Figure 1

MF nr:	Specificity:	Germline:	VH Sequence:
1337	TT	IGVH1-08	EVQLVETGAEVKKPGASVKVSCKASDYLFTKYDINWVRQAPGQGIEWMGWMSANTGNTGYAQKFQGRVTMTRDTSINTAYMELSSLTSGDTAVYFCARSSLFKTETAPYYHFALDVWGQGTTVTVSS
3125	HER3	IGVH3-30	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGSSGWFSYSNWGFDYWGQGTLVTVSS
3176	HER3	IGVH3-23	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDWWYPPYYWGFDYWGQGTLVTVSS
3178	HER3	IGVH1-2	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARDHGSRHFWSYWGFDYWGQGTLVTVSS
4863	HER3	IGVH7-4-1	EVQLVQSGSELKKPGASVKVSCKASGYTSIRYALNWVRQAPGQGLEWLGWINTNTGNPTYARGFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARDTYDSTGYLWFDYWGQGTLVTVSS
3370	EGFR	IGVH1-18	QVQLVQSGAEVKKPGASVKVSCKASGYTFISYGISWVRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCAKDRHWHWWLDAFDYWGQGTLVTVSS
3755	EGFR	IGVH7-4-1	QVQLVQSGSELKKPGASVKISCKASGYDFINYAMNWVRQAPGHGLEWMGWINANTGDPTYAQGFTGRFVFSLDTSVSTAYLQISSLKAEDSAVYYCTRERFLEWLHFDYWGQGTLVTVSS
4280	EGFR	IGVH1-24	QVQLVQSGAEVKKPGASVKVSCKVSGYTLTELSMHWVRQAPGKGLEWMGGFDPEYGKTIFFAQNFQGRVTMTEDTSADTAYMELSSLRSEDTAVYYCATEGYYETTYYYNLFDSWGQGTLVTVSS
4289	EGFR	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKTSGYTFTDYAMTWVRQAPGQGLEWMGWITTNTGDPTYAPGFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARVYHWLRGFEFWGQGTLVTVSS
5777	LGR4	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFTNYVMNWVRQAPGQGLEWMGWINTNTGNPTYAQGFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARWELLDYWGQGTLVTVSS
5781	LGR4	IGVH3-23	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSVISGSGGTTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGAGELDYWGQGTLVTVSS
5790	LGR5	IGVH4-39	QVQLQESGPGLVKPSETLSLTCTVSGGSFSSSSYWGWIRQPPGKGLEWIGSFYYSGNTYYNPSLKSRVTISEDTSKNQFSLKLSSVTAADTAVYYCARQTYSSSWDGVLVYFDYWGQGTLVTVSS
5803	LGR5	IGVH4-59	QVQLQESGPGLVKPSETLSLTCTVSNGSISYYWSWIRQPPGKGLEWIGYVYYTGRTKYNPSLKSRVTISVDTSKNQFSLNLSSVTAADTAVYYCARGGIVVVPAARDYYYYMDVWGKGTTVTVSS
5805	LGR5	IGVH5-51	EVQLVQSGAEVKKPGESLKISCKGSGFSFTSHWIGWVRQKPGRGLEWMGVIYPGDSDTRYSPSFQGQVTVSADKSINTAYLQWNSLKASDTAIYYCARPNSGSPRYFEFWGRGTLVTVSS
5808	LGR5	IGVH4-39	QVQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPGKGLEWIGSFYYSGNTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARQPYYYGSGSPSYYFDYWGQGTLVTVSS
5809	LGR5	IGVH5-51	EVQLVQSGAEVKKPGESLKISCKGSGDSFISHWIAWVRQMPGKGLEWMGIVYPGDSDTRYSPSFQGQVTISADKSITTAYLQWSSLKASDTAMYYCARHEWELLGPFDYWGQGTLVTVSS
5814	LGR5	IGVH1-69	EVQLVQSGAEVKKPGSSVKVSCKASGGTSINDALSWVRQTPGQGLEWMGSIIPILDTTDHAQKFQGRVTITADKSTNTAYMELNSLRSDDTAVYYCARSTNTAYMELNSLRSDDTAVYYCARGDCDSTSCYRYSYGYEDYWGQGTLVTVSS
5816	LGR5	IGVH7-4-1	EVQLVQSGSKLKKPGASVKVSCKASGYTFTSYTMNWVRQAPGQGLEWMGWINTDTGDPTYAQGFTGRFVFSLDTSVSTAFLQINSLKAETDTAVYYCARGDCDSTSCYRYSYGYEDYWGQGTLVTVSS
5817	LGR5	IGVH1-69	QVQLVQSGAEVKKPGSSVKVSCKVSGGTFRSYAISWVRQAPGQGLEWMGGIIPIFDTRNYAQILQGRVTITADLSTSTAYMELNSLRSEDTAIYYCARGSDEGDWFDPWGQGTLVTVSS
5818	LGR5	IGVH1-69	EVQLVQSGTEVRKPGSSVKVSCKASGGTFSNYAISWVRQAPGQGLEWMGSIIPILGTTDHAQKFQDRVTITADKSSNTTYMELSSLRSDDTAVYYCARETIAARLDYFDSWGQGTLVTVSS
5832	RNF43	IGVH3-13	EVQLVESGGGLVQPGGSLRLSCVVSGFTFSYYDMHWVRQVTGKGLEWVSAIGTAGATYYPGSVKGRFTISRENAKNSLYIQMNSLRAGDTAVYYCARDRGYSGVDAYYFDFWGQGTLVTVSS
5836	RNF43	IGVH4-39	QVQLQESGPGLVKPSETLSLTCTVSGGSISSSNYYWGWIRQPPGKGLEWIGNIYYRGYTYYNPSLKSRVTISVDTSKKQFSLTLSSVTAADTAMYYCARRGSDYGDYVGAFDIWDQGTMVTVSS
5839	RNF43	IGVH3-13	EVQLVQSGGGLVQPGGSLRLSCAASGFTFSYYDMHWVRQVTGKGLEWVSTIGATGDTYYSDSVKGRFTISRQNAKNSLYLQINSLRAGDTAVYYCVRDRGYIGYDSYYFDNWGQGTLVTVSS
5850	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFTPYPMNWVRQAPGQGLEWMGWINTNTGNPTYAQGFTGRFVFSLDTSVSTAFLQISSLKAEDTAVYYCARERTNFYDAFDIWGQGTMVTVSS
5853	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFNSYAMDWVRQAPGQGLEWMGWINTNTGNPTYAQAFTGRFVFSLDTSVSTAYLEISSLKAEDTAVYYCARERHGYFPAFDIWGQGTMVTVSS
5855	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFTKYVMNWVRQAPGQGLEWMGWINTNTGNPTYAQGFTGRFVFSLDTSVSTAYLQVSSLRAEDTALYYCARESNWNYDYFDYWGQGTLVTVSS
5862	ZNRF3	IGVH5-51	QVQLVQSGTEVKKPGESLKISCKGSGYSFTTYWIGWVRQMPGKGLEWMGIIYPGDSDTRYSPSFQGQVTISADKSISTAYLQLSSLKASDTAMYYCARRGLSMVPLSAFDVWGQGTIVTVSS
5882	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFTGNPTYAQGFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARDRGSYTYDAFDIWGQGTMVTVSS
5884	ZNRF3	IGVH7-4-1	EVQLVQSGSELKKPGASVKVSCKASGYTFTKYAMNWVRQVPGQGLEWMGWINTNTGNPTYAQGFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARKGGSYYDWFDPWGQGTLVTVSS
5887	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFTRYAMNWVRQAPGQGLEWMGWINTNTGKPTYAQGFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARDKGYNWNYMGALFDIWGQGTTVTVSS
5888	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGGSMKVSCKASGYTFTRYAMNWLRQAPGQGLEWMGWINTNTGNPTYAQGFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARRSGSYYDYEFDYWGQGTLVTVSS

MF nr:	Specificity:	Germline:	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
1337	TT	IGVH1-08	EVQLVETGAEVKKPGASVKVSCKASDYIFT	KYDIN	WVRQAPGQGLEWMG	WMSANTGNTGYAQKFQG	RVTMTRDTSINTAYMELSSLISGDTAVYFCAR	SSLFKTETAPYYHFALDV	WGQGTTVTVSS
3125	HER3	IGVH3-30	QVQLVESGGGVVQPGRSLRLSCAASGFTFS	SYGMH	WVRQAPGKGLEWVA	VISYDGSNKYYADSVKG	RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK	GSSGWFSYSNWGFDY	WGQGTLVTVSS
3176	HER3	IGVH3-23	EVQLLESGGGLVQPGGSLRLSCAASGFTFS	SYAMS	WVRQAPGKGLEWVS	AISGSGGSTYYADSVKG	RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR	DWWTPPYYWGFDY	WGQGTLVTVSS
3178	HER3	IGVH1-2	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	GYYMH	WVRQAPGQGLEWMG	WINPNSGGTNYAQKFQG	RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR	DIGSRHFWSYWGFDY	WGQGTLVTVSS
4863	HER3	IGVH7-4-1	EVQLVQSGSELKKPGASVKVSCKASGYTSI	RYALN	WVRQAPGQGLEWLG	WINTNTGNPTYARGFTG	RFVFSLDTSVSTAYLQISSLKAEDTAVYYCAR	DTYDSTGYLWFDY	WGQGTLVTVSS
3370	EGFR	IGVH1-18	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	SYGIS	WVRQAPGQGLEWMG	WISAYNGNTNYAQKLQG	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAK	DRHWHWWLDAFDY	WGQGTLVTVSS
3755	EGFR	IGVH7-4-1	QVQLVQSGSELKKPGASVKISCKASGYDFT	NYAMN	WVRQAPGHGLEWMG	WINANTGDPTYAQGFTG	RFVFSLDTSVSTAYLQISSLKAEDSAVYYCTR	ERFLEWLHFDY	WGQGTLVTVSS
4280	EGFR	IGVH1-24	QVQLVQSGAEVKKPGASVKVSCKVSGYTLT	ELSMH	WVRQAPGKGLEWMG	GFDPEYGKTIFAQNFQG	RVTMTEDTSADTAYMELSSLRSEDTAVYYCAT	EGYYETTTYYYNLFDS	WGQGTLVTVSS
4289	EGFR	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKTSGYTFT	DYAMT	WVRQAPGQGLEWMG	WITTNTGDPTYAPGFTG	RFVFSLDTSVSTAYLQISSLKAEDTAVYYCAR	VYHWIRGFEF	WGQGTLVTVSS
5777	LGR4	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFT	NYVMN	WVRQAPGQGLEWMG	WINTNTGNPTYAQGFTG	RFVFSLDTSVSTAYLQISSLKAEDTAVYYCAR	WELLDY	WGQGTLVTVSS
5781	LGR4	IGVH3-23	EVQLVESGGGLVQPGGSLRLSCAASGFTFS	SYAMS	WVRQAPGKGLEWVS	VISGSGGSTYYADSVKG	RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK	GAGELDY	WGQGTLVTVSS
5790	LGR5	IGVH4-39	QVQLQESGPGLVKPSETLSLTCTVSGGSFS	SSSYYWG	WIRQPPGKGLEWIG	SIYYSGNTYYNPSLKS	RVTISEDTSKNQFSLKLSSVTAADTAVYYCAR	QTYSSSWDGVLIYFDY	WGQGTLVTVSS
5803	LGR5	IGVH4-59	QVQLQESGPGLVKPSETLSLTCTVSNGSIS	TYYWS	WIRQPPGKGLEWIG	YVYYTGRTKYNPSLKS	RVTISVDTSKNQFSLNLSSVTAADTAVYYCAR	GGIVVVPAARDYYYMDV	WGKGTTVTVSS
5805	LGR5	IGVH5-51	EVQLVQSGAEVKKPGESLKISCKGSGFSFT	SHWIG	WVRQKPGKGLEWMG	VIYPGDSDTRYSPSFQG	QVTVSADKSINTAYLQWNSLKASDTAIYYCAR	PNSGSPRYFEF	WGRGTLVTVSS
5808	LGR5	IGVH4-39	QVQLQESGPGLVKPSETLSLTCTVSGGSIS	SSSYYWG	WIRQPPGKGLEWIG	SIYYSGNTYYNPSLKS	RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR	QRYYYGSGSPSYYFDY	WGQGTLVTVSS
5809	LGR5	IGVH5-51	EVQLVQSGAEVKKPGESLKISCKGSGDSFI	SHWIA	WVRQMPGKGLEWMG	IVYPGDSDTRYSPSFQG	QVTISADKSITTAYLQWSSLKASDTAMYYCAR	HEWELLGFFDY	WGQGTLVTVSS
5814	LGR5	IGVH1-69	EVQLVQSGAEVKKPGSSVKVSCKASGGTST	NDAIS	WVRQTPGQGLEWMG	SIIPILDTTDHAQKFQG	RVTITADKSTNTAYMELNSLRSDDTAVYYCAR	EHIAARQDYFDY	WGQGTLVTVSS
5816	LGR5	IGVH7-4-1	EVQLVQSGSELKKPGASVKVSCKASGYTFT	SYTMN	WVRQAPGQGLEWMG	WINTDTGDPTYAQGFTG	RFVFSLDTSVSTAFLQINSLKAEDTAVYYCAR	GDCDSTSCYKYSYGYEDY	WGQGTLVTVSS
5817	LGR5	IGVH1-69	QVQLVQSGAEVKKPGSSVKVSCKVSGGTFR	STAIS	WVRQAPGQGLEWMG	GIIPIFDTRNYAQILQG	RVTITADLSTSTAYMELNSLRSEDTAIYYCAR	GSDEGDWFDP	WGQGTLVTVSS
5818	LGR5	IGVH1-69	EVQLVQSGTEVKKPGSSVKVSCKASGGTFS	NYAIS	WVRQAPGQGLEWMG	SIIPILGTTDHAQKFQD	RVTITADKSSNTTYMELSSLRSDDTAVYYCAR	EYIAARLDYFDS	WGQGTLVTVSS
5832	RNF43	IGVH3-13	EVQLVESGGGLVQPGGSLRLSCVVSGFTFS	YYDMH	WVRQVTGKGLEWVS	AIGTAGATYYPGSVKG	RFTISRENAKNSLYLQMNSLRAGDTAVYYCAR	DRGYSGYDAYYFDF	WGQGTLVTVSS
5836	RNF43	IGVH4-39	QVQLQESGPGLVKPSETLSLTCTVSGGSIS	SSNYYWG	WIRQPPGKGLEWIG	NIYYRGYTYYNPSLKS	RVTISVDTSKKQFSLTLSSVTAADTAMYYCAR	EGSDYGDYVGAFDI	WDQGTMVTVSS
5839	RNF43	IGVH3-13	EVQLVQSGGGLVQPGGSLRLSCAASGFTFS	YYDMH	WVRQVTGKGLEWVS	TIGATGDTYYSDSVKG	RFTISRQNAKNSLYLQINSLRAGDTAVYYCVR	DRGYIGYDSYYFDN	WGQGTLVTVSS
5850	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFT	RYPMN	WVRQAPGQGLEWMG	WINTNTGNPTYAQGFTG	RFVFSLDTSVSTAFLQISSLKAEDTAVYYCAR	ERTNFYDAFDI	WGQGTMVTVSS
5853	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFN	SYAMD	WVRQAPGQGLEWMG	WINTNTGNPTYAQAFTG	RFVFSLDTSVSTAYLEISSLKAEDTAVYYCAR	ERHGYFEAFDI	WGQGTTVTVSS
5855	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFT	KYVMN	WVRQAPGQGLEWMG	WINTNTGNPTYAQGFTG	RFVFSLDTSVSTAYLQVSSLRAEDTAIYYCAR	ESNWNYDYFDY	WGQGTLVTVSS
5862	ZNRF3	IGVH5-51	QVQLVQSGTEVKKPGESLKISCKGSGYSFT	TYWIG	WVRQMPGKGLEWMG	IIYPGDSDTRYSPSFQG	QVTISADKSISTAYLQLSSLKASDTAMYYCAR	RGLSMVRLSAFDV	WGQGTLVTVSS
5882	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFT	RYAMN	WVRQAPGQGLEWMG	WINTKTGNPTYAQGFTG	RFVFSLDTSVSTAYLQISSLKAEDTAVYYCAR	DRGSYYDAFDI	WGQGTMVTVSS
5884	ZNRF3	IGVH7-4-1	EVQLVQSGSELKKPGASVKVSCKASGYTFT	KYAMN	WVRQVPGQGLEWMG	WINTNTGNPTYAQGFTG	RFVFSLDTSVRVTAYLQISSLKAEDTAVYYCAR	KGGSYYDWFDP	WGQGTLVTVSS
5887	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGASVKVSCKASGYTFT	RYAMN	WVRQAPGQGLEWMG	WINTNTGKPTYAQGFTG	RFVFSLDTSVSTAYLQISSLKAEDTAVYYCAR	DRGYNWNYMGAFDI	WGQGTTVTVSS
5888	ZNRF3	IGVH7-4-1	QVQLVQSGSELKKPGGSMKVSCKASGYTFT	RYAMN	WLRQAPGQGLEWMG	WINTNTGNPTYAQGFTG	RFVFSLDTSVSTAYLQISSLKAEDTAVYYCAR	RSGSYYDYFDY	WGQGTLVTVSS

