

VH domains:			
	CDR1	CDR2	CDR3
Ab1	QVQLQESGPGLVKPSQTLSTCTVSGYISISSDFAWN	WIRQPPGKGLEWMGVISYSGNTRYQP	SLKSRITISRDTSKNQFFLKLSVTAADTATYYCVTA
AbA	EVQLQESGPGLVKPSQTLSTCTVSGYISIRDFAWN	WIRQPPGKGLEWMGVISYNGNTRYQP	SLKSRITISRDTSKNQFFLKLSVTAADTATYYCVTA
VL domains: (Ab1 and AbA have the same VL sequence)			
Ab1	DIQMTQSPSSMSVSGDRVITITCHSSQDINSNIG	WLQQKPGKSFKGLIYHGTNLD	DGVPSRFSGSGTDYTLTISSLPEDFAFYCVQYAQFPWT
AbA	DIQMTQSPSSMSVSGDRVITITCHSSQDINSNIG	WLQQKPGKSFKGLIYHGTNLD	DGVPSRFSGSGTDYTLTISSLPEDFAFYCVQYAQFPWT

Figure 1

LC:
the same

DIQMTQSPSSMSVSVDGDRVTTITCHSSQDINSNIGWLQKPKGSKFKGLIYHGTNLDDGVPSRFSGSGSGT
DYTLTISSLQPEDFATYYCVQAQFPWTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLLNNFY
BREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSLSPVTKSF
NRGEC SEQ ID NO: 13

Ab1	QVQLQESGPGLVKPSQTLSTLTCTVSGYSISDFAWNWIRQPPGKGLEWMGYISYSGNTRYQPSLKSRTITI
AbA	EVQLQESGPGLVKPSQTLSTLTCTVSGYSISRDFAWNWIRQPPGKGLEWMGYISYNGNTRYQPSLKSRTITI
Ab1	SRDTSKNQFFFLKLSNVTAAADTATYYCVTAQRGFPPYWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGTA
AbA	SRDTSKNQFFFLKLSNVTAAADTATYYCVTAQRGFPPYWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGTA
Ab1	ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
AbA	ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
Ab1	VDKKVEPKSCDKTHHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVD
AbA	VDKKVEPKSCDKTHHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVD
Ab1	GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTT
AbA	GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTT
Ab1	LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQ
AbA	LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQ
Ab1	GNVFSCVMHEALHNHYTQKSLSLSPG SEQ ID NO: 14
AbA	GNVFSCVMHEALHNHYTQKSLSLSPG SEQ ID NO: 15

HC:
6 AA change

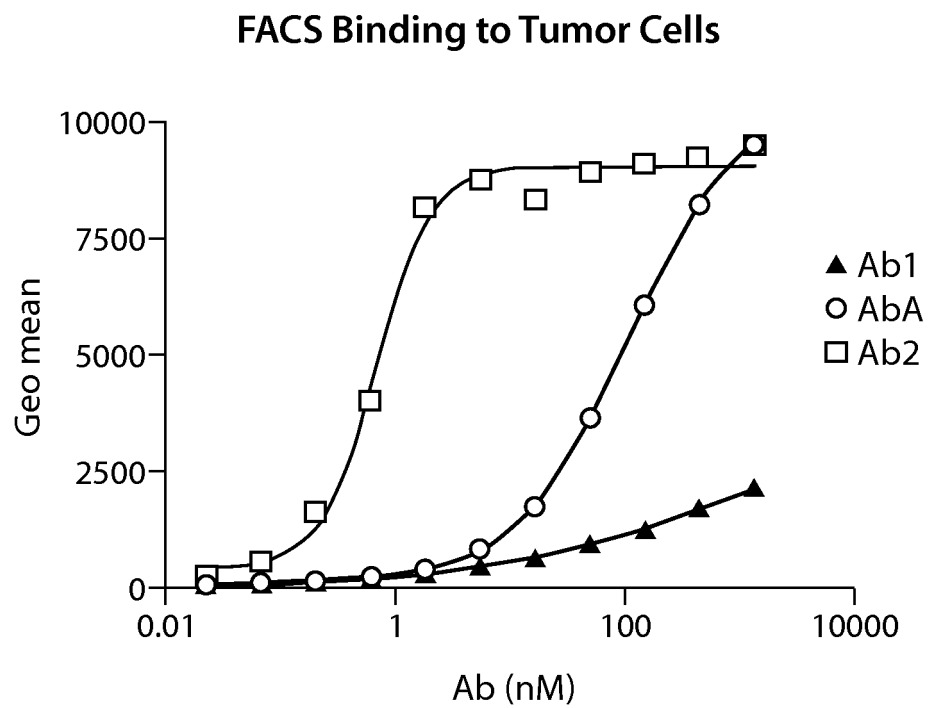
Figure 2

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mAb / DVD	EGFR (1-525)				EGFRvIII			
	k_a ($M^{-1} s^{-1}$)	k_d (s^{-1})	K_D (M)	K_D ratio (Ab1/variant Ab)	k_a ($M^{-1} s^{-1}$)	k_d (s^{-1})	K_D (M)	K_D ratio (Ab1/variant Ab)
Ab1	3.53E+03	8.02E-03	2.3E-06		8.43E+04	7.93E-04	9.4E-09	
Ab2	4.26E+05	1.71E-03	4.0E-09		3.46E+06	1.32E-03	3.8E-10	
AbK	4.78E+03	7.92E-06	1.7E-09	1372.6	1.30E+05	7.75E-05	6.0E-10	15.8
AbL	5.65E+03	1.78E-05	3.1E-09	722.5	2.00E+05	6.95E-05	3.5E-10	27.1
AbN	4.84E+03	1.71E-05	3.5E-09	641.7	1.37E+05	1.03E-04	7.5E-10	12.5
AbO	5.25E+03	2.05E-05	3.9E-09	582.4	1.96E+05	5.22E-05	2.7E-10	35.2
AbH	7.90E+03	4.07E-05	5.2E-09	441.0	3.27E+05	4.89E-05	1.5E-10	63.1
AbM	3.84E+03	2.26E-05	5.9E-09	386.6	1.87E+05	1.18E-04	6.3E-10	14.9
AbG	6.80E+03	5.88E-05	8.6E-09	263.0	3.74E+05	7.44E-05	2.0E-10	47.2
AbP	3.58E+03	7.67E-05	2.1E-08	106.0	1.17E+05	1.35E-04	1.2E-09	8.2
AbJ	2.20E+03	8.27E-05	3.8E-08	60.5	3.18E+05	9.40E-05	3.0E-10	31.8
AbB	5.46E+03	1.19E-03	2.2E-07	10.5	7.83E+04	1.73E-04	2.2E-09	4.2
AbA	3.26E+03	7.31E-04	2.2E-07	10.1	7.61E+04	1.73E-04	2.3E-09	4.1
AbF	1.98E+03	8.31E-04	4.2E-07	5.4	8.36E+04	3.24E-04	3.9E-09	2.4
AbD	5.82E+03	3.22E-03	5.5E-07	4.1	1.41E+05	8.66E-04	6.1E-09	1.5
AbE	6.17E+03	3.67E-03	5.9E-07	3.8	1.93E+05	1.58E-03	8.2E-09	1.2
AbC					2.20E+05	7.90E-04	3.6E-09	2.6
	poor fit, no kinetic info							

