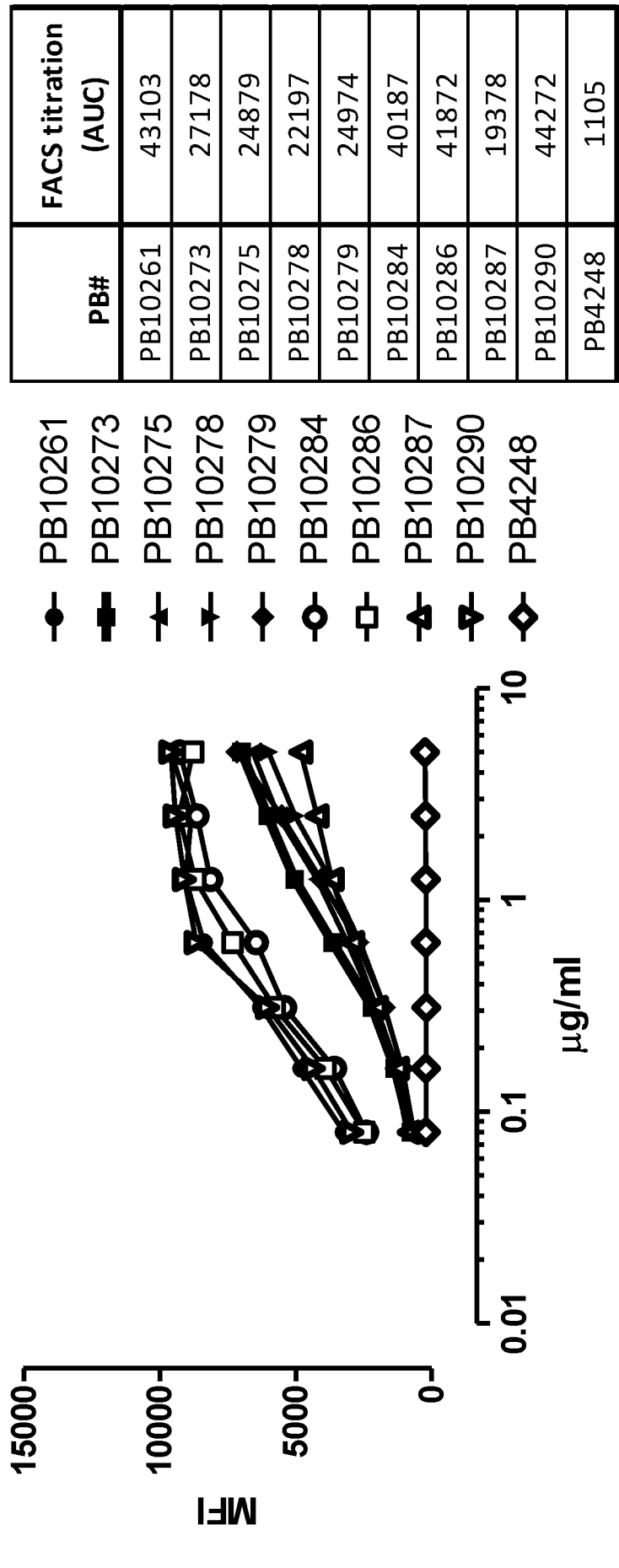


Figure 8

Figure 9

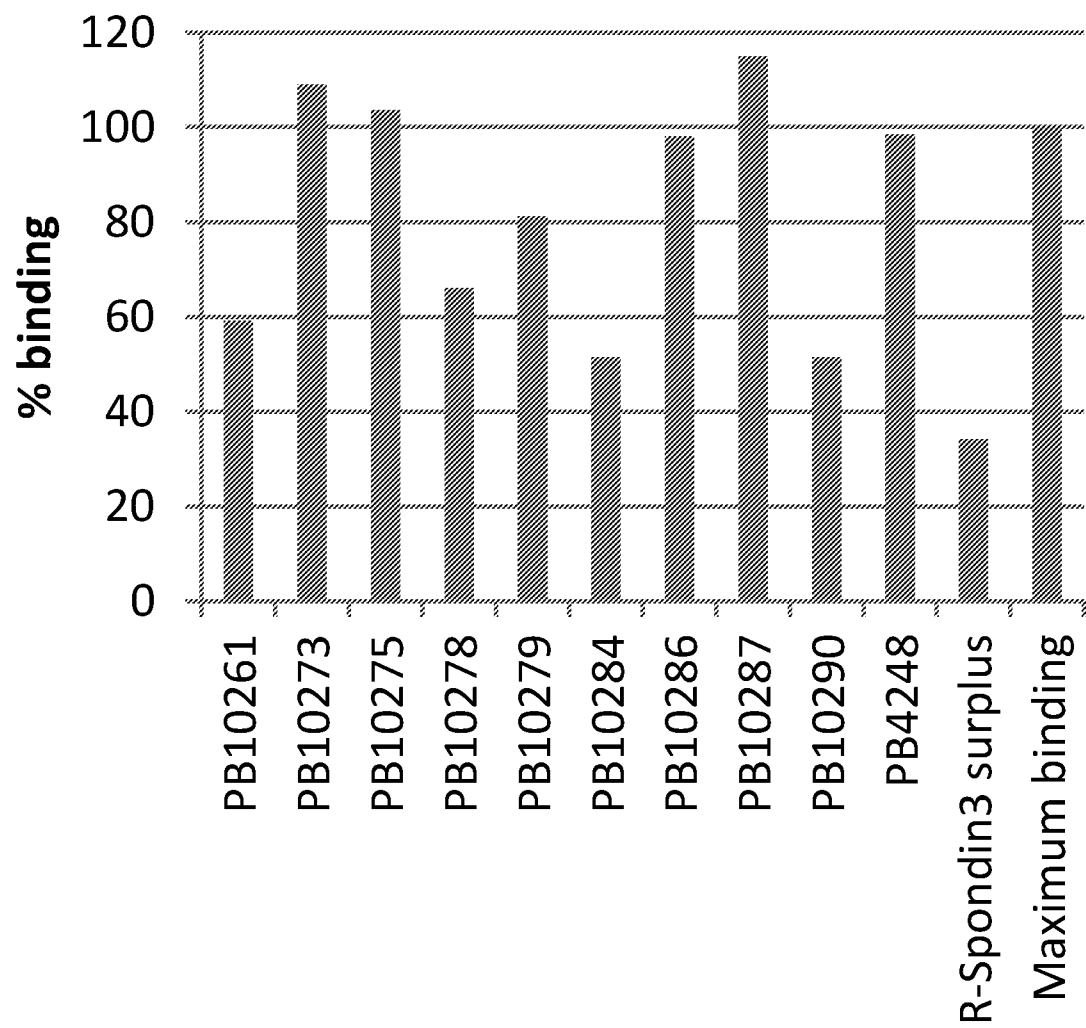


Figure 11

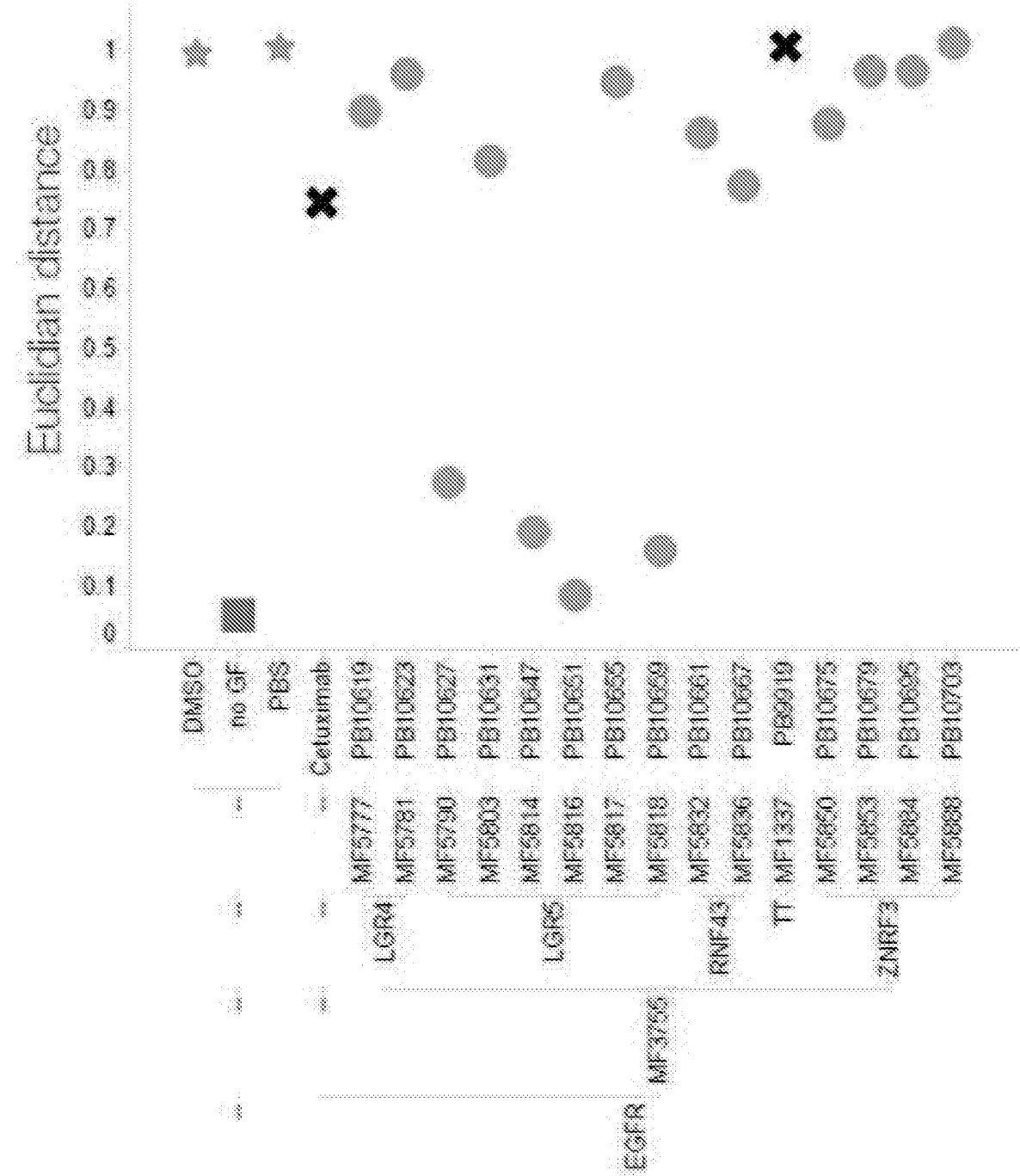


Figure 12

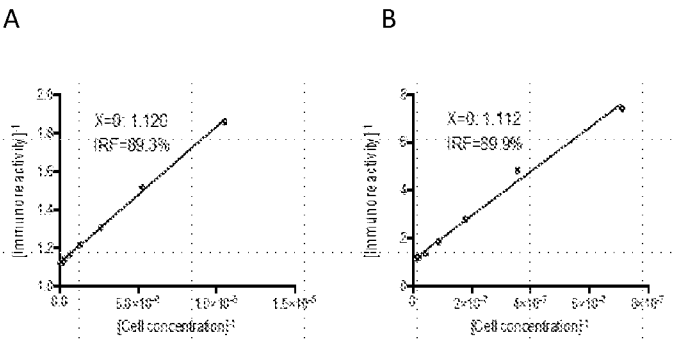


Figure 13

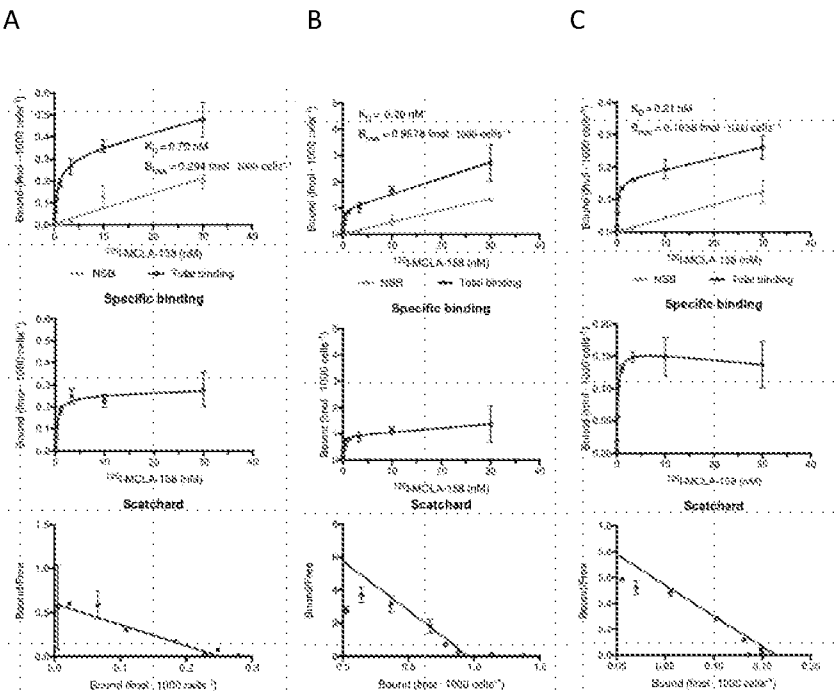


Figure 14

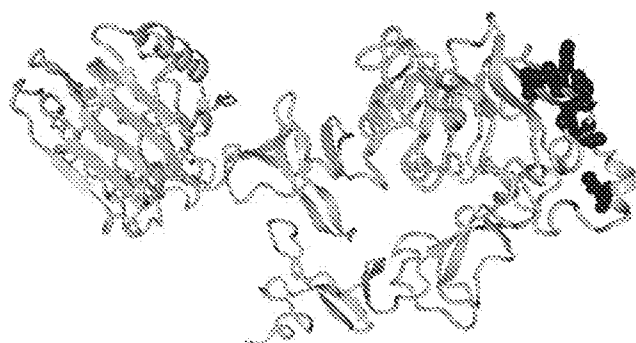