Figure 2

MF1337:
gaggtgcagctggtggagactggggctgaggtgaagaagccgggggcctcagtgaaggtctcctgcaagg
cttctgactacatcttcaccaaatatgacatcaactgggtgcgccaggcccctggacaagggcttgaatg
gatgggatggatgagcgctaacactggaaacacgggctatgcacagaagttccagggcagagtcaccatg
accagggacacgtccataaacacagcctacatggagctgagcagcctgacatctggtgacacggccgttt
atttctgtgcgaggagtagtcttttcaagacagagacggcgccctactatcacttcgctctggacgtctg
gggccaagggaccacggtcaccgtctccagt

MF3755:
caggtgcagctggtgcagtctgggtctgagttgaagaagcctggggcctcagtgaagatttcctgcaagg
cttctggatacgacttcactaactatgctatgaattgggtgcgacaggcccctggacacgggcttgagtg
gatgggatggatcaacgccaacactggggacccaacgtatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctgcagatcagcagtttaaaggctgaggactctgccgtgt
attactgtacgagagagcgatttttggagtggttacactttgactactggggccagggaaccctggtcac
cgtctccagt

MF3178:
caggtgcagctggtgcagtctggggctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaagg
cttctggatacaccttcaccggctactatatgcactgggtgcgacaggcccctggacaagggcttgagtg
gatgggatggatcaacccctaacagtggtggcacaaactatgcacagaagtttcagggcagggtcacgatg
accagggacacgtccatcagcacagcctacatggagctgagcaggctgagatctgacgacacggctgtgt
attactgtgcaagagatcatggttctcgtcatttctggtcttactggggctttgattattggggccaagg
taccctggtcaccgtctccagt

MF5790:
caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactg
tctctggtggctccttcagcagtagtagttcctactggggctggatccgccagcccccagggaaggggct
ggagtggattgggagtttctattatagtgggaacacctactacaacccgtccctcaagagtcgagtcacc
atatccgaagacacgtccaagaaccagttctccctgaagctgagctctgtgaccgccgcagacacggctg
tgtattactgtgcgagacagacgtatagcagcagctgggacggggtcctgtactactttgactactgggg
ccagggaaccctggtcaccgtctccagt

MF5816:

gaggtgcagctggtgcagtctgggtctaaattgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatacaccttcactagctatactatgaattgggtgcgacaggcccctggacaagggcttgagtg
gatgggatggatcaacaccgacactggggacccaacgtatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatttctacagatcaacagcctaaaggctgaggacactgccgtat
attactgtgcgagaggagattgtgatagtaccagctgctatagatacagttatggttacgaggactactg
gggccagggaaccctggtcaccgtctccagt

MF3125:
caggtgcagctggtggagtctgggggaggcgtggtccagcctgggaggtccctgagactctcctgtgcag
cctctggattcaccttcagtagctatggcatgcactgggtccgccaggctccaggcaaggggctggagtg
ggtggcagttatatcatatgatggaagtaataaatactatgcagactccgtgaagggccgattcaccatc
tccagagacaattccaagaacacgctgtatctgcaaatgaacagcctgagagctgaggacacggccgtgt
attactgtgcaaaaggttcttctggttggccgtcttactctaactggggctttgattattggggccaagg
taccctggtcaccgtctccagt

MF3176:
gaggtgcagctgttggagtctgggggaggcttggtacagcctgggggtccctgagactctcctgtgcag
cctctggattcacctttagcagctatgccatgagctgggtccgccaggctccagggaaggggctggagtg
ggtctcagctattagtggtagtggtggtagcacatactacgcagactccgtgaagggccggttcaccatc
tccagagacaattccaagaacacgctgtatctgcaaatgaacagcctgagagccgaggacacggctgtgt
attactgtgcaagagattggtggtacccgccgtactactggggctttgattattggggccaaggtaccct
ggtcaccgtctccagt

MF4863:
gaggtgcagctggtgcagtctgggtctgagttgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatacacctccattagatatgctttgaactgggtgcgacaggcccctggacaaggccttgagtg
gctgggatggatcaacaccaacactgggaacccaacgtatgcccggggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctgcagatcagcagcctaaaggctgaggacactgccgtgt
attactgtgcgagagatacttatgatagtactggttatctttggtttgactactggggccagggaaccct
ggtcaccgtctccagt

MF3370:
caggttcagctggtgcagtctggagctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaagg
cttctggttacacctttaccagctatggtatcagctgggtgcgacaggcccctggacaagggcttgagtg
gatgggatggatcagcgcttacaatggtaacacaaactatgcacagaagctccagggcagagtcaccatg
accacagacacatccacgagcacagcctacatggagctgaggagcctgagatctgacgacacggctgtgt
attactgtgcaaaagatcgtcattggcattggtggctggacgcctttgattattggggccaaggtaccct
ggtcaccgtctccagt

MF4280:
caggtgcagctggtgcagtctggggctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaagg
tttccggatacaccctcactgaattatccatgcactgggtgcgacaggctcctggtaaagggcttgaatg
gatgggaggctttgatcctgagtatggtaaaacattcttcgcacagaacttccagggcagagtcaccatg
accgaggacacatctgcagacacagcctacatggagctaagcagcctgagatctgaggacacggccgtgt
attactgtgcaacagaggggtattatgagactactacttattactacaacctttttgactcctggggcca
gggaaccctggtcaccgtctccagt

MF4289:
caggtgcagctggtgcaatctgggtctgaattgaagaagcctggggcctcagtgaaggtttcctgcaaga
cttctggatacaccttcactgactatgctatgacttgggtgcgacaggcccctggacaagggcttgaatg
gatgggatggatcaccaccaacactggggacccaacgtatgccccgggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctgcagatcagcagcctaaaggccgaggacactgccgtat
attactgtgcgagagtgtatcattggatacggggatttgagttttggggccagggaaccctggtcaccgt
ctccagt

MF5777:
caggtgcagctggtgcaatctgggtctgagttgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatacaccttcactaactatgttatgaattgggtgcgacaggcccctggacaagggcttgagtg
gatgggatggatcaacaccaacactgggaacccaacgtatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctgcagatcagcagcctaaaggctgaggacactgccgtgt
attactgtgcgaggtgggagctactagactactggggccagggaaccctggtcaccgtctccagt

MF5781:
gaggtgcagctggtggagtctgggggaggcttggtacagcctgggggtccctgagactctcctgtgcag
cctctggattcacctttagcagctatgccatgagctgggtccgccaggctccagggaaggggctggagtg
ggtctcagttattagtggtagtggtgggaccacatactacgcagactccgtgaagggccggttcaccatc

tccagagacaattccaagaacacgctgtatctgcaaatgaacagcctgagagccgaggacacggccgtat
attactgtgcgaaaggggctggggagcttgactactggggccagggaaccctggtcaccgtctccagt

MF5803:

caggtgcagctgcaggagtcggggccaggactggtgaagccttcggagaccctgtccctcacctgcactg
tctctaatggctccatcagtacttactactggagctggatccggcagcccccagggaaggggctggagtg
gattggatatgtctattacactgggcgcaccaagtacaacccctccctcaagagtcgagtcaccatatca
gtagacacgtccaagaaccagttctccctgaacctgagttctgtgaccgctgcggacacggccgtgtatt
actgtgcgagaggggtattgtagtagtcccagctgcgcgggactattactactacatggacgtctgggg
caaagggaccacggtcaccgtctccagt

MF5805:

gaggtgcaactggtgcagtctggagcagaggtgaaaaagcccggggagtctctgaagatcgcctgtaagg
gttctggattcagttttaccagccactggatcggctgggtgcgccagaagcccgggagaggcctggagtg
gatgggggtcatctatcctggtgactctgataccagatacagcccgtccttccaaggccaggtcaccgtc
tcagccgacaagtccatcaataccgcctacctgcagtggaacagcctgaaggcctcggacaccgccatat
attactgtgcgagaccgaacagtgggagtccccggtacttcgagttctggggccgtggcaccctggtcac
cgtctccagt

MF5808:

caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactg
tctctggtggctccatcagcagtagtagttactactggggctggatccgccagcccccagggaaggggct
ggagtggattgggagtttctattatagtgggaacacctactacaacccgtccctcaagagtcgagtcacc
atatccgtagacacgtccaagaaccagttctccctgaagctgagctctgtgaccgccgcagacacggctg
tgtattactgtgcgagacaggagtattactatggttcggggagtccttcgtactactttgactactgggg
ccagggaaccctggtcaccgtctccagt

MF5809:

gaggtgcagctggtgcagtctggagcagaggtgaaaaagcccggggagtctctgaagatctcctgtaagg
gttctggagacagttttatcagccactggatcgcctgggtgcgccagatgcccgggaaaggcctggagtg
gatggggatcgtctatcctggtgactctgataccagatacagcccgtccttccaaggccaggtcaccatc
tcagccgacaagtccatcaccaccgcctacttgcagtggagcagcctgaaggcctcggacaccgccatgt
attactgtgcgagacacgagtgggaactacttggccccctttgactactggggccagggaaccctggtcac
cgtctccagt

MF5814:

gaggtgcagctggtgcagtctggggctgaggtgaagaagcctgggtcctcggtgaaggtctcctgcaagg
cttctggaggcacctccactaacgatgctatcagttgggtgcgacagacccctggacaagggcttgagtg
gatgggaagtatcatccctatccttgatacaacagaccacgcacagaagttccagggcagagtcacgatt
accgcggacaaatccacgaacacagcctacatggagctgaacagcctgagatctgatgacacggccgtgt
attactgtgcgagagagcatatagcagctcgtcaggactactttgactattggggccagggaaccctggt
caccgtctccagt

MF5817:

caggtgcagctggtgcagtctggggctgaggtgaagaagcctgggtcctcggtgaaggtctcctgcaagg
tttctggaggcaccttcaggagctatgctatcagctgggtgcgacaggcccctggacaagggcttgagtg
gatgggagggatcatccctatctttgatacaagaaactacgcacagattcttcagggcagagtcacgatt
accgcggacttatccacgagcacagcctacatggagctgaacagtctgagatctgaggacacggccattt
attactgtgcgagagggagcgacgaggggactggttcgacccctggggccaaggaaccctggtcaccgt
ctccagt

MF5818:
gaggtgcagctggtgcagtctgggactgaggtgaggaagcctgggtcctcggtgaaggtctcctgcaagg
cttctggaggcaccttcagcaactatgctatcagctgggtgcgacaggcccctggacaggggcttgagtg
gatgggaagtatcatccctatccttggaacaacagaccacgcacagaagttccaggacagagtcacgatt
accgcggacaaatcctcgaacacaacctacatggagctgagcagcctgagatctgatgacacggccgtat
attactgtgcgagagagtatatagcagctcgtctggactactttgactcttggggccagggaaccctggt
caccgtctccagt

MF5832:
gaggtgcagctggtggagtctgggggaggcttggtacagcctgggggtccctgagactctcctgtgtag
tctctggattcaccttcagttactacgacatgcactgggtccgccaagtcacaggaaaaggtctggagtg
ggtctcagctattggcactgctggtgccacatactatccaggctccgtgaagggccgattcaccatctcc
agagaaaatgccaagaactccttgtatcttcaaatgaatagcctgagagccggggacacggctgtgtatt
actgtgcaagagatcgtggatatagtggctacgatgcgtactactttgacttctggggccagggaaccct
ggtcaccgtctccagt

MF5836:
caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactg
tctctggtggctccatcagcagtagtaattactactggggctggatccgccagcccccagggaaggggct
ggagtggattgggaatatctattatagagggtacacctattataacccgtccctcaagagtcgagtcacc
atatccgtagacacgtccaagaagcagttctccctgacgctgagctctgtgaccgccgcagacacggcta
tgtattactgtgcgagagaggggagtgactacggtgactacgtaggagcttttgatatctgggaccaagg
gacaatggtcaccgtctccagt

MF5839:
gaggtgcagctggtgcagtctgggggaggcttggtacagcctgggggtccctgagactctcctgtgcag
cctctggattcaccttcagttactacgacatgcactgggtccgccaagttacaggaaaaggtctggagtg
ggtctcaactattggtgctactggtgacacatactattcagactccgtgaagggccgatttaccatctcc
agacaaaatgccaagaactccttgtatcttcaaataaacagcctgagagccggggacacggctgtatatt
actgtgtaagagatcgtggatatattggctacgattcgtactactttgacaactggggccagggaaccct
ggtcaccgtctccagt

MF5850:
caggtgcagctggtgcagtctgggtctgagttgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatacaccttcactaggtatcctatgaattgggtgcgacaggcccctggacaagggcttgagtg
gatgggatggatcaacaccaacactgggaacccaacatatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatttctgcagatcagcagcctaaaggctgaggacactgccgtgt
attactgtgcgagagagaggactaacttttatgatgcttttgatatctggggccaagggacaatggtcac
cgtctccagt

MF5853:
caggtgcagctggtgcaatctgggtctgagttgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatataccttcaatagctatgctatggattgggtgcgacaggcccctggacaagggcttgagtg
gatgggatggatcaacaccaatactgggaacccaacgtatgcccaggccttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctggagatcagcagcctaaaggctgaggacactgccgtgt
attactgtgcgagagagaggcatggatattttgaagcttttgatatctggggccaagggaccacggtcac
cgtctccagt

MF5855:
caggtgcagctggtgcaatctgggtctgagttgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatacaccttcactaagtatgttatgaattgggtgcgacaggcccctggacaagggcttgagtg

gatgggatggatcaacaccaacactgggaacccaacgtatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctgcaggtcagcagtctaagggctgaggacactgccctgt
attactgtgcgagagagtctaactggaactacgactactttgactactggggccagggcaccctggtcac
cgtctccagt

MF5862:
caggtgcagctggtgcagtctggaacagaggtgaaaaagcccggggagtctctgaagatctcctgtaagg
gttctggatacagctttaccacctactggatcggctgggtgcgccagatgcccgggaaaggcctggagtg
gatgggaatcatctatcctggtgactctgataccagatacagcccgtccttccaaggccaggtcaccatc
tcagccgacaagtccatcagcaccgcctacctgcagttgagcagcctgaaggcctcggacaccgccatgt
attactgtgcgagacggggtcttagtatggttcggttgagcgcttttgatgtctggggccaaggaaccct
ggtcaccgtctccagt

MF5882:
caggtgcagctggtgcaatctgggtctgagttgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatacaccttcactagatatgctatgaattgggtgcgacaggcccctggacaagggcttgagtg
gatgggatggatcaacaccaaaactgggaacccaacgtatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctgcagatcagcagcctaaaggctgaggacactgccgtgt
attactgtgcgagagatcgtgggagctactatgatgcttttgatatctggggccaagggacaatggtcac
cgtctccagt

MF5884:
gaggtgcagctggtgcagtctgggtctgaattgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatacaccttcactaagtatgctatgaattgggtgcgacaggtccctggacaagggcttgagtg
gatgggatggatcaacaccaacactgggaacccaacgtatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtccgcacggcatatctgcagatcagcagcctaaaggctgaggacactgccgtgt
attactgtgcgagaaaaggggggagctactacgactggttcgacccctggggccagggaaccctggtcac
cgtctccagt

MF5887:
caggtgcagctggtgcagtctgggtctgagttgaagaagcctggggcctcagtgaaggtttcctgcaagg
cttctggatacaccttcactcgctatgctatgaattgggtgcgacaggcccctggacaagggcttgagtg
gatgggatggatcaacaccaacactgggaaaccaacgtatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctgcagatcagcagcctgaaggctgaggacactgccgtgt
attactgtgcgagagataagggctataactggaactacatgggtgcttttgatatctggggccaagggac
cacggtcaccgtctccagt

