

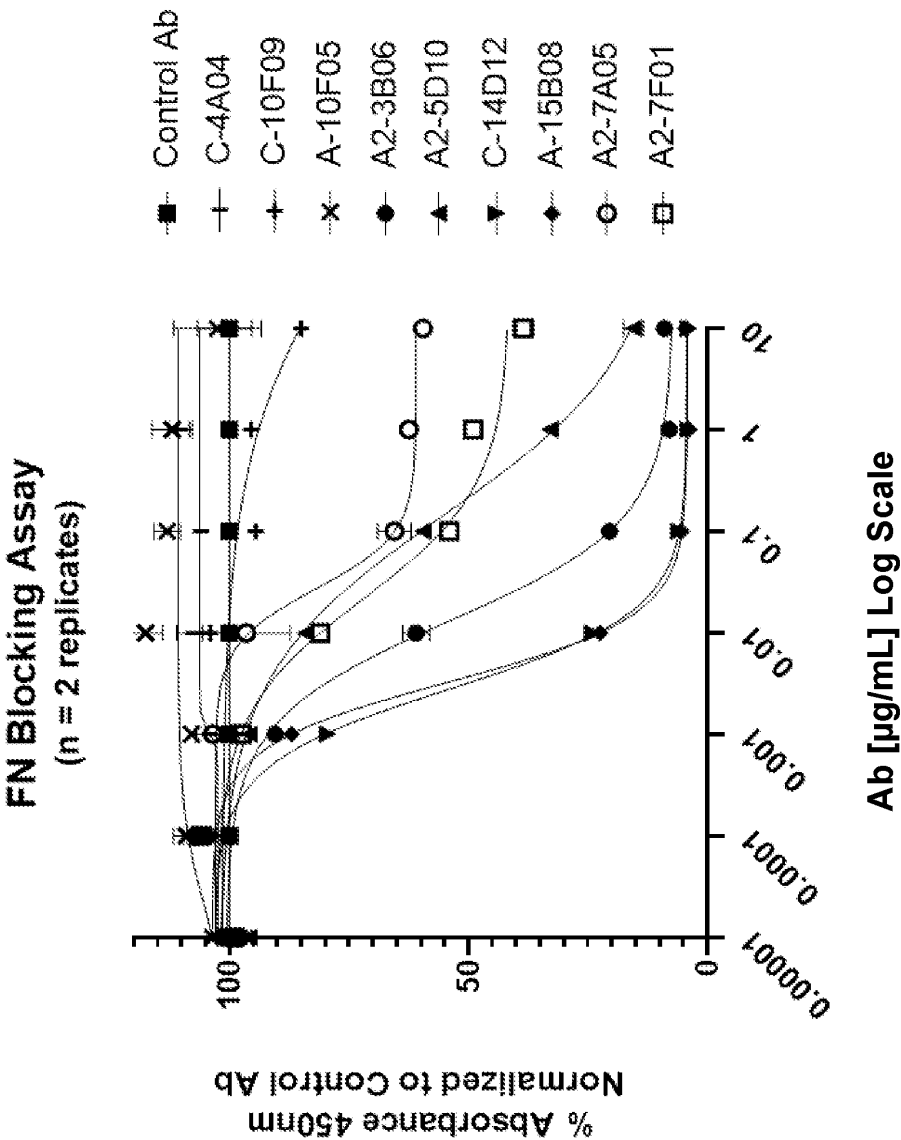


FIG. 1

FIG. 2A

VH Domain									
Kabat	1	10	22	31--35	40	50--a-----60----	65		
AbM	1	10	22	26-----ab-----35	40	50--a-----58	65		
Chothia	1	10	22	26-----ab32	40	a-55	65		
Contact	1	10	22	30ab-----35	40	47-----a-----58	65		
IMGT	1	23	27-----38	41		56-----65	74		
A-15B08	QVQLKESGPGLVAPSQSLSTCTIS	GFSLT--SYGVH	WVRQPPGKGLEWL	VIW-SDGSTTYNSTLKS					
A2-3B06	QVQLKESGPGLVAPSQSLSTCTIS	GFSLT--TYGVH	WVRQPPGKGLEWL	VIW-SDGSTTYNSALKS					
A2-5D10	QVQLKESGPGLVAPSQSLSTCTIS	GFSLT--SYGVH	WVRQPPGKGLEWL	VIW-SDGSTTYNSTLKS					
C-14D12	QVQLKESGPDVLAPSQSLSTCTVS	GFSLT--DYG	WVRQPPGKGLEWL	VIW-SDGSTTYNSALKS					
consensus	GFSLT--xYGVH			(SEQ ID NO:120)		(SEQ ID NO:121)			
A2-7A05	QVQLQQPGAELVKPGASVKLSCKAS	GYTFT--IYWIN	WVKQRPQGGLWIG	KIYPGSISTDYNEKFKS					
A2-7F01	QVQLQQPGAELVKPGASVKLSCKAS	GYTFT--IYWIN	WVKQRPQGGLWIG	NIYPGSSSTNYNEKFKT					
consensus	GYTFT--IYWIN			xIYPGSxSTxYNEKFKx					
				(SEQ ID NO:127)		(SEQ ID NO:128)			

Kabat	70	80	abc	90	95	110
AbM	70	80	abc	90	95	110
Chothia	70	80	abc	90	96	110
Contact	70	80	abc	90	93	110
IMGT	75	89		105	117	
A-15B08	RLSISKD	NSKQVFFK	MNSLQTDD	TAMYYCAR	HYDYDGDWF	(SEQ ID NO:25)
A2-3B06	RLNITKD	NSKQVFLK	MNSLQTDD	TAMYYCVR	HGGLLRDAM	(SEQ ID NO:42)
A2-5D10	RLSISKD	NSKQVFLK	MNSLQTDD	TAMYYCAR	HYDYDGDWF	(SEQ ID NO:51)
C-14D12	RLSITKDT	SKRQVFLK	MNSLQTDD	TAMYYCAR	HAPSFIRYGSRYDALDY	(SEQ ID NO:109)
consensus	HxxxxxxxxxxRYDALxY (SEQ ID NO:123)					
A2-7A05	KATLTVD	TSSSTAYMQ	LSSLTSD	DSAVYYCAI	TGTGGL	(SEQ ID NO:77)
A2-7F01	KATLTVD	TSSSTAYMQ	LSSLTSD	DSAVYYCAI	TGTGGF	(SEQ ID NO:91)
consensus	TGTGGx (SEQ ID NO:129)					

FIG. 2A (cont.)