Figure 15

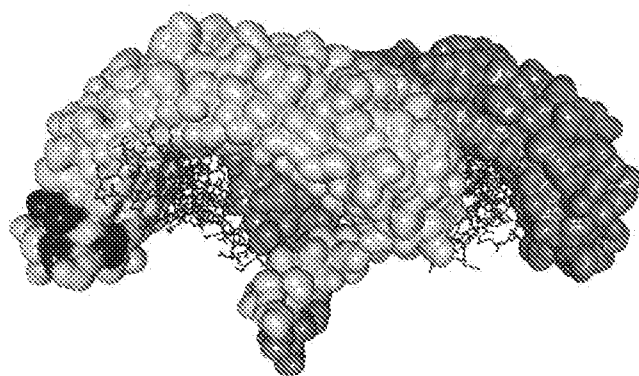


Figure 16

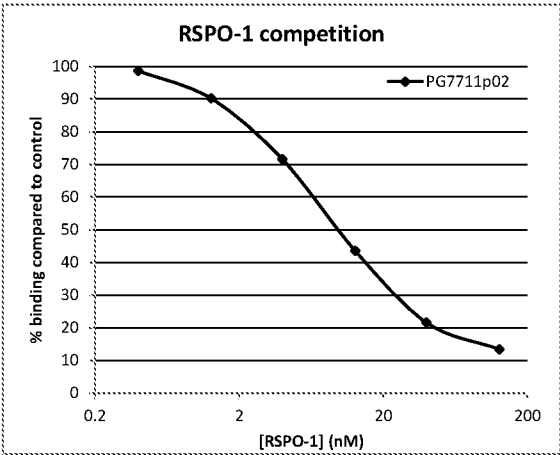


Figure 17

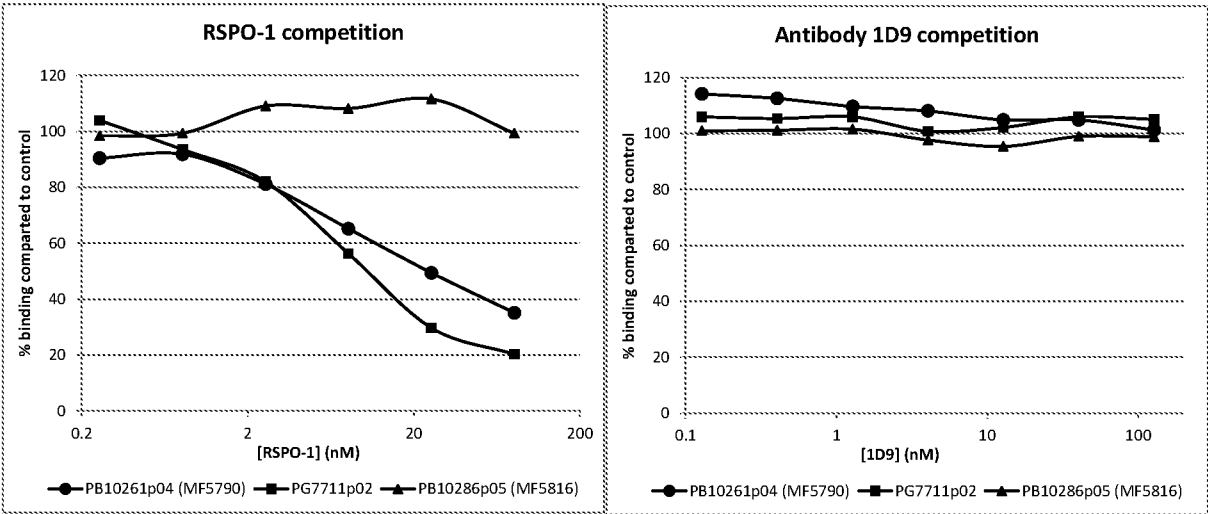


Figure 18

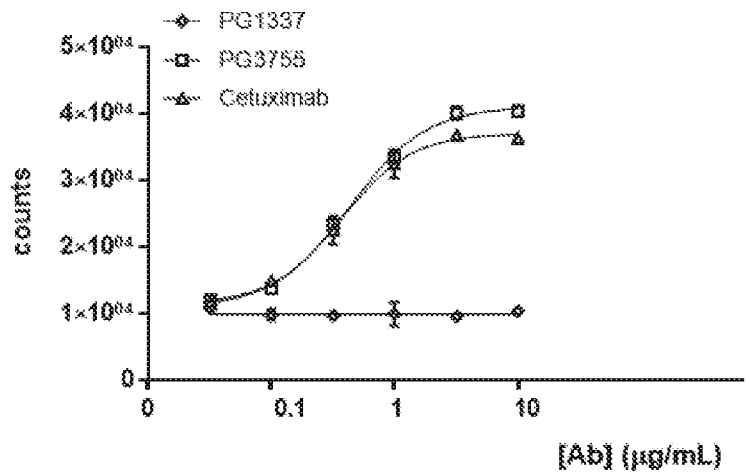


Figure 19

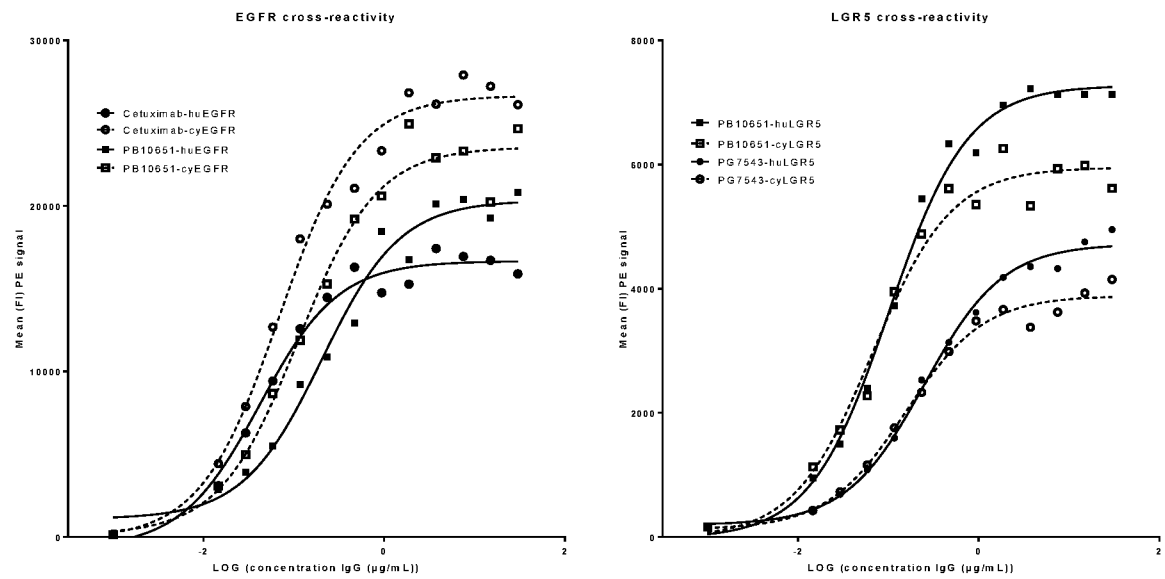
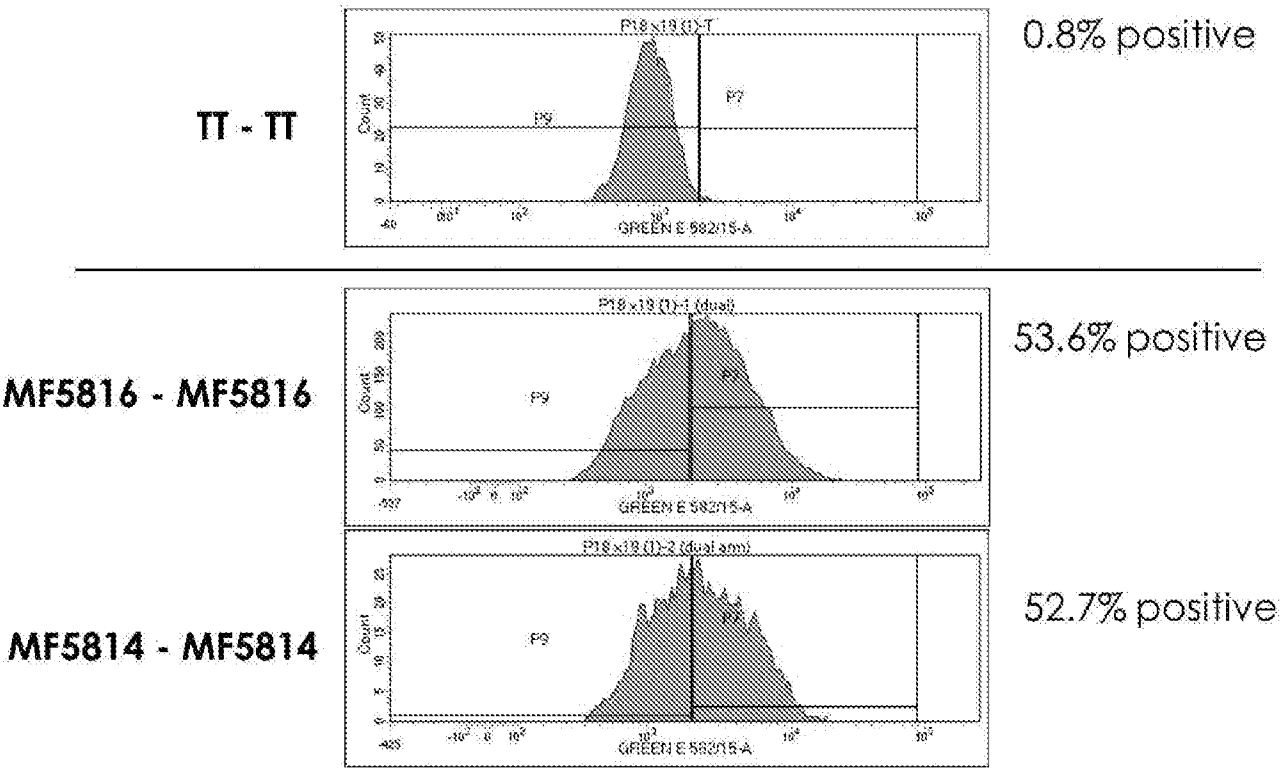