MF5888:
caggtgcagctggtgcagtctgggtctgagttgaagaagcccgggggctcaatgaaggtttcctgcaagg
cttctggatacaccttcactagatatgctatgaattggttgcgacaggcccctggacaagggcttgagtg
gatgggatggatcaacaccaacactgggaacccaacgtatgcccagggcttcacaggacggtttgtcttc
tccttggacacctctgtcagcacggcatatctgcagatcagcagcctaaaggctgaggacactgccgtct
attattgtgcgagacggagtgggagctactacgactactttgactactggggccagggaaccctggtcac
cgtctccagt

Figure 3

Common Light Chain amino acid (A.A.) sequence
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQ
PEDFATYYCQQSYSTPPTFGQGTKVEIK
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA
DYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Annotated sequence:
VL:

```
gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcacc
 D  I  Q  M  T  Q  S  P  S  S  L  S  A  S  V  G  D  R  V  T
atcacttgccgggcaagtcagagcattagcagctacttaaattggtatcagcagaaacca
 I  T  C  R  A  S  Q  S  I  S  S  Y  L  N  W  Y  Q  Q  K  P
gggaaagcccctaagctcctgatctatgctgcatccagtttgcaaagtggggtcccatca
 G  K  A  P  K  L  L  I  Y  A  A  S  S  L  Q  S  G  V  P  S
aggttcagtggcagtggatctgggacagatttcactctcaccatcagcagtctgcaacct
 R  F  S  G  S  G  S  G  T  D  F  T  L  T  I  S  S  L  Q  P
gaagattttgcaacttactactgtcaacagagttacagtacccctccaacgttcggccaa
 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
tggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggac
 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
agcttcaacaggggagagtgttag
 S  F  N  R  G  E  C  -
```

Figure 4

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

CH1:

```
gctagcaccaagggcccatcggtcttcccctggcaccctcctccaagagcacctctggg
 A  S  T  K  G  P  S  V  F  P  L  A  P  S  S  K  S  T  S  G
ggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgtcg
 G  T  A  A  L  G  C  L  V  K  D  Y  F  P  E  P  V  T  V  S
tggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctca
 W  N  S  G  A  L  T  S  G  V  H  T  F  P  A  V  L  Q  S  S
ggactctactccctcagcagcgtcgtgaccgtgccctccagcagcttgggcacccagacc
 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:

```
gagcccaaatcttgtgacaaaactcacacatgcccaccgtgccca
 E  P  K  S  C  D  K  T  H  T  C  P  P  C  P
```

CH2:

```
gcacctgaactcctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacacc
 A  P  E  L  L  G  G  P  S  V  F  L  F  P  P  K  P  K  D  T
ctcatgatctcccggaccccctgaggtcacatgcgtggtggtggacgtgagccacgaagac
 L  M  I  S  R  T  P  E  V  T  C  V  V  V  D  V  S  H  E  D
cctgaggtcaagttcaactggtacgtggacggcgtggaggtgcataatgccaagacaaag
 P  E  V  K  F  N  W  Y  V  D  G  V  E  V  H  N  A  K  T  K
ccgcgggaggagcagtacaacagcacgtaccgtgtggtcagcgtcctcaccgtcctgcac
 P  R  E  E  Q  Y  N  S  T  Y  R  V  V  S  V  L  T  V  L  H
caggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagcc
 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

```
gggcagccccgagaaccacaggtgtacaccaagcccccatcccgggaggagatgaccaag
 G  Q  P  R  E  P  Q  V  Y  T  K  P  P  S  R  E  E  M  T  K
aaccaggtcagcctgaagtgcctggtcaaaggcttctatcccagcgacatcgccgtggag
 N  Q  V  S  L  K  C  L  V  K  G  F  Y  P  S  D  I  A  V  E
tgggagagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactcc
 W  E  S  N  G  Q  P  E  N  N  Y  K  T  T  P  P  V  L  D  S
gacggctccttcttcctctatagcaagctcaccgtggacaagagcaggtggcagcagggg
 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

```
gggcagccccgagaaccacaggtgtacaccgacccccccatcccgggaggagatgaccaag
 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
tgggagagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactcc
 W   E   S   N   G   Q   P   E   N   N   Y   K   T   T   P   P   V   L   D   S
gacggctccttcttcctctatagcaagctcaccgtggacaagagcaggtggcagcagggg
 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

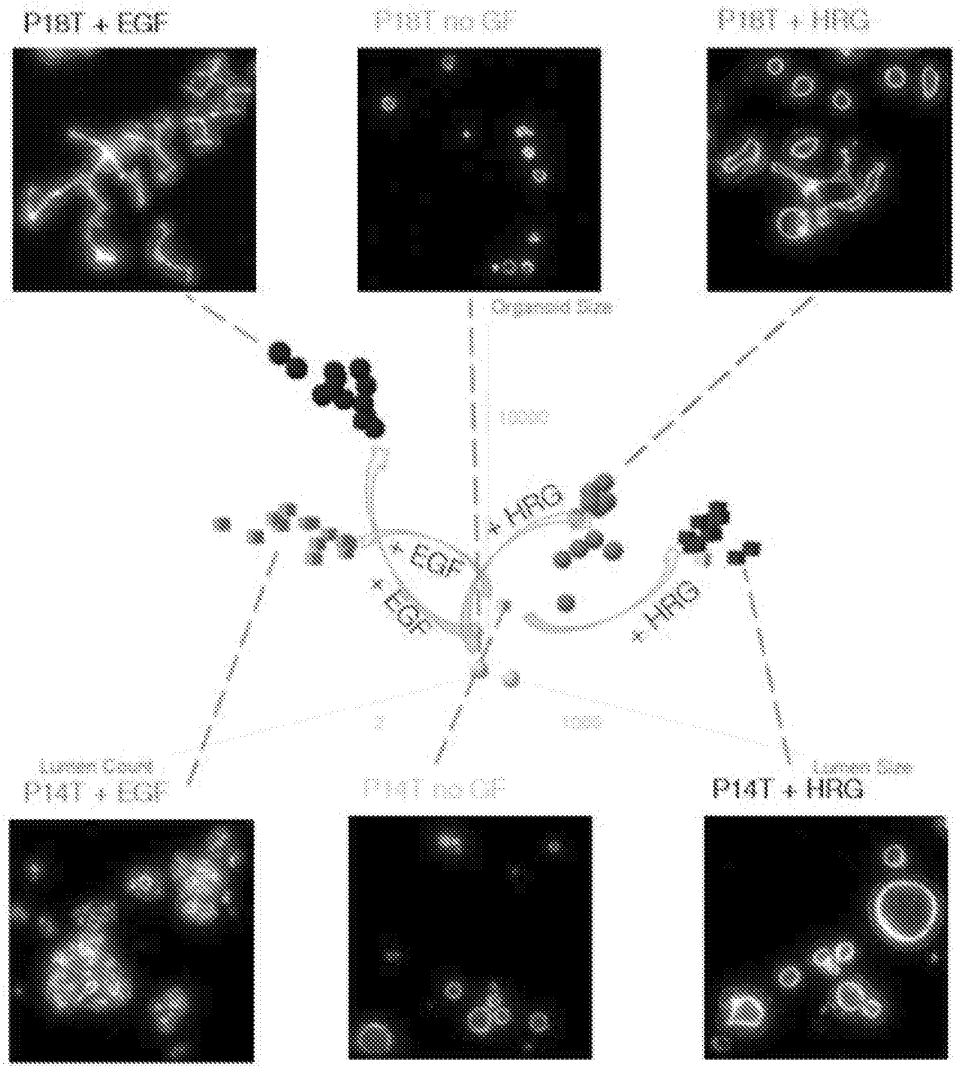
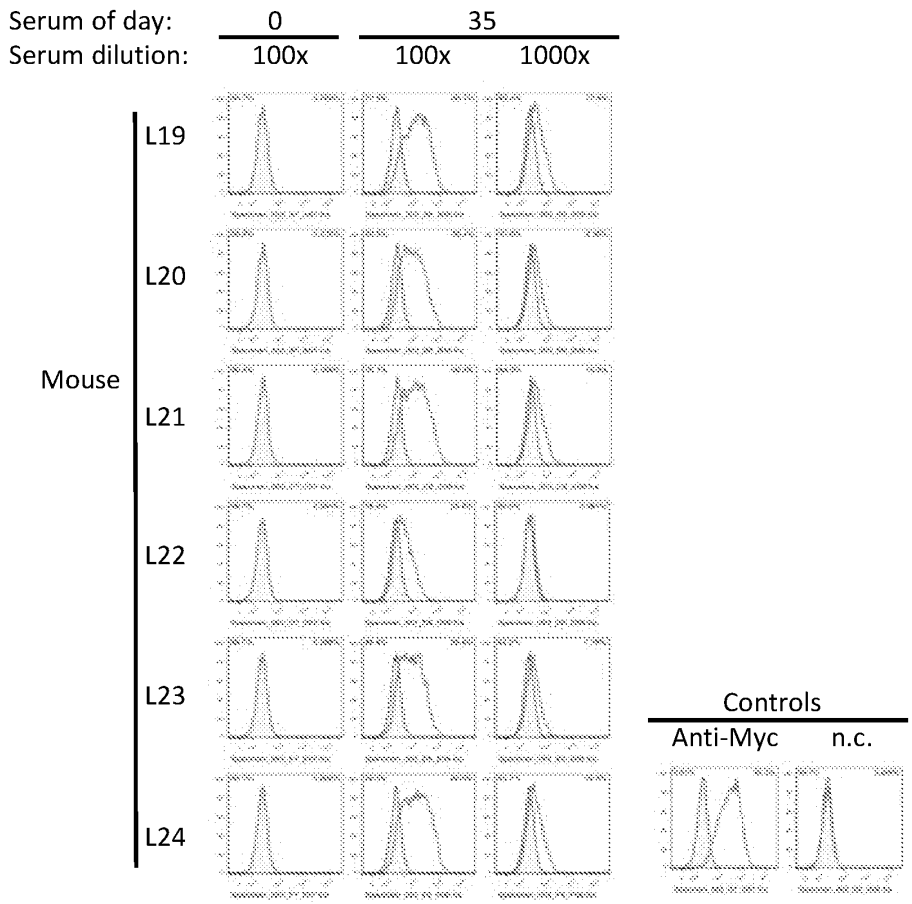

P18T + EGF
P18T no GF
P18T + HRG
Organoid Size
+ HRG
+ EGF
+ EGF
+ HRG
Lumen Count
Lumen Size
P14T + EGF
P14T no GF
P14T + HRG

Figure 6


Serum of day:
0
35
Serum dilution:
100x
100x
1000x
Mouse
L19
L20
L21
L22
L23
L24
Controls
Anti-Myc
n.c.

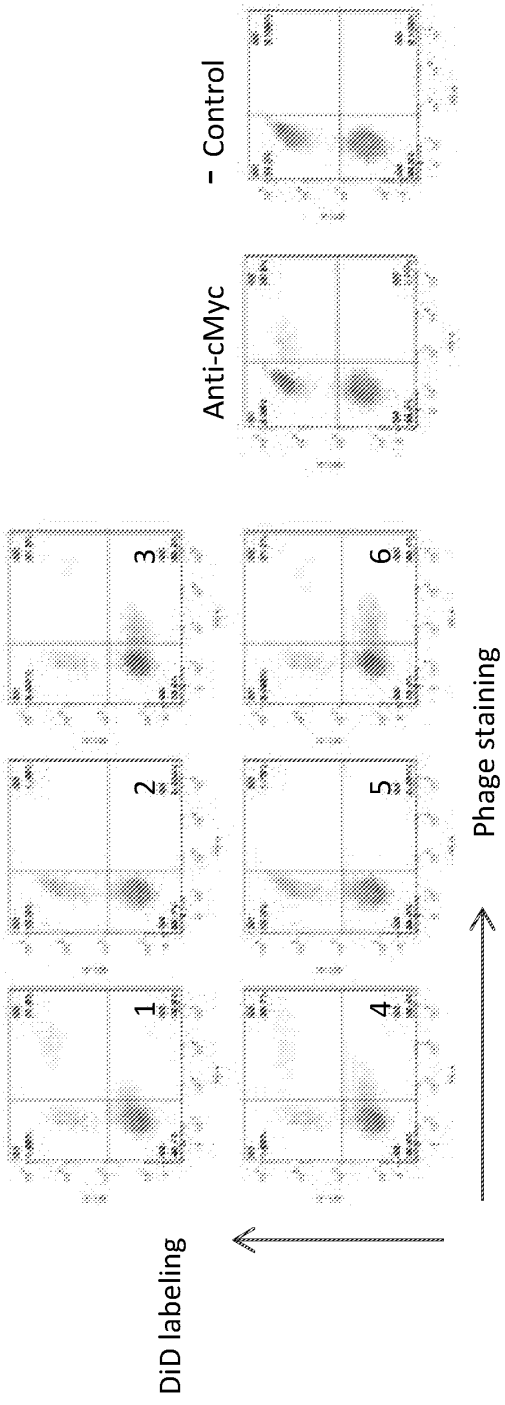
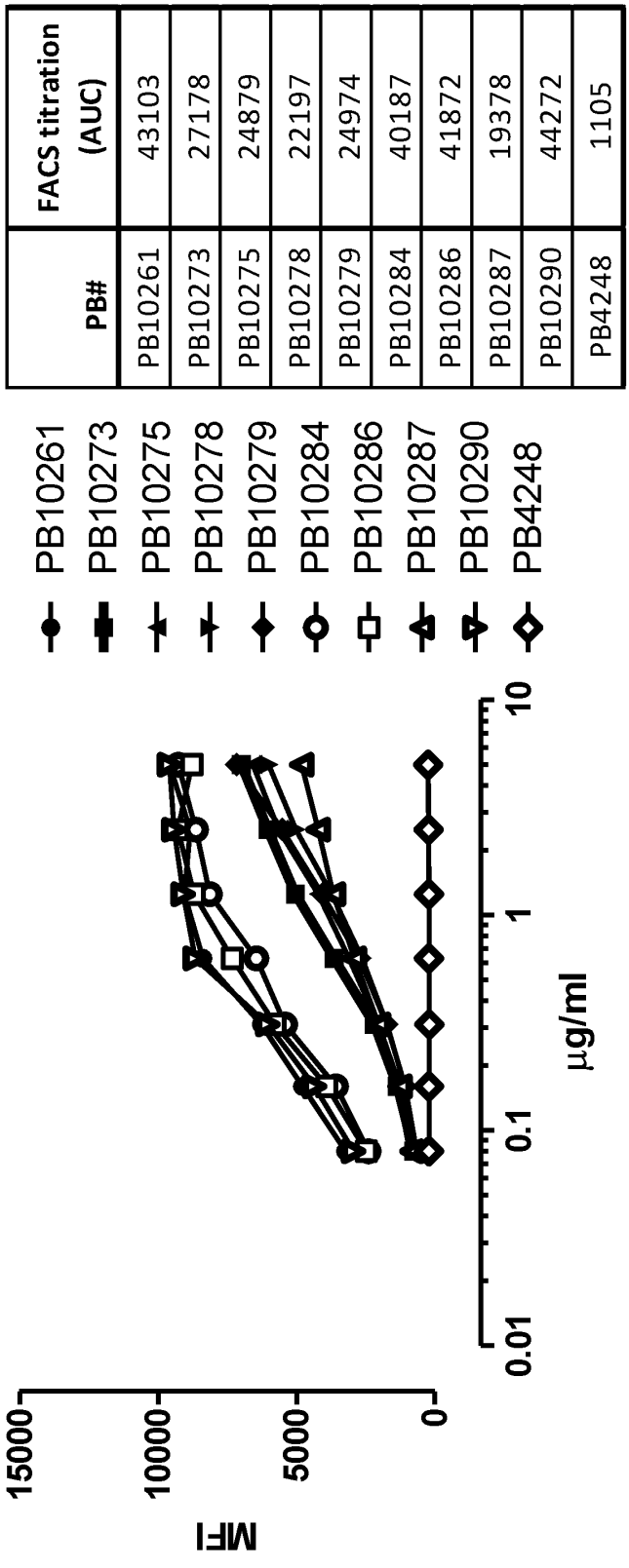


Figure 7



PB#	FACS titration (AUC)
PB10261	43103
PB10273	27178
PB10275	24879
PB10278	22197
PB10279	24974
PB10284	40187
PB10286	41872
PB10287	19378
PB10290	44272
PB4248	1105

