PRLR VH alignment

	FR1			CDR1	FR2		CDR2		
	1	2	3		4		5	6	
	123456789012345678901234567890			12345a	67890123456789		012a3456789012345		
Ab5 VH	QVQLQQPGAELVRPGTSVKLSCKASGYTFT			SFWMH-	WVKQRPGQGLEWIG		VIDPSDTYTNYNQKFKG		
Ab13 VH	QVQLQQPGAELVRPGTSVKLSCKASGYTFT			SFWMH-	WVKQRPGQGLEWIG		VIDPSDSHTNYNQKFKG		
Ab7 VH	QVQLQQPGAELVMPGTSVKLSCKASGYTFT			SYWIH-	WVKQRPGQGLEWIG		EIDPSDSYTNYNQKFKG		
Ab6 VH	QVQLQQPGAELVMPGSSVKLSCKASGYTFT			TYWMH-	WVKQRPGQGLEWIG		EIDPSDSYSNYNQKFKD		
Ab8 VH	EVQLQQSGPELVKPGASVKISCKASGYTFT			DYNIH-	WVKQSHGKSLEWIG		YIYPNNDGTGYNQKFKS		
Ab9 VH	EVQLQQSGPELVRPGASVKISCKASGYSFT			DYNMH-	WVKQSHGKSLEWIG		YIYPYNGGAGYNQKFKS		
Ab10 VH	EVQLHQSGPELVKPGASVKISCKASGYTFT			DYNMH-	WMKQSHGKSLEWIG		YFYPYNGGTGYNQEFKN		
Ab11 VH	EVKLVESGGGLVQPGGSLKLSCAASGFTFS			DYYMF-	WVRQTPEKSLEWVA		YISNGGGSTYYPDTVKG		
Ab12 VH	DVQLQESGPGLVKPSQSLSLTCTVTGYSIT			SDYAWN	WIRQFPGNKLEWMG		YIG-YSGRTSFNPSLKS		

	FR3			CDR3	FR4	
	7	8	9	1 0	1 1	
	67890123456789012abc345678901234			567890abcde12	34567890123	
Ab5 VH	KATLTVDTSSSTAYMQLSSLTSEDSAVYYCAR			GDYSNWF-----TY	WGQGTLVTVSA	(IGHJ3*01)
Ab13 VH	KATLTVNTSSSTAYMHLSSLTSEDSAVYYCAR			GDYSNWF-----TY	WGQGTLVTVSA	(IGHJ3*01)
Ab7 VH	KATLTVDRSSSTAYMQLSSLTSEDSAVYYCGR			SFFTNWF-----AY	WGQGTLVTVSA	(IGHJ3*01)
Ab6 VH	KATLTVDKSSSTAYMQLSSLTSEDSAVYYCAR			NGGLGPAWF--SY	WGQGTLVTVSA	(IGHJ3*01)
Ab8 VH	KATLTVDNSSSTAYMEVRSLTSEDSAVYYCAR			GDGNYVGDM--DY	WGQGTSVTVSS	(IGHJ4*01)
Ab9 VH	KATMNVGISSSTAYMELRSLTSEDSAVYYCAR			GDGNYVGDM--DY	WGQGTSVTVSS	(IGHJ4*01)
Ab10 VH	KATLTVDISSSTAYMELRRLTSEDSAVYYCAR			GGWGIYYAM--DY	WGQGTSVTVSS	(IGHJ4*01)
Ab11 VH	RFTISRDNAKNTLYLQMSRLKSEDTAMYYCSR			QLFYYGSRGAMGY	WGQGTSVTVSS	(IGHJ4*01)
Ab12 VH	RISITRDTSKNQFFLQLNSVTTEDTATYYCAR			GGFAM------DY	WGQGTSVTVSS	(IGHJ4*01)