Figure 20



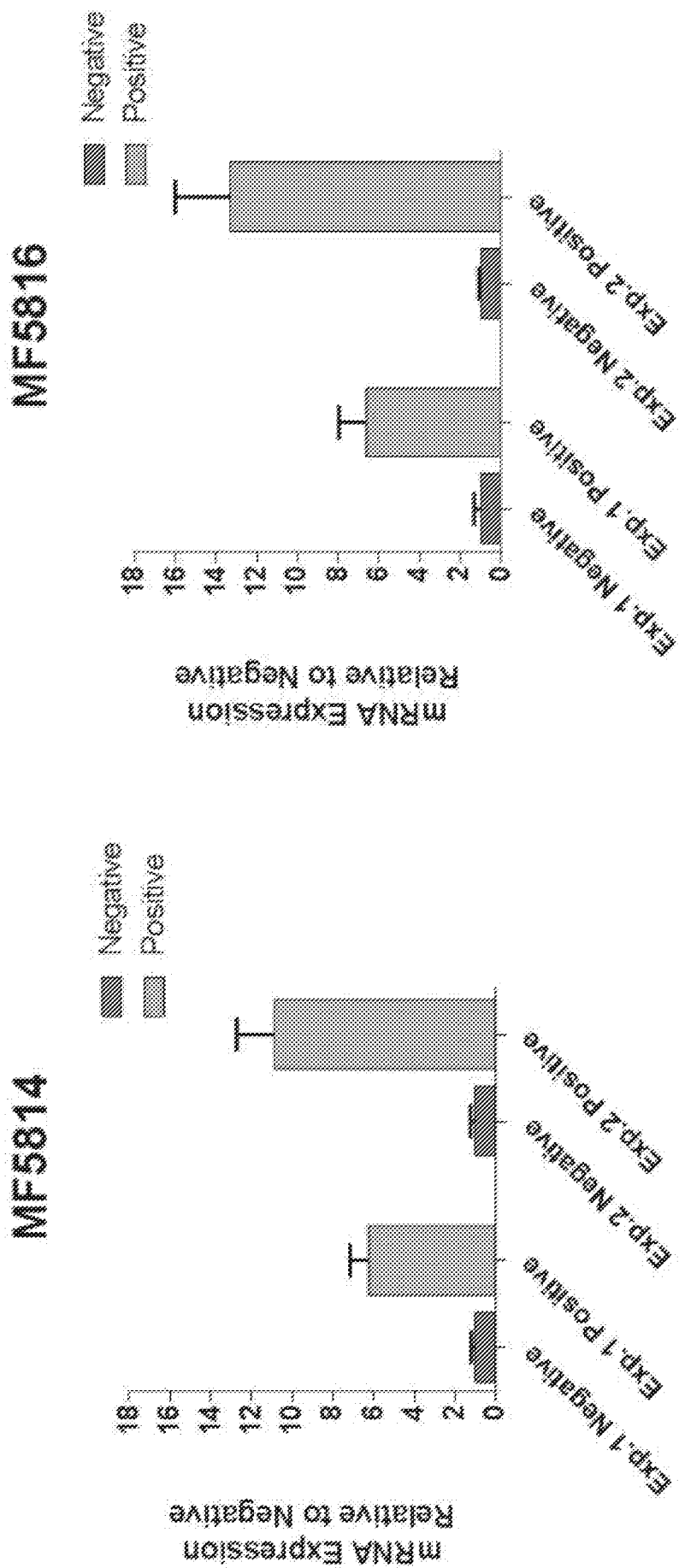


Figure 21

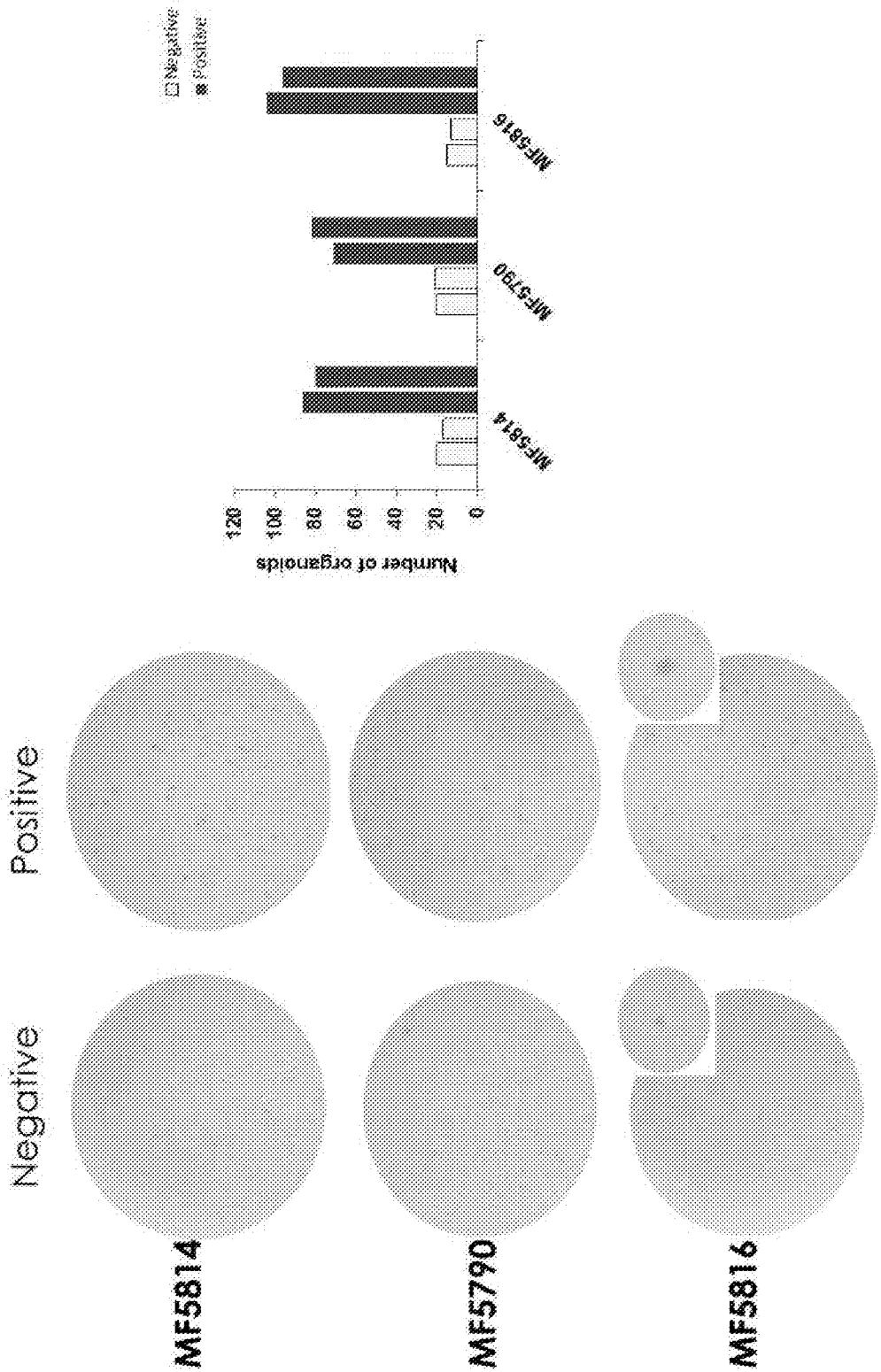


Figure 22

Figure 23

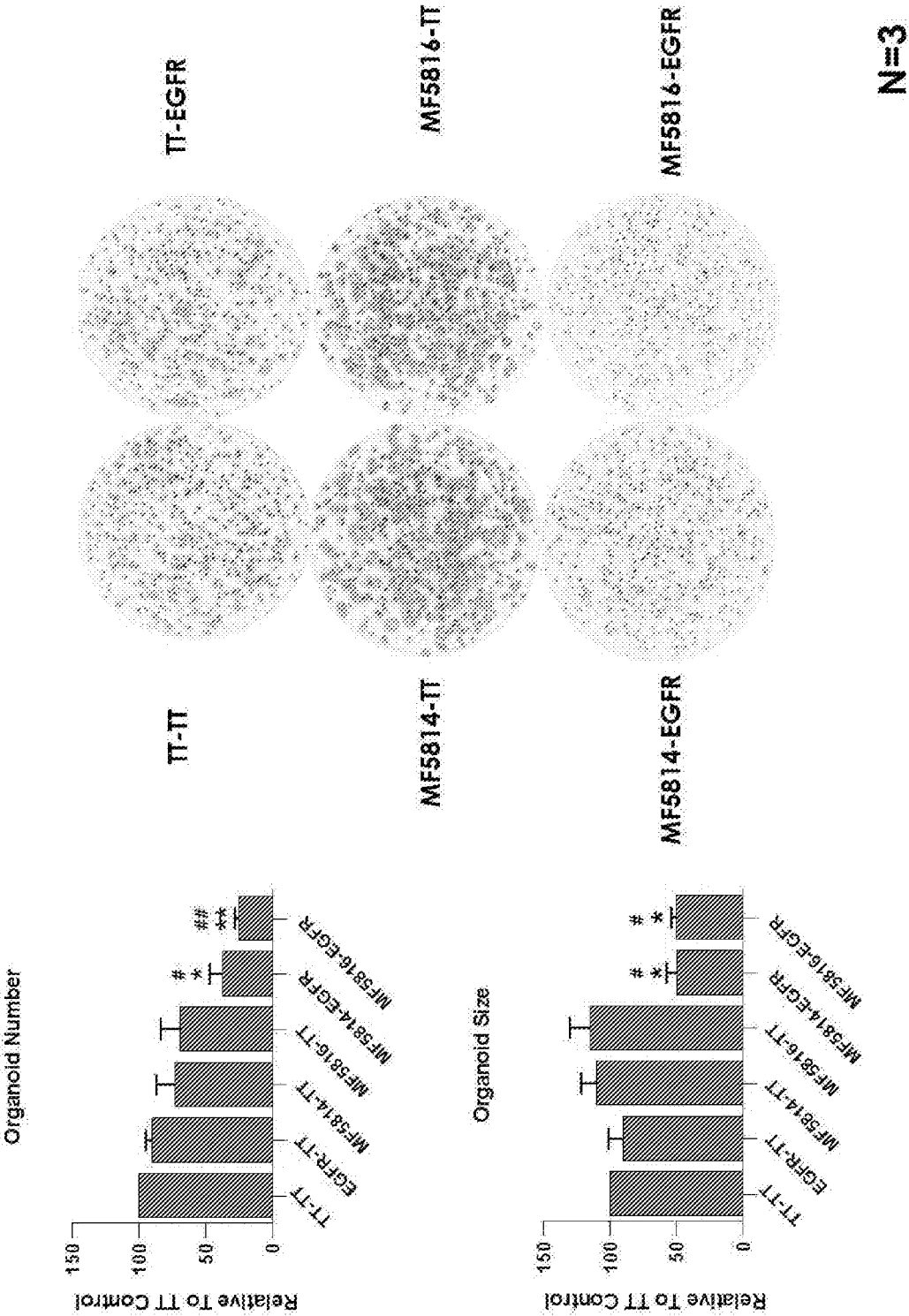


Figure 24

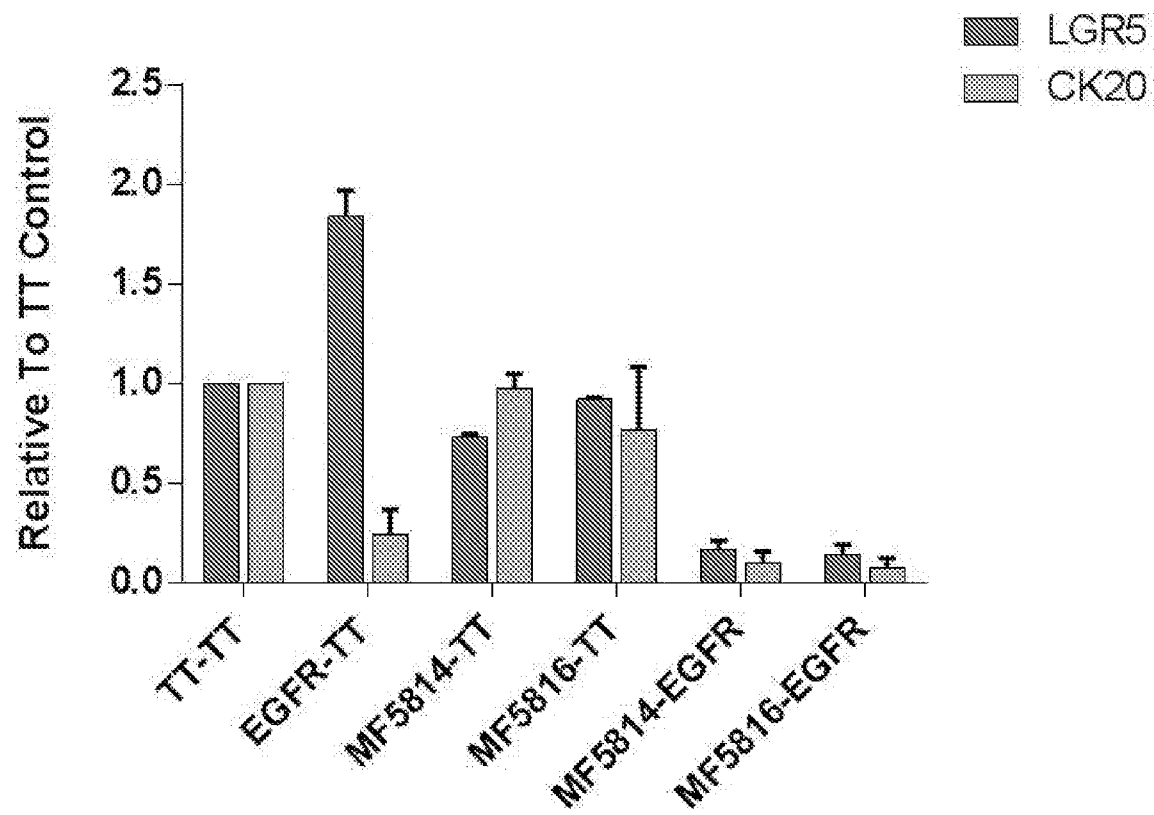