Figure 8

Figure 9

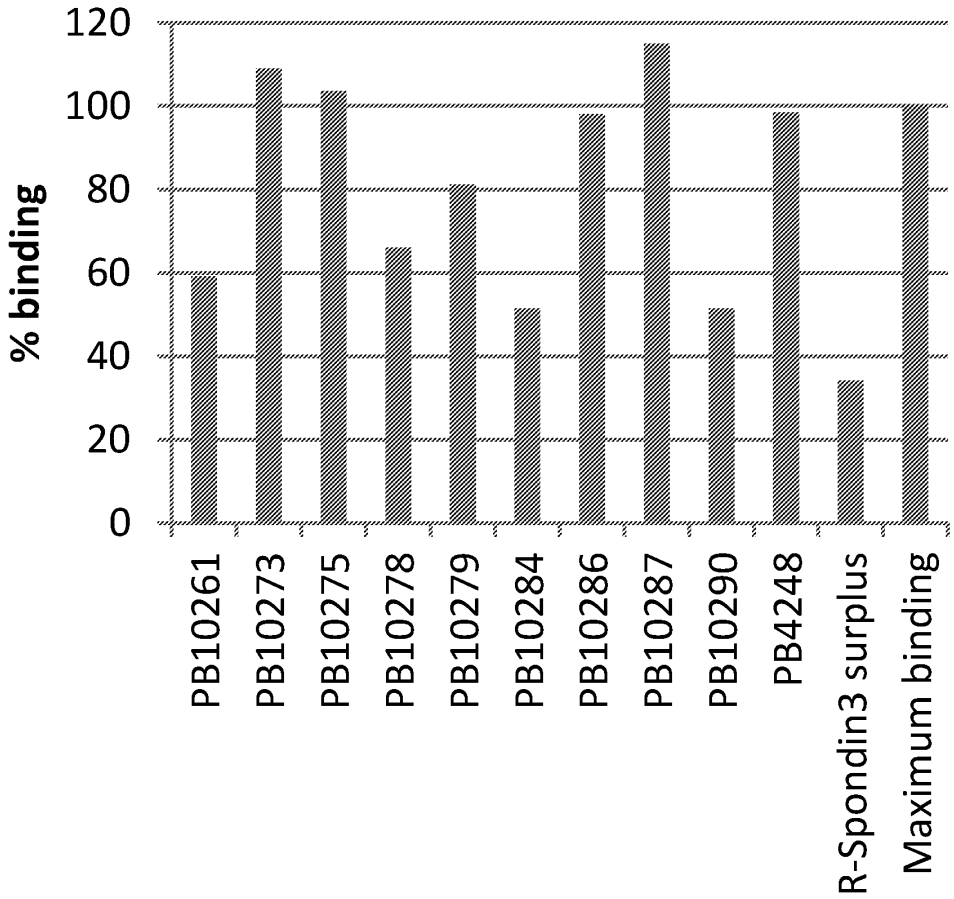

% binding
120
100
80
60
40
20
0
PB10261
PB10273
PB10275
PB10278
PB10279
PB10284
PB10286
PB10287
PB10290
PB4248
R-Spondin3 surplus
Maximum binding

Figure 11

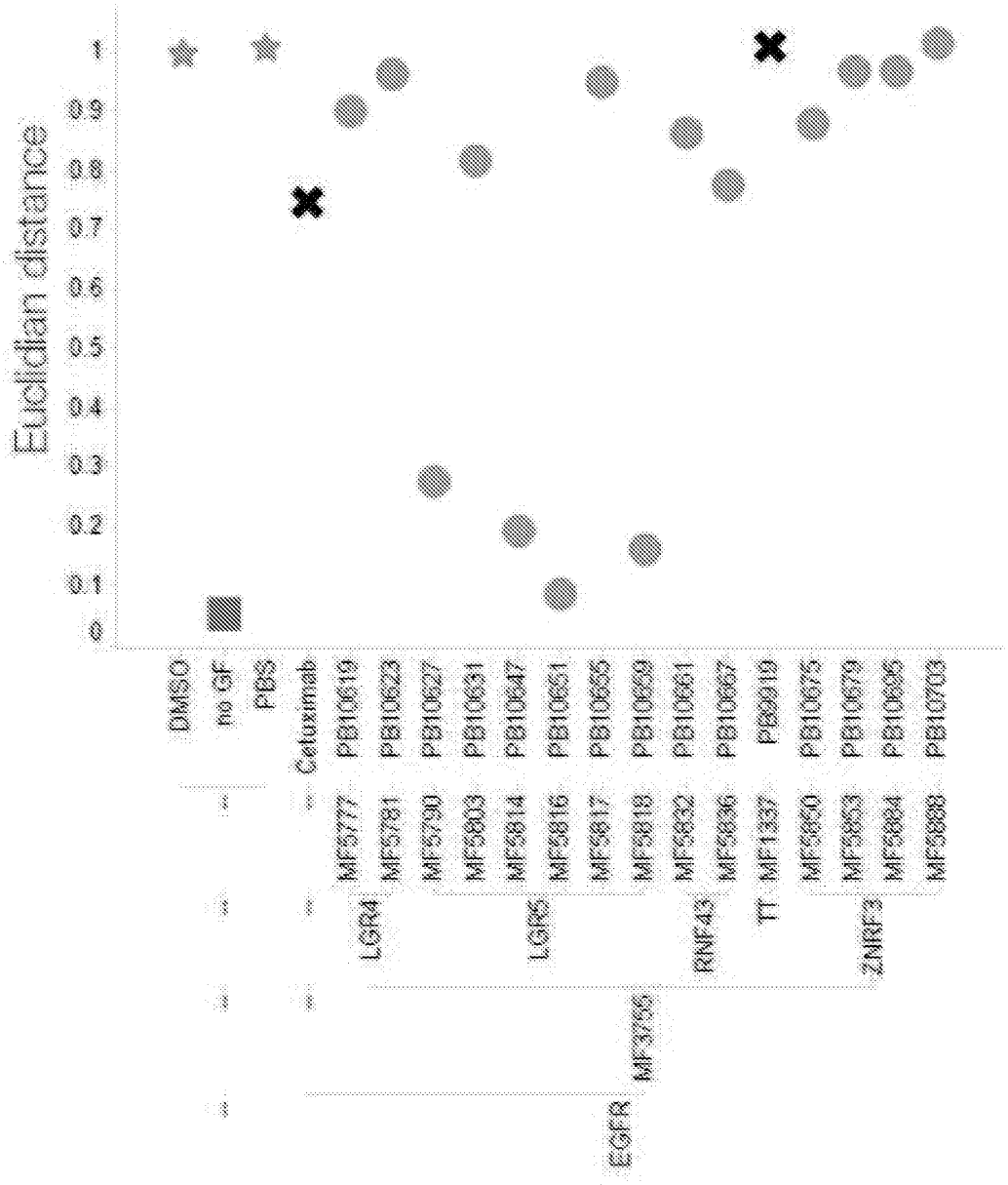

Euclidian distance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
DMSO
no GF
PBS
Cetuximab
PB10619
PB10623
PB10627
PB10631
PB10647
PB10651
PB10655
PB10659
PB10661
PB10667
PB00919
PB10675
PB10679
PB10695
PB10703
MF5777
MF5781
MF5790
MF5803
MF5814
MF5816
MF5817
MF5818
MF5832
MF5836
MF1337
MF5850
MF5853
MF5824
MF5888
LGR4
LGR5
RNF43
TT
ZNRF3
EGFR
MF3755

Figure 12

A B

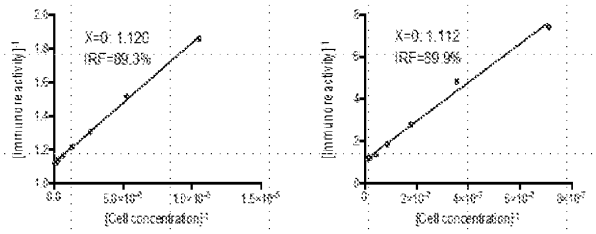


Figure 13

A B C

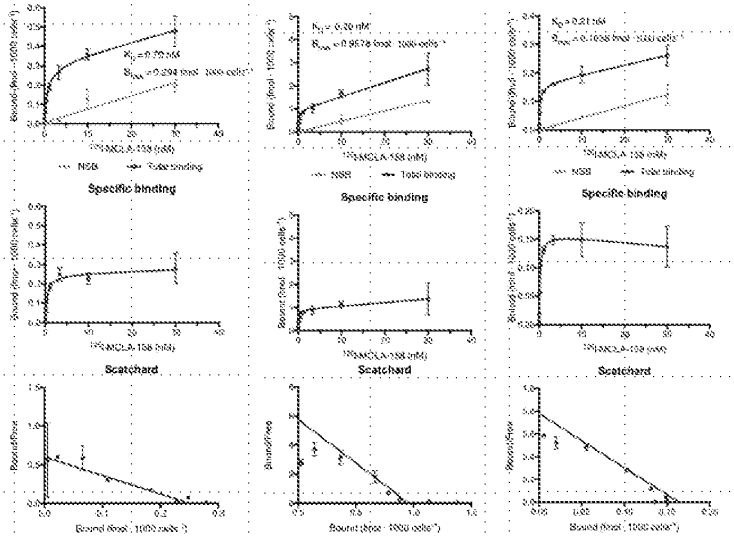


Figure 14

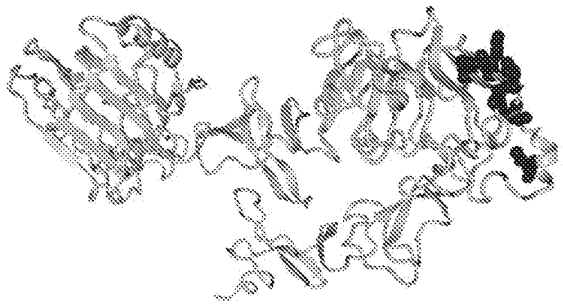


Figure 15

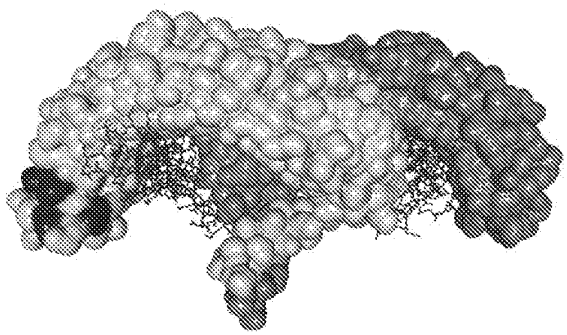


Figure 16

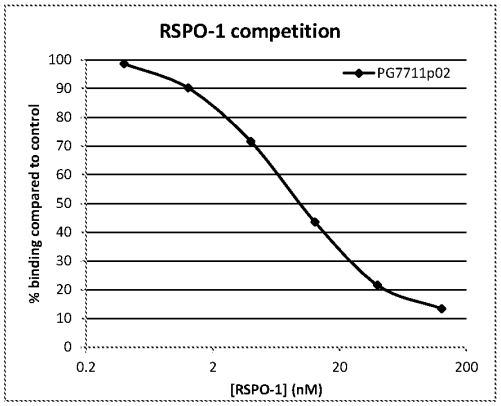


Figure 17

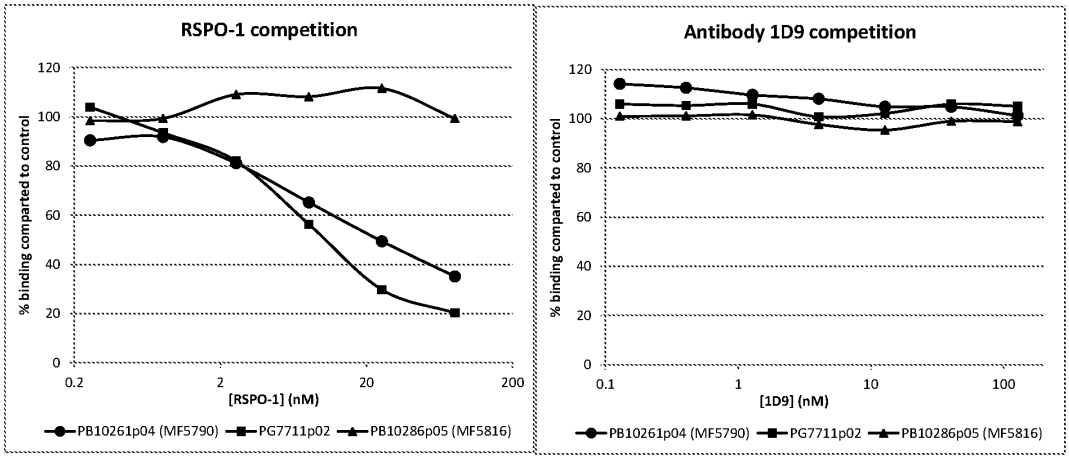


Figure 18

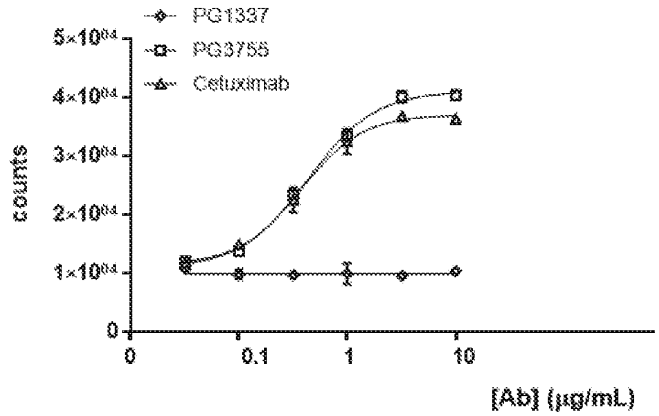


Figure 19

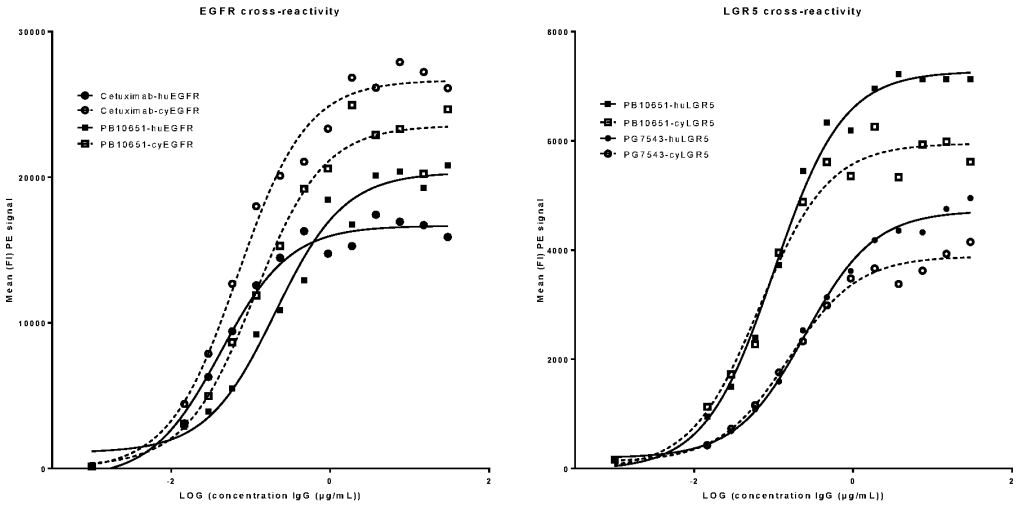
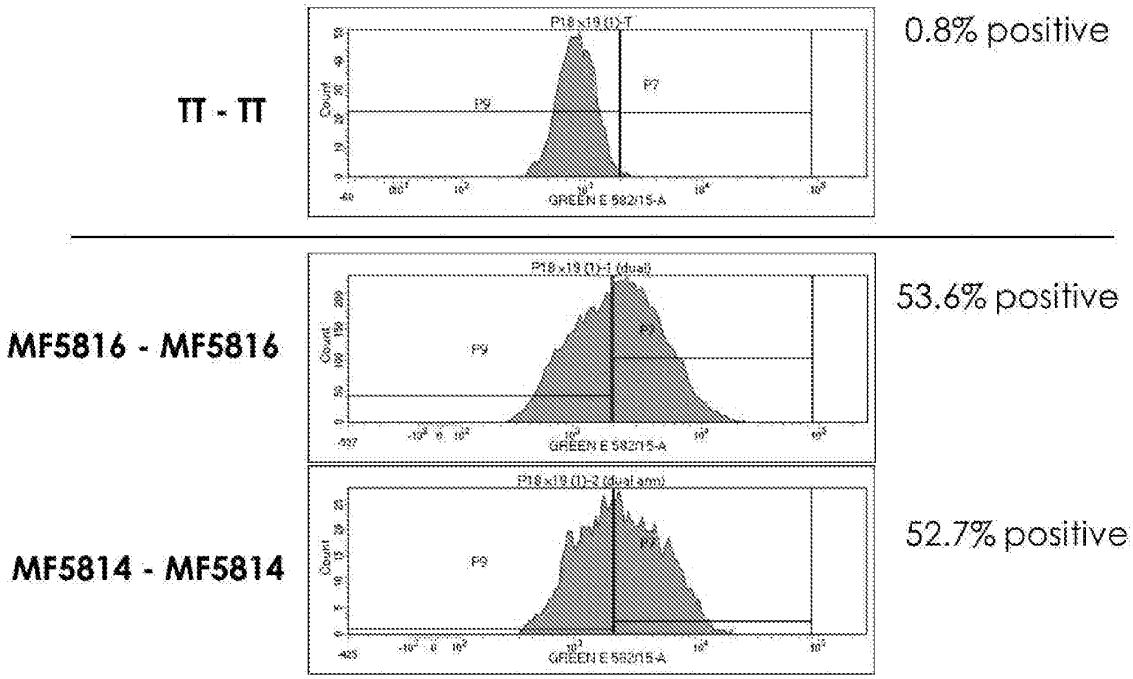