Figure 3

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**Figure 4**

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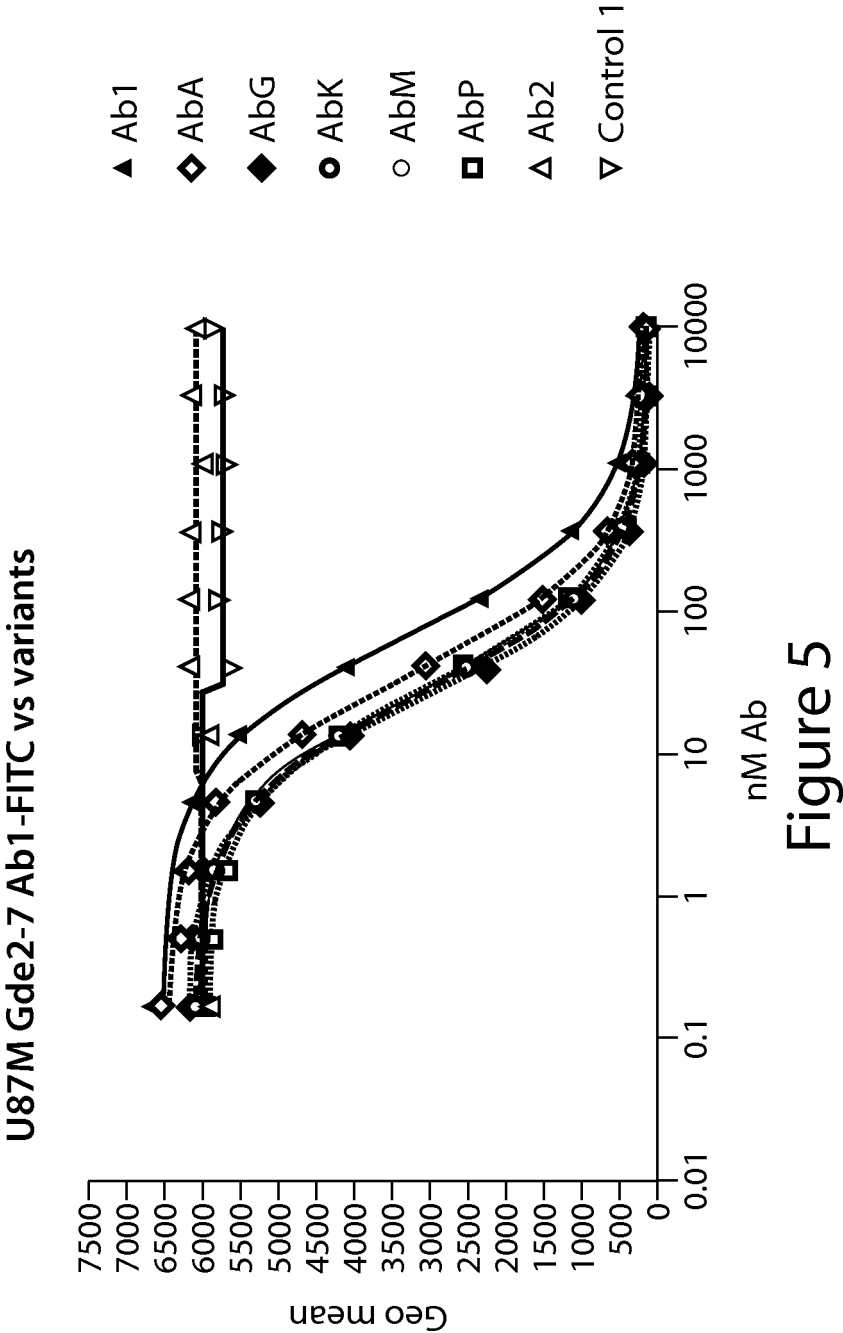


Figure 5

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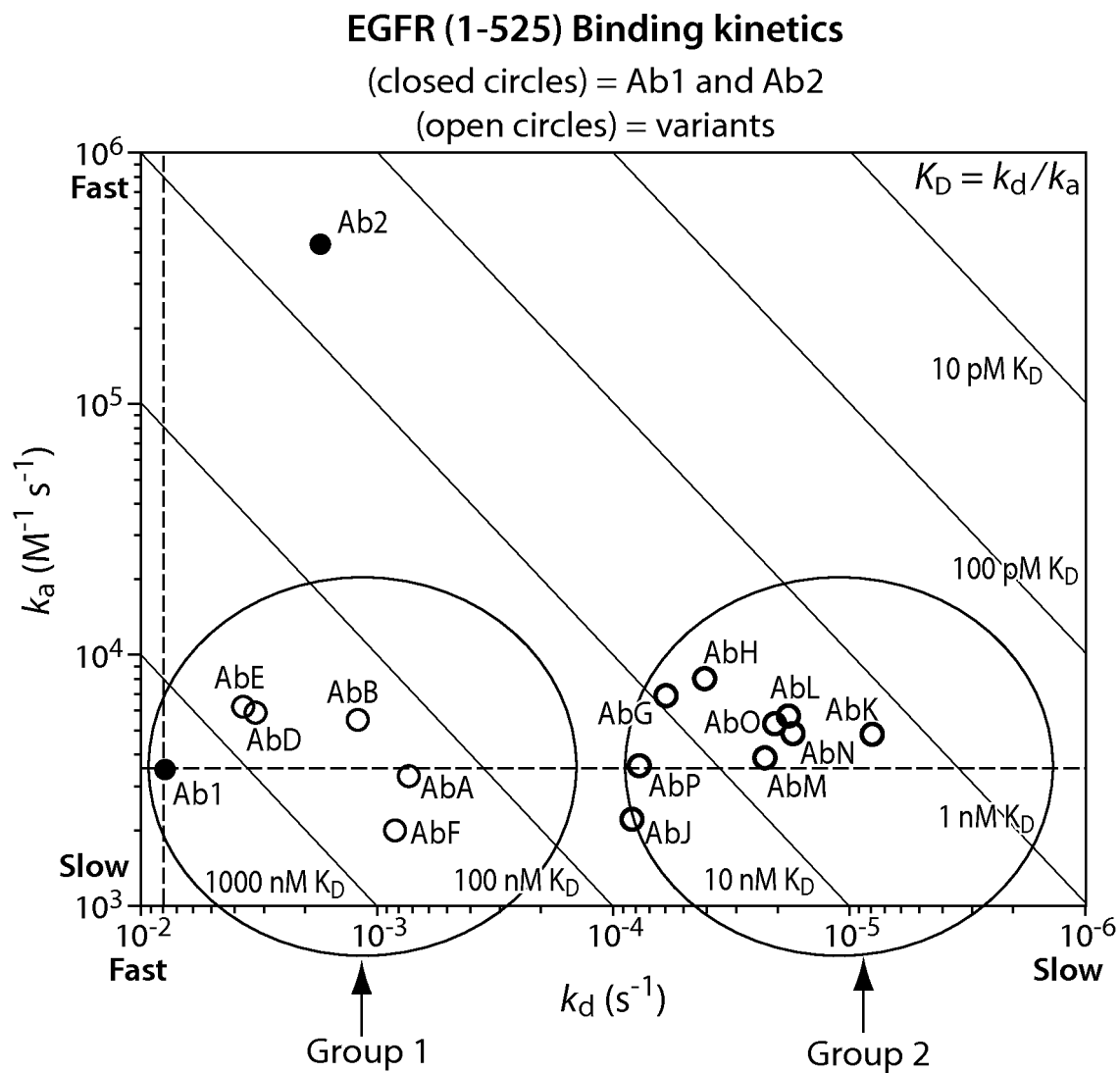


Figure 6

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SCC-15 (Ab1 Sensitive)

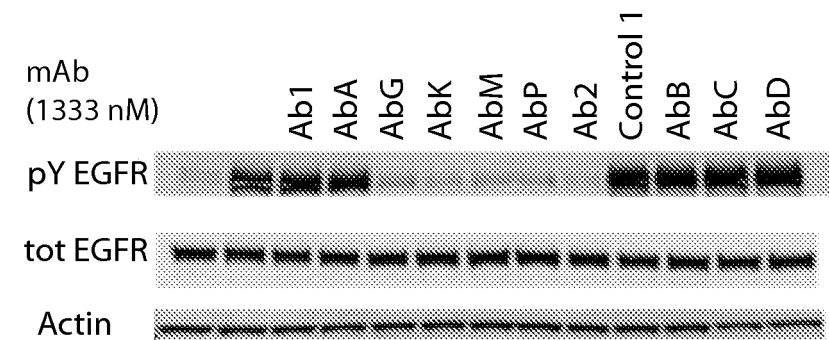


Figure 7A

H292 (Ab1 Resistant)