Figure 25

Figure 25A

Supercluster 1 (MF5814 and MF5818)

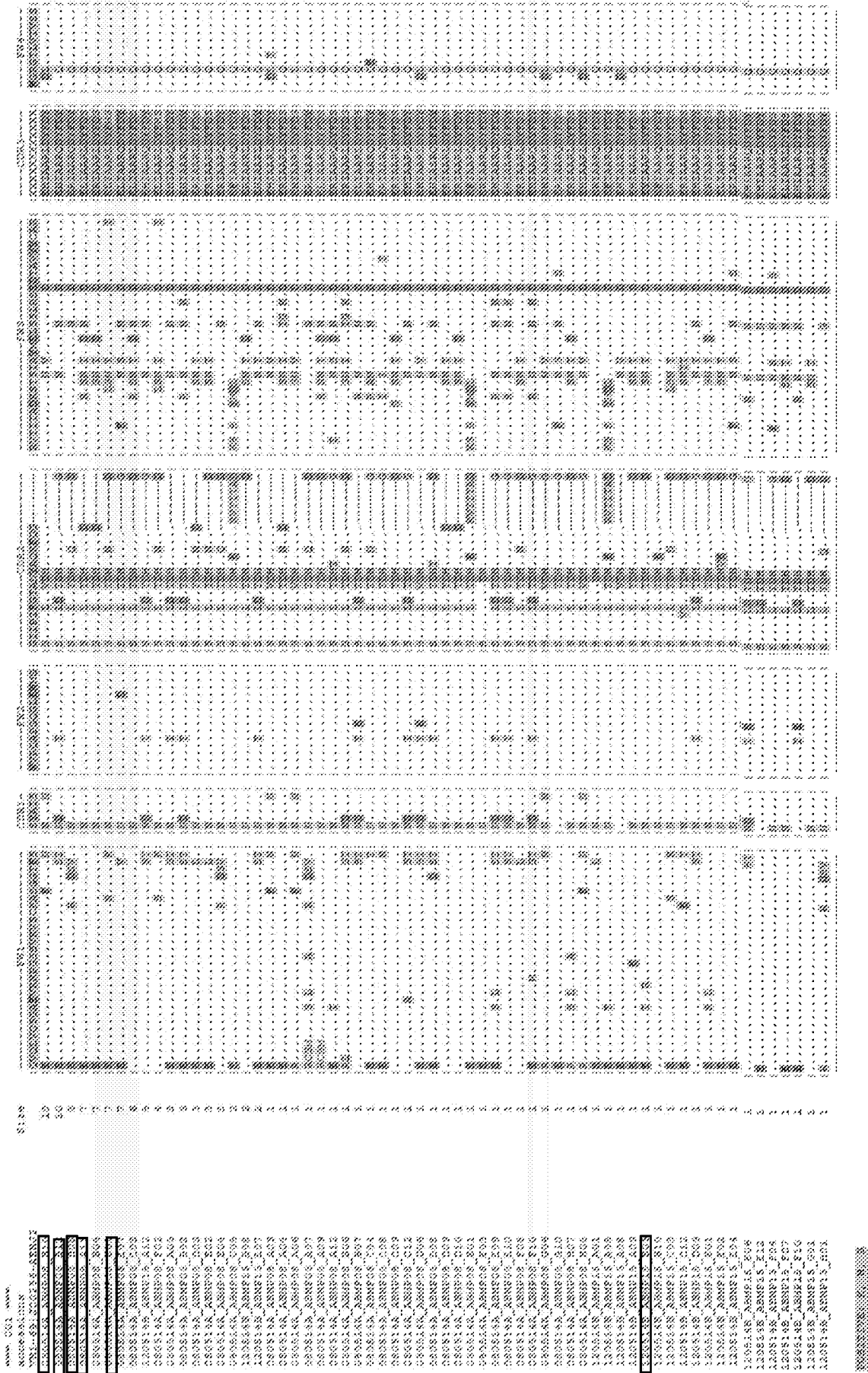


Figure 25B

Supercluster 8 (MF5790)

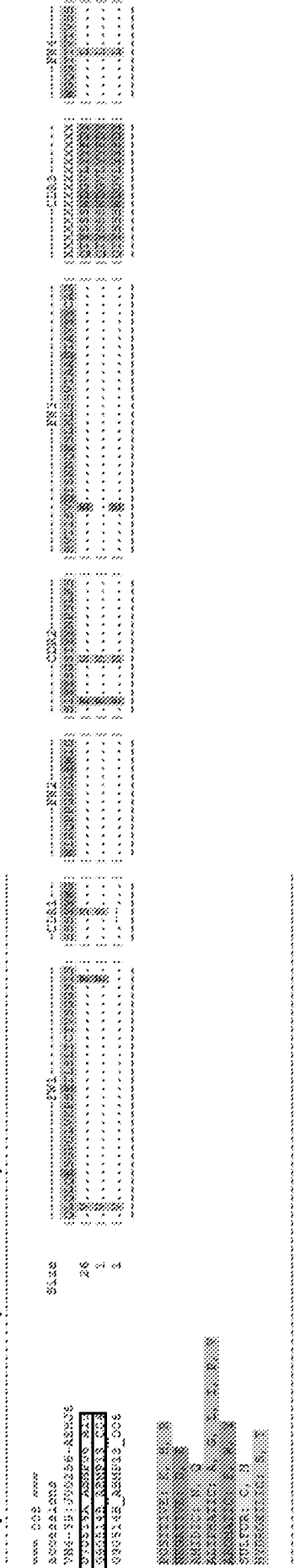


Figure 25C

Supercluster 10 (MF5816)