Figure 20


TT - TT
0.8% positive
MF5816 - MF5816
53.6% positive
MF5814 - MF5814
52.7% positive
Count
GREEN E 582/15-A

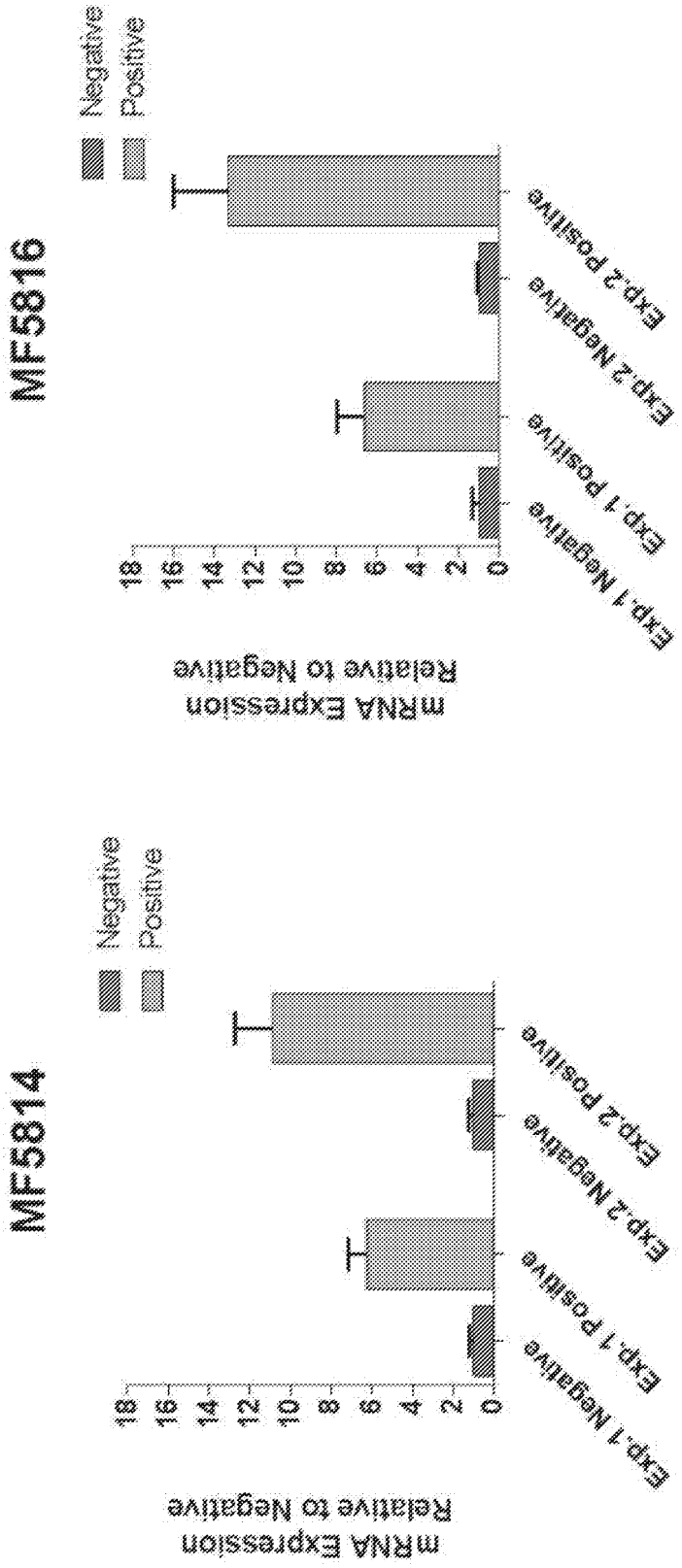

MF5816
Negative
Positive
mRNA Expression
Relative to Negative
0
2
4
6
8
10
12
14
16
18
Exp.1 Negative
Exp.1 Positive
Exp.2 Negative
Exp.2 positive
MF5814
Negative
Positive
mRNA Expression
Relative to Negative
0
2
4
6
8
10
12
14
16
18
Exp.1 Negative
Exp.1 Positive
Exp.2 Negative
Exp.2 positive

Figure 21

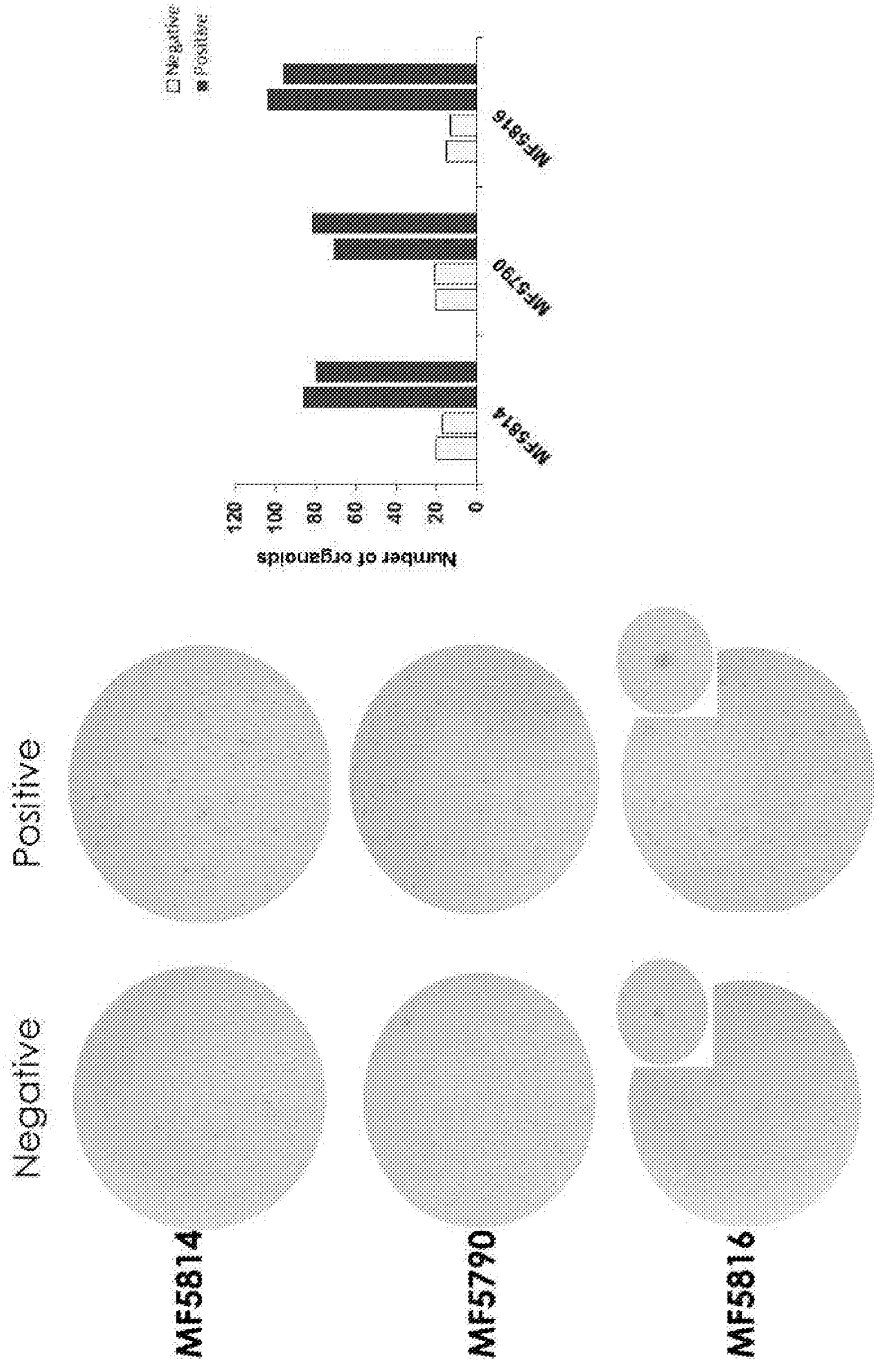

Negative
Positive
MF5814
MF5790
MF5816
Negative
Positive
Number of organoids
0
20
40
60
80
100
120
MF-5814
MF-5790
MF-5816

Figure 22

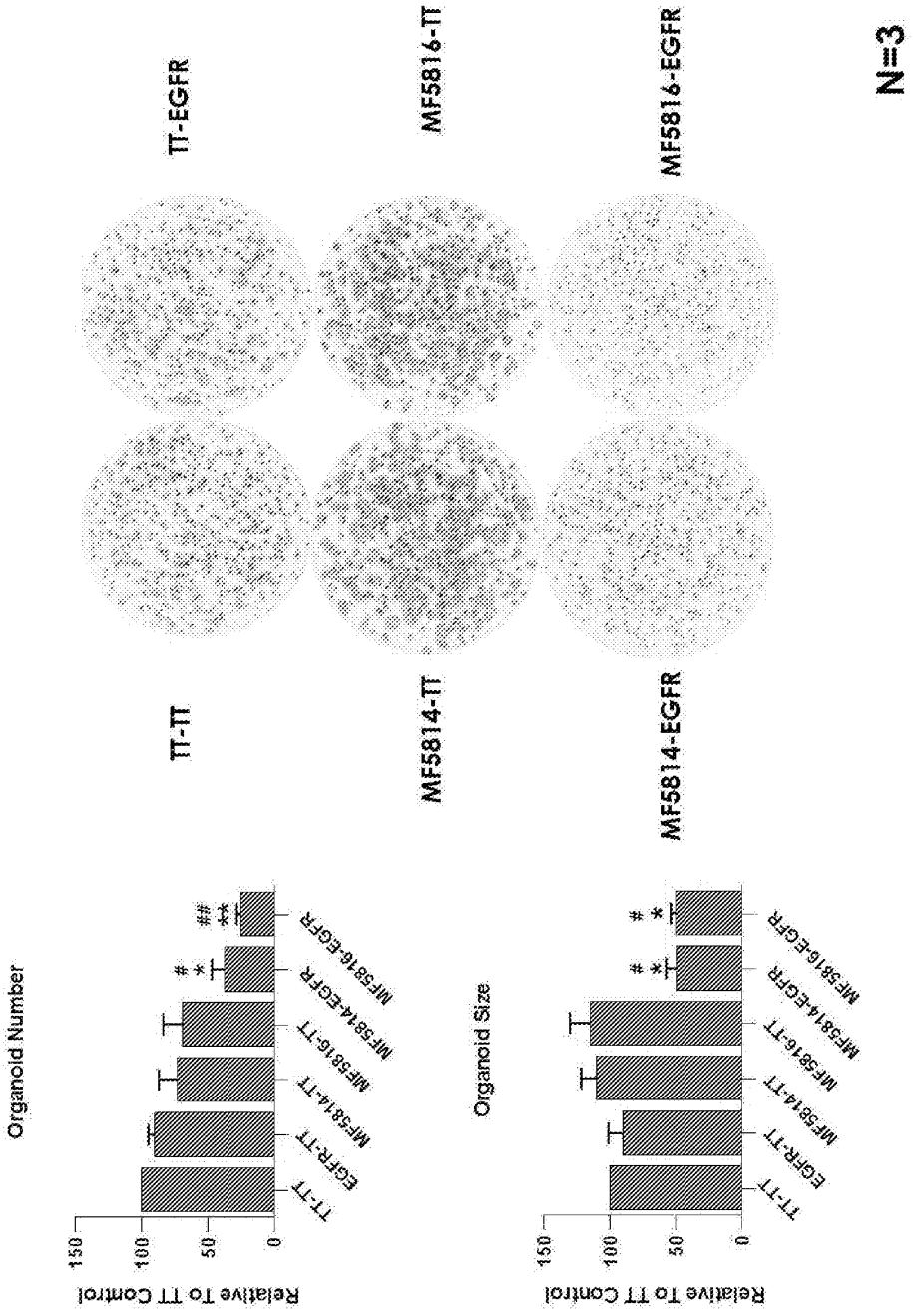

TT-EGFR
MF5816-TT
MF5816-EGFR
N=3
TT-TT
MF5814-TT
MF5814-EGFR
Organoid Number
Relative To TT Control
150
100
50
0
TT-TT
EGFR-TT
MF5814-TT
MF5816-TT
MF5814-EGFR
MF5816-EGFR
#
*
**
##
Organoid Size
Relative To TT Control
150
100
50
0
TT-TT
EGFR-TT
MF5814-TT
MF5816-TT
MF5814-EGFR
MF5816-EGFR
#
*
**

Figure 23

Figure 24

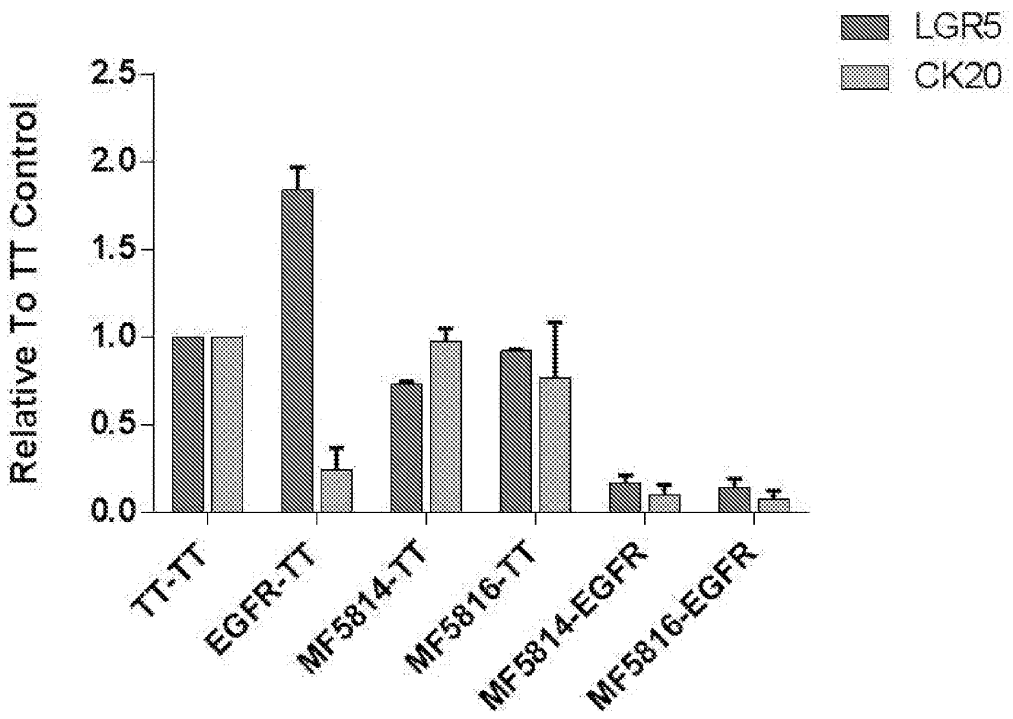

LGR5
CK20
Relative To TT Control
2.5
2.0
1.5
1.0
0.5
0.0
TT-TT
EGFR-TT
MF5814-TT
MF5816-TT
MF5814-EGFR
MF5816-EGFR

Figure 25

Figure 25A

Supercluster 1 (MF5814 and MF5818)