Figure 1

PRLR VL alignment

```
                FR1                    CDR1            FR2          CDR2
                ---------------------- --------------- ------------ -------
                          1         2              3         4          5
                1234567890123456789012 3 4567abcde8901234 5678901234567890 123456
Ab5 VL          DVVMTQTPLSLPVSLGDQASISC RSSQRLVHSNGNTYLH WYLQKPGQSPKLLIY KVSNRFS
Ab13 VL         DVVMTQTPFSLPVSLGDQASISC RSSQSLVHSNGNTYLH WYLQKPGQSPKLLIY KVSNRFS
Ab7 VL          DVVMTQTPLSLPVSLGDQASISC RSSQSLVHSNGNTYLH WYLQKPGQSPKLLIY KVSNRFS
Ab11 VL         DVLMTQTPLSLPVSLGDQASISC RSSQSIVHSNGNTYLE WYLQKPGQSPKLLIY KVSNRFS
Ab8 VL          DIQMTQSPASLSASVGETVTITC RASE------NIYSYLA WYQQKQGKPPQLLVY NAKTLAE
Ab9 VL          DIQMTQSPASLSASVGETVTITC RASE------NIYSYLA WYQQKQGKSPQLLVY NAKTLAE
Ab10 VL         DIQMTQSPASLSASVGETVTITC RASE------NIYSYLT WYQQKQGKSPQLLVY NAKTLAE
Ab6 VL          DIVMTQSQKFMSTTVGDRVSITC KASQ------YVGTAVA WYQQKPGQSPKLLIY SASNRYT
Ab12 VL         QIVLTQSPGIMSASPGEKVTMTC SASS-------SVTYMY WYQQKPRSSPKPWIY LTSNLAS

                FR3                              CDR3      FR4
                -------------------------------- --------- ----------
                                                           1
                   6         7         8          9        0
                789012345678901234567890123456789 0123456a78 9012345678
Ab5 VL          GVPDRFSGSGSGTDFTLKISRVEAEDLGVYFC SQSTHVP-WT FGGGTKLEIK (IGKJ1*01)
Ab13 VL         GVPDRFSGSGSGTDFTLKISRVEAEDLELYFC SQSTHVP-WT FGGGTKLEIK (IGKJ1*01)
Ab7 VL          GVPDRFSGSGSGTDFTLKINRVEAEDLGVYFC SQSTHVP-FT FGSGTKLEIK (IGKJ4*01)
Ab11 VL         GVPDRFSGSGSGTDFTLKISRVEAEDLGVYYC FQGSHVP-FT FGSGTKLEIK (IGKJ4*01)
Ab8 VL          GVPSRFSGGGSGTQFSLKINSLQPEDFGSYYC QHHYATP-FT FGSGTKLEIK (IGKJ4*01)
Ab9 VL          GVPSRFSGSGSGTQFSLKINSLQPEDFGSYYC QHHSGTP-FT FGSGTKLEIK (IGKJ4*01)
Ab10 VL         GVPSRFSGSGSGTQFSLKINSLQPEDFGSYHC QHHSVTP-LT FGAGTKLELK (IGKJ5*01)
Ab6 VL          GVPDRFTDSGSGTDFTLTISNLQSEDLADYFC QQYSSYP-WT FGGGTKLEIK (IGKJ1*01)
Ab12 VL         GVPARFSGSGSGTSYSLTISSMEAEDGATYYC QQWSSTPPLT FGGGTKLELN (IGKJ1/5*01)
```