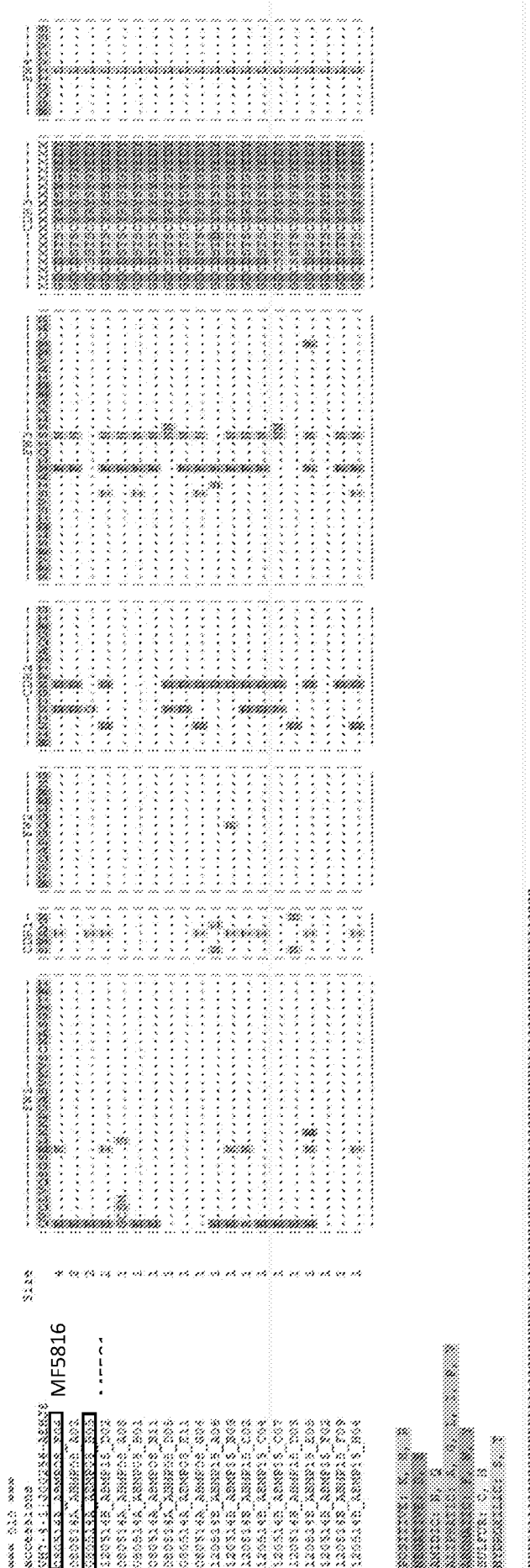


Figure 26
Figure 26A

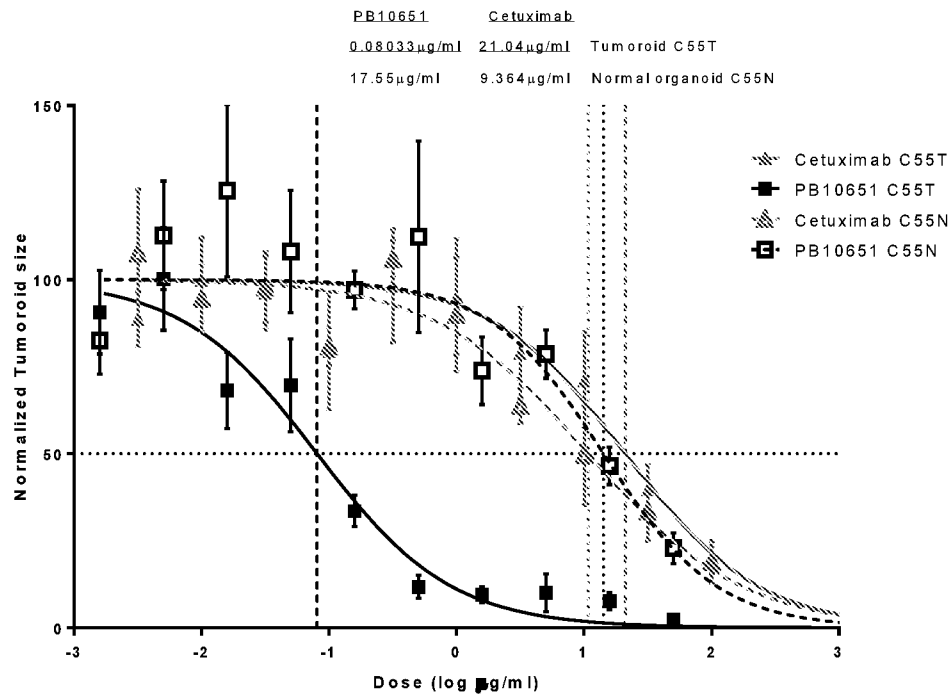


Figure 26B

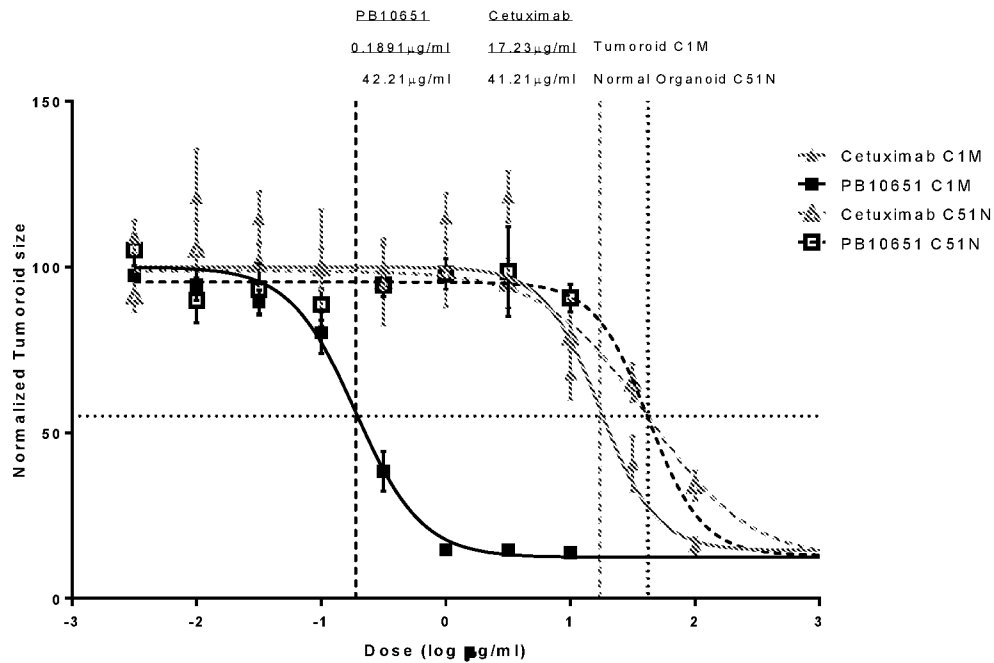


Figure 26C

		IC50 (µg/ml)		
Organoid type	Name	Cetuximab	PB10651	Ratio
Normal	C7N	13.43	19.05	0.7
Normal	C51N	52	67.45	0.8
Normal	C71N	1.37	3.09	0.4
Normal	C57N	1.08	4.52	0.2
Normal	C55N	11.17	14.86	0.8
Tumoroid	C55T	19.63	0.08	245
Tumoroid	C57T	22.75	1.25	18.2
Tumoroid	C0M	10.12	0.39	25.9
Tumoroid	C1M	24.21	0.25	96.8
Tumoroid	C65M	18.92	0.99	19.1
Tumoroid	P18T	5.17	0.25	20.7

Figure 27

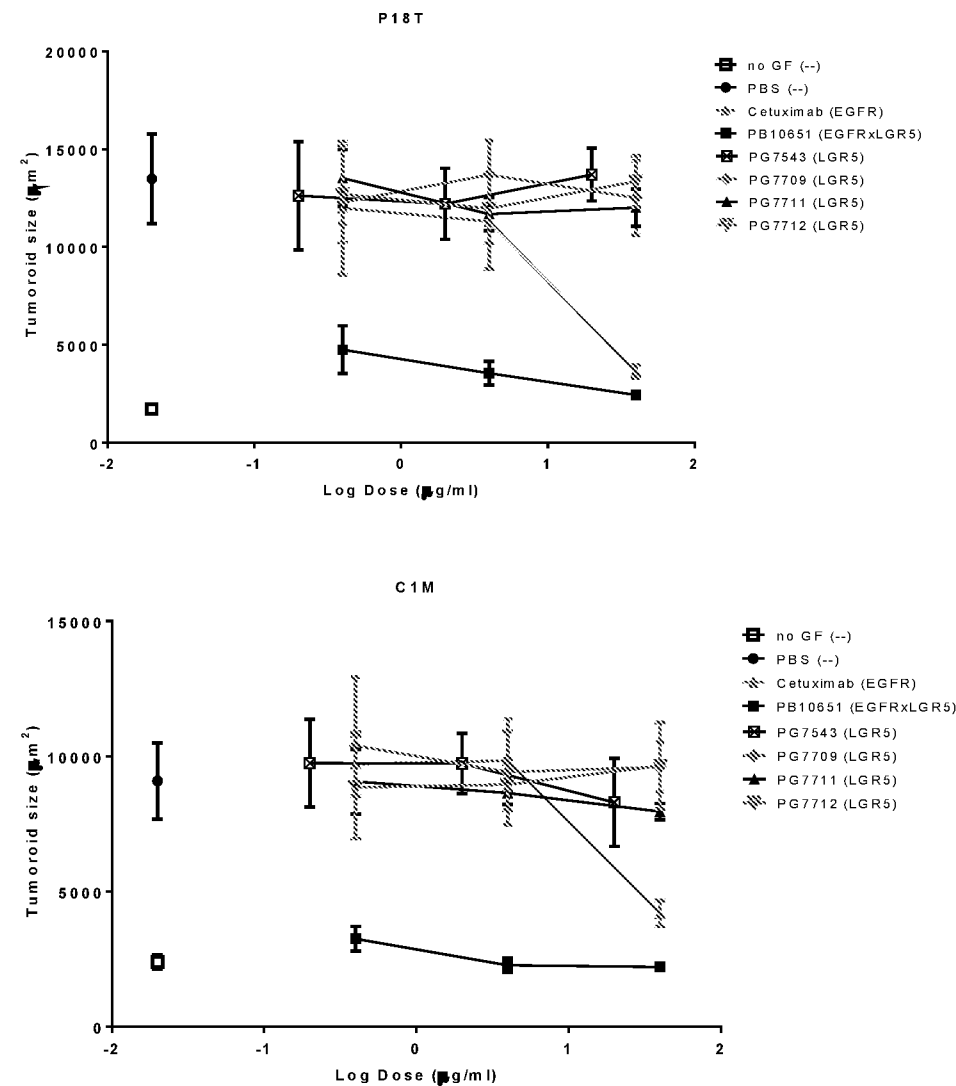


Figure 28
Figure 28A

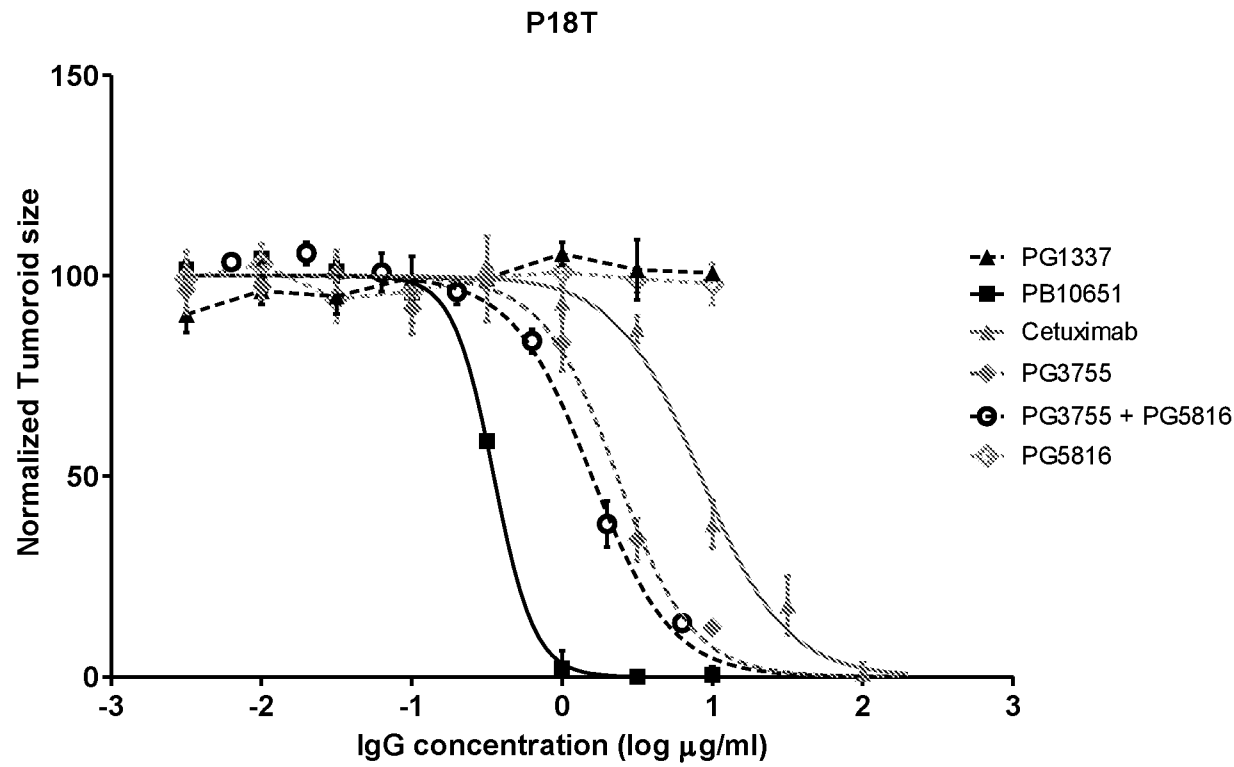
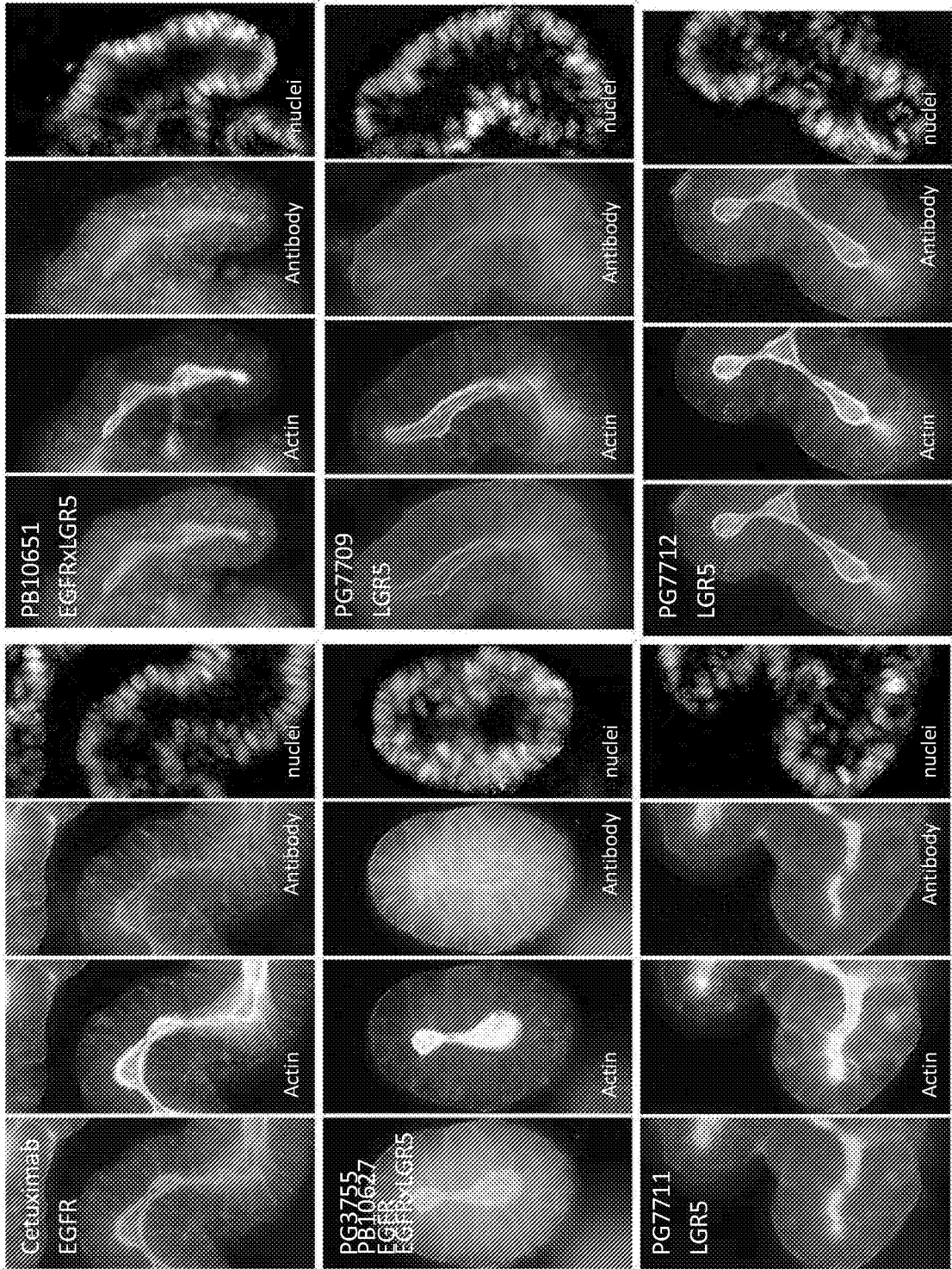