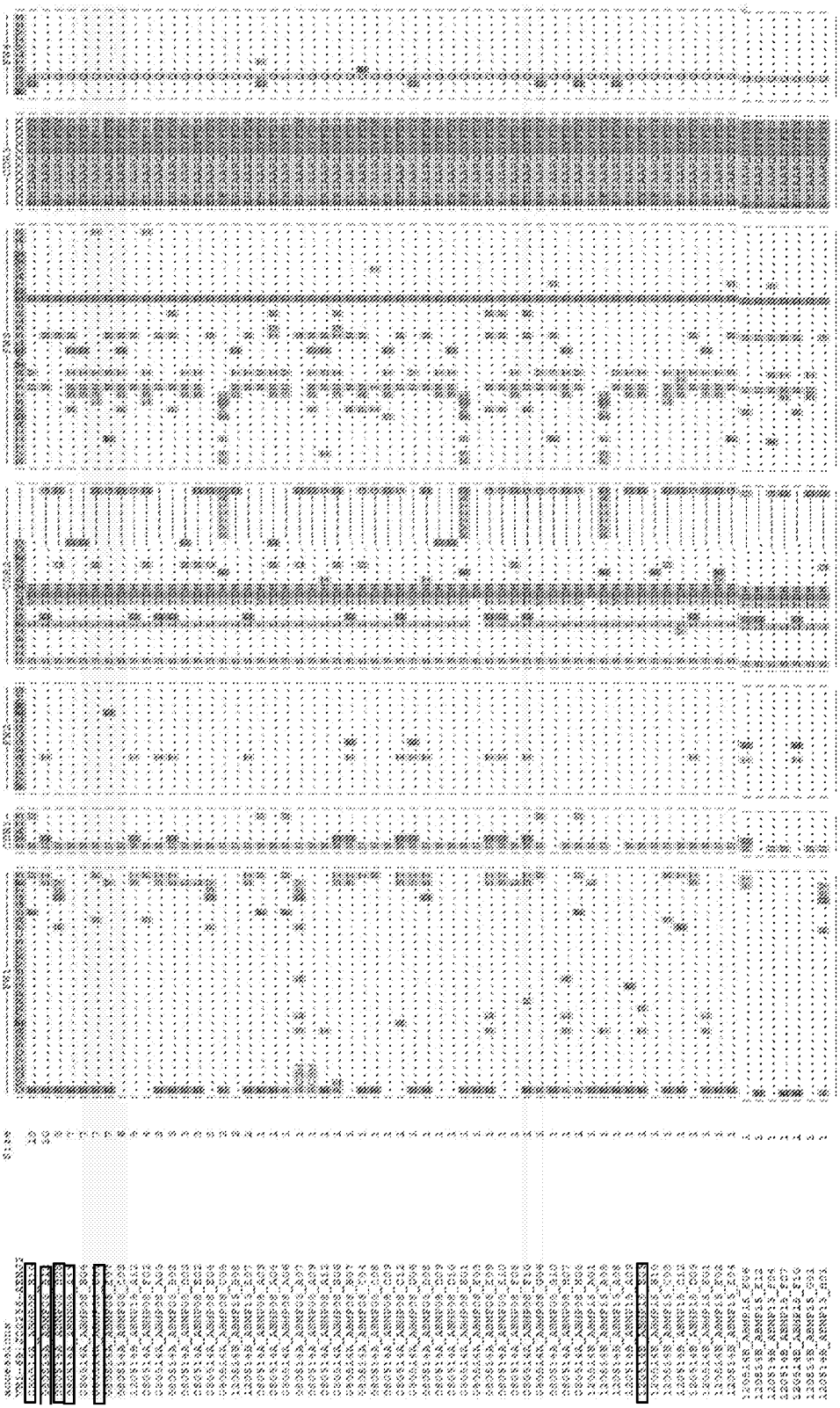


Figure 25B

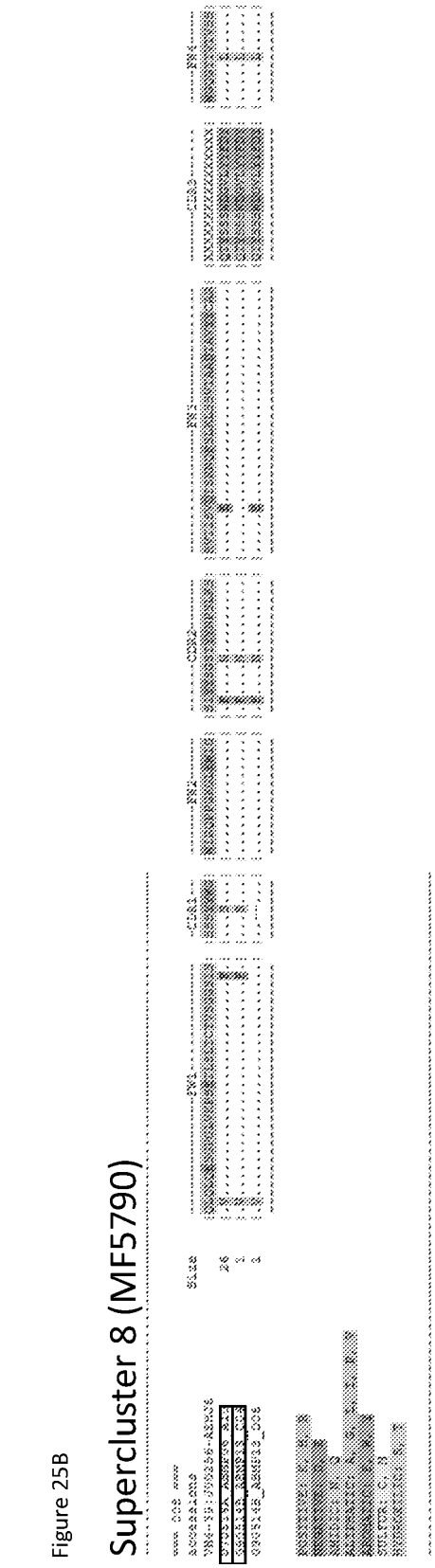


Figure 25C

Supercluster 10 (MF5816)

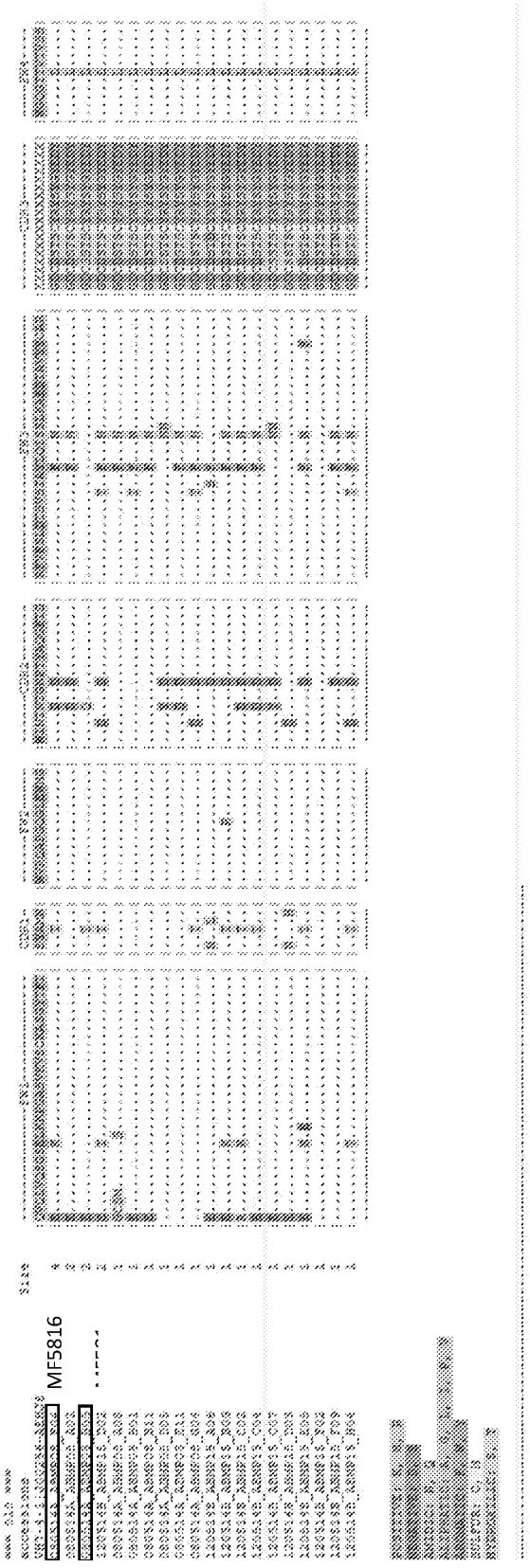


Figure 26

Figure 26A

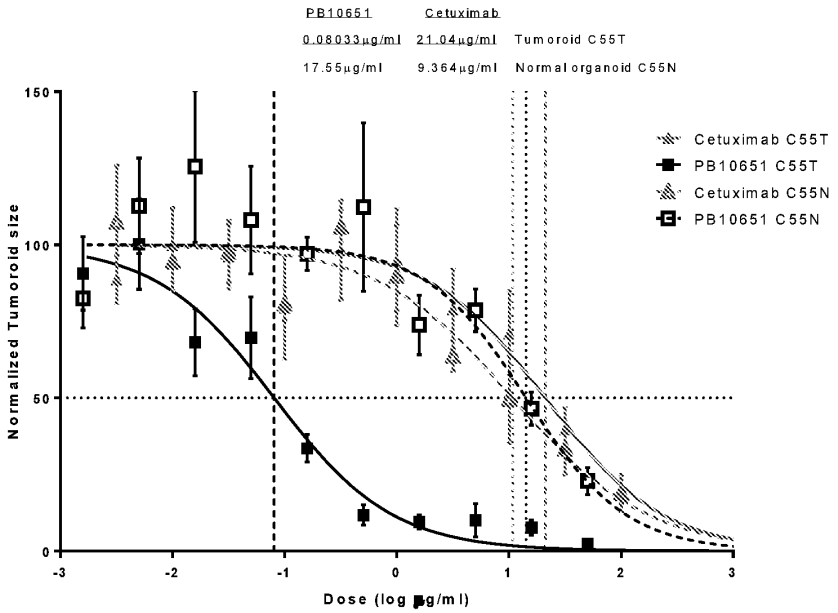


Figure 26B

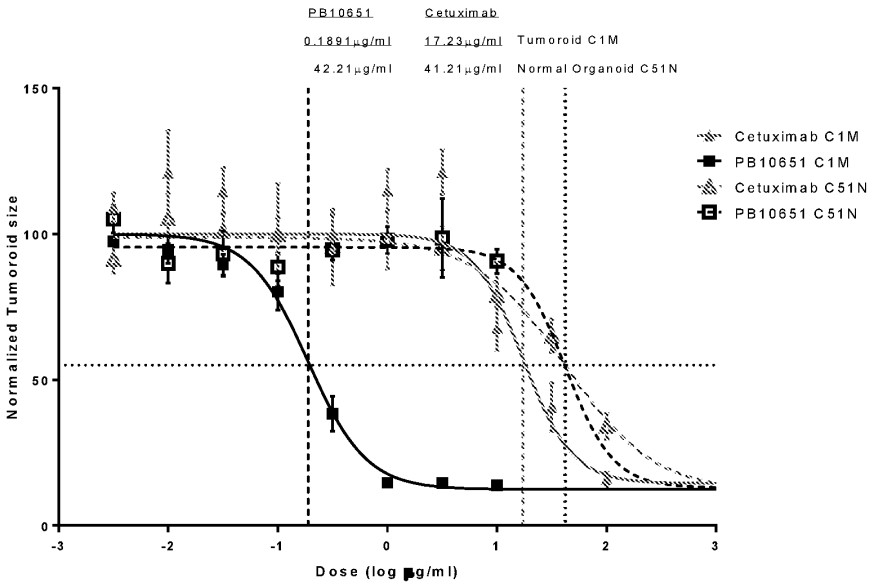


Figure 26C

		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

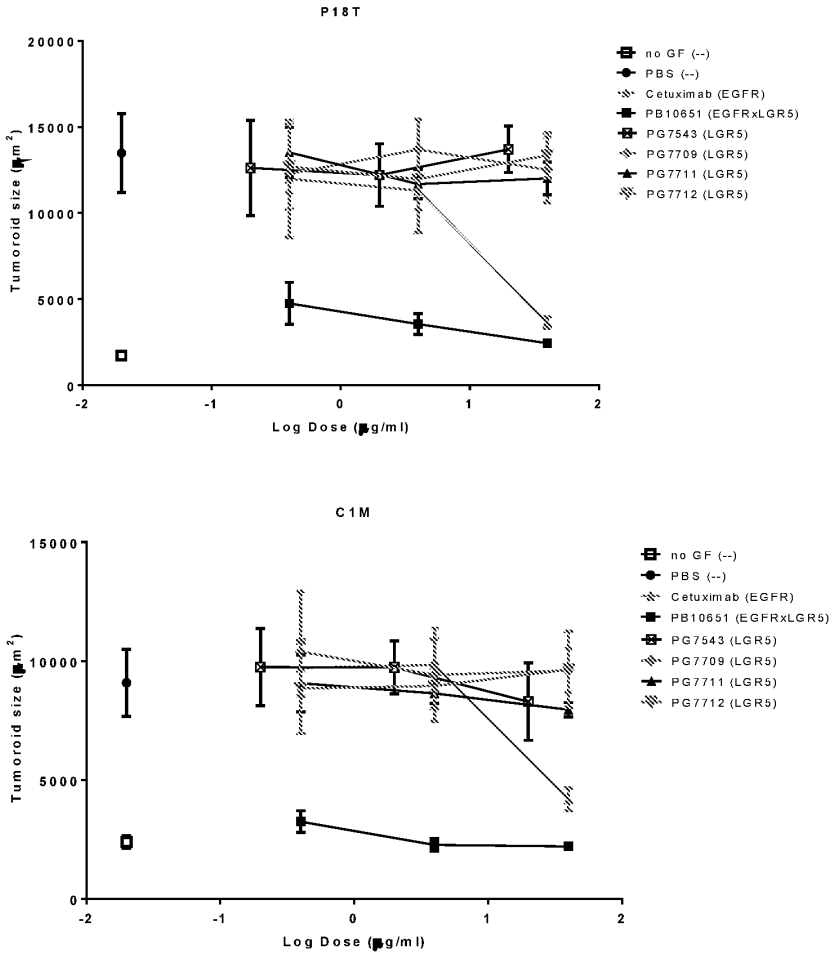

P18T
Tumoroid size (µm²)
20000
15000
10000
5000
0
-2
-1
0
1
2
Log Dose (µg/ml)
no GF (--)
PBS (--)
Cetuximab (EGFR)
PB10651 (EGFRxLGR5)
PG7543 (LGR5)
PG7709 (LGR5)
PG7711 (LGR5)
PG7712 (LGR5)
C1M
Tumoroid size (µm²)
15000
10000
5000
0
-2
-1
0
1
2
Log Dose (µg/ml)
no GF (--)
PBS (--)
Cetuximab (EGFR)
PB10651 (EGFRxLGR5)
PG7543 (LGR5)
PG7709 (LGR5)
PG7711 (LGR5)
PG7712 (LGR5)