Figure 2

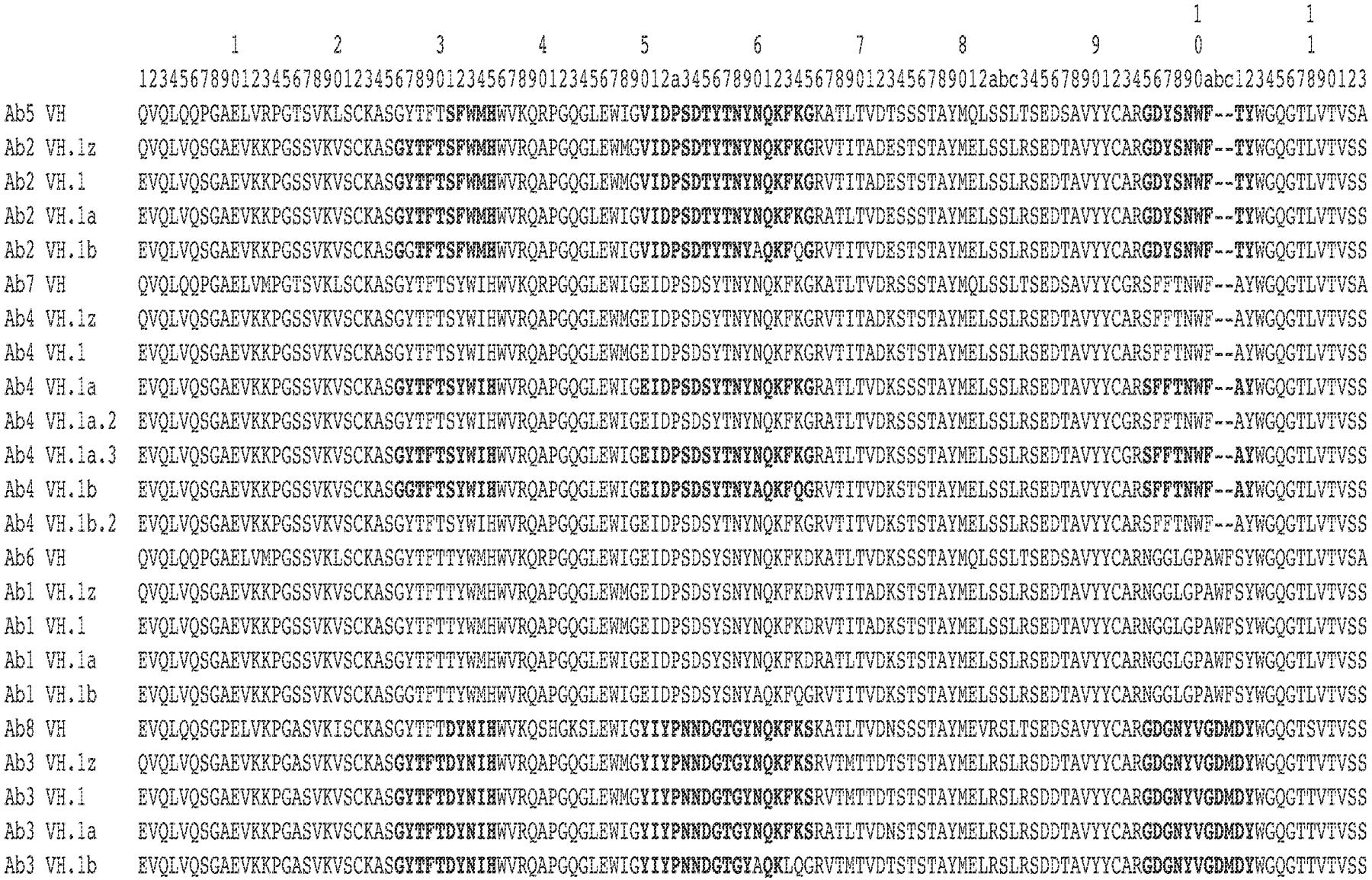

1 1
1 2 3 4 5 6 7 8 9 0 1
12345678901234567890123456789012345678901234567890123456789012a3456789012345678901234567890123456789012abc3456789012345678901abc1234567890123
Ab5 VH QVQLQQPGAELVRPGTSVKLSCKASGYTFTSFWMHWVKQRPGQGLEWIGVIDPSDTYTNYNQKFKGKATLTVDTSSSTAYMQLSSLTSEDSAVYYCARGDYSNWF--TYWGQGTLVTVSA
Ab2 VH.1z QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSFWMHWVRQAPGQGLEWMGVIDPSDTYTNYNQKFKGRVTITADESTSTAYMELSSLRSEDTAVYYCARGDYSNWF--TYWGQGTLVTVSS
Ab2 VH.1 EVQLVQSGAEVKKPGSSVKVSCKASGYTFTSFWMHWVRQAPGQGLEWMGVIDPSDTYTNYNQKFKGRVTITADESTSTAYMELSSLRSEDTAVYYCARGDYSNWF--TYWGQGTLVTVSS
Ab2 VH.1a EVQLVQSGAEVKKPGSSVKVSCKASGYTFTSFWMHWVRQAPGQGLEWIGVIDPSDTYTNYNQKFKGRATLTVDESSSTAYMELSSLRSEDTAVYYCARGDYSNWF--TYWGQGTLVTVSS
Ab2 VH.1b EVQLVQSGAEVKKPGSSVKVSCKASGGTFTSFWMHWVRQAPGQGLEWIGVIDPSDTYTNYAQKFQGRVTITVDESTSTAYMELSSLRSEDTAVYYCARGDYSNWF--TYWGQGTLVTVSS
Ab7 VH QVQLQQPGAELVMPGTSVKLSCKASGYTFTSYWIHWVKQRPGQGLEWIGEIDPSDSYTNYNQKFKGKATLTVDRSSSTAYMQLSSLTSEDSAVYYCGRSFFTNWF--AYWGQGTLVTVSA
Ab4 VH.1z QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYWIHWVRQAPGQGLEWMGEIDPSDSYTNYNQKFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARSFFTNWF--AYWGQGTLVTVSS
Ab4 VH.1 EVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYWIHWVRQAPGQGLEWMGEIDPSDSYTNYNQKFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARSFFTNWF--AYWGQGTLVTVSS
Ab4 VH.1a EVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYWIHWVRQAPGQGLEWIGEIDPSDSYTNYNQKFKGRATLTVDKSSSTAYMELSSLRSEDTAVYYCARSFFTNWF--AYWGQGTLVTVSS
Ab4 VH.1a.2 EVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYWIHWVRQAPGQGLEWIGEIDPSDSYTNYNQKFKGRATLTVDRSSSTAYMELSSLRSEDTAVYYCGRSFFTNWF--AYWGQGTLVTVSS
Ab4 VH.1a.3 EVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYWIHWVRQAPGQGLEWIGEIDPSDSYTNYNQKFKGRATLTVDKSSSTAYMELSSLRSEDTAVYYCGRSFFTNWF--AYWGQGTLVTVSS
Ab4 VH.1b EVQLVQSGAEVKKPGSSVKVSCKASGGTFTSYWIHWVRQAPGQGLEWIGEIDPSDSYTNYAQKFQGRVTITVDKSTSTAYMELSSLRSEDTAVYYCARSFFTNWF--AYWGQGTLVTVSS
Ab4 VH.1b.2 EVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYWIHWVRQAPGQGLEWIGEIDPSDSYTNYNQKFKGRVTITVDKSTSTAYMELSSLRSEDTAVYYCARSFFTNWF--AYWGQGTLVTVSS
Ab6 VH QVQLQQPGAELVMPGSSVKLSCKASGYTFTTYWMHWVKQRPGQGLEWIGEIDPSDSYSNYNQKFKDKATLTVDKSSSTAYMQLSSLTSEDSAVYYCARNGGLGPAWFSYWGQGTLVTVSA
Ab1 VH.1z QVQLVQSGAEVKKPGSSVKVSCKASGYTFTTYWMHWVRQAPGQGLEWMGEIDPSDSYSNYNQKFKDRVTITADKSTSTAYMELSSLRSEDTAVYYCARNGGLGPAWFSYWGQGTLVTVSS
Ab1 VH.1 EVQLVQSGAEVKKPGSSVKVSCKASGYTFTTYWMHWVRQAPGQGLEWMGEIDPSDSYSNYNQKFKDRVTITADKSTSTAYMELSSLRSEDTAVYYCARNGGLGPAWFSYWGQGTLVTVSS
Ab1 VH.1a EVQLVQSGAEVKKPGSSVKVSCKASGYTFTTYWMHWVRQAPGQGLEWIGEIDPSDSYSNYNQKFKDRATLTVDKSTSTAYMELSSLRSEDTAVYYCARNGGLGPAWFSYWGQGTLVTVSS
Ab1 VH.1b EVQLVQSGAEVKKPGSSVKVSCKASGGTFTTYWMHWVRQAPGQGLEWIGEIDPSDSYSNYAQKFQGRVTITVDKSTSTAYMELSSLRSEDTAVYYCARNGGLGPAWFSYWGQGTLVTVSS
Ab8 VH EVQLQQSGPELVKPGASVKISCKASGYTFTDYNIHWVKQSHGKSLEWIGYIYPNNDGTGYNQKFKSKATLTVDNSSSTAYMEVRSLTSEDSAVYYCARGDGNYVGDMDYWGQGTSVTVSS
Ab3 VH.1z QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYNIHWVRQAPGQGLEWMGYIYPNNDGTGYNQKFKSRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARGDGNYVGDMDYWGQGTTVTVSS
Ab3 VH.1 EVQLVQSGAEVKKPGASVKVSCKASGYTFTDYNIHWVRQAPGQGLEWMGYIYPNNDGTGYNQKFKSRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARGDGNYVGDMDYWGQGTTVTVSS
Ab3 VH.1a EVQLVQSGAEVKKPGASVKVSCKASGYTFTDYNIHWVRQAPGQGLEWIGYIYPNNDGTGYNQKFKSRATLTVDNSTSTAYMELRSLRSDDTAVYYCARGDGNYVGDMDYWGQGTTVTVSS
Ab3 VH.1b EVQLVQSGAEVKKPGASVKVSCKASGYTFTDYNIHWVRQAPGQGLEWIGYIYPNNDGTGYAQKLQGRVTMTVDTSTSTAYMELRSLRSDDTAVYYCARGDGNYVGDMDYWGQGTTVTVSS