Figure 28B

IC ₅₀ table (µg/ml)		Primary tumour			Metastasis			Normal				
		P18T	C55T	C57T	C65M	C1M	C0M	C51N	C7N	C71N	C55N	C57N
		IC ₅₀	IC ₅₀	IC ₅₀	IC ₅₀	IC ₅₀	IC ₅₀	IC ₅₀	IC ₅₀	IC ₅₀	IC ₅₀	IC ₅₀
EGFR	Cetuximab	8.39	28.51	15.63	15.70	17.10	3.35	26.36	16.11	3.14	2.18	4.80
EGFRxLGR5	PB10651	0.35	0.11	1.20	3.57	0.19	0.14	53.83	17.51	4.77	6.03	8.24
EGFR + LGR5	PG3755 +PG5816	1.59	7.87	16.94	8.89	2.58	1.36	2.17	2.39	0.32	0.47	1.32

Figure 29



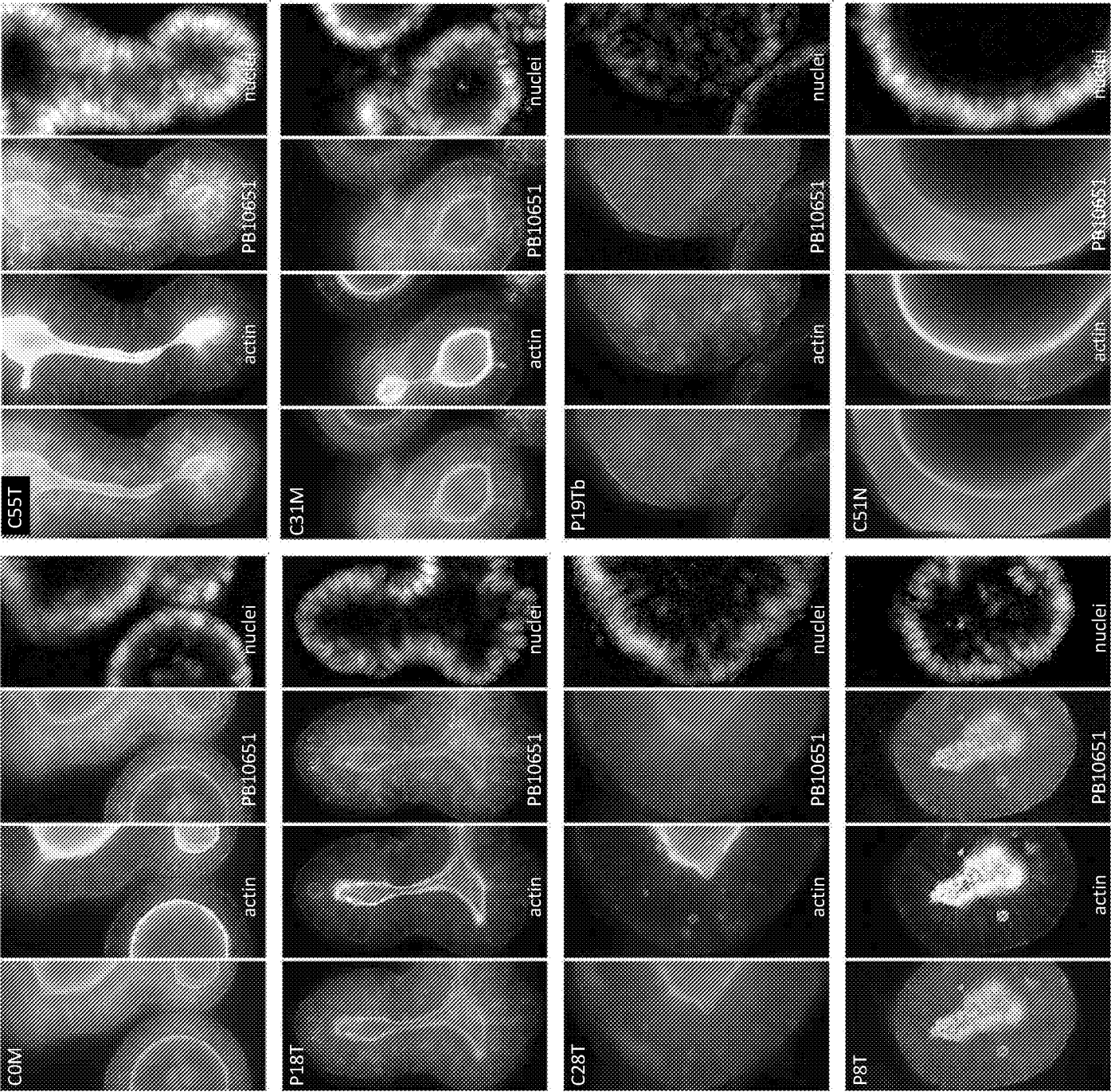


Figure 30

Figure 31

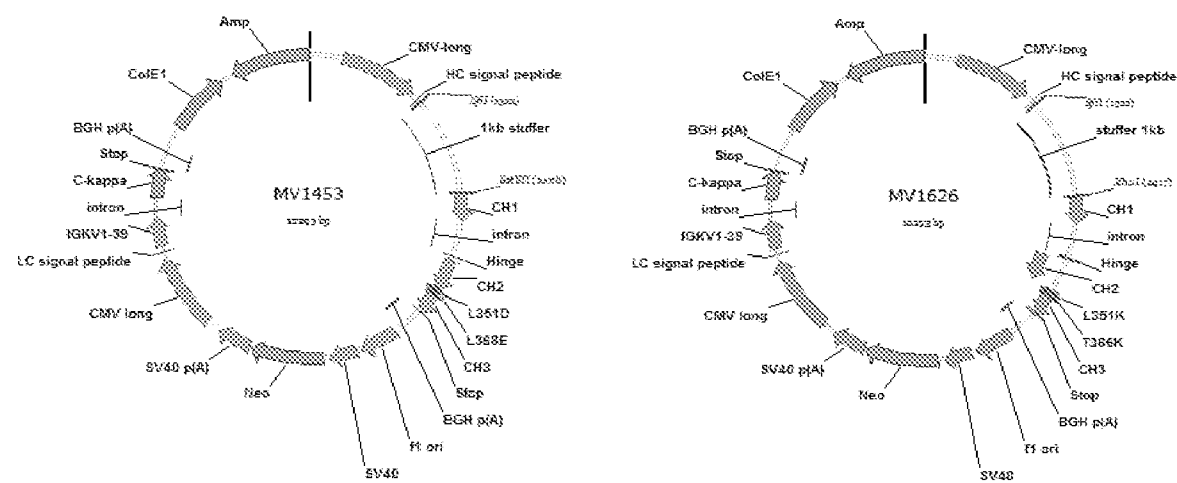


Figure 32

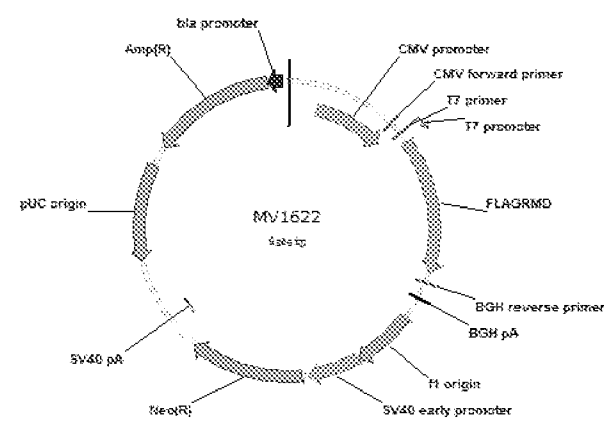


Figure 33

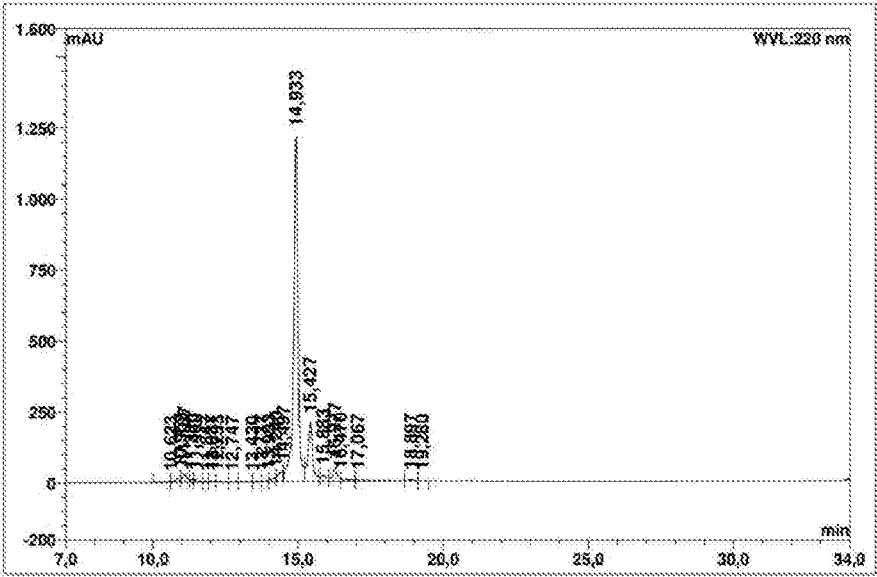


Figure 34

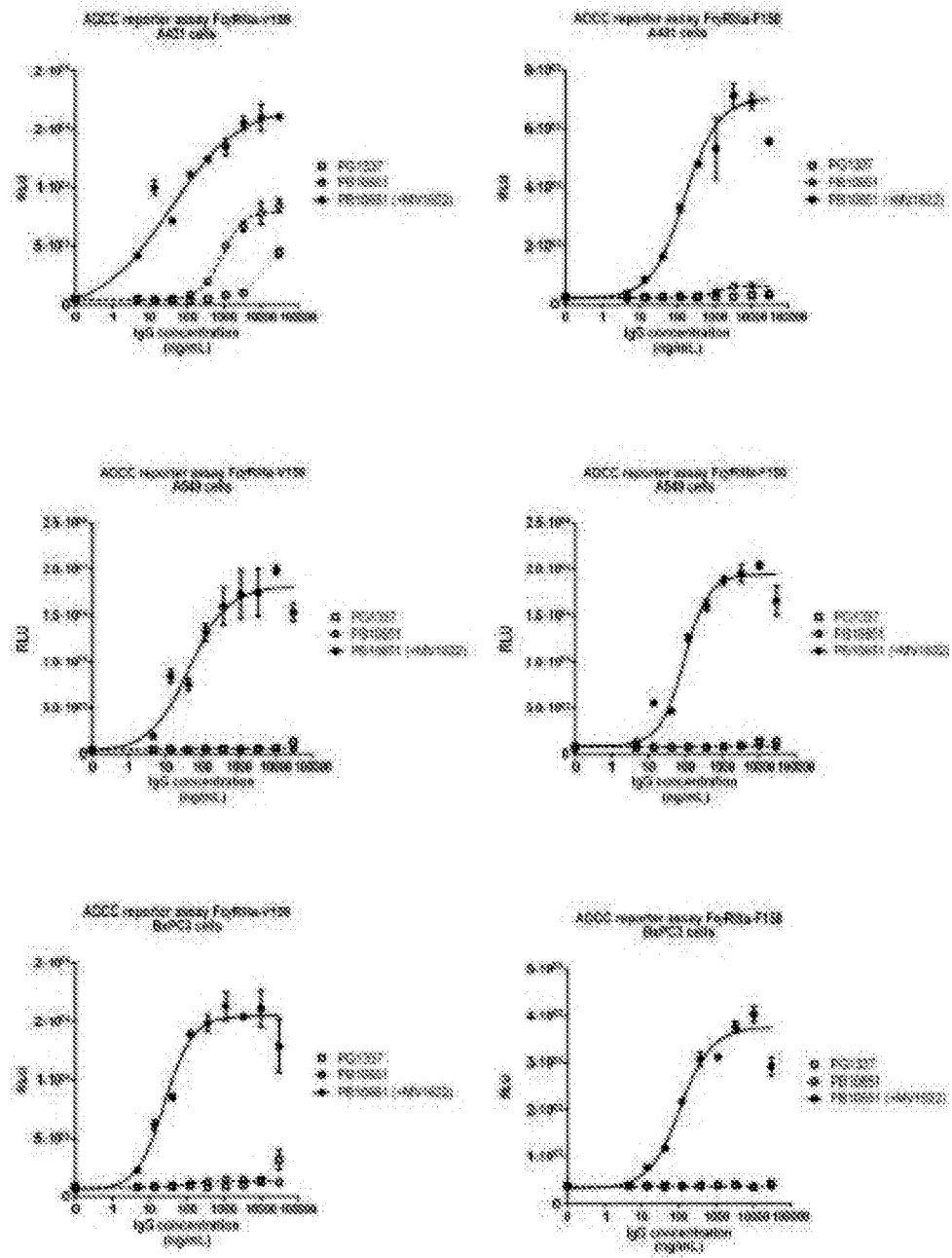


Figure 35

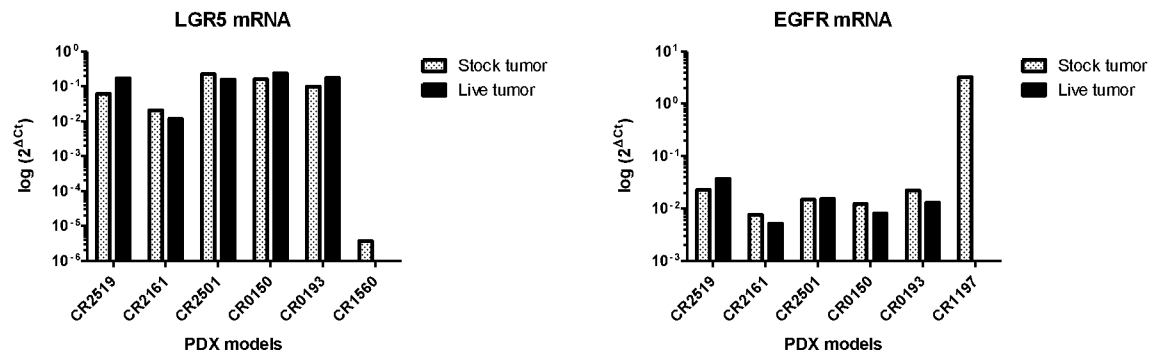


Figure 36

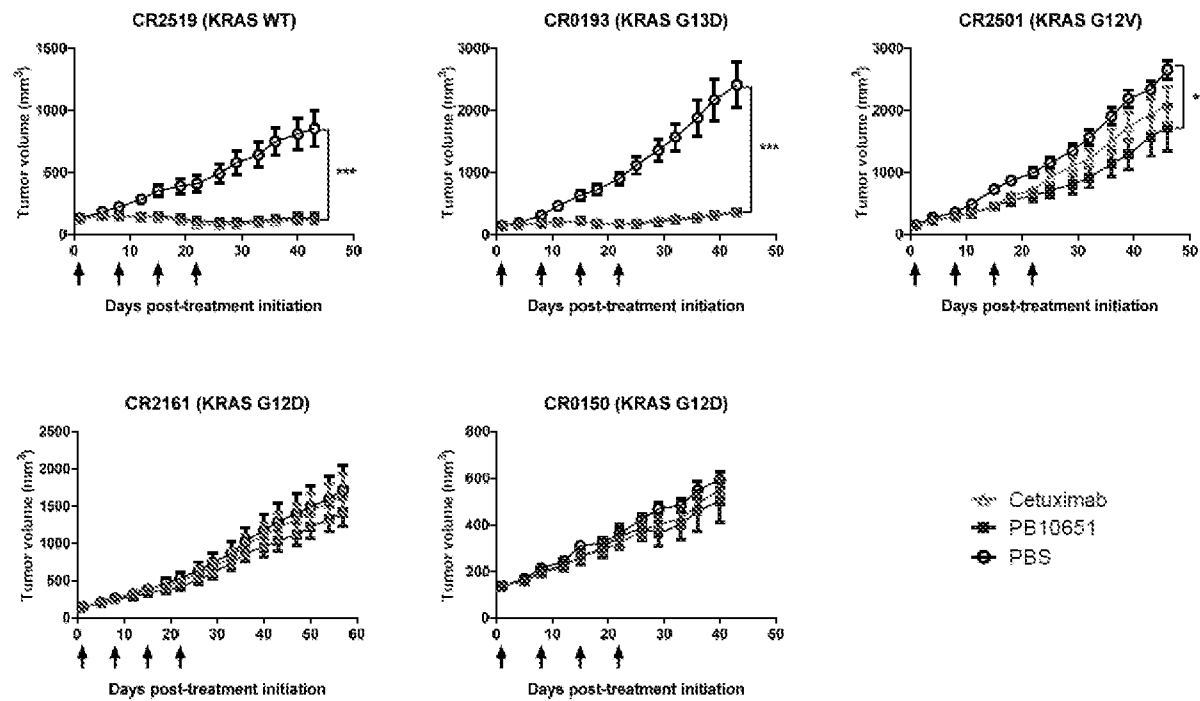


Figure 37

48hrs After Addition of Antibodies

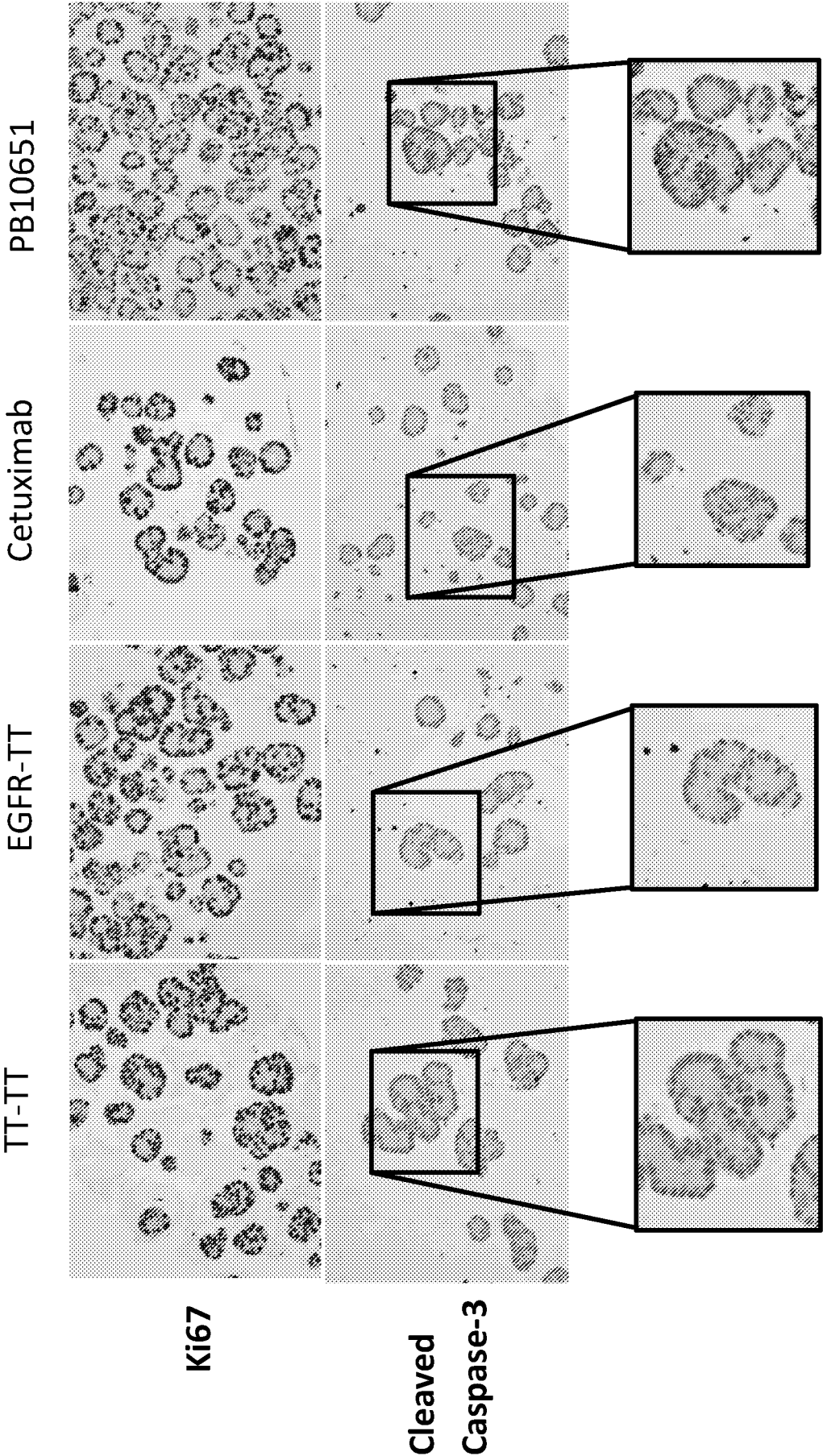


Figure 38

Figure 38A

Average Tumor Volume on Day 0

	Day 0
PBS	46.9
PB10651	47.3
CET	44.3

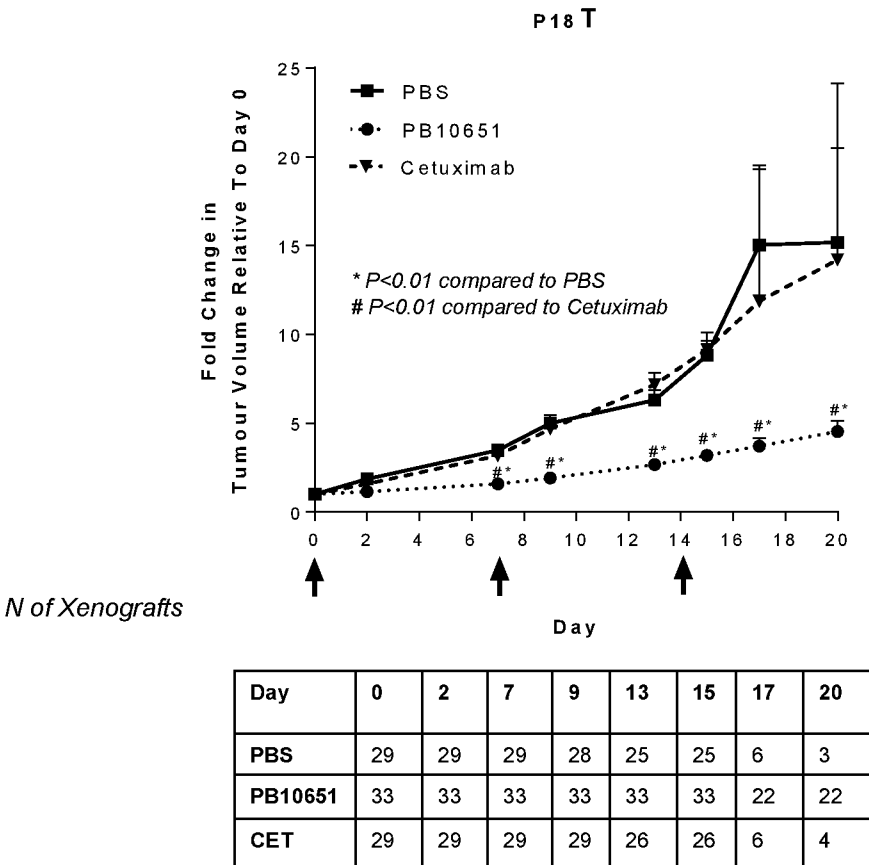


Figure 39

SEQ ID NO:1

MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPHCHCEPDGRMLLRVDCSDLGLSELPSNLSVFTSYLDL
 SMNNISQLLPNPLPSLRFLEELRLAGNALTYPKGAFSTGLYSLKVLMLQNNQLRHVPTEALQNLRLQSLRLD
 ANHISYVPPSCFSGHSLRHLWLDDNALTEIPVQAFRSLALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHN
 NRIHSLGKKCFDGLHSLETLDLNYNNLDEFPTAIRTLNLKELGFHSNNIRSIPEKAFVGNPSLITIHFYDNPIQ
 FVGRSAFQHLPELRTLTLNGASQITEFPDLTG TANLES LTLTGAQISSLPQTVCNQLPNLQVLDLSYNLLEDLP
 SFSVCQKLQKIDLRHNEIYEIKVDTFQQLSLRSLNLAWN KIAIHPNAFSTLPSLIKLDLSSNLLSSFPITGLHG
 LTHLKL TGNHALQSLISSENFPELKVIEMPYAYQCCAFGVCENAYKISNQWNKGDNSSMDDLHKKDAGMFQ
 AQDERDLEDLDFEEDLKALHSVQCSPSPGPFKPEHLLDGWLIRIGVWTIAVLALTCNALVTSTVFRSPLYI
 SPIKLLIGVIAAVNMLTGVS SAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLTLAALERG
 FSVKYS AKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGEPTMGYMVALILLNSLCFL
 MMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNCPVAFLSFSSLINLTFISPEVIKFILLVVVPLPA
 CLNPLLYILFNPHFKEDLVSLRKQTYVWTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPPSSVPSP
 AYPVTE SCHLSSVAFVPCL