VL Domain						
Kabat	1	10	20	24-27-----34	40	50-----56
AbM	1	10	20	24-----30a--34	40	50-----56
Chothia	1	10	20	26-----32	40	50--
Contact	1	10	20	30a-----36	40	46-----55
IMGT	1		23	27-----38	41	56-65 69
A-15B08	QIVLTQSPAIMASLGERVTMTC TASSRVSSNSLH WYQQKPGSSPKLWIY STSNLAS					
A2-3B06	QIVLTQSPAIMASLGERVTMTC TASSSVSSNSFH WYQQKPGSSPKLWLY STSNLAS					
A2-5D10	QILLTQSPAIMASLGERVTMTC TASSSVSSRCLH WYQQKPGSSPKLWIY STSNLAS					
C-14D12	QIVLTQSPAIMASLGERVTLLTC TASSSVTSSFLH WYQQKPGSSPKLWIY STSNLAS					
consensus	TASSxVxSxxH (SEQ ID NO:124) (SEQ ID NO:125)					
A2-7A05	ENVLTQSPAIMASLGEKVTMTC RASSVN--YMY WYQQKSDASPKLWIY FTSSLAP					
A2-7F01	ENVLTQSPAIMASLGEKVTMSC RASSVN--YMY WYQQKSDASPKLWIY FTSSLAP					
consensus	RASSVN--YMY (SEQ ID NO:130) (SEQ ID NO:131)					

FIG. 2B

Kabat	60	70	80	89-----97
AbM	60	70	80	89-----97
Chothia	60	70	80	91----96
Contact	60	70	80	89-----96
IMGT	70	89		105-----117
A-15B08	GVPARFSGSGGTSYSLTISSMEAEADAATYYC			HQYLRSPPT FGGGTKLEIK (SEQ ID NO:26)
A2-3B06	GVPARFSGSGGTSYSLTISSMEAEADAATYYC			HQYLRSPPT FGGGTKLEIK (SEQ ID NO:43)
A2-5D10	GVPARFRGSGGTSYSLTISSMEAEADAATYYC			HQYRSPPT FGGGTKLEIK (SEQ ID NO:52)
C-14D12	GVPARFSGSGGTSYSLTISSMEAEADAATYYC			HQYHRSPPT FGGGTKLEIK (SEQ ID NO:110)
consensus	HQYxRSPPT			(SEQ ID NO:126)
A2-7A05	GVPGRFSGSGGNSYSLTISTMEGEDAATYYC			QQFTTSPPT FGSGTKLEIK (SEQ ID NO:78)
A2-7F01	GVPTRFSGSGGNSFSLTISSMEGEDAATYYC			QQLTGSPPT FGSGTRLEIK (SEQ ID NO:92)
consensus	QQxTxSPPT			(SEQ ID NO:132)

FIG. 2B (cont.)

VH Domain									
Kabat	1	10	22	31--35	40	50-----60----	65		
AbM	1	10	22	26-----35	40	50-----58	65		
Chothia	1	10	22	26-----32	40	-55	65		
Contact	1	10	22	30--35	40	47-----58	65		
IMGT	1		23	27-----38	41	56-----65	74		
A-15B08-T62A	QVQLKESGPGLVAPSQSLISITCTIS GFSLTSYGVH WVRQPPGKGLEWLVIWSDGSTTYSALKS								
A-15B08_HC_Low	QVTLKESGPTLVKPTQTLLITCTIS GFSLTSYGVH WVRQPPGKGLEWLVIWSDGSTTYSALKS								
A-15B08_HC_Low+Mod	QVTLKESGPTLVKPTQTLLITCTIS GFSLTSYGVH WVRQPPGKALEWLVIWSDGSTTYSALKS								
Kabat	70	80	abc	90	95-----102	110			
AbM	70	80	abc	90	95-----102	110			
Chothia	70	80	abc	90	96-----101	110			
Contact	70	80	abc	90	93-----101	110			
IMGT	75	89		105-----117					
A-15B08-T62A	RLSISKDNSKSQVFFKMNSLQTDVTATAMYYCAR HYDYGDFWFGWQGTTLVTVSA (SEQ ID NO:135)								
A-15B08_HC_Low	RLTISKDNSKSQVFFMTNLDVTATAMYYCAR HYDYGDFWFGWQGTTLVTVSS (SEQ ID NO:136)								
A-15B08_HC_Low+Mod	RLTISKDTSKNQVFFMTNLDVTATAMYYCAR HYDYGDFWFGWQGTTLVTVSS (SEQ ID NO:138)								