Figure 3

	1 2 3 4 5 6 7 8 9 10
	1234567890123456789012345 67abcde8901234567890123456789012345678901234567890123456789012345678901234567890123456a
Ab5 VL	DVVMTQTPLSLPVSLGDQASISC**RSSQRLVHSNGNTYLH**WYLQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLKISRVEAEDLGVYFC**SQSTHVPWT**FGGGTKLEIK
Ab2 VL.1	DIVMTQTPLSLSVTPGQPASISC**RSSQRLVHSNGNTYLH**WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**SQSTHVPWT**FGGGTKVEIK
Ab2 VL.1a	DVVMTQTPLSLSVTPGQPASISC**RSSQRLVHSNGNTYLH**WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLKISRVEAEDVGVYFC**SQSTHVPWT**FGGGTKVEIK
Ab2 VL.1b	DVVMTQTPLSLSVTPGQPASISC**RSSQRLVHSNGNTYLH**WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**SQSTHVPWT**FGGGTKVEIK
Ab7 VL	DVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKINRVEAEDLGVYFCSQSTHVPFTFGSGTKLEIK
Ab4 VL.1	DIVMTQTPLSLSVTPGQPASISCRSSQSLVHSNGNTYLHWYLQKPGQSPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPFTFGGGTKVEIK
Ab4 VL.1a	DVVMTQTPLSLSVTPGQPASISCRSSQSLVHSNGNTYLHWYLQKPGQSPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPFTFGGGTKVEIK
Ab4 VL.1b	DVVMTQTPLSLSVTPGQPASISCRSSQSLVHSNGNTYLHWYLQKPGQSPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPFTFGGGTKVEIK
Ab6 VL	DIVMTQSQKFMSTTVGDRVSITCKASQ-----YVGTAVAWYQQKPGQSPKLLIYSASNRYTGVPDRFTDSGSGTDFTLTISNLQSEDLADYFCQQYSSYPWTFGGGTKLEIK
Ab1 VL.1	DIQMTQSPSSVSASVGDRVTITCKASQ-----YVGTAVAWYQQKPGKAPKLLIYSASNRYTGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYSSYPWTFGGGTKVEIK
Ab1 VL.1a	DIQMTQSPSSVSASVGDRVTITCKASQ-----YVGTAVAWYQQKPGKSPKLLIYSASNRYTGVPSRFSDSGSGTDFTLTISSLQPEDFATYFCQQYSSYPWTFGGGTKVEIK
Ab1 VL.2	EIVMTQSPATLSVSPGERATLSCKASQ-----YVGTAVAWYQQKPGQAPRLLIYSASNRYTGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYSSYPWTFGGGTKVEIK
Ab1 VL.2a	EIVMTQSPATLSVSPGERATLSCKASQ-----YVGTAVAWYQQKPGQSPRLLIYSASNRYTGVPARFSDSGSGTEFTLTISSLQSEDFAVYFCQQYSSYPWTfGGGTKVEIK
Ab8 VL	DIQMTQSPASLSASVGETVTITC**RASE**-----**NIYSYLA**WYQQKQGKPPQLLVY**NAKTLAE**GVPSRFSGGGSGTQFSLKINSLQPEDFGSYYC**QHHYATPFT**FGSGTKLEIK
Ab3 VL.1	DIQMTQSPSSLSASVGDRVTITC**RASE**-----**NIYSYLA**WYQQKPGKAPKLLIY**NAKTLAE**GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC**QHHYATPFT**FGQGTKLEIK
Ab3 VL.1a	DIQMTQSPSSLSASVGDRVTITC**RASE**-----**NIYSYLA**WYQQKPGKPPKLLVY**NAKTLAE**GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC**QHHYATPFT**FGQGTKLEIK
Ab3 VL.1b	DIQMTQSPSSLSASVGDRVTITC**RASE**-----**NIYSYLA**WYQQKPGKAPKLLVY**NAKTLAE**GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC**QHHYATPFT**FGQGTKLEIK