Annotated sequence No1:

Mdtsrlgvllslpvllqlat

Signal peptide

GgssprsgvllrgcpthchcepdgrmlrrvdcSDLGLSELPSNLSVFTSY N-region

Ldlsmn nisqlpnplpslrflee	LRR1
Lrlagnaltypkgafstglyslkv	LRR2
Lmlqnnqlrhvp tealqnlrslqs	LRR3
Lrldanhisyvppscfsglslrh	LRR4
Lwlddnalteipvqafsrslsalqa	LRR5
mtlalnkiihipdyafgnlsslvv	LRR6
Lhlhnnrihslgkkcf dglhsletl	LRR7
Dlnynnldefptairtl sn	LRR8
Lkelgfhsnnirsipekafvgnpslit	LRR9
Ihfydnpiqfvgrsafqhlpelrt	LRR10
Ltlngasqitefpdltgtanles	LRR11
Ltl tgaqisslpqtvcnqlpnlqv	LRR12
Ldlsynlledlp sfsvcqklqk	LRR13
Idlrhneiyeikvdtfqqlslr	LRR14
Slnlawnkiaiihpnafstlpslik	LRR15
Ldlssnllssfpitglhglthlk	LRR16
Ltgnhalqslissenfpelkvie m	LRR17

pyayqccafgvcenayk isnqwnkgdnssmddl hkkdagmfqaqderd

46/48

Ledflldfeedlkalhsvqcspspgpfkpcelhldgwlir

CRL region

igvwtiavlaltcnalvtstvf

predicted TM1

*rsplyispi**klligviaavnmltgvsavlagvda*

predicted TM2

*ftfgsfarhgawwengvgchv**igflsifasessvfltltaaler*

predicted TM3

*gfsvkysakfetakpfss**lkviillcallaltmaavpllggsk*

predicted TM4

*ygasplclplpfgepstn**gymvalillnslcflmmtiaytkly*

predicted TM5

*cnldkgdleniwdcsmvk**hialllftncilncpvafsfssl*

predicted TM6

*inltfispevi**kfillvvvplpaclnpllyilfnp*

predicted TM7

*hfkedlvslrkqtyvwtrskhpslmsinsddvekqscdstqalvtft**sssitydlppssvspaypvteschlssvafvpcl*

C-terminal tail

Figure 40

SEQ ID NO: 2

MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLS
 LQRMFNNEEVVLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIP
 LENLQIIRGNMYYENSALAVLSNYDANKTGLKELPMRNLQEILHGAVRF
 SNNPALCNVESIQWRDIVSSDFLSNMSMDFQNLHGSCQKCDPSCPNGSCW
 GAGEENCQKLTKIICAQQCSGRCRGKSPSDCCHNQCAAGCTGPRESCLV
 CRKFRDEATCKDTCPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV
 VTDHGSCVRACGADSYEMEEDGVRKCKKCEGPCRKVCNGIGIGEFKDSLS
 INATNIKHFKNCTSIGDLHILPVAFRGDSFTHTPPLDPQELDILKTVKE
 ITGFLLIQAWPENRTDLHAFENLEIIRGRKQHGQFSLAVVSLNITSLGL
 RSLKEISDGDVVISGNKNLCYANTINWKKLFGTSGQKTKIISNRGENSCK
 ATGQVCHALCSPEGCWGPEPRDCVSCRNVSRGRECVDKCNLLEGEPREFV
 ENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPAGVM
 GENNTLVWKYADAGHVCHLCHPNCTYGCTGPGLEGCPPTNGPKIPSIATGM
 VGALLLLLVLVALGIGLFMRRRHIVRKRTLRLRLQERELVEPLTPSGEAPN
 QALLRILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREA
 TSPKANKEILDEAYVMASVDNPHVCRLLGICLTSTVQLITQLMPFGCLLD
 YVREHKDNIGSQYLLNWCVQIAKGMNYLEDRLVHRDLAARNVLVKTPQH
 VKITDFGLAKLLGAEKEYHAEGKVPIKWMALLESILHRIYTHQSDVWSY
 GVTVWELMTFGSKPYDGIPASEISSILEKGERLPQPPICTIDVYMIMVKC
 WMIDADSRPKFRELIIEFSKMARDPQRYLVIQGDERMHLPSPDTSNFYRA
 LMDEEDMDVDVDADEYLIPOQGFSSPSTSRTPLLSSLSATSNNSTVACI
 DRNGLQSCPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSVPKR
 PAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTPVQPTCVNST
 FDSAPAHWAQKGSQISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRV
 APQSSEFIGA

Annotated seq. No: 2

MRPSGTAGAALLALLAALCPASRA **signal peptide**

LEEKKVCQGTSNKLTQLGTFEDHFLS
 LQRMFNNEEVVLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIP
 LENLQIIRGNMYYENSALAVLSNYDANKTGLKELPMRNLQEILHGAVRF
 SNNPALCNVESIQWRDIVSSDFLSNMSMDFQNLHGSCQKCDPSCPNGSCW
 GAGEENCQKLTKIICAQQCSGRCRGKSPSDCCHNQCAAGCTGPRESCLV
 CRKFRDEATCKDTCPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV
 VTDHGSCVRACGADSYEMEEDGVRKCKKCEGPCRKVCNGIGIGEFKDSLS
 INATNIKHFKNCTSIGDLHILPVAFRGDSFTHTPPLDPQELDILKTVKE
 ITGFLLIQAWPENRTDLHAFENLEIIRGRKQHGQFSLAVVSLNITSLGL
 RSLKEISDGDVVISGNKNLCYANTINWKKLFGTSGQKTKIISNRGENSCK
 ATGQVCHALCSPEGCWGPEPRDCVSCRNVSRGRECVDKCNLLEGEPREFV
 ENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPAGVM
 GENNTLVWKYADAGHVCHLCHPNCTYGCTGPGLEGCPPTNGPKIPSIAT

Extra-cellular domainGMVGALLLLLVLVALGI **predicted transmembrane domain**

GLFMRRRHIVRKRTLRLRLQERELVEPLTPSGEAPN

QALLRILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREA
TSPKANKEILDEAYVMASVDNPHVCRLLGICLTSTVQLITQLMPFGCLLD
YVREHKDNIGSQYLLNWCVQIAKGMNYLEDRLVHRDLAARNVLVKTPQH
VKITDFGLAKLLGAEKEYHAEGGKVPIKWMALESILHRIYTHQSDVWSY
GVTVWELMTFGSKPYDGIPASEISSILEKGERLPQPPICTIDVYMIMVKC
WMIDADSRPKFRELIIEFSKMARDPQRYLVIQGDERMHLPSPDTSNIFYRA
LMDEEDMDDVVDADAYLIPQQGFFSSPSTSRTPLLSSLATSNNSTVACI
DRNGLQSCPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSVPKR
PAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNST
FDSPAHWAAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRV
APQSSEFIGA

Intra-cellular tyrosine kinase and C-terminal tail