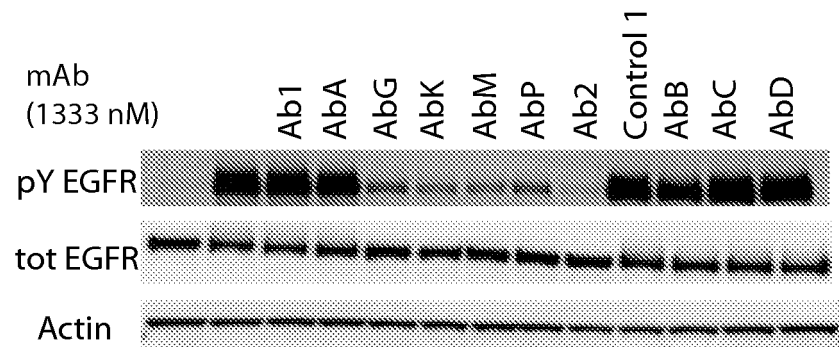


Figure 7B

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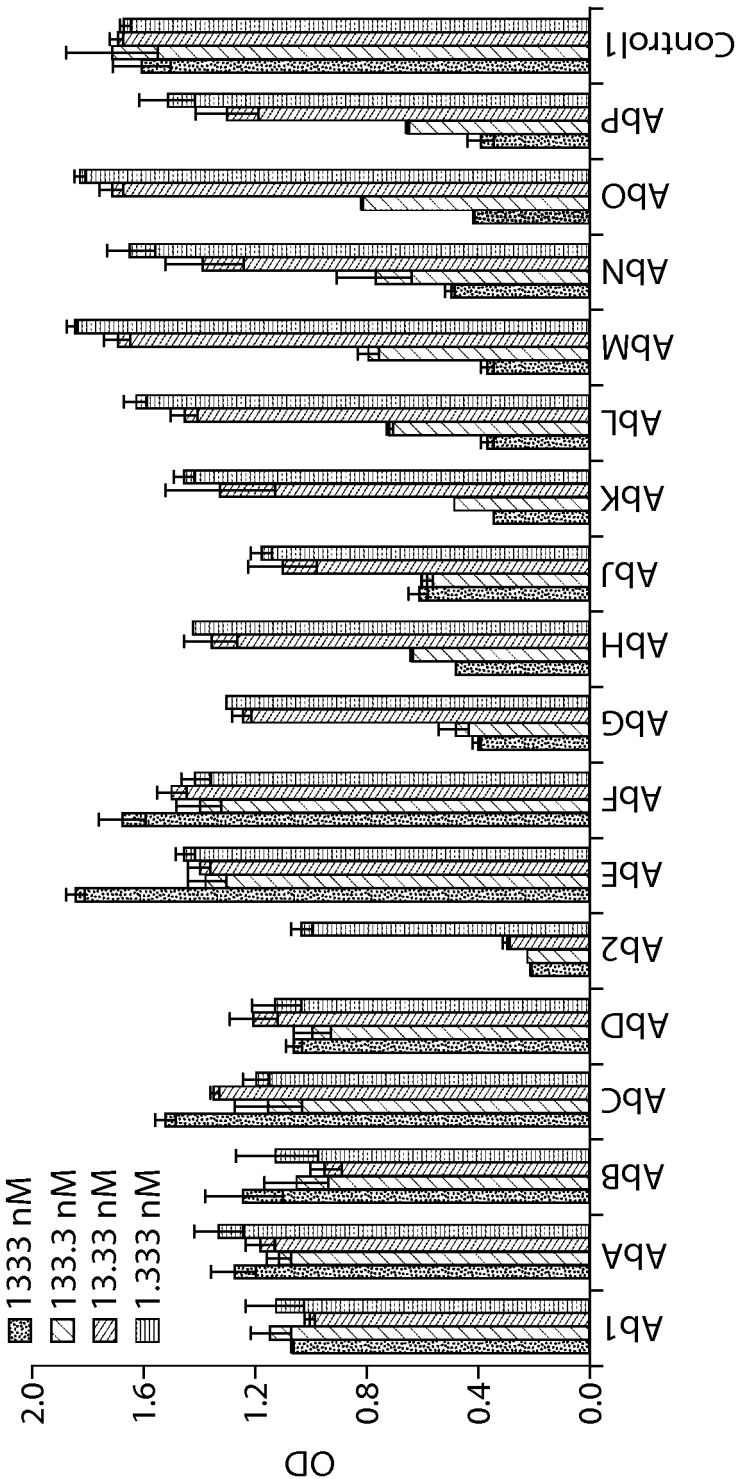


Figure 8A

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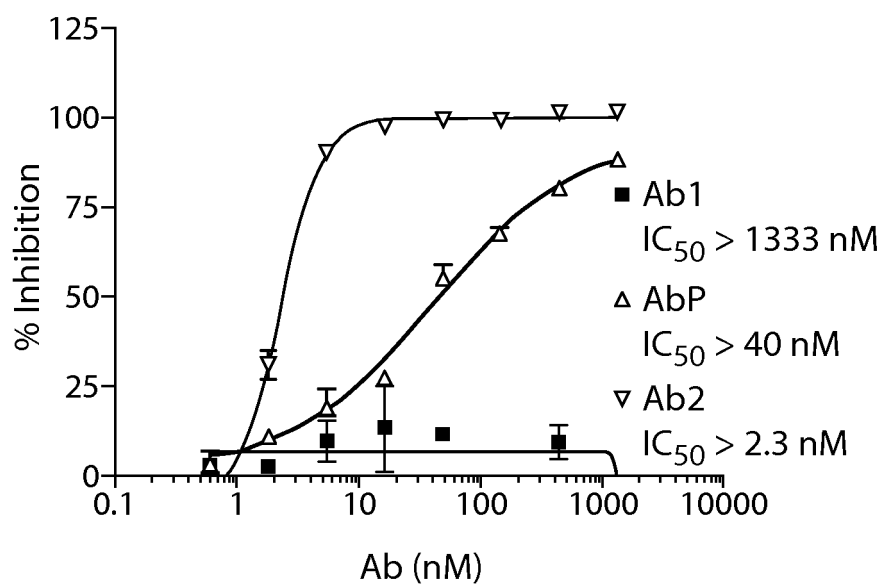


Figure 8B

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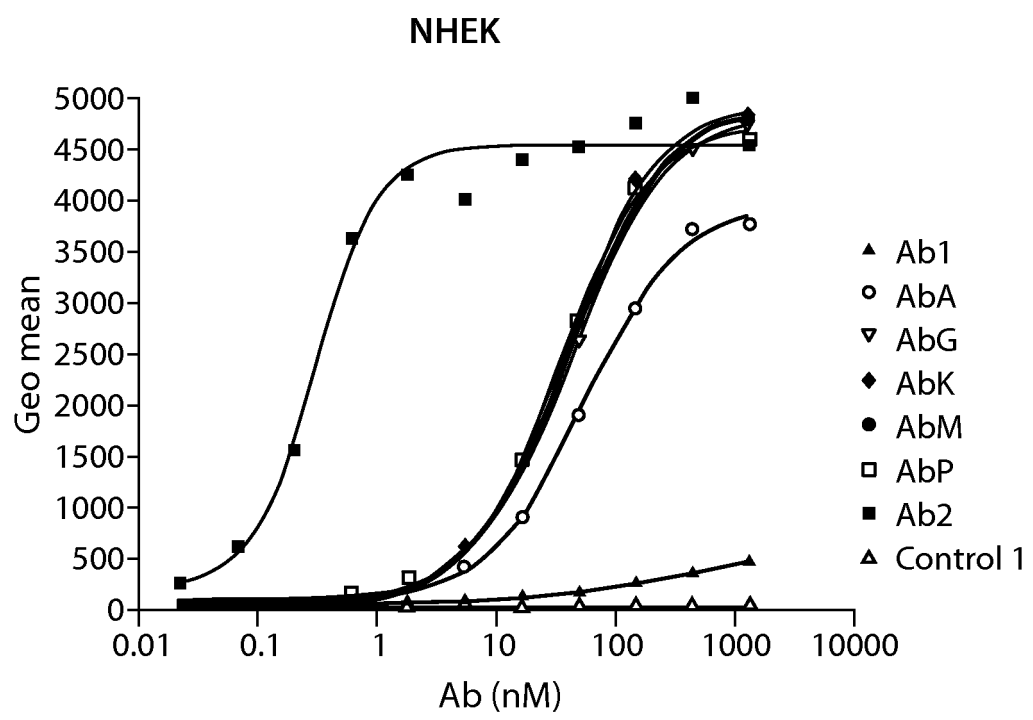


Figure 9

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NCI-H292 Human NSCLC Carcinoma Xenograft