FIG. 2C

VL Domain									
Kabat	1	10	20	24-27-----34	40	50-----56			
AbM	1	10	20	24-----30a--34	40	50-----56			
Chothia	1	10	20	26-----32	40	50--			
Contact	1	10	20	30a-----36	40	46-----55			
IMGT	1		23	27-----38	41	56-65	69		
A-15B08-T62A*	QIVLTQSPAIMSASLGERVTMTC TASSRVSSNSLH WYQQKPGSSPKLWIY STSNLAS								
A-15B08_LC_Low	EIVLTQSPGIMSASLGERVTMSC RASSRVSSNSLH WYQQKPGQSPKLWIY STSNRAS								
A-15B08_LC_Low+Mod	EIVLTQSPGILSASLGERVTMSC RASSRVSSNSLH WYQQKPGQAPRLWIY STSNRAT								
Kabat	60	70	80	89-----97					
AbM	60	70	80	89-----97					
Chothia	60	70	80	91---96					
Contact	60	70	80	89-----96					
IMGT	70		89	105-----117					
A-15B08-T62A*	GVPARFSGSGGTSYSLTISMEAEADAATYYC HQYLRSPPT FGGGTKLEIK (SEQ ID NO:26)								
A-15B08_LC_Low	GVPDFRFGSGGTDYTLTISRMEAEADFATYYC HQYLRSPPT FGGGTKLEIK (SEQ ID NO:137)								
A-15B08_LC_Low+Mod	GVPDFRFGSGGTDYTLTISRMEAEADFATYYC HQYLRSPPT FGGGTKLEIK (SEQ ID NO:139)								
*VL domain sequence is the same between A-15B08 and A-15B08-T62A									

FIG. 2D

VH Domain									
Kabat	1	10	22	31--35	40	50--a-----60----	65		
AbM	1	10	22	26-----35	40	50--a-----58	65		
Chothia	1	10	22	26-----32	40	a-55	65		
Contact	1	10	22	30-----35	40	47-----a-----58	65		
IMGT	1		23	27-----38	41	56-----65	74		
A2-7A05_HC	QVQLQQPGAELVKPGASVKLSCKAS GYTFTIYWIN WVKQRPQGLEWIG KIYPGISTDYNEKFKS								
A2-7A05_HC_Low	QVQLVQPGAEVVKPGASVKLSCKAS GYTFTIYWIN WVKQAPQGLEWIG KIYPGISTDYNEKFKG								
A2-7A05_HC_Low+Mod	QVQLVQPGAEVVKPGASVKLSCKAS GYTFTIYWIN WVRQAPQGLEWIG KIYPGISTDYNQKFQG								
Kabat	70	80	abc	90	95-----102	110			
AbM	70	80	abc	90	95-----102	110			
Chothia	70	80	abc	90	96--101	110			
Contact	70	80	abc	90	93-----101	110			
IMGT	75	89		105-----117					
A2-7A05_HC	KATLTVDTSSTAYMQLSLTSDDSAVYYCAI TGTGGLAY WGQGTLLVTVSA (SEQ ID NO:77)								
A2-7A05_HC_Low	KATLTVDTSSTAYMELSSLRSEDTAVYYCAI TGTGGLAY WGQGTLLVTVSS (SEQ ID NO:140)								
A2-7A05_HC_Low+Mod	RATLTVDTSSTAYMELSSLRSEDTAVYYCAI TGTGGLAY WGQGTLLVTVSS (SEQ ID NO:142)								

FIG. 2E

VL Domain									
Kabat	1	10	20	24-27-----34	40	50-----56			
AbM	1	10	20	24-----30-34	40	50-----56			
Chothia	1	10	20	26-----32	40	50--			
Contact	1	10	20	30-----36	40	46-----55			
IMGt	1		23	27--38	41	56-65	69		
A2-7A05_LC	ENVLTQSPAIMSASLGEKVTMTC RASSVNMY WYQKSDASPKLWIY FTSSLAP								
A2-7A05_LC_Low	ENVLTQSPGIMSASLGERVTMSC RASSVNMY WYQKSGQSPKLWIY FTSSRAP								
A2-7A05_LC_Low+Mod	ENVLTQSPGILSASLGERVTMSC RASSVNMY WYQKSGQAPRLWIY FTSSRAP								
Kabat	60	70	80	89-----97					
AbM	60	70	80	89-----97					
Chothia	60	70	80	91----96					
Contact	60	70	80	89-----96					
IMGt	70	89		105-----117					
A2-7A05_LC	GVPGRFSGSGSGNSYSLTISTMEGEDAATYIC QQFTTSPFT FGSGTKLEIK (SEQ ID NO:78)								
A2-7A05_LC_Low	GVPDRFSGSGSGTSYTLTISRMEGEDFATYIC QQFTTSPFT FGQGTKLEIK (SEQ ID NO:141)								
A2-7A05_LC_Low+Mod	GVPDRFSGSGSGTSYTLTISRMEGEDFATYIC QQFTTSPFT FGQGTKLEIK (SEQ ID NO:143)								

FIG. 2F

VH Domain									
Kabat	1	10	22	31--35	40	50-----60----	65		
AbM	1	10	22	26-----35	40	50-----58	65		
Chothia	1	10	22	26-----32	40	-55	65		
Contact	1	10	22	30-----35	40	47-----58	65		
IMGT	1		23	27-----38	41	56-----65	74		
C-14D12	QVQLKESGPDLVAPSQSLITCTVS GFSLTDYGVH WVRQPPGKGLEWLVIWSDGSTTYSALKS								
C-14D12_HC_Low	QVTLKESGPTLVKPTQTLLTITCTVS GFSLTDYGVH WVRQPPGKGLEWLVIWSDGSTTYSALKS								
C-14D12_HC_Low+Mod	QVTLKESGPTLVKPTQTLLTITCTVS GFSLTDYGVH WVRQPPGKALEWLVIWSDGSTTYSALKS								
Kabat	70	80	abc	90	95-----102	110			
AbM	70	80	abc	90	95-----102	110			
Chothia	70	80	abc	90	96-----101	110			
Contact	70	80	abc	90	93-----101	110			
IMGT	75	89		105-----117					10/21
C-14D12	RLSITKDTSKRQVFLKMNSLQTDDTAMYICAR HAPSFIRYGSRYDALDY WGQGTSTVTVSS (SEQ ID NO:109)								
C-14D12_HC_Low	RLTISKDTSKRQVVLWTNLDVTVDTAMYICAR HAPSFIRYGSRYDALDY WGQGTTLVTVSS (SEQ ID NO:144)								
C-14D12_HC_Low+Mod	RLTISKDTSKNQVVLWTNLDVTVDTATYYICAR HAPSFIRYGSRYDALDY WGQGTTLVTVSS (SEQ ID NO:146)								

