

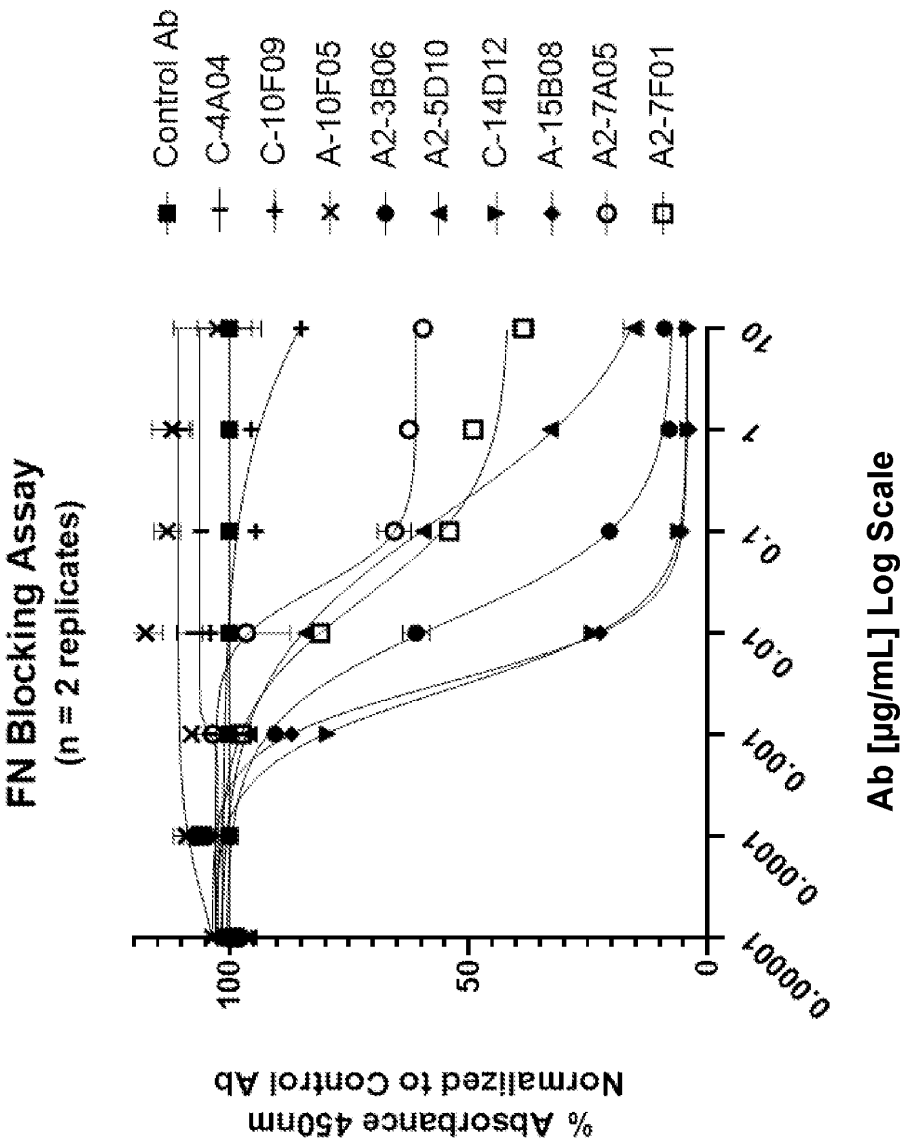


FIG. 1

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	QVQLKESGPGLVAPSQSL	ITCTIS	GFSLT--SYGVH	WVRQPPGKGLEWL	VIW-SDGSTTYNSTLKS				
A2-3B06	QVQLKESGPGLVAPSQSL	ITCTIS	GFSLT--TYGVH	WVRQPPGKGLEWL	VIW-SDGSTTYNSALKS				
A2-5D10	QVQLKESGPGLVAPSQSL	ITCTIS	GFSLT--SYGVH	WVRQPPGKGLEWL	VIW-SDGSTTYNSTLKS				
C-14D12	QVQLKESGPDVLAPSQSL	ITCTVS	GFSLT--DYG	WVRQPPGKGLEWL	VIW-SDGSTTYNSALKS				
consensus	GFSLT--xYGVH		(SEQ ID NO:120)		(SEQ ID NO:121)				
A2-7A05	QVQLQQPGAELVKPGASV	KLSC	KAS	GYTFT--IYWIN	WVKQRPGQGLEWIG	KIYPGSISTDYNEKFKS			
A2-7F01	QVQLQQPGAELVKPGASV	KLSC	KAS	GYTFT--IYWIN	WVKQRPGQGLEWIG	NIYPGSSSTNYNEKFKT			
consensus	GYTFT--IYWIN		(SEQ ID NO:127)			xIYPGSxSTxYNEKFKx			
						(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	NSK	QVFFK	MNSLQTDD	TAMYYCAR	HYDYDGDWF (SEQ ID NO:25)
A2-3B06	RLNITK	DNSK	SQVFLK	MNSLQTDD	TAMYYCVR	HGGLLRDAM (SEQ ID NO:42)
A2-5D10	RLSISK	DNSK	SQVFLK	MNSLQTDD	TAMYYCAR	HYDYDGDWF (SEQ ID NO:51)
C-14D12	RLSITK	DTSK	RQVFLK	MNSLQTDD	TAMYYCAR	HAPSFIRYGSRYDALDY (SEQ ID NO:109)
consensus	HxxxxxxxxxRYDALxY (SEQ ID NO:123)					
A2-7A05	KATLTVD	TSSST	AYMQ	LSSLT	SDDSAVYYCAI	TGTGGL (SEQ ID NO:77)
A2-7F01	KATLTVD	TSSST	AYMQ	LSSLT	SDDSAVYYCAI	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	QIVLTQSPAIMASLGERVTMTCTASSRVSSNSLHWYQQKPGSSPKLWIYSTSNLAS					
A2-3B06	QIVLTQSPAIMASLGERVTMTCTASSSVSSNSFHWYQQKPGSSPKLWLYSTSNLAS					