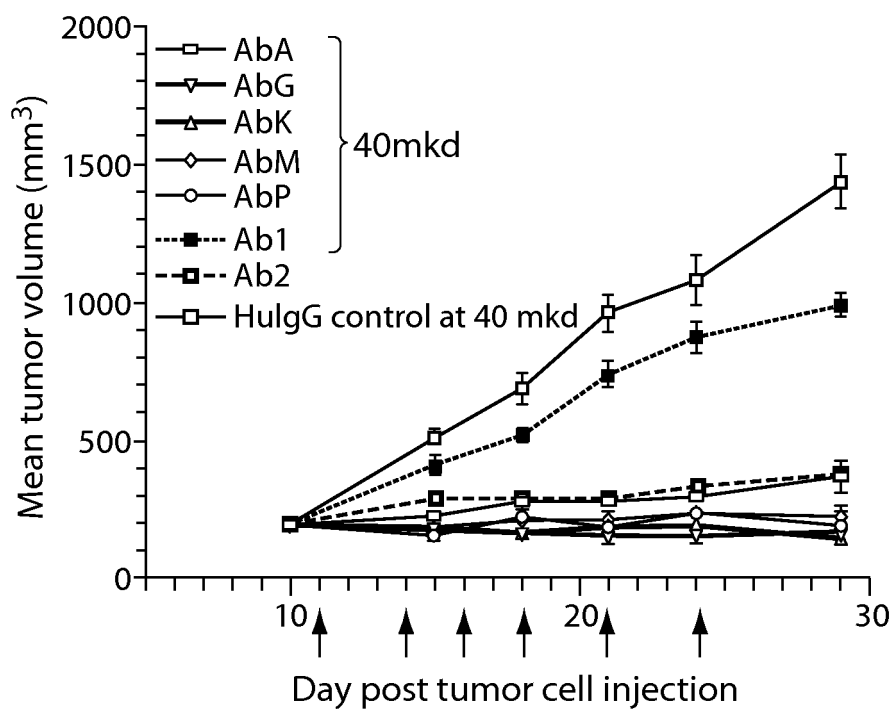


Figure 10

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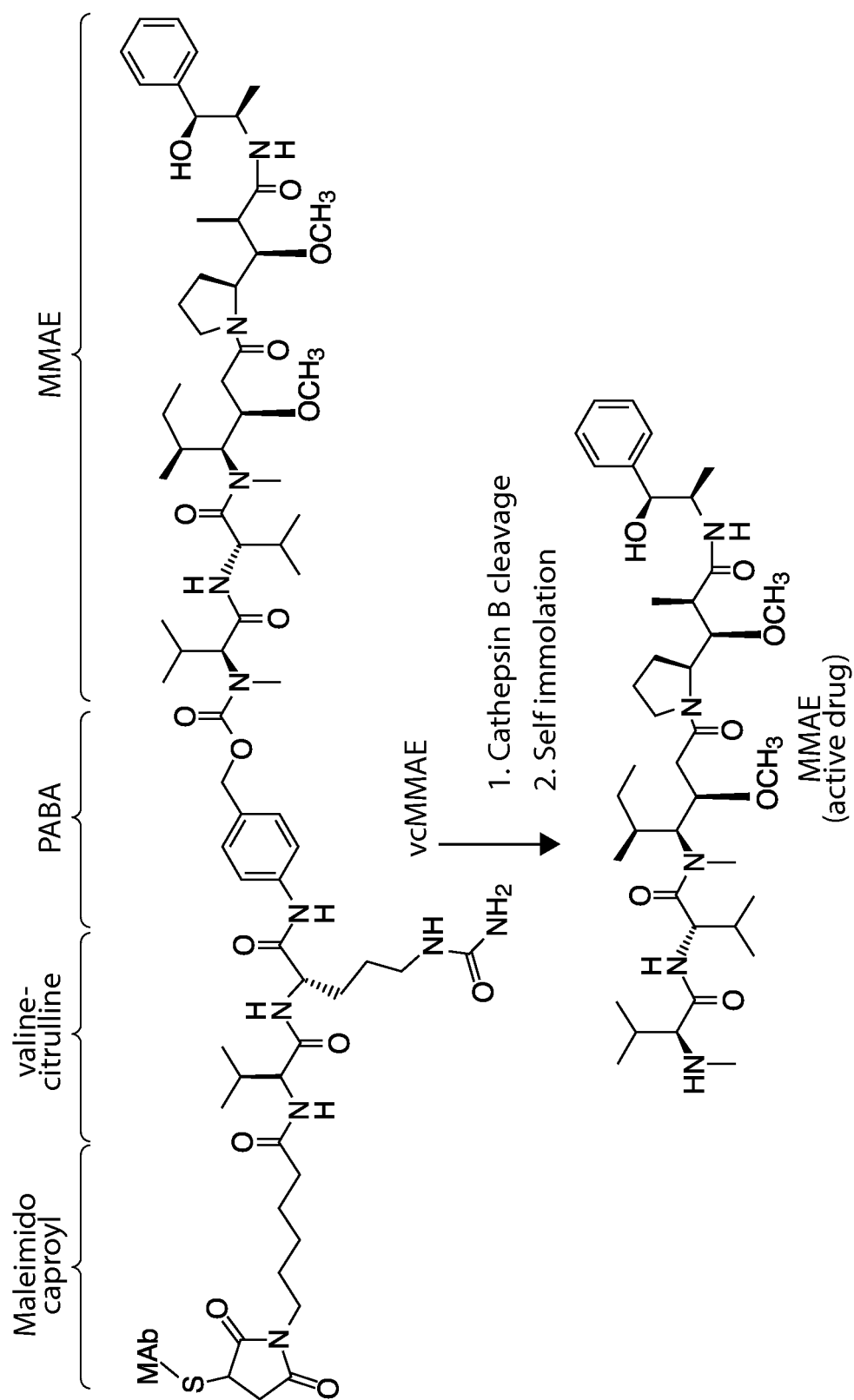