FIG. 2G

VL Domain									
Kabat	1	10	20	24-27-----34	40	50-----56			
AbM	1	10	20	24-----30a--34	40	50-----56			
ChoThia	1	10	20	26-----32	40	50--			
Contact	1	10	20	30a-----36	40	46-----55			
IMGT	1		23	27-----38	41	56-65	69		
C-14D12	QIVLTQSPAIMSASLGERVT LTC TASSSVTSSFLH WYQKPGSSPKLWIY STSNLAS								
C-14D12_LC_Low	EIVLTQSPGTMSASLGERVT LSC RASSSVTSSFLH WYQKPGQSPK LWIY STSNRAS								
C-14D12_LC_Low+Mod	EIVLTQSPGTLSASLGERVT LSC RASSSVTSSFLH WYQKPGQAPRLWIY STSNRAT								
Kabat	60	70	80	89-----97					
AbM	60	70	80	89-----97					
ChoThia	60	70	80	91---96					
Contact	60	70	80	89-----96					
IMGT	70	89		105-----117					
C-14D12	GVPARFSGSGSGTSYSLTISSRMEAEADAATY C HQYHRSPPT FGGGTKLEIK (SEQ ID NO:110)								
C-14D12_LC_Low	GVPDRFSGSGSGTDYTLTISRMEAEADFATY C HQYHRSPPT FGQGTKLEIK (SEQ ID NO:145)								
C-14D12_LC_Low+Mod	GVPDRFSGSGSGTDYTLTISRMEAEADFATY C HQYHRSPPT FGQGTKLEIK (SEQ ID NO:147)								

FIG. 2H

	240	250	260	270	280
	*	*	*	*	*
IgG1	CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH				
IgG4	CPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH				
N297A/Q	CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH				
LALA	CPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH				
LALAPS	CPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH				
LALAPG	CPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH				
TM	CPPCPAPEFEGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH				
	290	300	310	320	330
	*	*	*	*	*
IgG1	NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE				
IgG4	NAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE				
N297A/Q	NAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE				
LALA	NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE				
LALAPS	NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE				
LALAPG	NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPRE				
TM	NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPRE				

FIG. 3

	350	360	370	380	390	400
IgG1	*	*	*	*	*	*
IgG4	PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF					
N297A/Q	PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF					
LALA	PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF					
LALAPS	PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF					
LALAPG	PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF					
TM	PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF					
	410	420	430	440	447	
IgG1	*	*	*	*	*	
IgG4	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:148)					
N297A/Q	LYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:149)					
LALA	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:150)					
LALAPS	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:151)					
LALAPG	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:152)					
TM	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:153)					
	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:154)					

FIG. 3 (cont.)