Figure 4

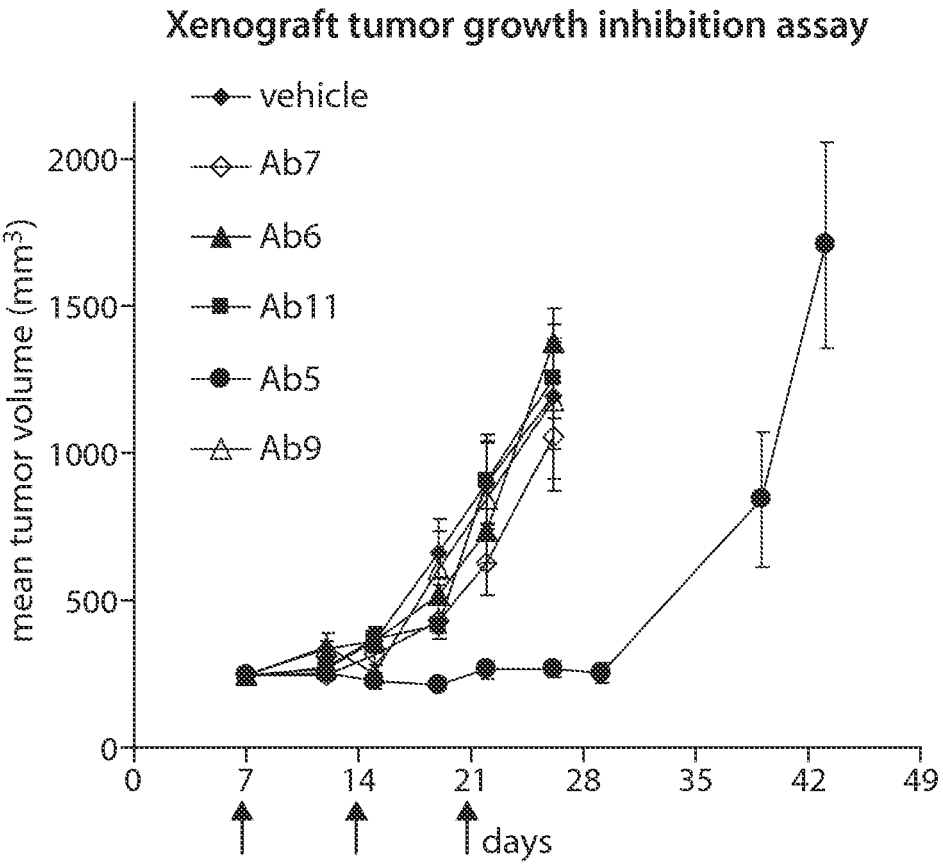

Xenograft tumor growth inhibition assay
vehicle
Ab7
Ab6
Ab11
Ab5
Ab9
mean tumor volume (mm3)
2000
1500
1000
500
0
0
7
14
21
28
35
42
49
days