A2-5D10	QILLTQSPAIMASLGERVTMTCTASSSVSSRCLHWYQQKPGSSPKLWIYSTSNLAS					
C-14D12	QIVLTQSPAIMASLGERVTTLTCTASSSVTSSFLHWYQQKPGSSPKLWIYSTSNLAS					
consensus	TASSxVxSxxH (SEQ ID NO:124) (SEQ ID NO:125)					
A2-7A05	ENVLTQSPAIMASLGEKVTMTCTASSSVN--YMYWYQQKSDASPKLWIYFTSSLAP					
A2-7F01	ENVLTQSPAIMASLGEKVTMSCRASSSVN--YMYWYQQKSDASPKLWIYFTSSLAP					
consensus	RASSSVN--YMYFTSSLAP (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			HQYYRSPPT 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	QVQLKESGPGLVAPSQSLSTICTTIS	GFSLTSYGVH	WVRQPPGKGLEWL	VIWSDGSTTYSALKS					
A-15B08_HC_Low	QVTLKESGPTLVKPTQTTLTITCTIS	GFSLTSYGVH	WVRQPPGKGLEWL	VIWSDGSTTYSALKS					
A-15B08_HC_Low+Mod	QVTLKESGPTLVKPTQTTLTITCTIS	GFSLTSYGVH	WVRQPPGKALEWL	VIWSDGSTTYSALKS					
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	RLSISKDNSKSQLVFFKMNSLQTD	TAMYICAR	HYDYGDFW	FAY	WGQGLVTVSA	(SEQ ID NO:135)			
A-15B08_HC_Low	RLTISKDNSKSQLVFTMTNLD	TVDTAMYICAR	HYDYGDFW	FAY	WGQGLVTVSS	(SEQ ID NO:136)			
A-15B08_HC_Low+Mod	RLTISKDTSKNQVFTMTNLD	TVDTATYICAR	HYDYGDFW	FAY	WGQGLVTVSS	(SEQ ID NO:138)			

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 KIYPGISISTDYNEKFKS								
A2-7A05_HC_Low	QVQLVQPGAEVVKPGASVKLSCKAS GYTFTIYWIN WVKQAPQGLEWIG KIYPGISISTDYNEKFKG								
A2-7A05_HC_Low+Mod	QVQLVQPGAEVVKPGASVKLSCKAS GYTFTIYWIN WVRQAPQGLEWIG KIYPGISISTDYNQKFQG								
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