Figure 11

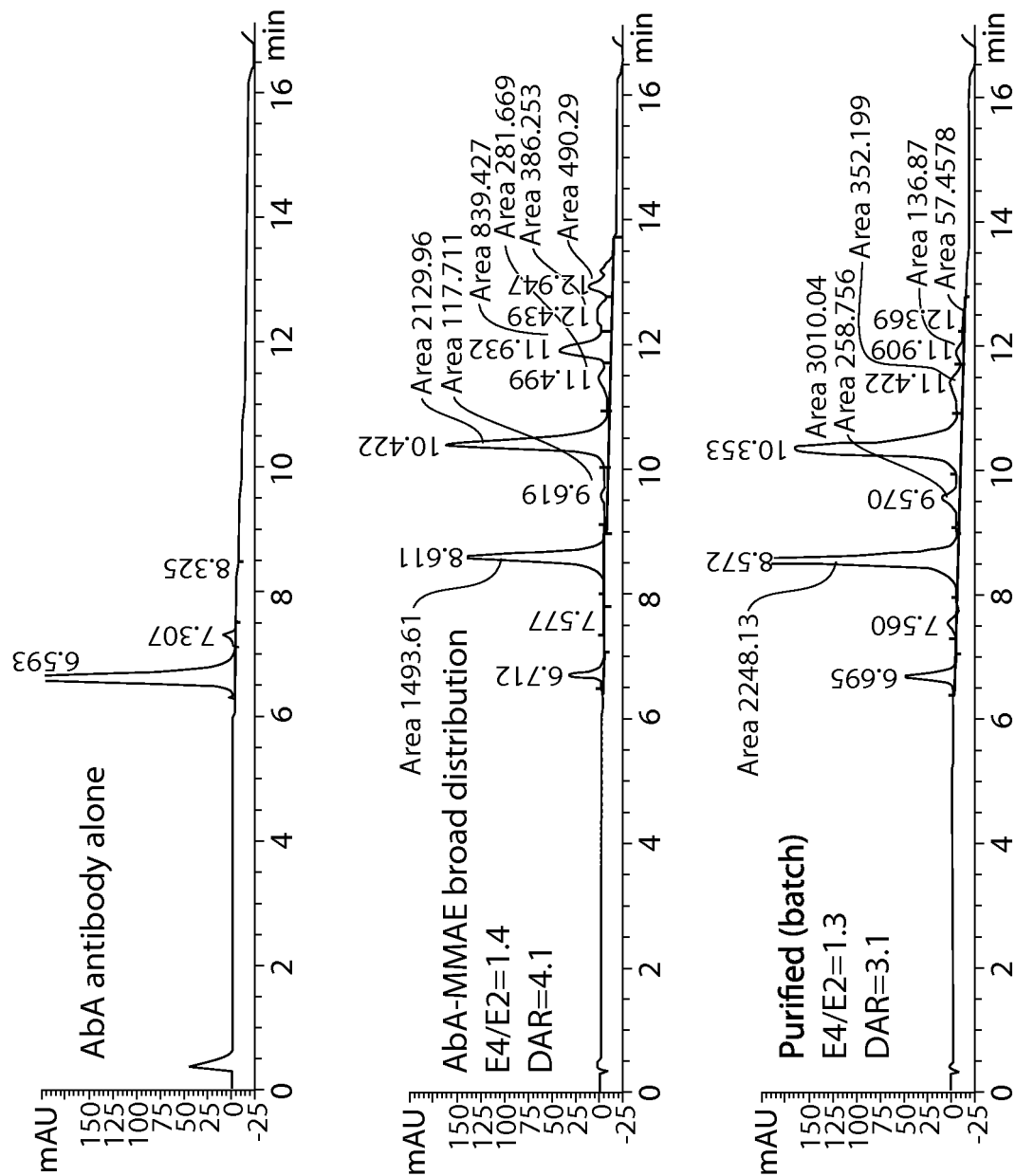


Figure 12-1

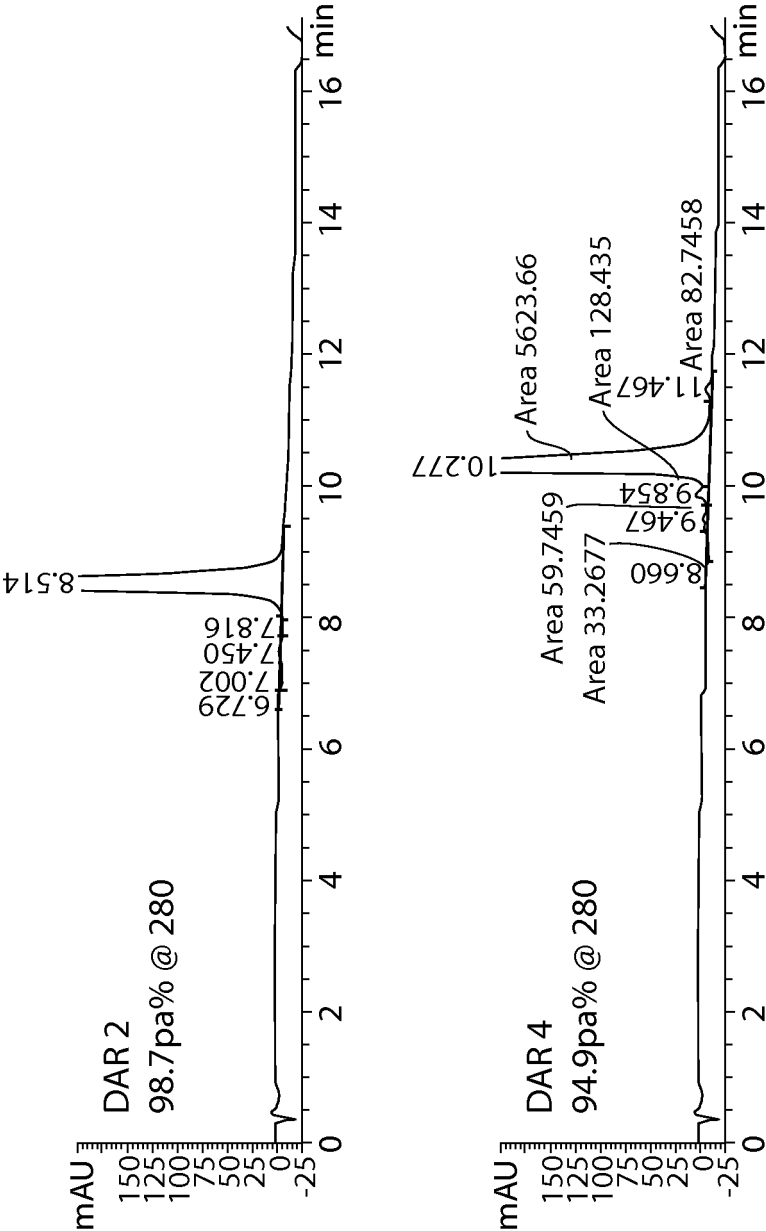


Figure 12-2

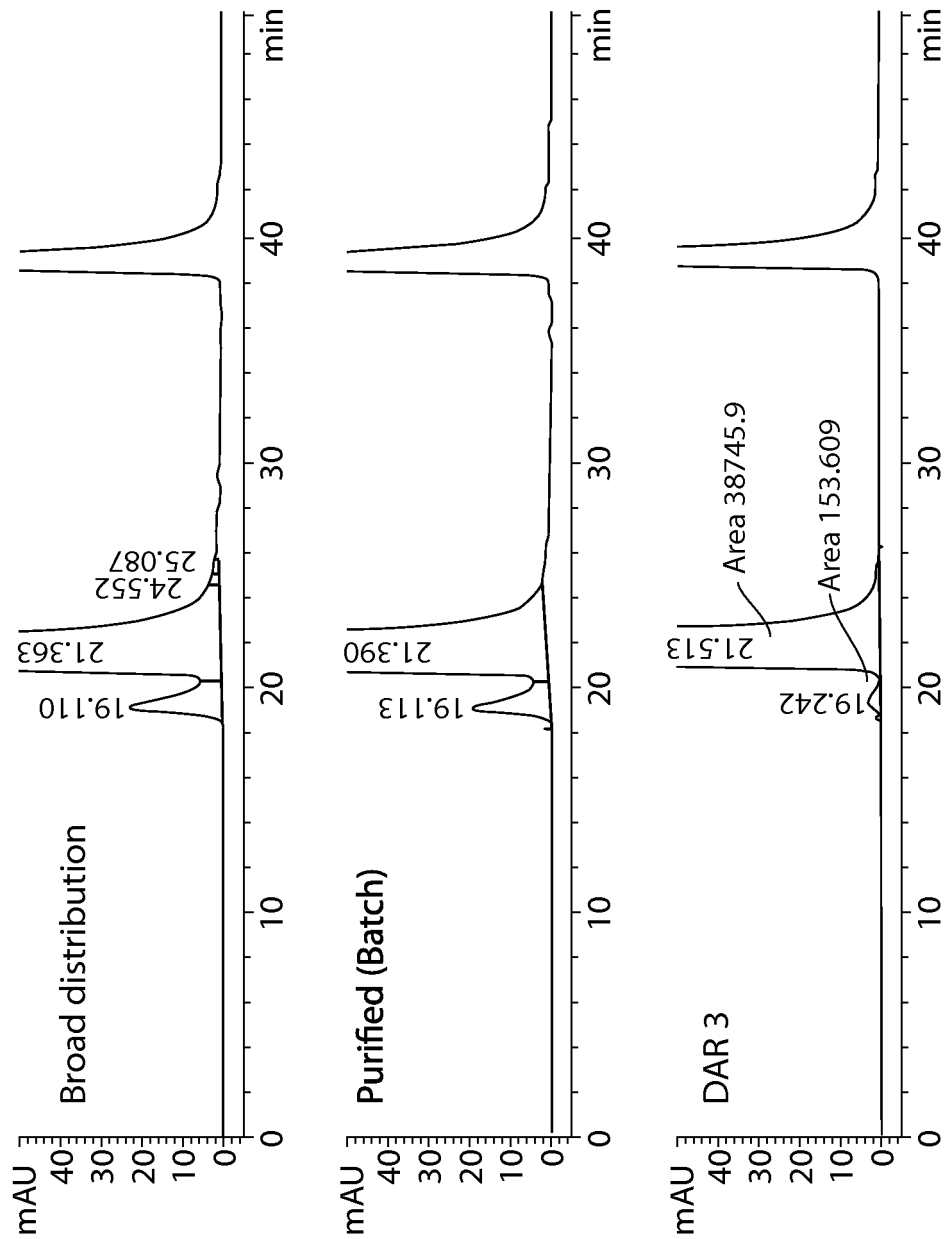


Figure 13-1

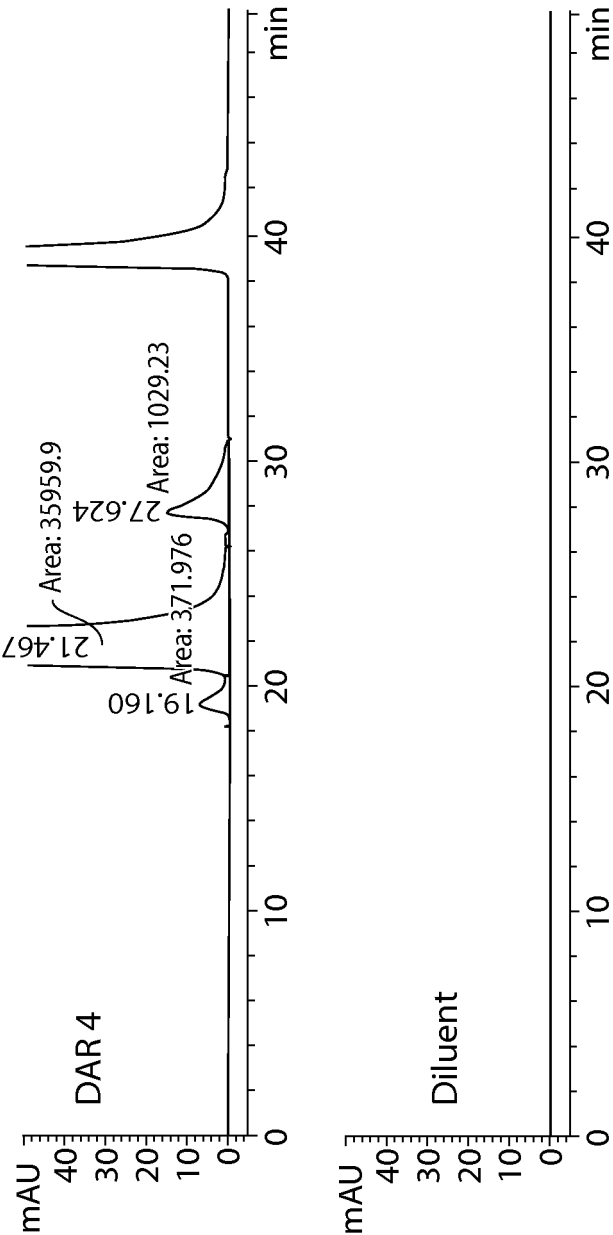


Figure 13-2