Figure 5

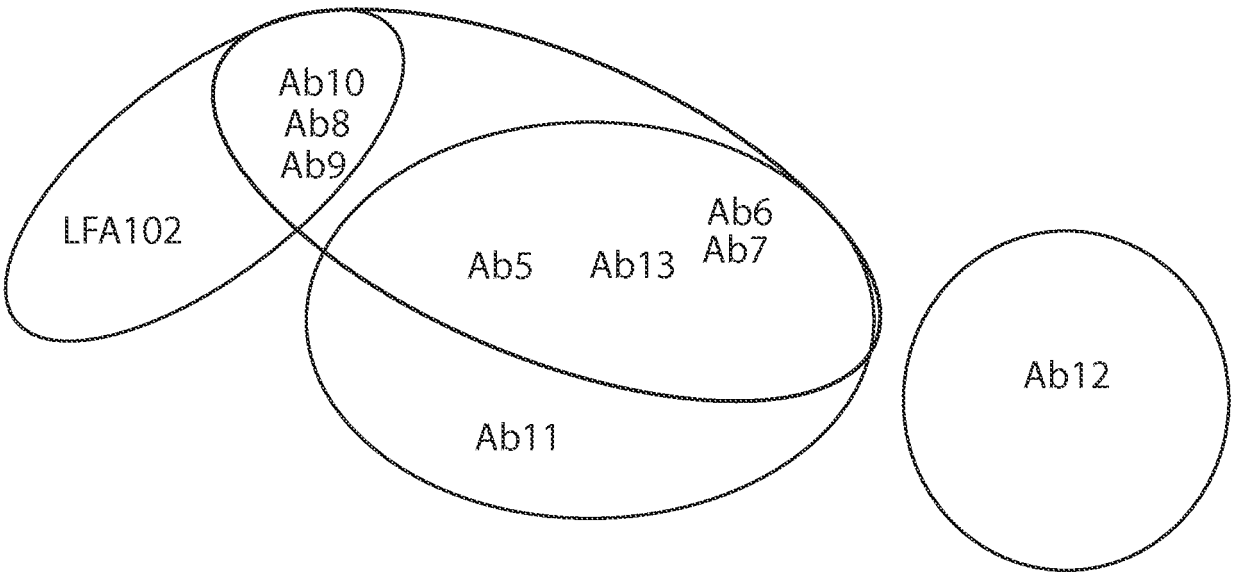


Figure 6

simultaneous binding assay results

surface mAb		solution mAb#											
		01	02	03	04	05	06	07	08	09	10	11	12
chAb7	01 - chAb7	0	1	1	0	0	1	0	0	0	0	0	39
Ab39	02 - Ab39	-2	-2	-2	-2	-2	-2	-2	-2	-2	-2	-2	36
Ab40	03 - Ab40	-2	-2	-2	-2	-2	-2	-2	-2	-2	-2	-3	40
chAb5	04 - chAb5	-1	0	0	0	0	0	0	-1	0	0	0	32
Ab30	05 - Ab30	-1	0	-1	-1	-1	-1	-1	-1	-1	-1	-1	35
chAb6	06 - chAb6	-1	0	-1	-1	-1	-1	0	-1	-1	-2	-2	26
Ab19	07 - Ab19	-1	-1	-1	0	-1	-1	-1	-1	-1	-1	-1	19
Ab21	08 - Ab21	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	21
chAb8	09 - chAb8	2	1	0	7	6	0	0	0	-1	-1	-1	1
Ab48	10 - Ab48	1	2	0	8	6	0	0	1	-1	-1	0	-1
Ab49	11 - Ab49	2	2	0	7	6	0	1	0	-1	-2	-1	1
LFA102	12 - LFA102	48	92	35	102	103	90	122	104	-2	-2	-2	-2

Values shown are solution mAb binding magnitudes expressed as the percentage of the respective PRLR binding magnitudes.

simultaneous binding (different epitopes)

no simultaneous binding (overlapping epitopes)