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 WGQGTSTVTSS (SEQ ID NO:109)								
C-14D12_HC_Low	RLTISKDTSKRQVVLWTNLDVTVDTAMYICAR HAPSFIRYGSRYDALDY WGQGTSLVTSS (SEQ ID NO:144)								
C-14D12_HC_Low+Mod	RLTISKDTSKNQVVLWTNLDVTVDTATYYICAR HAPSFIRYGSRYDALDY WGQGTSLVTSS (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	QIVLTQSPAIMSASLGERVTLC TASSSVTSSFLH WYQKPGSSPKLWIY STSNLAS								
C-14D12_LC_Low	EIVLTQSPGTMSASLGERVTLSC RASSSVTSSFLH WYQKPGQSPKLWIY STSNRAS								
C-14D12_LC_Low+Mod	EIVLTQSPGTLSASLGERVTLSC 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	GVPARFSGSGSGTSYSLTISSMEAEADAATYYC HQYHRSPPT FGGGTKLEIK (SEQ ID NO:110)								
C-14D12_LC_Low	GVPDFRFGSGSGTDYTLTISRMEAEADFATYYC HQYHRSPPT FGQGTKLEIK (SEQ ID NO:145)								
C-14D12_LC_Low+Mod	GVPDFRFGSGSGTDYTLTISRMEAEADFATYYC 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	PQVYTLPPSRDEL	TKNQVSLTCLVKGF	YPSDIAVEWESNGQPENNYK	TTPPVLDSDGSFF		
N297A/Q	PQVYTLPPSQEEM	TKNQVSLTCLVKGF	YPSDIAVEWESNGQPENNYK	TTPPVLDSDGSFF		
LALA	PQVYTLPPSRDEL	TKNQVSLTCLVKGF	YPSDIAVEWESNGQPENNYK	TTPPVLDSDGSFF		
LALAPS	PQVYTLPPSRDEL	TKNQVSLTCLVKGF	YPSDIAVEWESNGQPENNYK	TTPPVLDSDGSFF		
LALAPG	PQVYTLPPSRDEL	TKNQVSLTCLVKGF	YPSDIAVEWESNGQPENNYK	TTPPVLDSDGSFF		
TM	PQVYTLPPSRDEL	TKNQVSLTCLVKGF	YPSDIAVEWESNGQPENNYK	TTPPVLDSDGSFF		
	410	420	430	440	447	
IgG1	*	*	*	*	*	
IgG4	LYSKLTVDKSRWQ	QGNVFCSCVMHEALHNHYTQKSLSLSPGK	(SEQ ID NO:148)			
N297A/Q	LYSRLTVDKSRWQ	EGNVFSCSCVMHEALHNHYTQKSLSLSPGK	(SEQ ID NO:149)			
LALA	LYSKLTVDKSRWQ	QGNVFCSCVMHEALHNHYTQKSLSLSPGK	(SEQ ID NO:150)			
LALAPS	LYSKLTVDKSRWQ	QGNVFCSCVMHEALHNHYTQKSLSLSPGK	(SEQ ID NO:151)			
LALAPG	LYSKLTVDKSRWQ	QGNVFCSCVMHEALHNHYTQKSLSLSPGK	(SEQ ID NO:152)			
TM	LYSKLTVDKSRWQ	QGNVFCSCVMHEALHNHYTQKSLSLSPGK	(SEQ ID NO:153)			
	LYSKLTVDKSRWQ	QGNVFCSCVMHEALHNHYTQKSLSLSPGK	(SEQ ID NO:154)			

FIG. 3 (cont.)