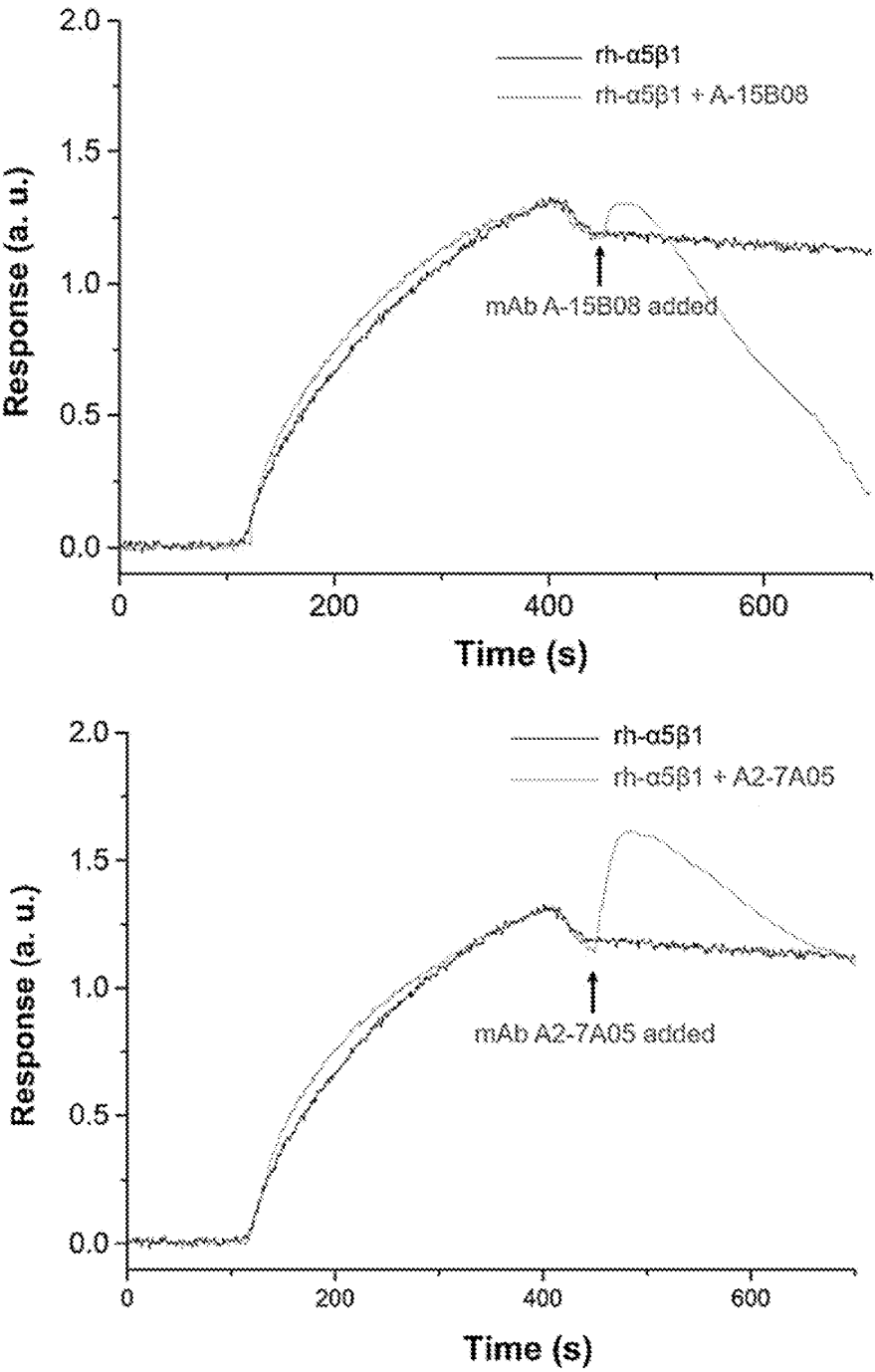
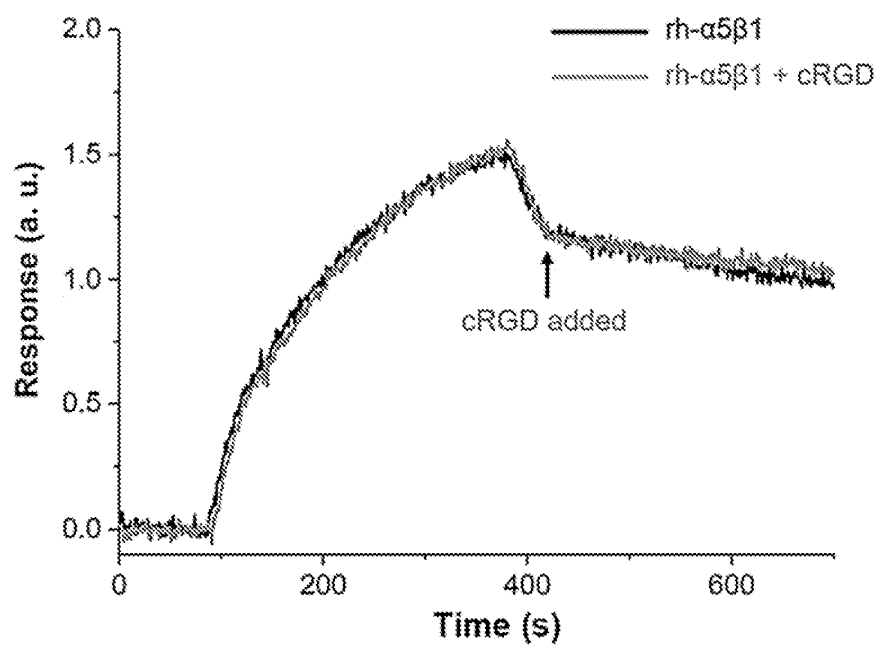
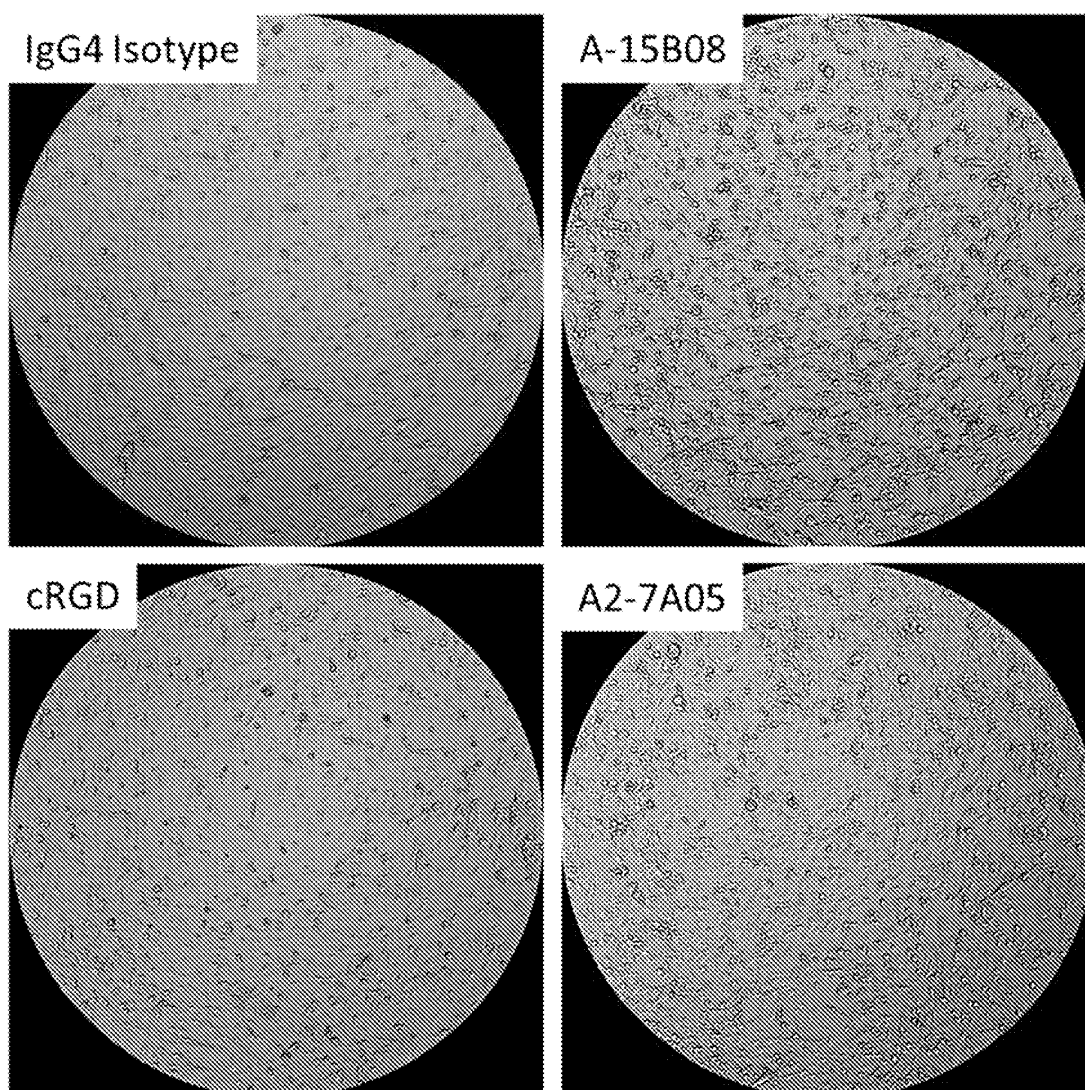