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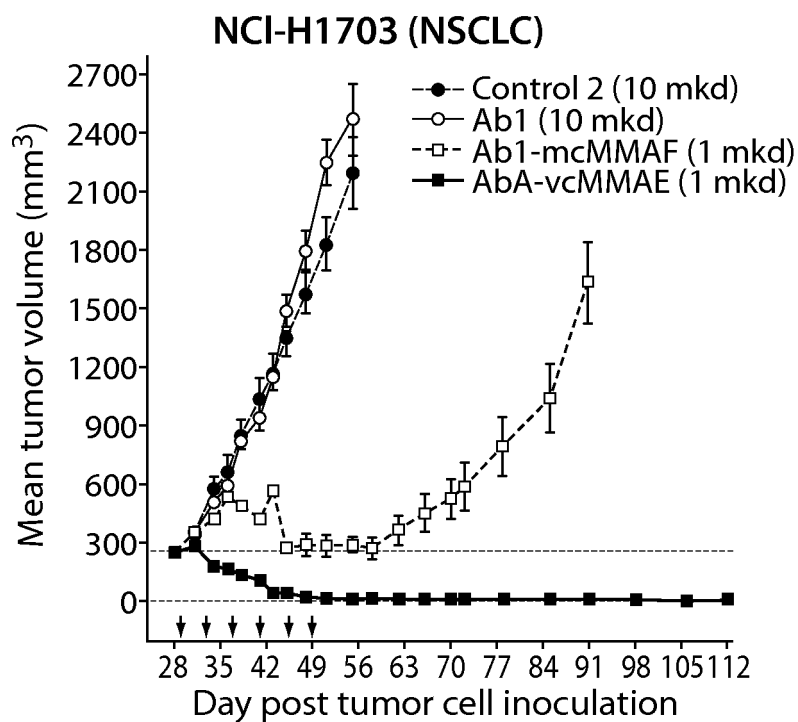


Figure 14A

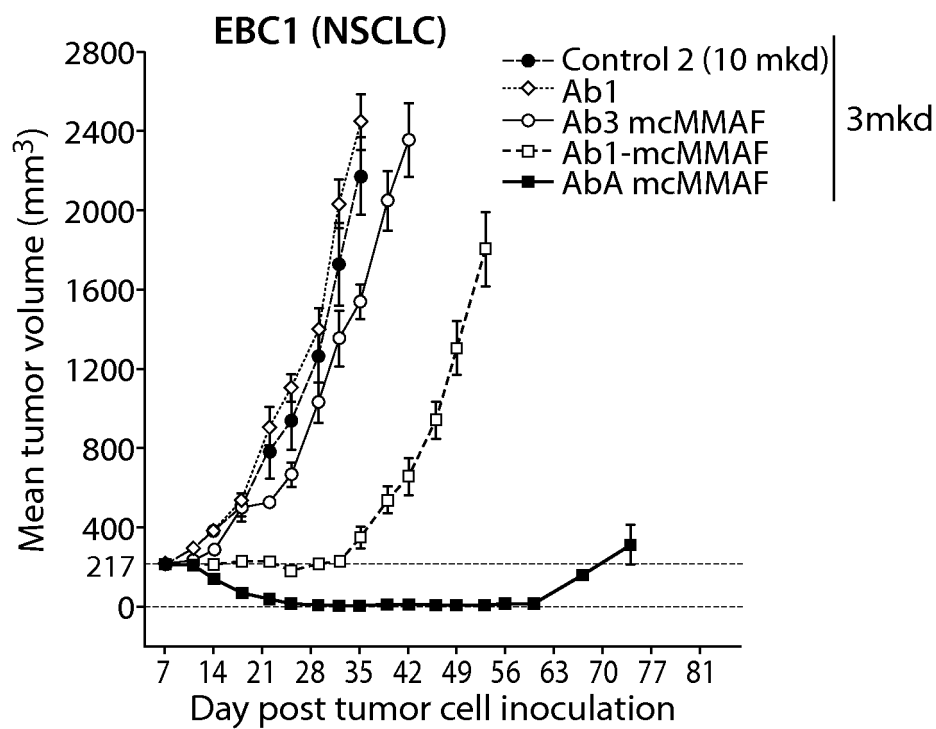


Figure 14B

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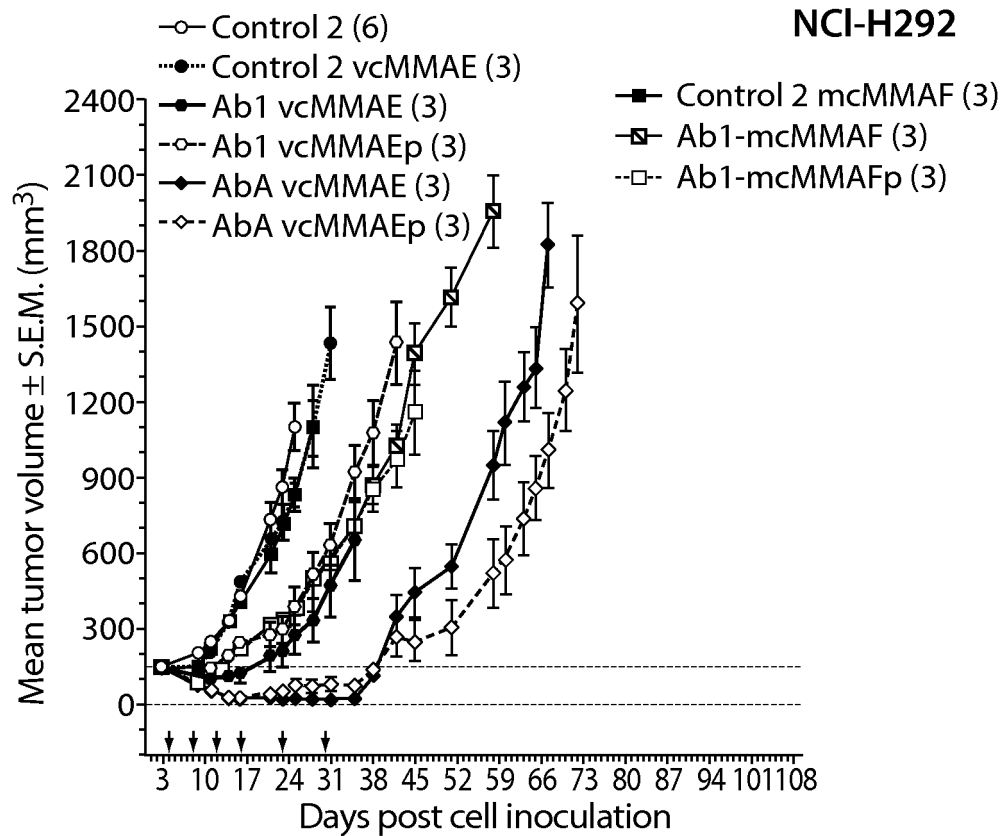