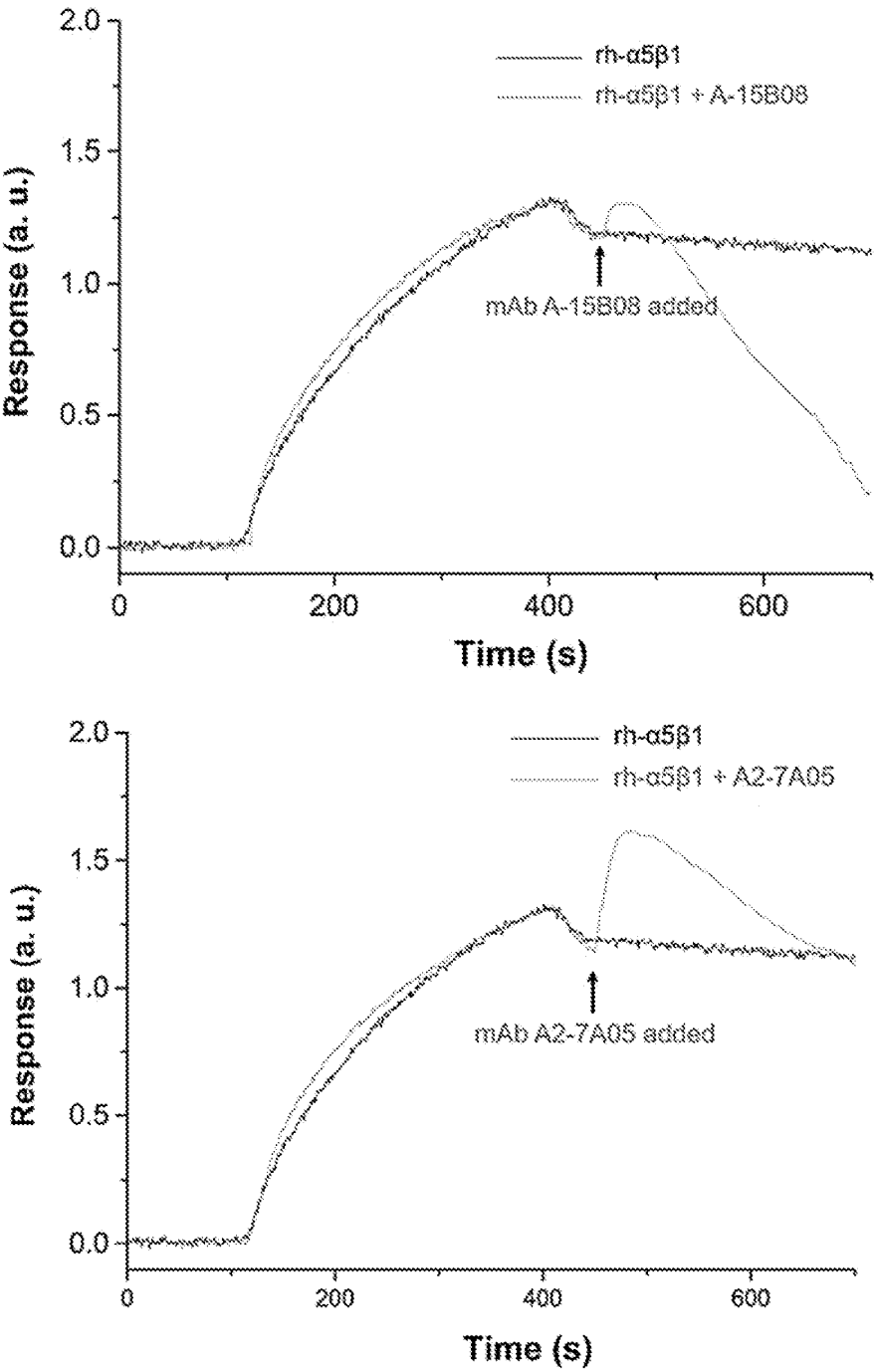
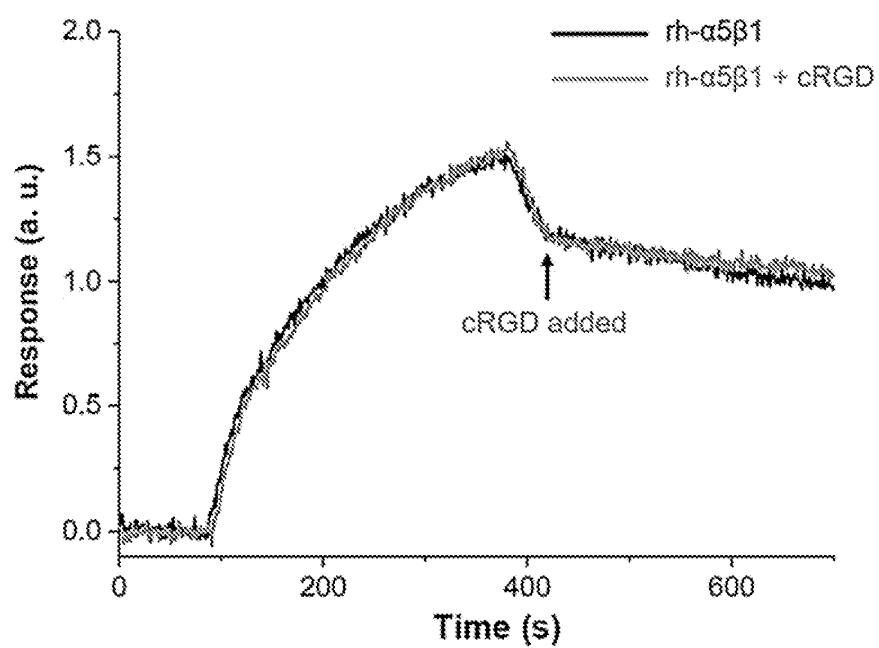