FIG. 4A

**FIG. 4A (cont.)**

**FIG. 4B**

$\alpha 5\beta 1$ Integrin FN Blocking Assay
4°C vs. 3x Freeze/Thaw -80°C
(n = 2 replicates)

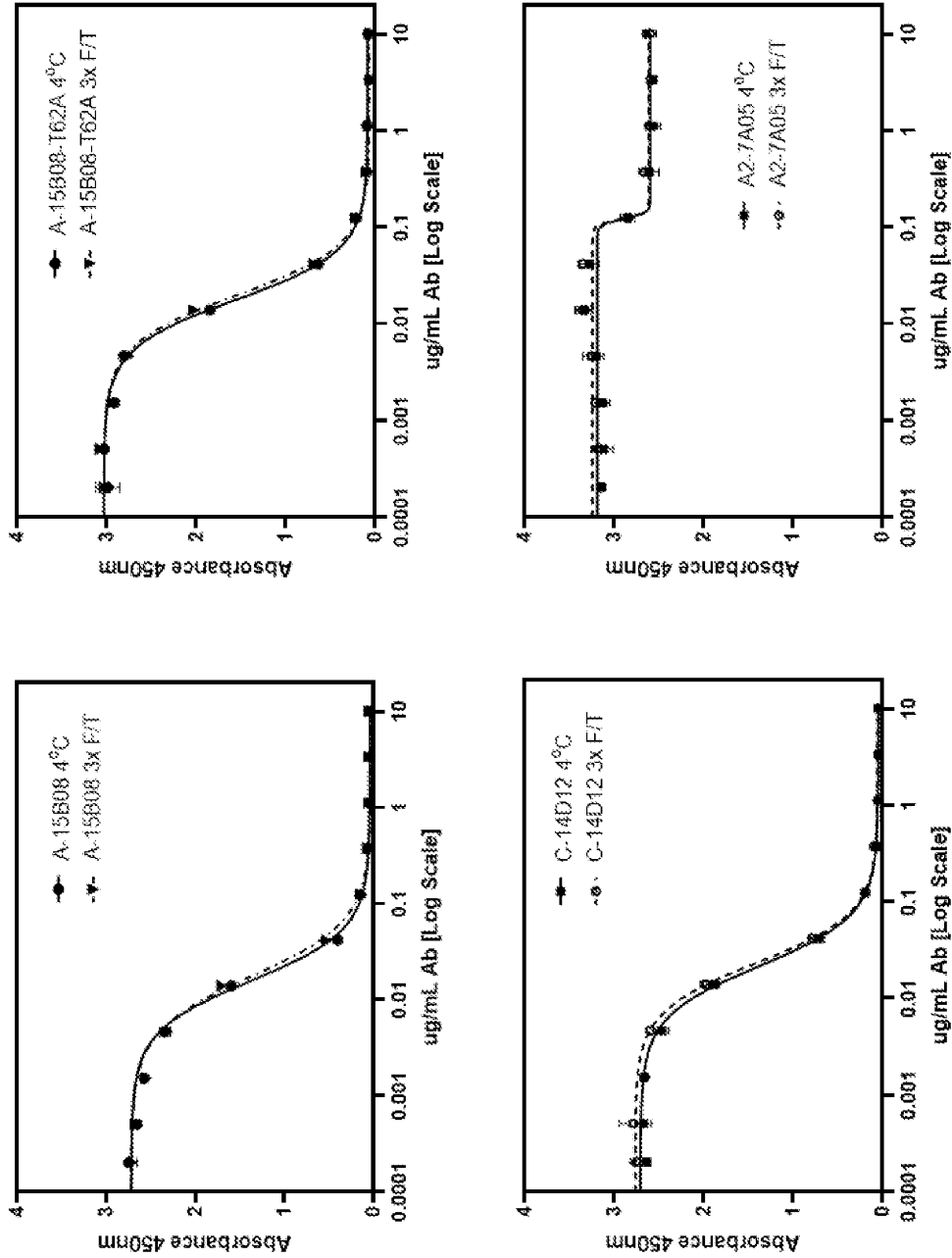


FIG. 5

Potency of Hybridomas vs. IgG4 Chimeras

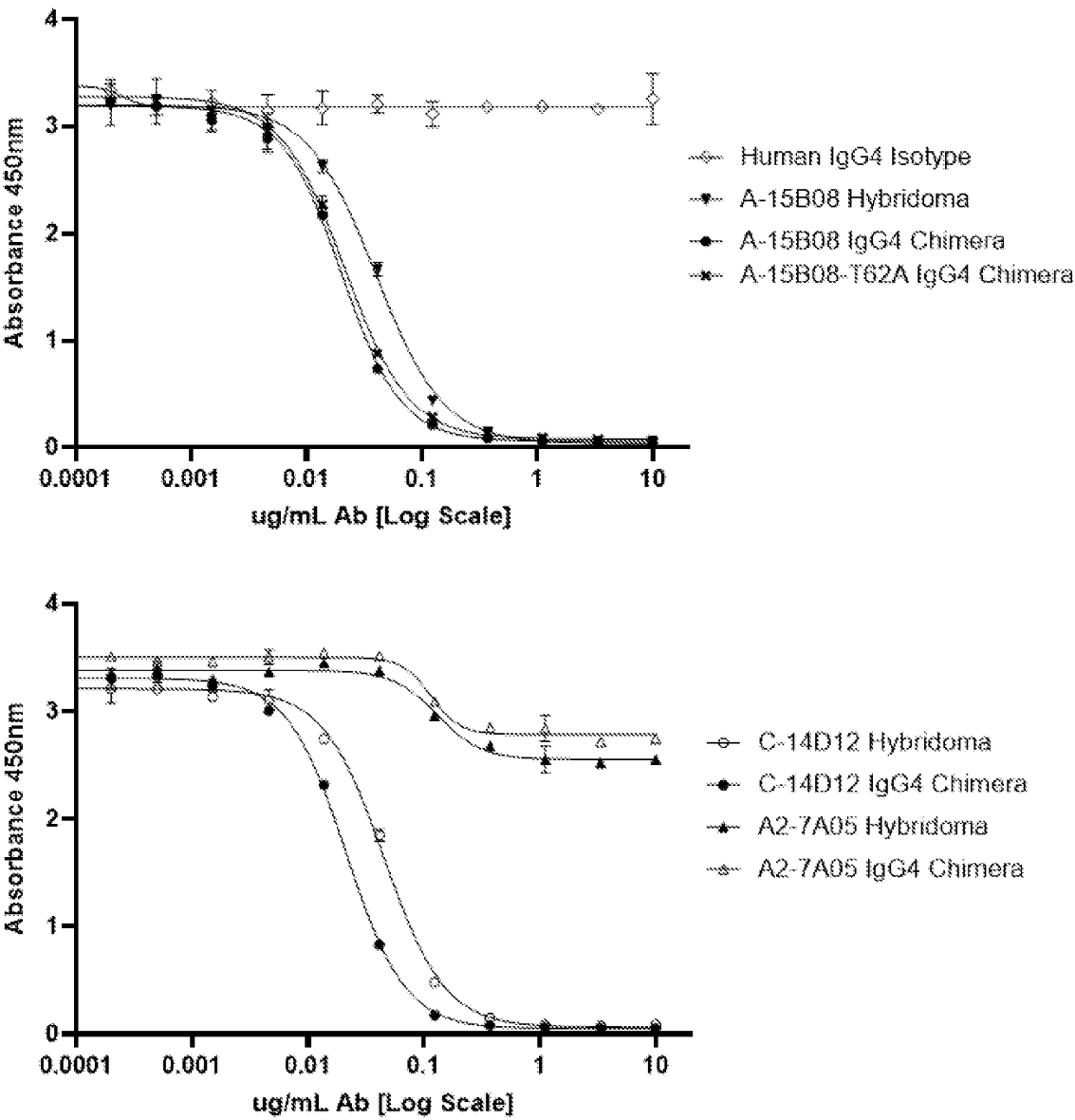


FIG. 6

SDS-PAGE of IgG4 Chimeric Antibodies