small non-reciprocal simultaneous binding

Figure 7

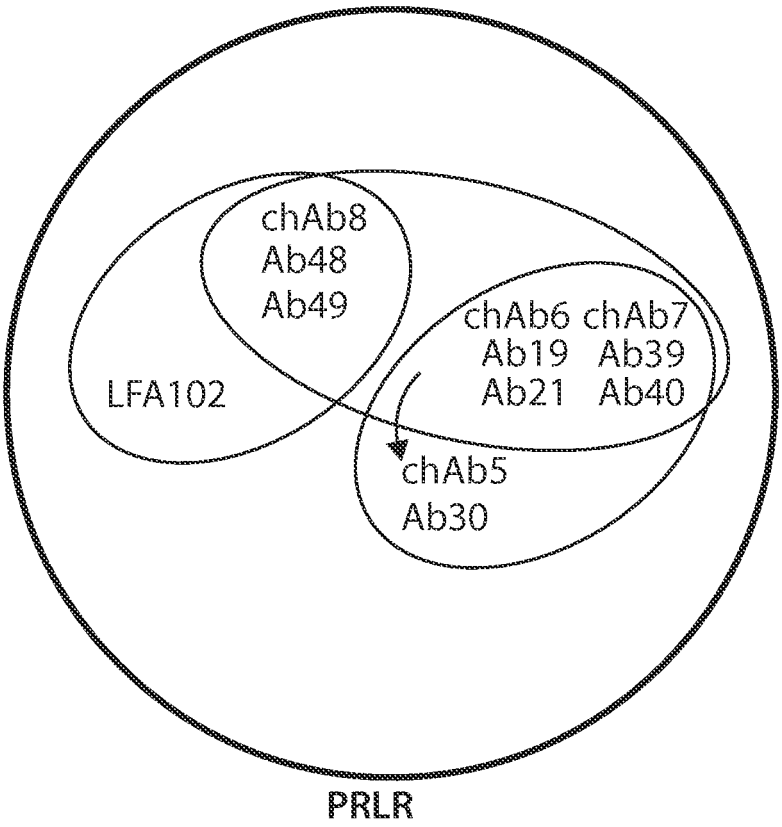

chAb8
Ab48
Ab49
chAb6 chAb7
Ab19 Ab39
Ab21 Ab40
LFA102
chAb5
Ab30
PRLR

Figure 8

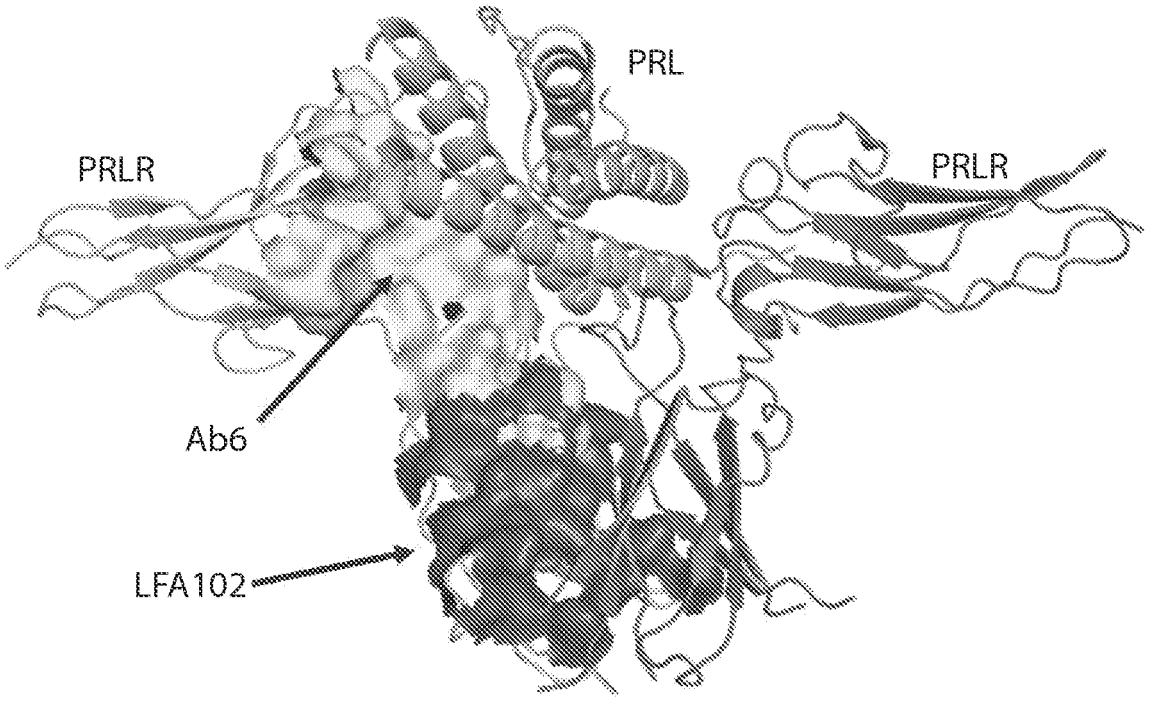


Figure 9

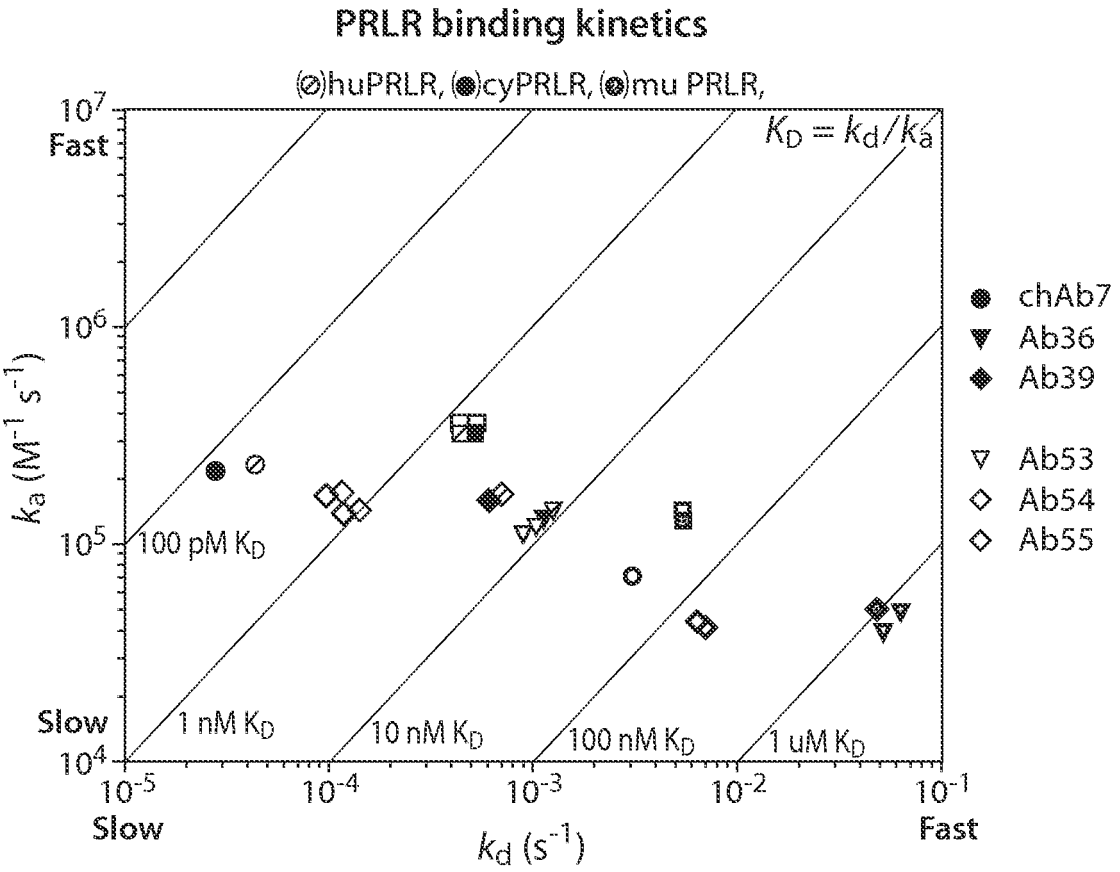

PRLR binding kinetics
⊘huPRLR, ●cyPRLR, ◉mu PRLR,
$K_D = k_d/k_a$
10^7
Fast
10^6
10^5
10^4
Slow
k_a (M^{-1} s^{-1})
100 pM K_D