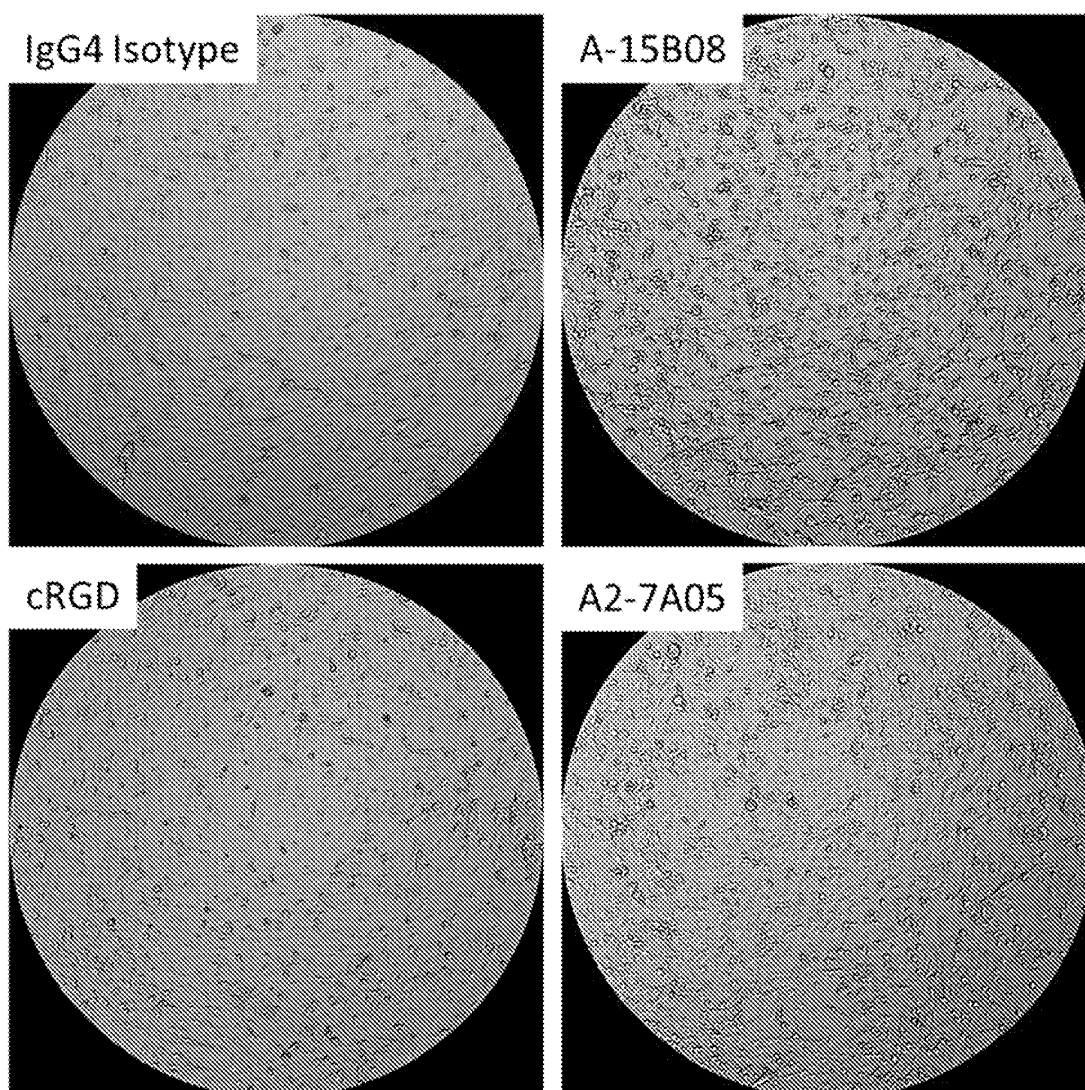