Figure 15A

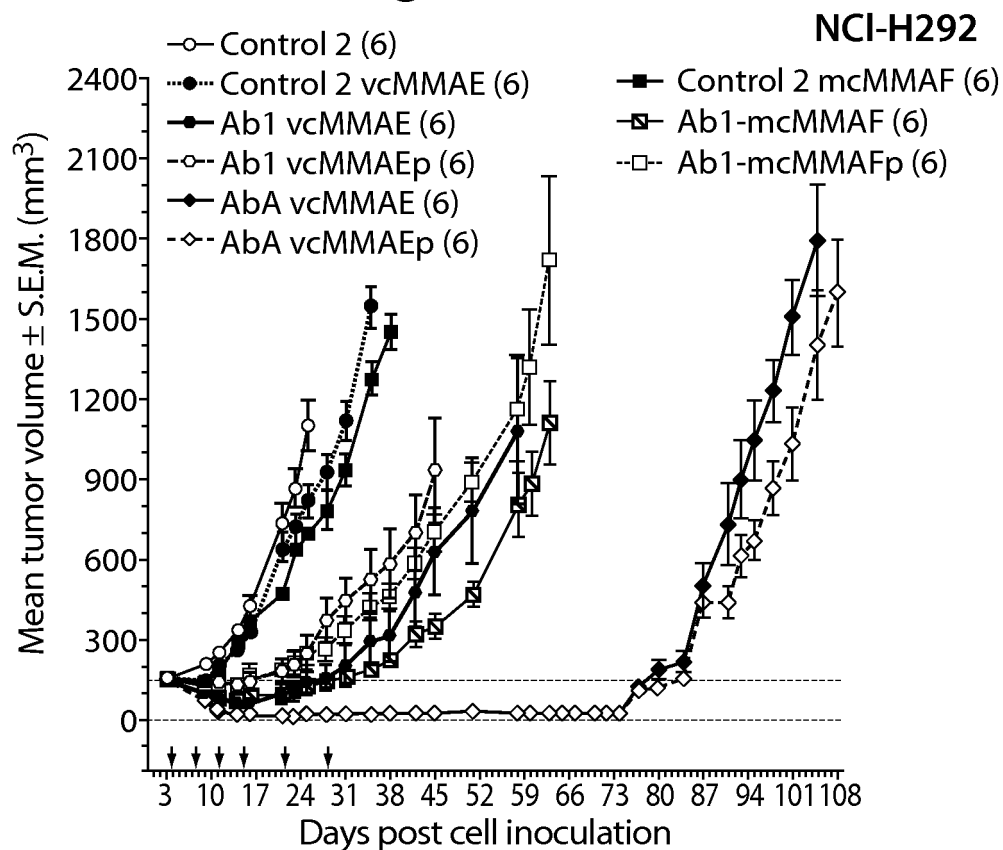


Figure 15B

A. Ab1 variant (Ab1v) VH library design

	1	2	3	4	5	6	7	8	9	1	1
	1234567890123456789012345678901234567890123456789012345678901234567890123										
VH4-4	QVQLQESGPGLVKPSGTL	SLTCAVSGGSISSSNWWSWVRQPPGKGL	EWTEIYHSGSTNYP	PSLKS	RITIS	VDKSKNQFFL	KLSSV	TAADTAV	YCAR		
Ab1vVH	QVQLQESGPGLVKPSQ	TLSTCTVSGYSISSDFAWNI	WIRQPPGKGL	EWMGVTSYSGNTRYQ	PSLKS	RITIS	RDTSKNQFFL	KLNSV	TAADTATYYCVT	ACRG	FPYWGQGTLVTVSS
Lib.	E	XXX	XXX	XXX	XXX	XXX	XXXXXX	XXXXXX	XXXXXX	XXXXXX	XXXXXX
		CDR1				CDR2				CDR3	

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B. Ab1 variant (Ab1v) VL library design

	1	2	3	4	5	6	7	8	9	1	0
	1234567890123456789012345678901234567890123456789012345678901234567890123456a										
IGKV1-12	DIQMTQSPSSMSASVGDRVTIT	CRASQGIS	SLAWYQQKPKAPKLLIYAAS	SLQSGVPSRFS	SGSGTDF	TLTIS	SLQPED	FATYYC	QQANSFP		
Ab1vVL	DIQMTQSPSSMSVSGDRVTIT	CHSSQDINS	NIQWLQQKPGKSF	KGILYHG	TNLD	DDGVPSRFS	SGSGTDTLT	TISS	LQPEDFATYYC	VQYAQFP	PWT
Lib.		X XXX1	X XXX1	X 2X XX	X 2X XX	XXX	XXX	XXX	XXX	XXX	XXX
		CDR1				CDR2				CDR3	

Figure 16

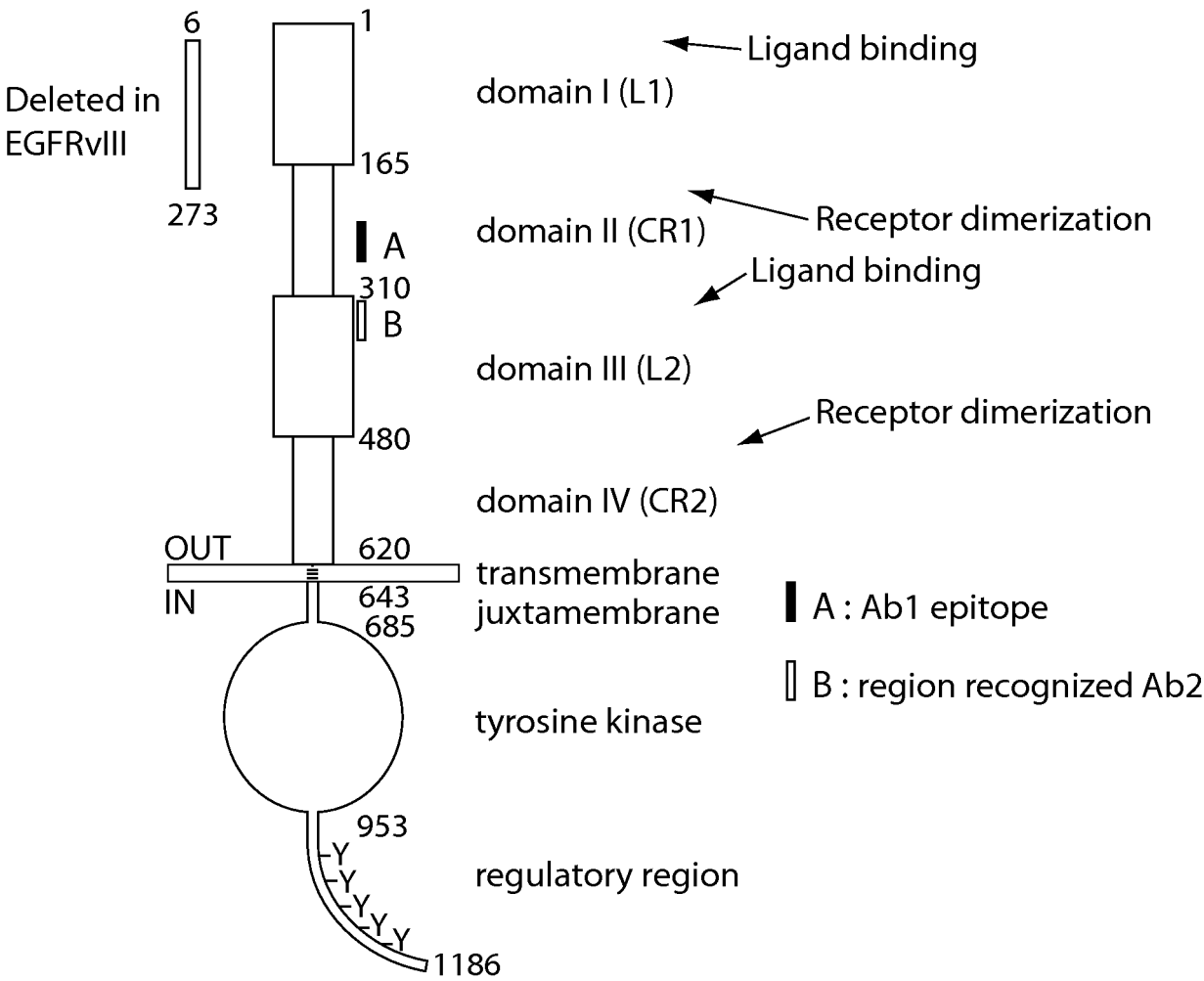
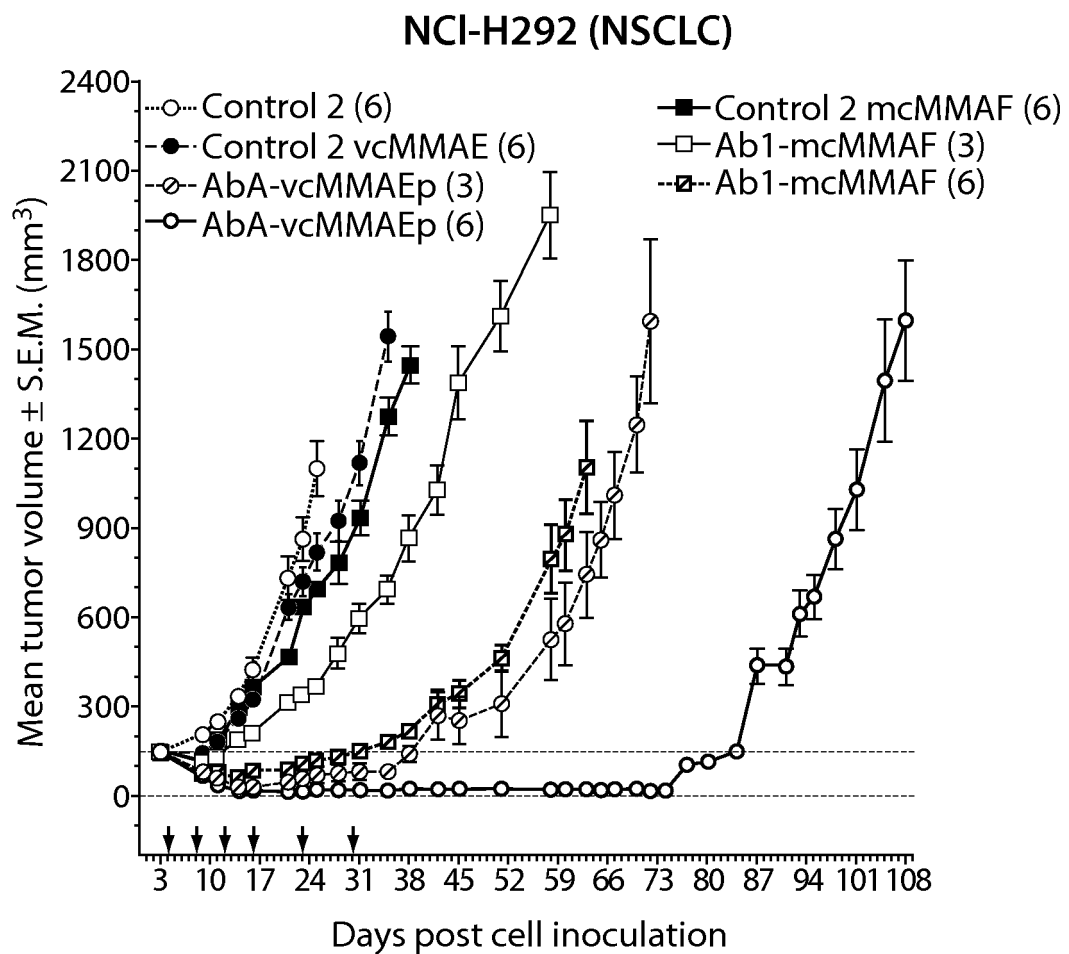
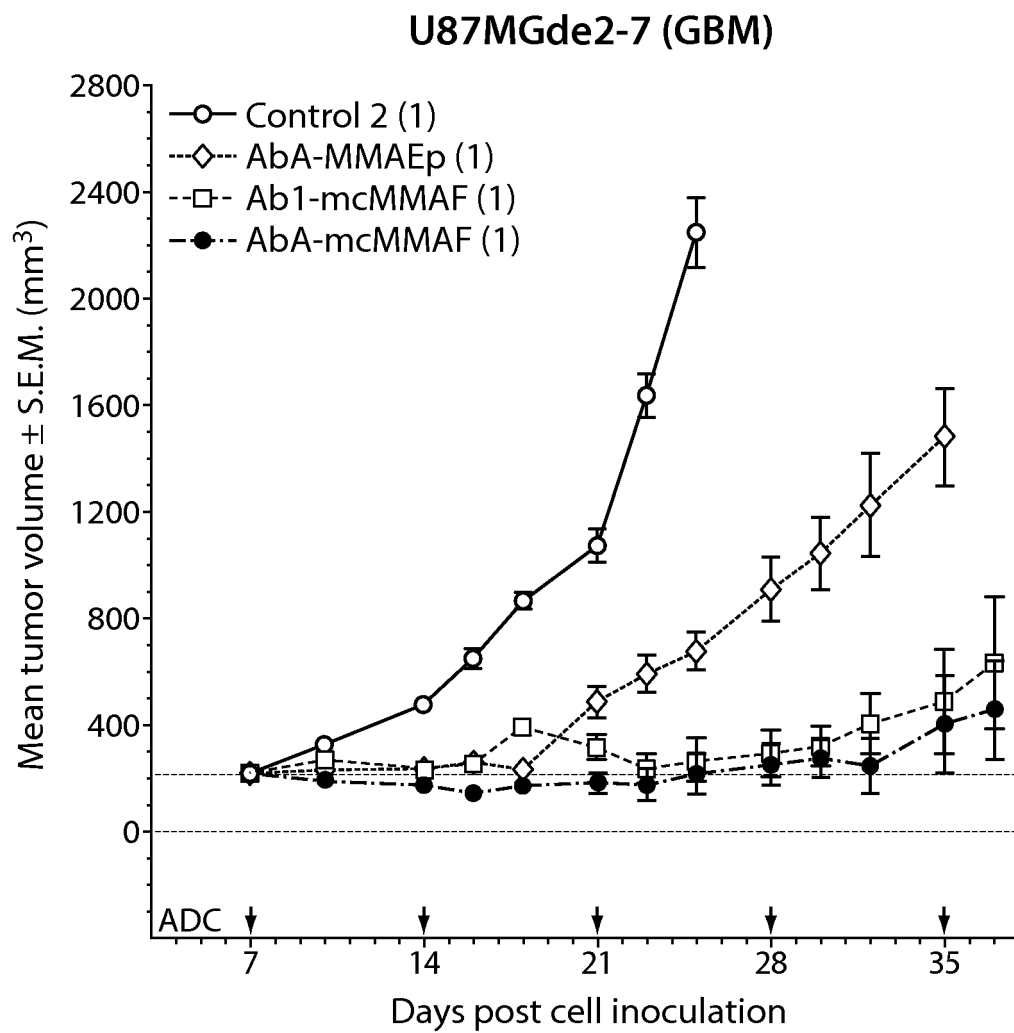