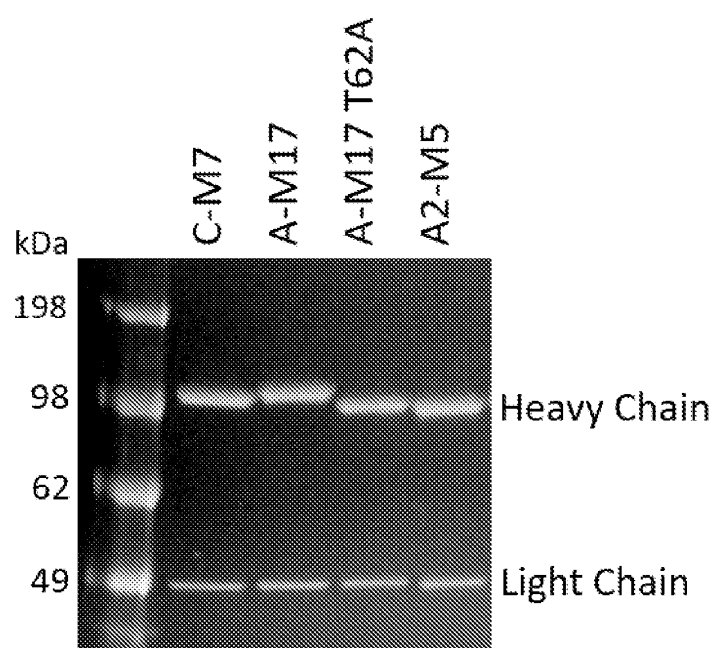


FIG. 7

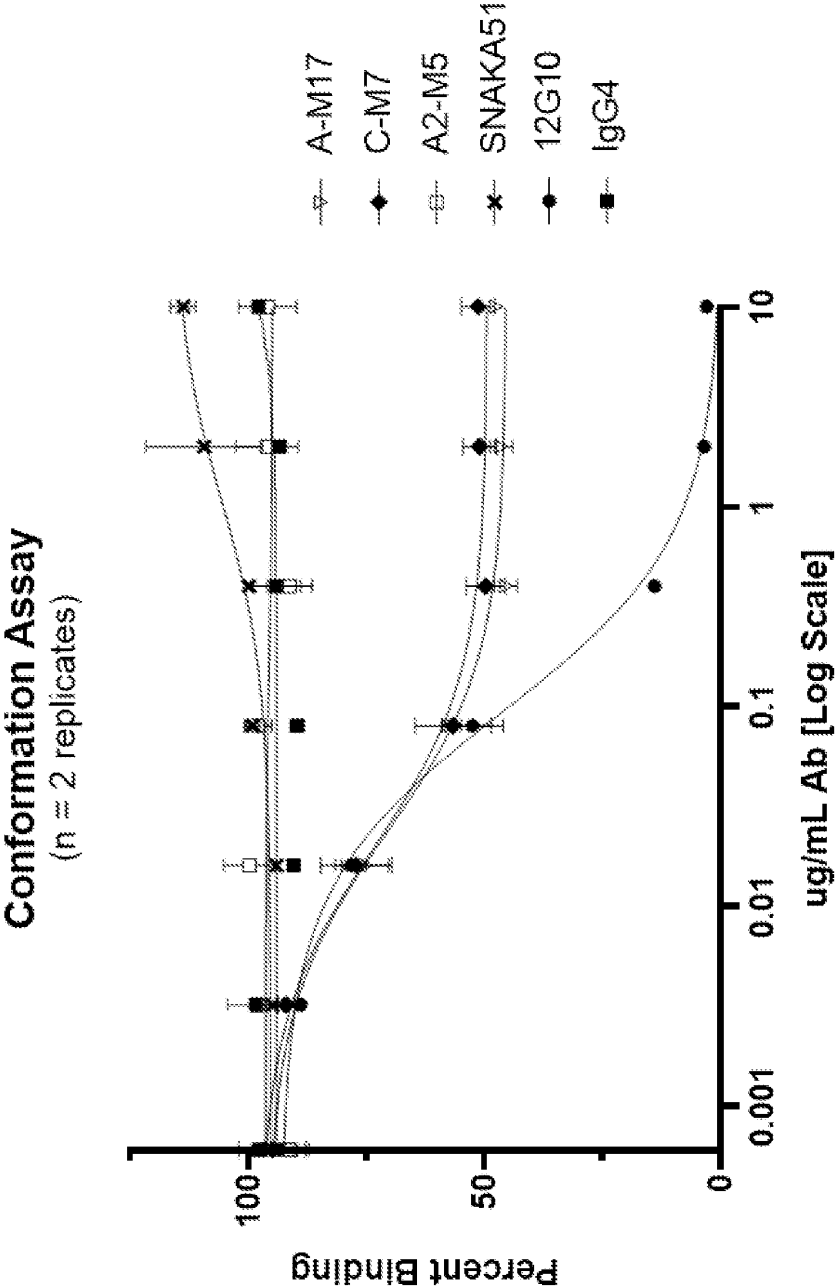


FIG. 8

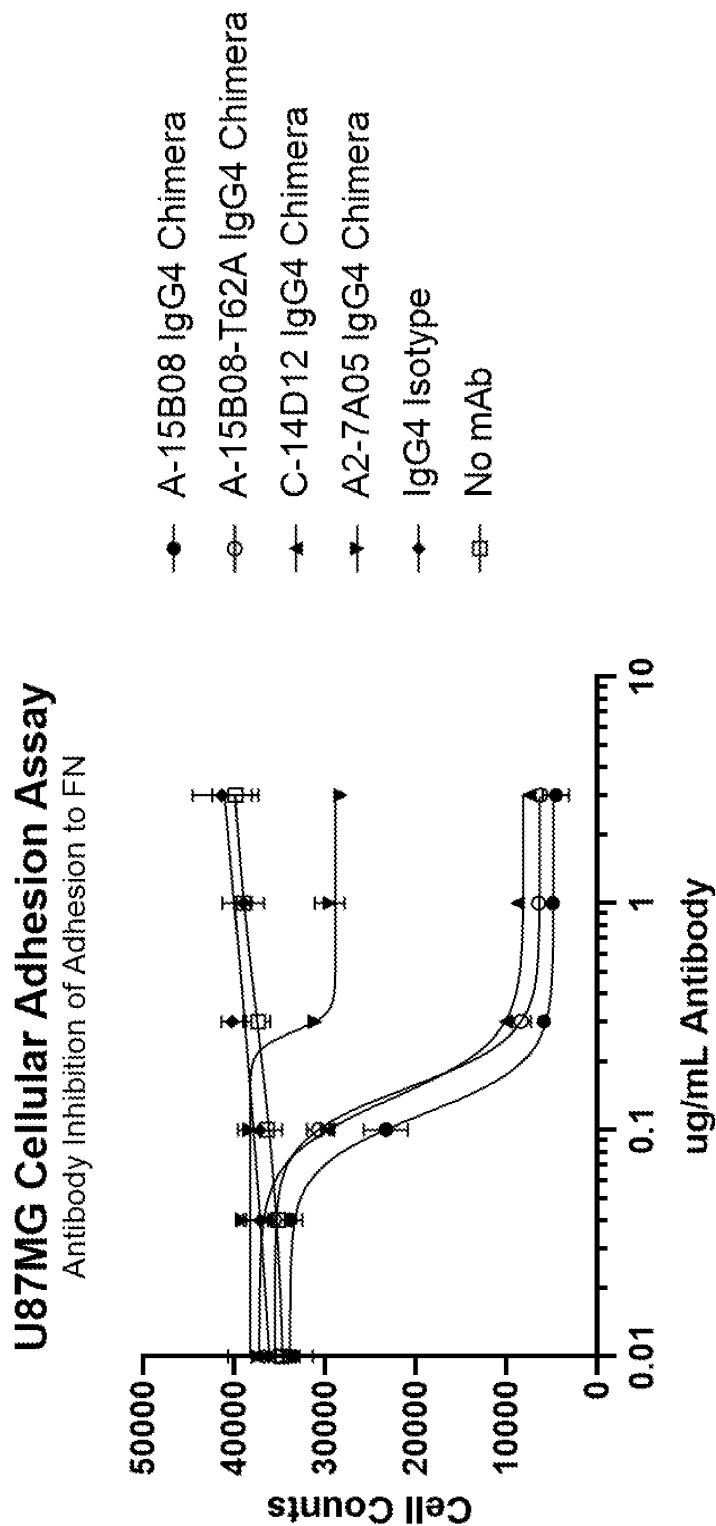


FIG. 9