FIG. 4A

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

**FIG. 4B**

$\alpha 5\beta 1$ Integrin FN Blocking Assay

4°C vs. 3x Freeze/Thaw -80°C

(n = 2 replicates)

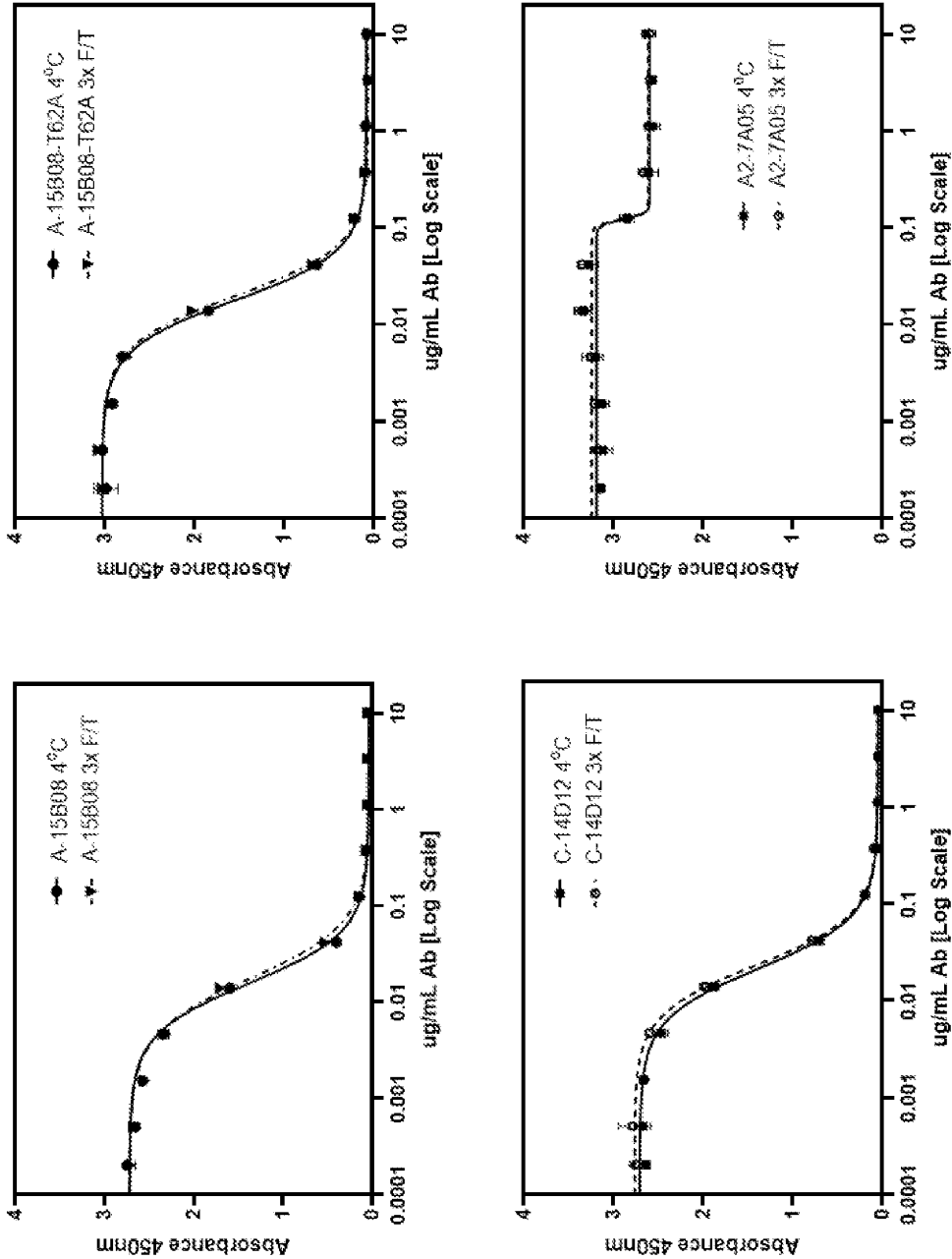


FIG. 5

Potency of Hybridomas vs. IgG4 Chimeras

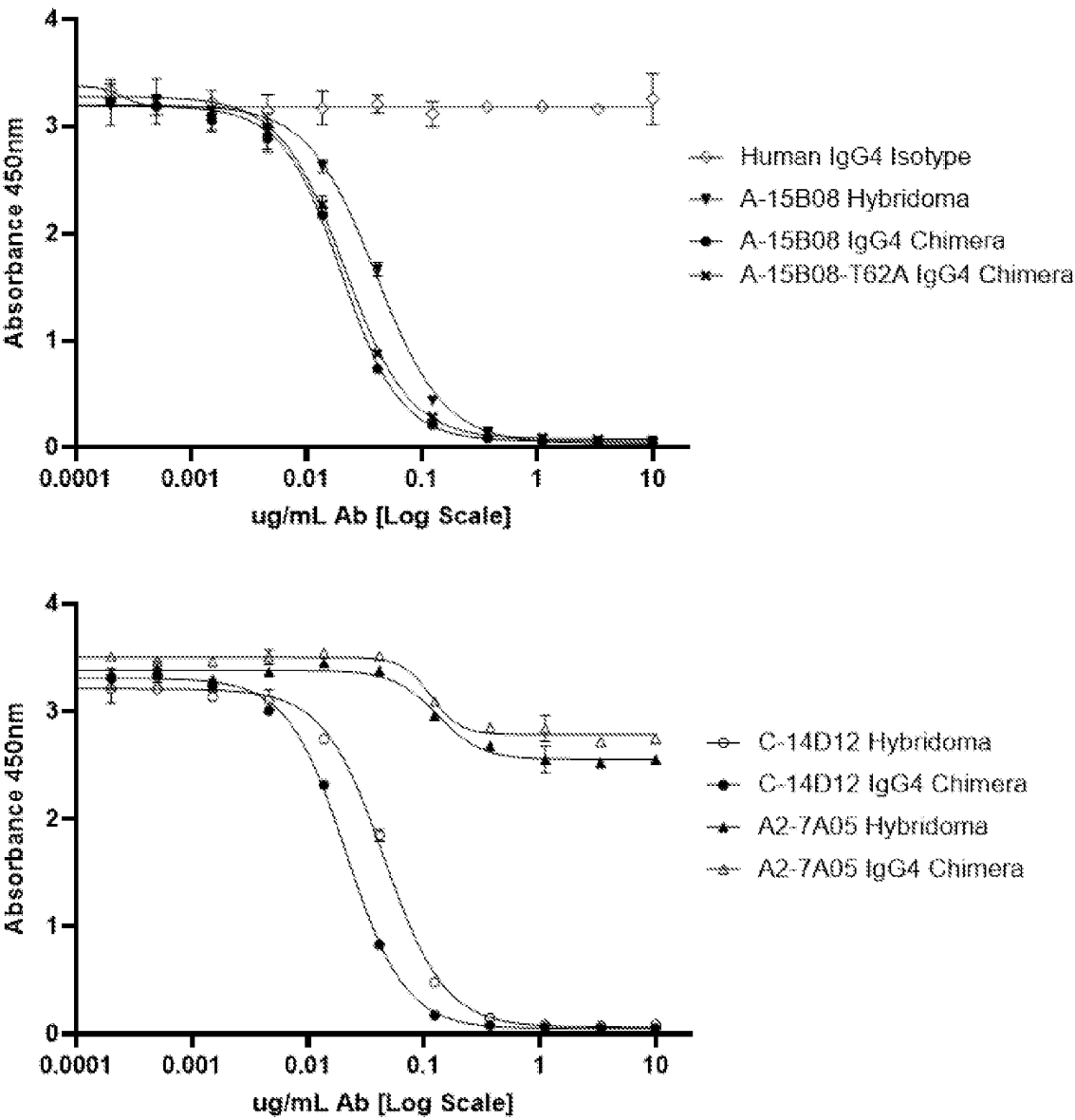


FIG. 6

SDS-PAGE of IgG4 Chimeric Antibodies