Figure 28

Figure 28A

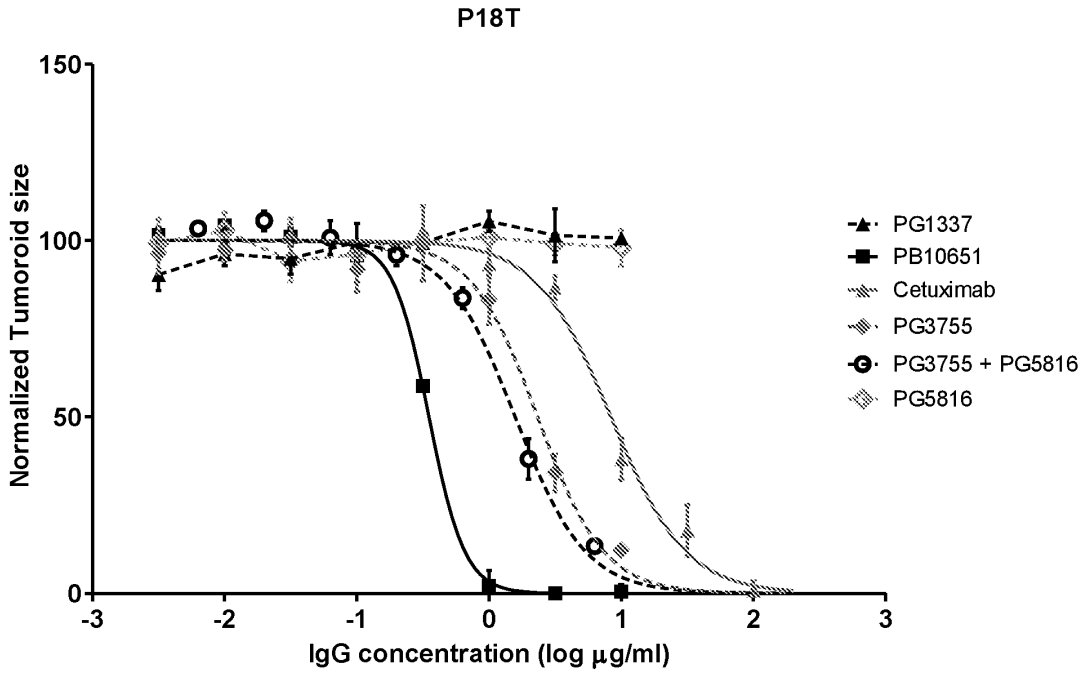
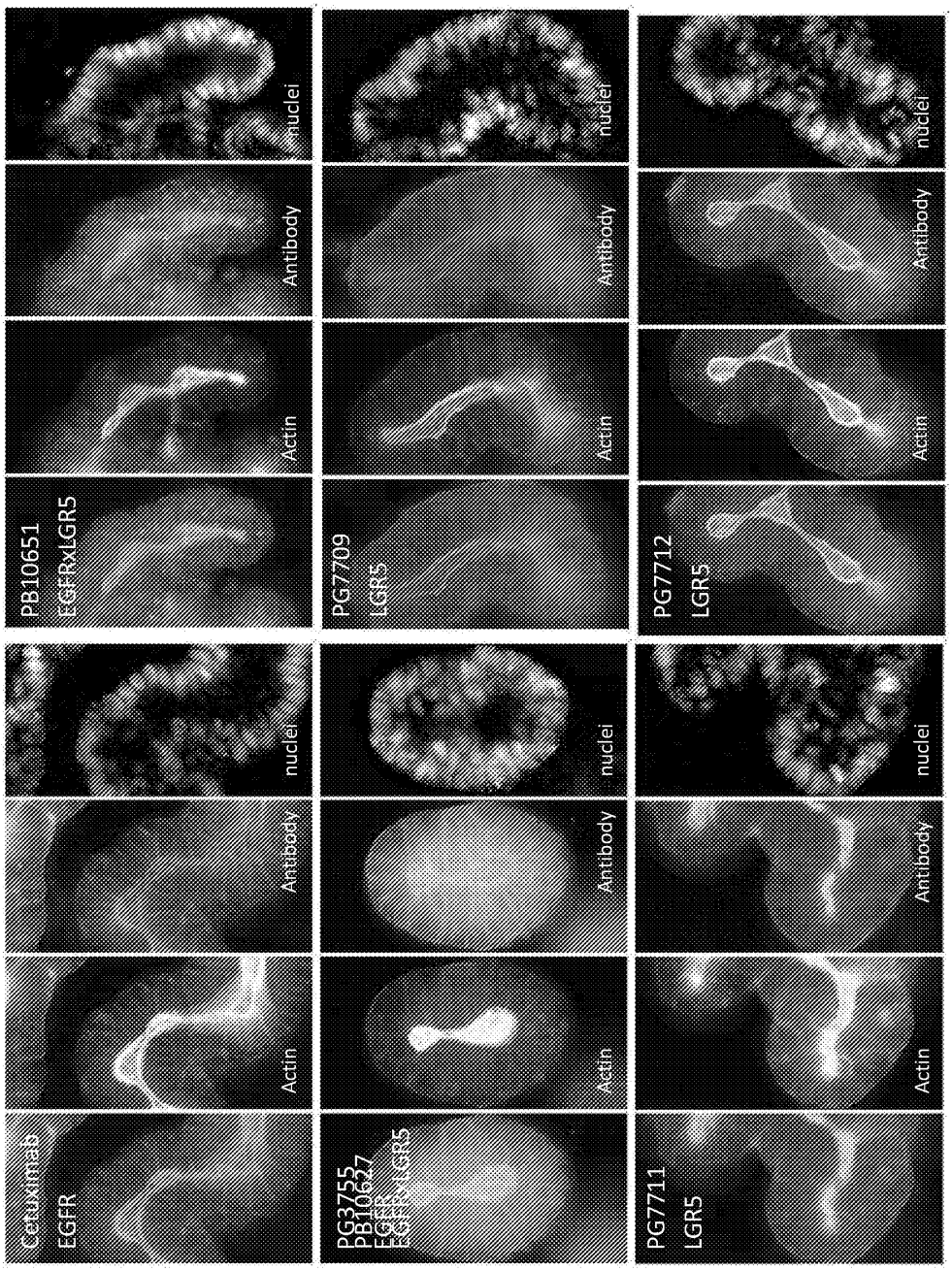


Figure 28B

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


Cetuximab
EGFR
Actin
Antibody
nuclei
PB10651
EGFRxLGR5
PG7709
LGR5
PG7712
LGR5
PG7711
LGR5

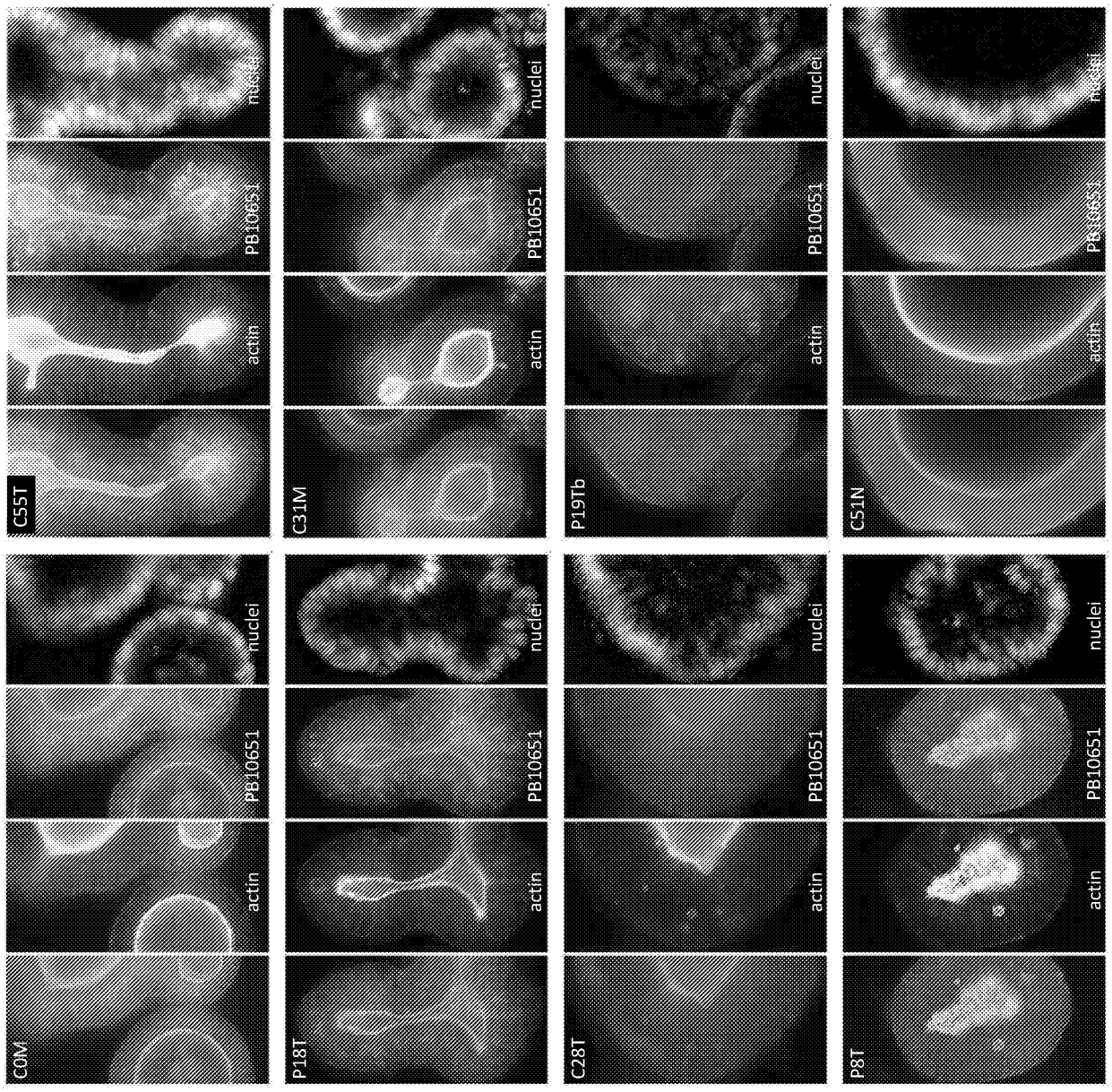


Figure 30

Figure 31

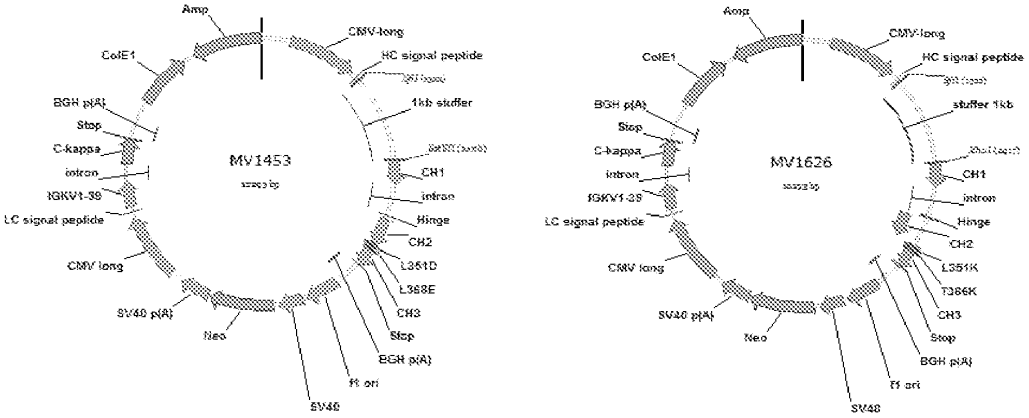


Figure 32

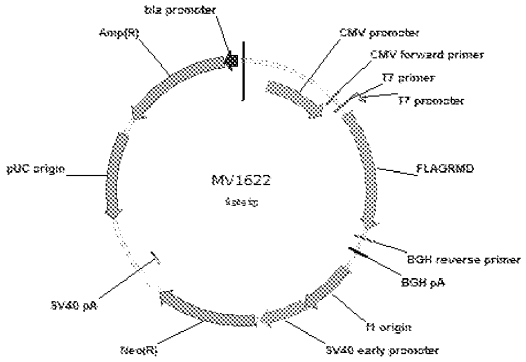


Figure 33

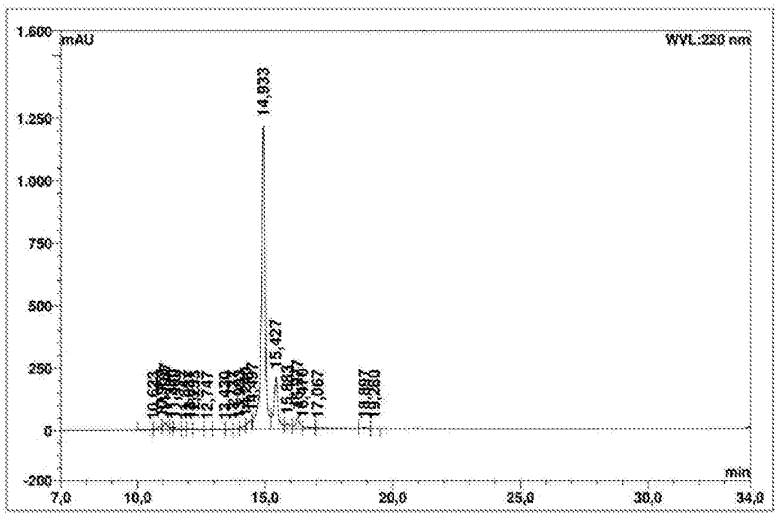

mAU
WVL:220 nm
14,933
15,427
17,067
min
1.600
1.250
1.000
750
500
250
0
-200
7,0
10,0
15,0
20,0
25,0
30,0
34,0

Figure 34

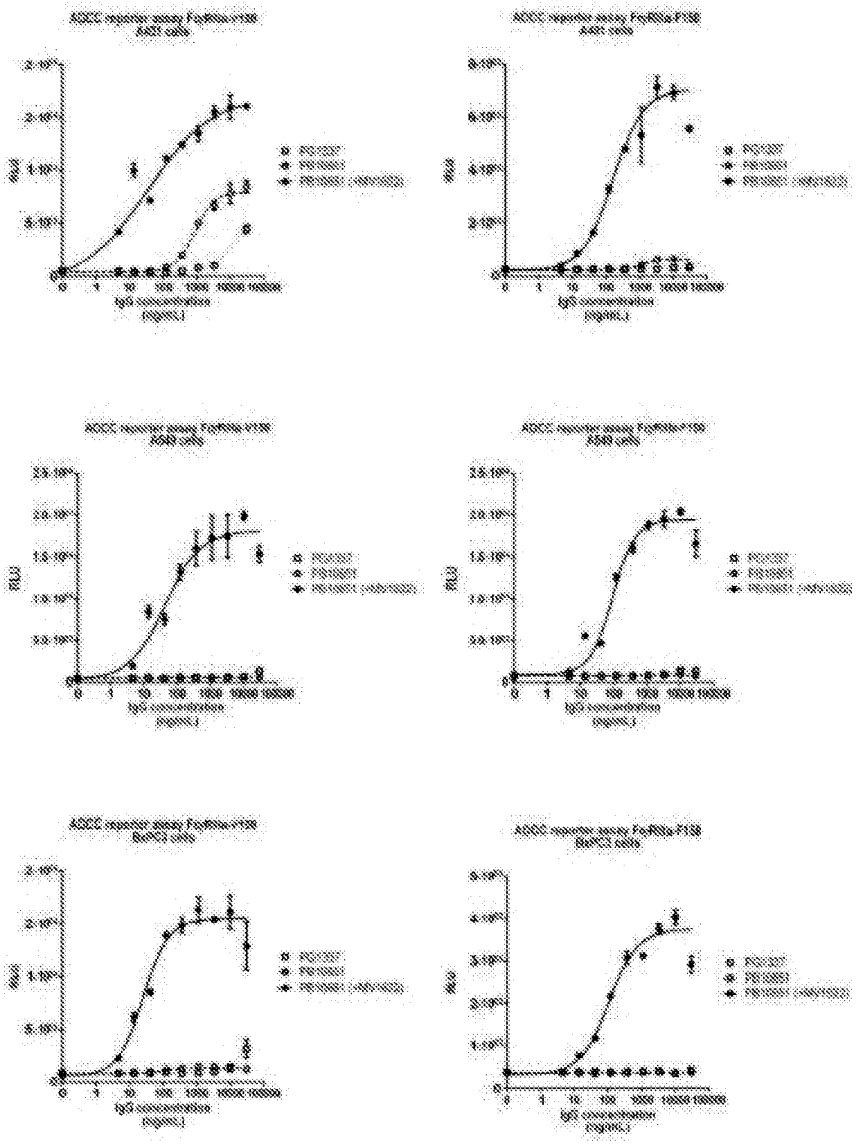


Figure 35

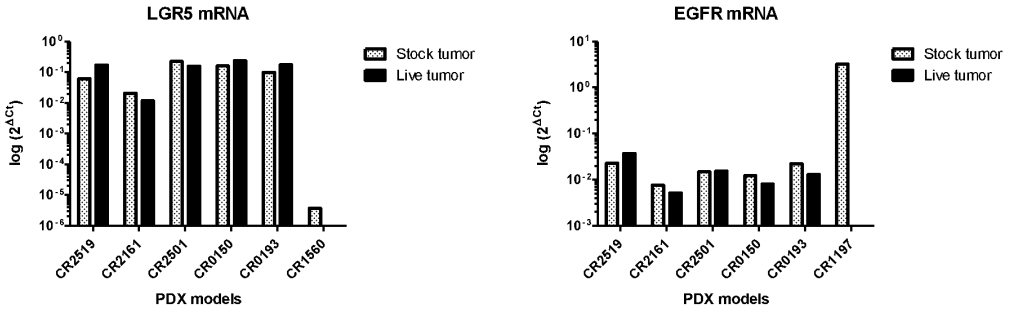

LGR5 mRNA
log (2^ΔCt)
Stock tumor
Live tumor
CR2519
CR2161
CR2501
CR0150
CR0193
CR1560
PDX models
EGFR mRNA
log (2^ΔCt)
Stock tumor
Live tumor
CR2519
CR2161
CR2501
CR0150
CR0193
CR1197
PDX models