1 nM K_D
10 nM K_D
100 nM K_D
1 uM K_D
10^{-5}
10^{-4}
10^{-3}
10^{-2}
10^{-1}
Slow
Fast
k_d (s^{-1})
chAb7
Ab36
Ab39
Ab53
Ab54
Ab55

Figure 10

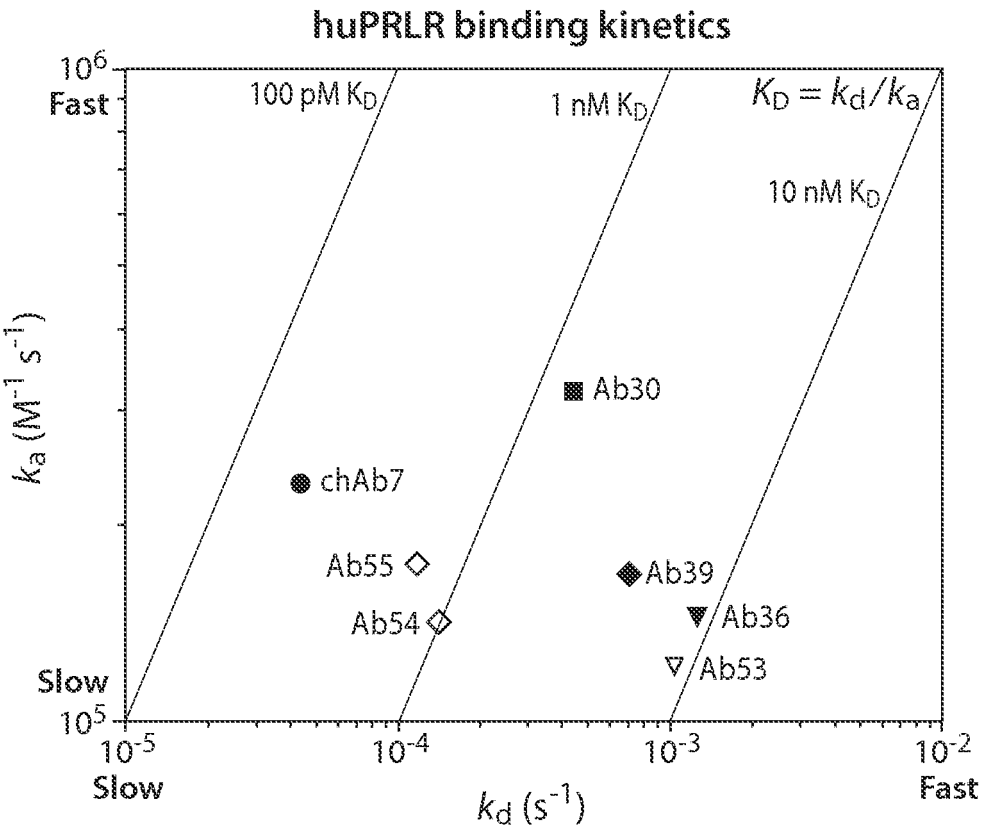

huPRLR binding kinetics
10^6
Fast
100 pM K_D
1 nM K_D
$K_D = k_d/k_a$
10 nM K_D
k_a (M^{-1} s^{-1})
Ab30
chAb7
Ab55
Ab39
Ab54
Ab36
Ab53
Slow
10^5
10^{-5}
Slow
10^{-4}
10^{-3}
10^{-2}
Fast
k_d (s^{-1})

Figure 11