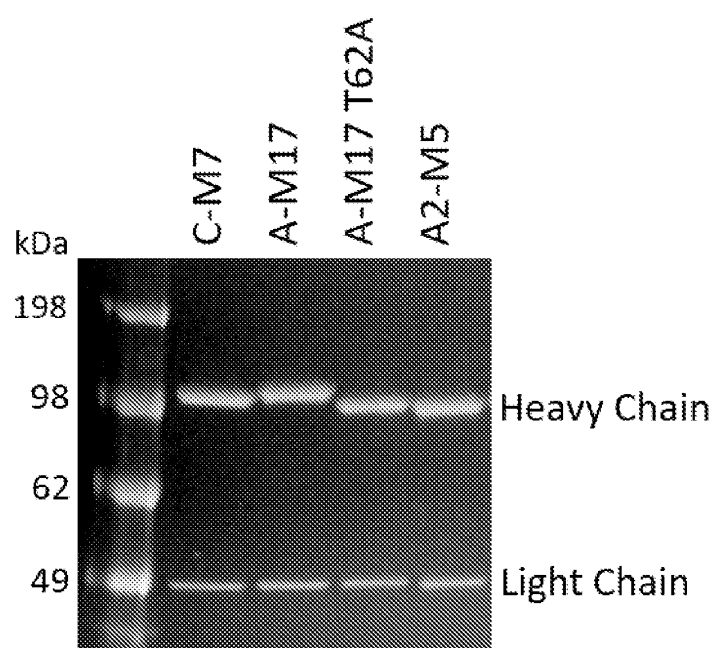


FIG. 7

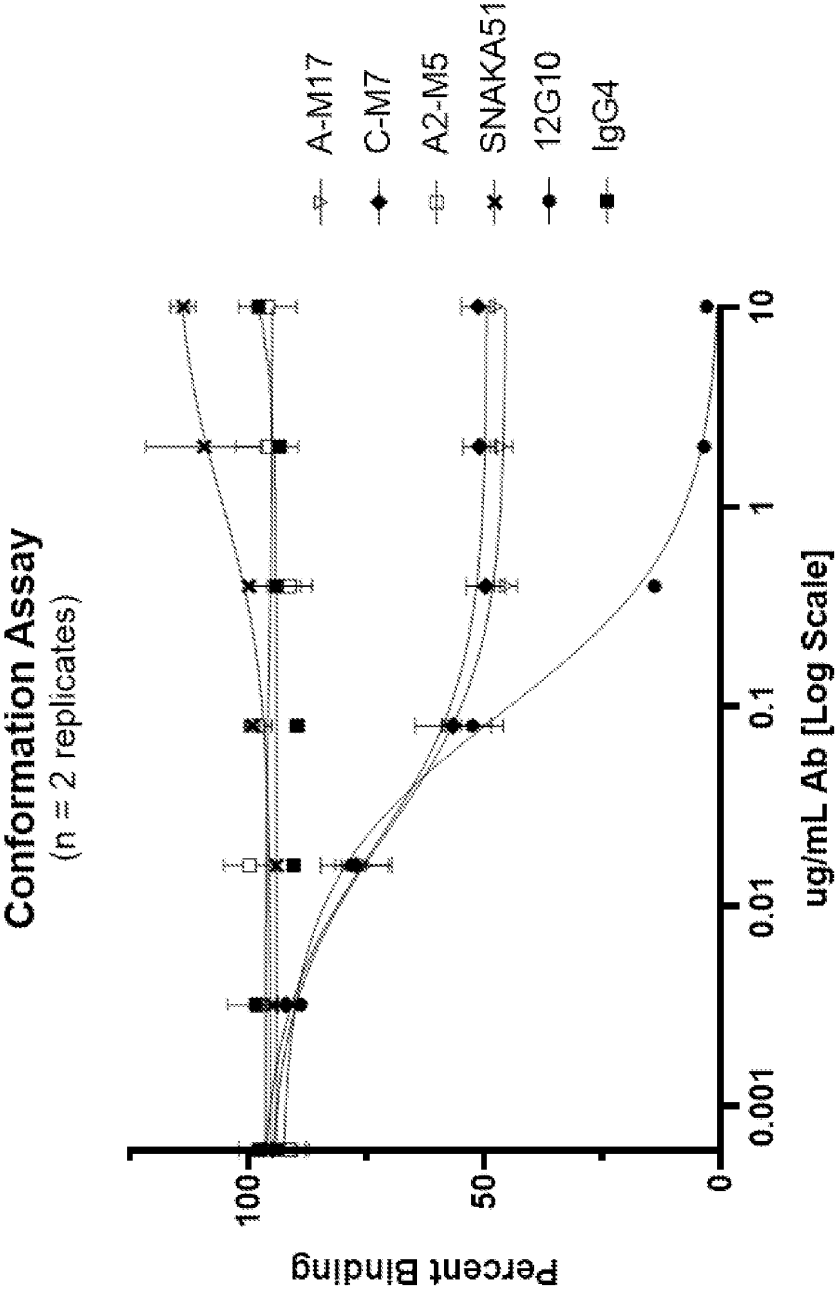


FIG. 8

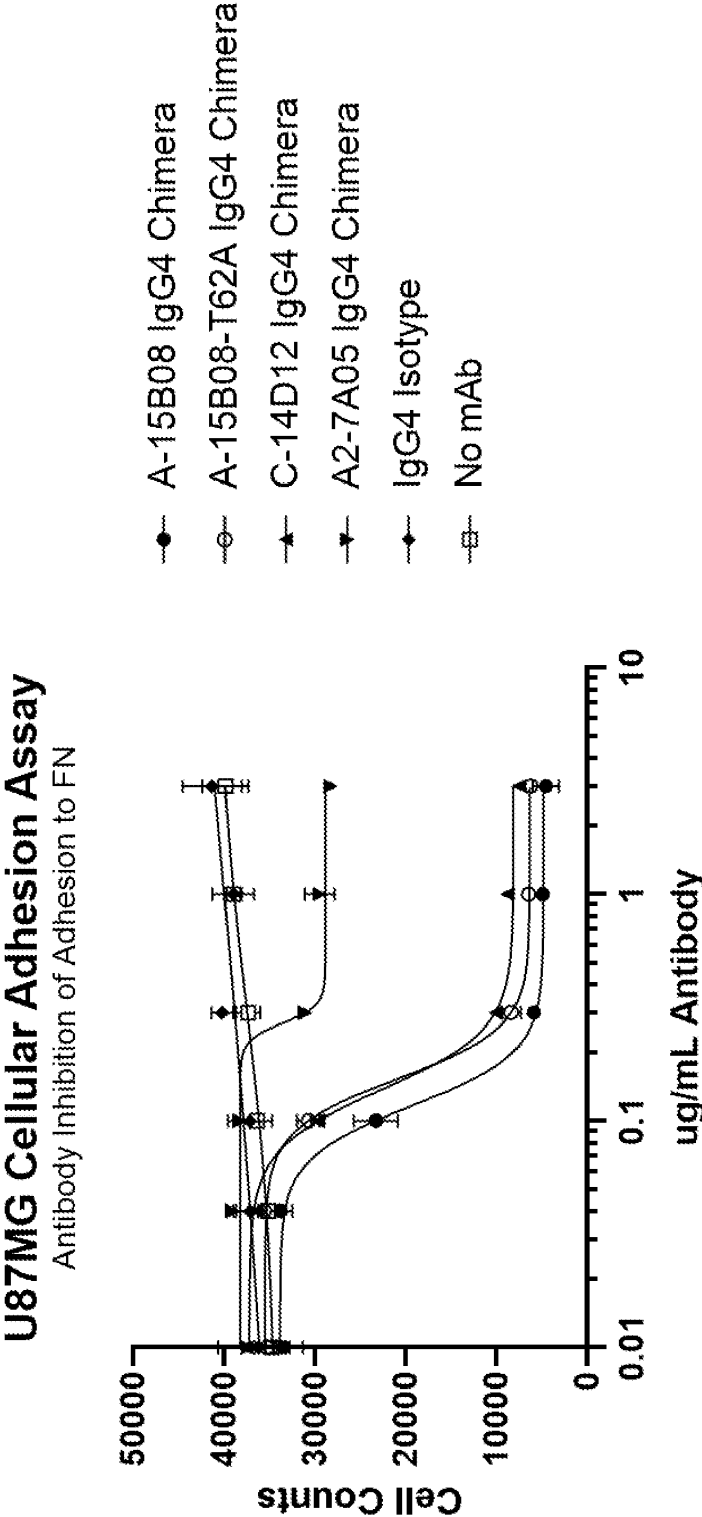


FIG. 9