Figure 17

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**Figure 18**

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**Figure 19**

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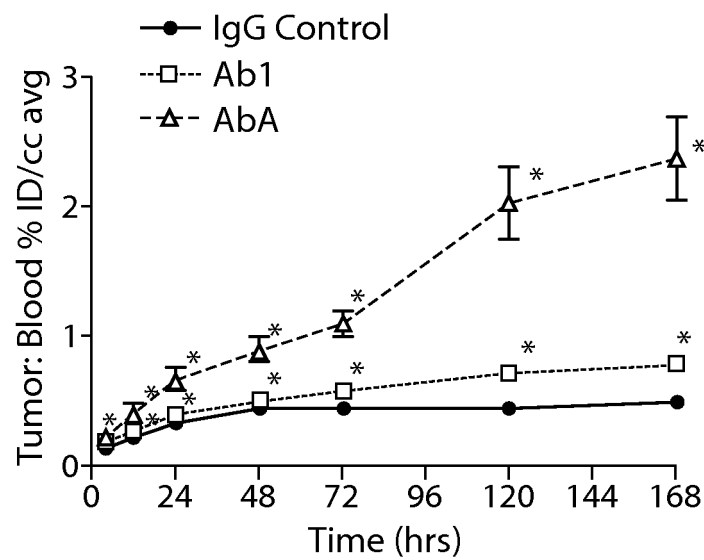


Figure 20A

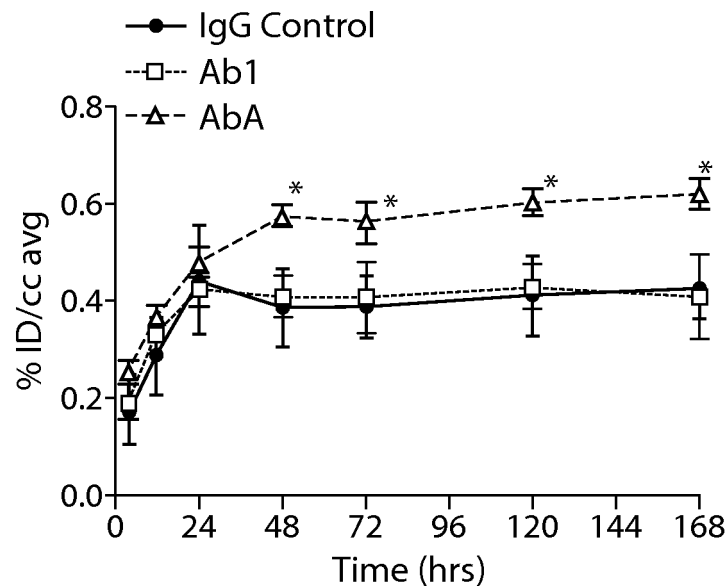


Figure 20B

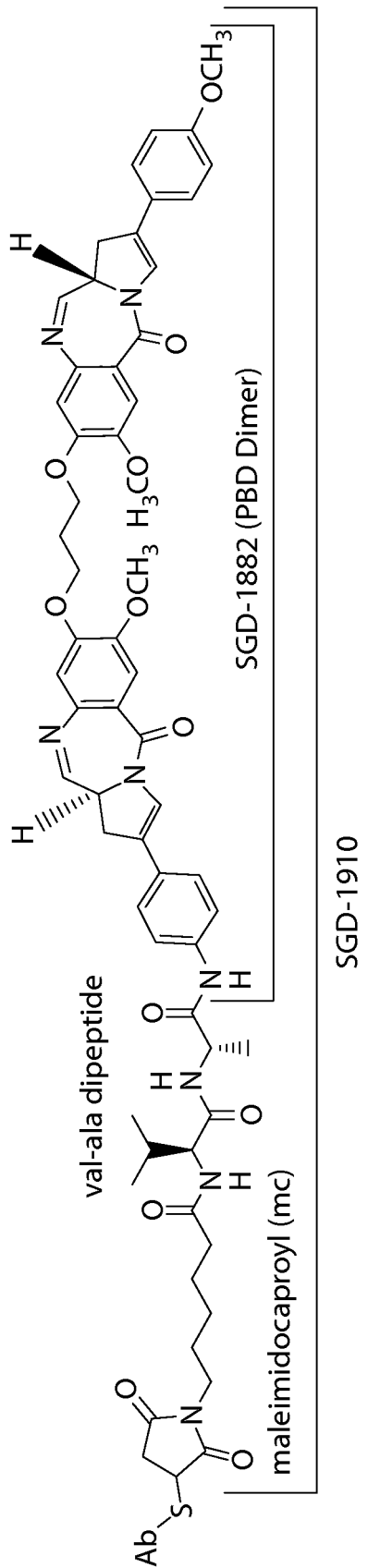


Figure 21