Figure 36

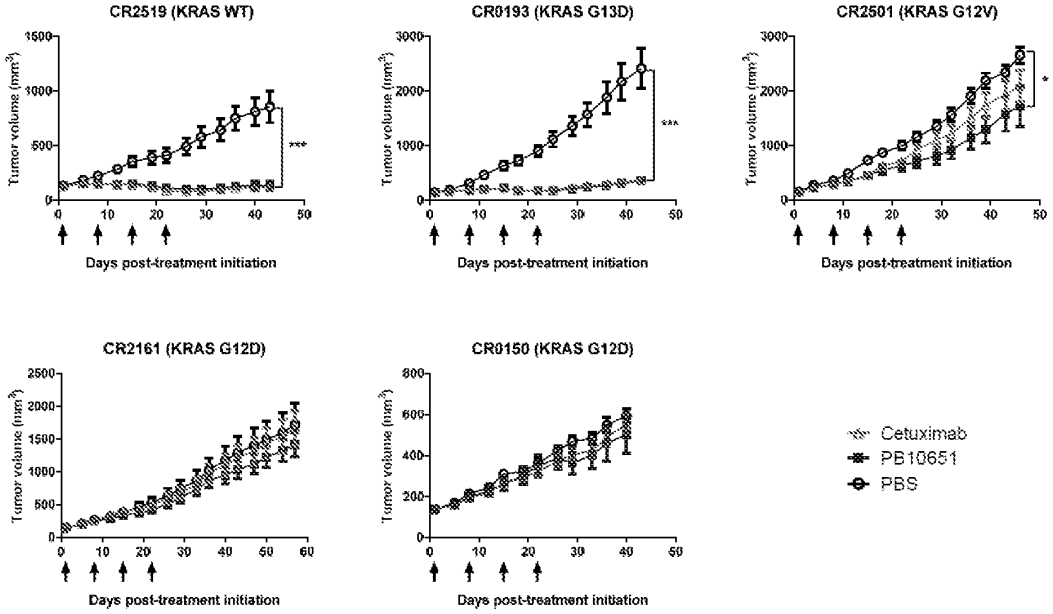

CR2519 (KRAS WT)
CR0193 (KRAS G13D)
CR2501 (KRAS G12V)
CR2161 (KRAS G12D)
CR0150 (KRAS G12D)
Tumor volume (mm3)
Days post-treatment initiation
***
*
Cetuximab
PB10651
PBS

Figure 37

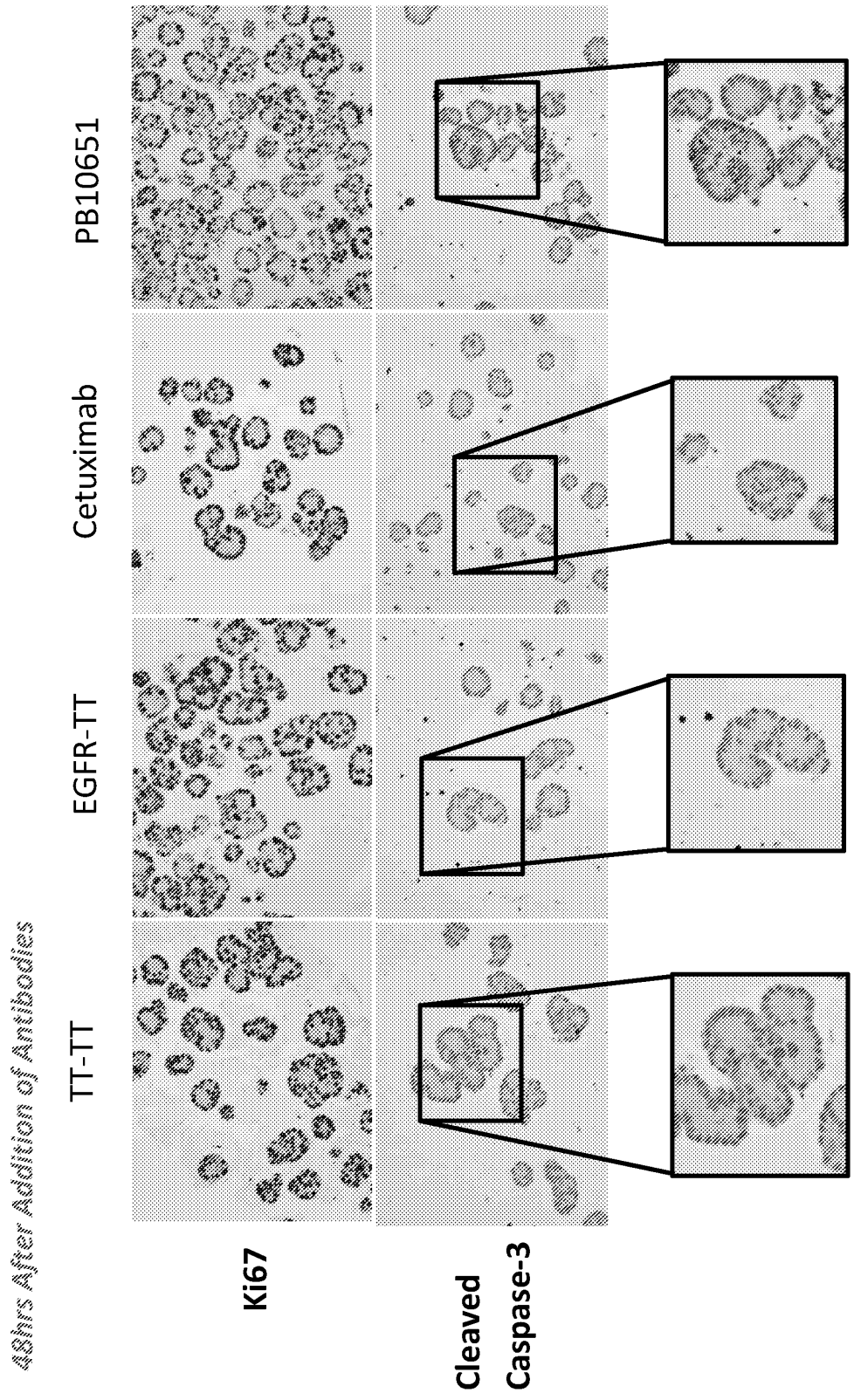
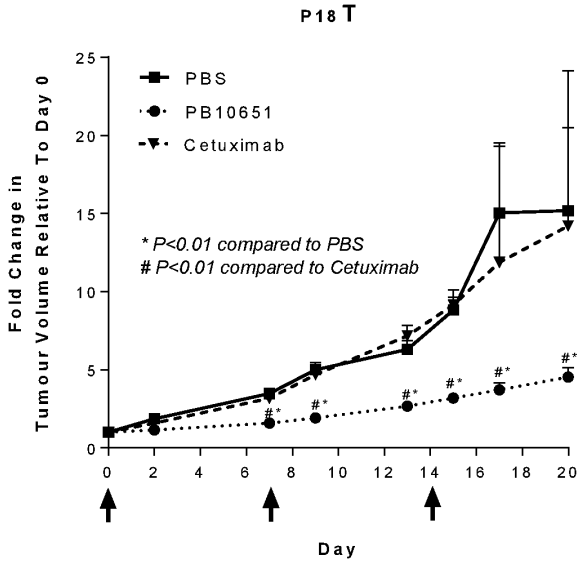

48hrs After Addition of Antibodies
TT-TT
EGFR-TT
Cetuximab
PB10651
Ki67
Cleaved Caspase-3

Figure 38

Figure 38A

Average Tumor Volume on Day 0

	Day 0
PBS	46.9
PB10651	47.3
CET	44.3



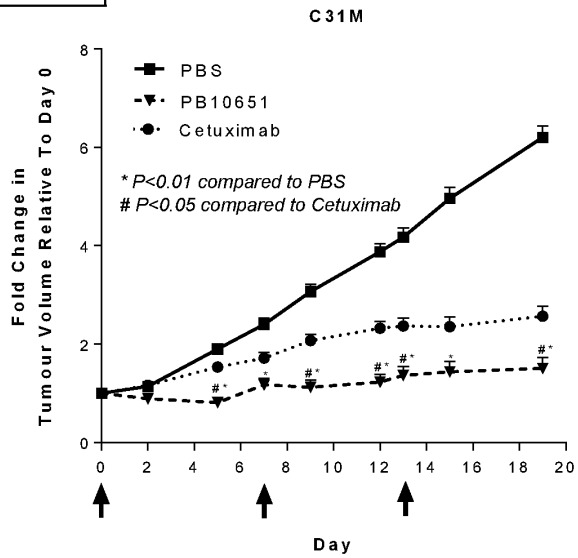
N of Xenografts

Day	0	2	7	9	13	15	17	20
PBS	29	29	29	28	25	25	6	3
PB10651	33	33	33	33	33	33	22	22
CET	29	29	29	29	26	26	6	4

Figure 38B

Average Tumor Volume on Day 0

	Day 0
PBS	29.1
PB10651	29.6
CET	31.2



N of Xenografts

Day	0	2	5	7	9	12	13	15	19
PBS	18	18	18	18	18	18	18	18	18
PB10651	22	22	22	22	22	22	22	22	22
CET	21	21	21	21	21	21	21	21	21

Figure 39

SEQ ID NO:1

MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSELPSNLSVFTSYLDL
SMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVLMLQNNQLRHVPTEALQNLRSLQSLRLD
ANHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQAFRSLSALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHN
NRIHSLGKKCFDGLHSLETLDLNYNNLDEFPTAIRTLSNLKELGFHSNNIRSIPEKAFVGNPSLITIHFYDNPIQ
FVGRSAFQHLPELRTLTLNGASQITEFPDLTGTANLESLTLTGAQISSLPQTVCNQLPNLQVLDLSYNLLEDLP
SFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSLRSLNLAWNKIAIIHPNAFSTLPSLIKLDLSSNLLSSFPITGLHG
LTHLKLTGNHALQSLISSENFPELKVIEMPYAYQCCAFGVCENAYKISNQWNKGDNSSMDDLHKKDAGMFQ
AQDERDLEDFLLDFEEDLKALHSVQCSPSPGPFKPCEHLLDGWLIRIGVWTIAVLALTCNALVTSTVFRSPLYI
SPIKLLIGVIAAVNMLTGVSSAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTLAALERG
FSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGEPSTMGYMVALILLNSLCFL
MMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNCPVAFLSFSSLINLTFISPEVIKFILLVVVPLPA
CLNPLLYILFNPHFKEDLVSLRKQTYVWTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPPSSVPSP
AYPVTESCHLSSVAFVPCL

Annotated sequence No1:

Mdtsrlgvllslpvllqlat Signal peptide

Ggssprsgvllrgcpthchcepdgrmllrvdcsdlglselpsnlsvftsy N-region

Ldlsmnnisqllpnplpslrflee LRR1
Lrlagnaltyipkgaftglyslkv LRR2
Lmlqnnqlrhvptealqnlrslqs LRR3
Lrldanhisyvppscfsglhslrh LRR4
Lwlddnalteipvqafrslsalqa LRR5
mtlalnkihhipdyafgnlsslvv LRR6
Lhlhnnrihslgkkcfdglhsletl LRR7
Dlnynnldefptairtlsn LRR8
Lkelgfhsnnirsipekafvgnpslit LRR9
Ihfydnpiqfvgrsafqhlpelrt LRR10
Ltlngasqitefpdltgtanles LRR11
Ltltgaqisslpqtvcnqlpnlqv LRR12
Ldlsynlledlpsfsvcqklqk LRR13
Idlrhneiyeikvdtfqqllslr LRR14
Slnlawnkiaiihpnafstlpslik LRR15
Ldlssnllssfpitglhglthlk LRR16
Ltgnhalqslissenfpelkviem LRR17

pyayqccafgvcenaykisnqwnkgdnssmddlhkkdagmfqaqderd

Ledflldfeedlkalhsvqcspspgpfkpcehlldgwlir CRL region

igvwtiavlaltcnalvtstvf predicted TM1
rsplyispi
klligviaavnmltgvssavlagvda predicted TM2
ftfgsfarhgawwengvgchv
igflsifasessvflltlaaler predicted TM3
gfsvkysakfetkapfss
lkviillcallaltmaavpllggsk predicted TM4
ygasplclplpfgepstm
gymvalillnslcflmmtiaytkly predicted TM5
cnldkgdleniwdcsmvk
hialllftncilncpvaflsfssl predicted TM6
inltfispevi
kfillvvvplpaclnpllyilfnp predicted TM7

hfkedlvslrkqtyvwtrskhpslmsinsddvekqscdstqalvtft
sssitydlppssvpspaypvteschlssvafvpcl C-terminal tail

Figure 40

SEQ ID NO: 2
MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLS
LQRMFNNCEVVLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIP
LENLQIIRGNMYYENSYALAVLSNYDANKTGLKELPMRNLQEILHGAVRF
SNNPALCNVESIQWRDIVSSDFLSNMSMDFQNHLGSCQKCDPSCPNGSCW
GAGEENCQKLTKIICAQQCSGRCRGKSPSDCCHNQCAAGCTGPRESDCLV
CRKFRDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV
VTDHGSCVRACGADSYEMEEDGVRKCKKCEGPCRKVCNGIGIGEFKDSLS
INATNIKHFKNCTSISGDLHILPVAFRGDSFTHTPPLDPQELDILKTVKE
ITGFLLIQAWPENRTDLHAFENLEIIRGRTKQHGQFSLAVVSLNITSLGL
RSLKEISDGDVIISGNKNLCYANTINWKKLFGTSGQKTKIISNRGENSCK
ATGQVCHALCSPEGCWGPEPRDCVSCRNVSRGRECVDKCNLLEGEPREFV
ENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPAGVM
GENNTLVWKYADAGHVCHLCHPNCTYGCTGPGLEGCPTNGPKIPSIATGM
VGALLLLLVVALGIGLFMRRRHIVRKRTLRRLLQERELVEPLTPSGEAPN
QALLRILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREA
TSPKANKEILDEAYVMASVDNPHVCRLLGICLTSTVQLITQLMPFGCLLD
YVREHKDNIGSQYLLNWCVQIAKGMNYLEDRRLVHRDLAARNVLVKTPQH
VKITDFGLAKLLGAEEKEYHAEGGKVPIKWMALESILHRIYTHQSDVWSY
GVTVWELMTFGSKPYDGIPASEISSILEKGERLPQPPICTIDVYMIMVKC
WMIDADSRPKFRELIIEFSKMARDPQRYLVIQGDERMHLPSPTDSNFYRA
LMDEEDMDDVVDADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNSTVACI
DRNGLQSCPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSVPKR
PAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNST
FDSPAHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRV
APQSSEFIGA

Annotated seq. No: 2

MRPSGTAGAALLALLAALCPASRA signal peptide

LEEKKVCQGTSNKLTQLGTFEDHFLS
LQRMFNNCEVVLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIP
LENLQIIRGNMYYENSYALAVLSNYDANKTGLKELPMRNLQEILHGAVRF
SNNPALCNVESIQWRDIVSSDFLSNMSMDFQNHLGSCQKCDPSCPNGSCW
GAGEENCQKLTKIICAQQCSGRCRGKSPSDCCHNQCAAGCTGPRESDCLV
CRKFRDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV
VTDHGSCVRACGADSYEMEEDGVRKCKKCEGPCRKVCNGIGIGEFKDSLS
INATNIKHFKNCTSISGDLHILPVAFRGDSFTHTPPLDPQELDILKTVKE
ITGFLLIQAWPENRTDLHAFENLEIIRGRTKQHGQFSLAVVSLNITSLGL
RSLKEISDGDVIISGNKNLCYANTINWKKLFGTSGQKTKIISNRGENSCK
ATGQVCHALCSPEGCWGPEPRDCVSCRNVSRGRECVDKCNLLEGEPREFV
ENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPAGVM
GENNTLVWKYADAGHVCHLCHPNCTYGCTGPGLEGCPTNGPKIPSIAT
Extra-cellular domain

GMVGALLLLLVVALGI predicted transmembrane domain

GLFMRRRHIVRKRTLRRLLQERELVEPLTPSGEAPN

QALLRILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREA
TSPKANKEILDEAYVMASVDNPHVCRLLGICLTSTVQLITQLMPFGCLLD
YVREHKDNIGSQYLLNWCVQIAKGMNYLEDRRLVHRDLAARNVLVKTPQH
VKITDFGLAKLLGAEEKEYHAEGGKVPIKWMALESILHRIYTHQSDVWSY
GVTVWELMTFGSKPYDGIPASEISSILEKGERLPQPPICTIDVYMIMVKC
WMIDADSRPKFRELIIEFSKMARDPQRYLVIQGDERMHLPSPTDSNFYRA
LMDEEDMDDVVDADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNSTVACI
DRNGLQSCPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSVPKR
PAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNST
FDSPAHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRV
APQSSEFIGA

Intra-cellular tyrosine kinase and C-terminal tail