

FIG. 1

				▼ V _H		*		
CaIgG-A	MESVFCWVFL	VVILKGVQGE	VQLVESGGDL	VKPGGSLRLS	GVASGFTFSS		50	
CaIgG-B	----LF----	-T-----	-R-----T-	-----K--	-----RR		50	
CaIgG-C	----LY----	-A-----D			-----		50	
CaIgG-D	----L-----	-S-----			-----D		50	
CaIgG-A	YYMHVIRQAP	CKGLQ RVAHI	RGDGRTHYA	DAMKGRFTIS	RDNAKNTLYE		100	
CaIgG-B	-S-D-V- - -	-S--W--G-	N--TG-S-S	QTV- - - -	-----		100	
CaIgG-C	CA-S-V- - -	-P-W--T-	-Y--SDIY--	-----S--	-----V--		100	
CaIgG-D	-G-S-V- - -	-----W--AV	SNR- D-Y--	-----	-----		100	
CaIgG-A	QMSLTVEDT	AIYYCVKDI	YYGVG D	YWQGTLVTV	SSASTTAPSV		150	
CaIgG-B	-I---RA--S	-V--A-S W	SRNG DL-		-----		150	
CaIgG-C	-----RA--	-V--A-A P	PYDS-HY-M-	---P--SLF-	-----		150	
CaIgG-D	--S--KA--	-I-H-VTG VW	PRH--M -	H--N--SLF-	-----		150	
CaIgG-A	FPLAPSCGST	SGSTVALACL	VSGYFPEPVT	VSWNSGSLTS	GVHTFPSVLQ		200	
CaIgG-B	-----				-----		200	
CaIgG-C	-----Q		---I----	-----V----	-----		200	
CaIgG-D	-----				-----		200	
CaIgG-A	SSGLHSLSSM	VTVPSSRWPS	ETFTCNVVHP	ASNTKVDPKV	FNECRCTDT		250	
CaIgG-B	----Y-----		-----A-	P-K-----	PKRENGRVPR		250	
CaIgG-C	----Y-----		-----A-	-T-----	AK--E-KC N		250	
CaIgG-D	----Y-----T				PK-ST-KCI		250	
CaIgG-A	PPCPVP	EPLGGPSVLI	FPPKPKDILR	ITRTPEVTCV	VLDLGREDPE		300	
CaIgG-B	PPDC-K--A-	-M-----F-	-----TLL	-A-----	-V--DP----		300	
CaIgG-C	CNNC- --GC	GL-----F-	-----V	TA--T----	-V--DP-N--		300	
CaIgG-D	SP-----	ES-----F-		-----I--	-----		300	
CaIgG-A	VQISWFVDGK	EVHTAKTQSR	EQQFNGTYRV	VSVLPIDHQD	WLTGKEFKCR		350	
CaIgG-B	-----	QMQ-----P-	-E- - - - -	-----G--	--K--Q-T-K		350	
CaIgG-C	-----S-	Q-Q--N--P-	-E-S- - - -	-----G--	--S--Q--K		350	
CaIgG-D	-----	-----P-	-S- - - - -	-----	-----		350	
CaIgG-A	VNHIDLPSP	ERTISKARGR	AHKPSVYVLP	PSPKELSSSD	TVSITCLIKD		400	
CaIgG-B	--NKA-----	-----Q	--Q-----	--RE--K N	---L-----		400	
CaIgG-C	--NKA-----	-EI--TP-Q	--Q-N-----	--RD-M-K N	--TL--V--		400	
CaIgG-D	----G-----	-----Q	--Q-----		--TL-----		400	
CaIgG-A	FYPDPIDVEW	QSNQQEPPER	KHRMTTPQLD	EDGSYFLYSK	LSVDKSRWQQ		450	
CaIgG-B	-F-----	-----S	-Y-T-----		-----R		450	
CaIgG-C	-F--E-----	-----S	-Y-M-----		-----R		450	
CaIgG-D	-F--E-----	-----P--S	-YHT-A----		-----		450	
CaIgG-A	GDPFTCAVMH	ETLQNHYTEL	SLSHSPGK				500	
CaIgG-B	--T-I-----	-A-H----QE					500	
CaIgG-C	--T-I-----	-A-H----QI					500	
CaIgG-D	--T-----	-A-----					500	

FIG.2

Canine.IgG.A	GPSVLIFPPKPKDILIRITRTP ~~EV~~ TCVVDLDLGREDPEVQISWFDGKEVHT
Canine.IgG.D	GPSVFIFPPKPKDILIRITRTP ~~ET~~ ITCVVDLDLGREDPEVQISWFDGKEVHT
Canine.IgG.B	GPSVFIFPPKPKDILLIARTPEVTCVVVDLDPEDPEVQISWFDGKQMQT
canine.IgG.C	GPSVFIFPPKPKDILLVTARTPTVTCVVVDLDPENPEVQISWFD ~~SK~~ QVQT
	****:***** * :*** :****:***. *.*****.***.***:*
Canine.IgG.A	AKTQSREQQFNGTYRVVSVLPIEHQ ~~DL~~ WTGKEFKCRVNHIDLPSPIERTISKAR
Canine.IgG.D	AKTQPREQQFNSTYRVVSVLPIEHQ ~~DL~~ WTGKEFKCRVNHIGLPSPIERTISKAR
Canine.IgG.B	AKTQPREEQNGTYRVVSVLPIGHQ ~~DL~~ WLGKQFTCKVNNKALPSPIERTISKAR
Canine.IgG.C	ANTQPREEQSNGTYRVVSVLPIGHQ ~~DL~~ SGKQFKCKVNNKALPSPIEEIIISKTP
	*:***:*** *.*****.***.***:***:****. *****. ***:

FIG. 3

Canine.IgG.A	KPSVYVLPSPKELSSDTSITCLIKDFYPPDIDVEWQSNQGQPEPERKHRMTPPQLDED
Canine.IgG.D	QPSVYVLPSPKELSSDVTLTCLIKDFFPPEIDVEWQSNQGQPEPESEKYHTTAPQLDED
Canine.IgG.B	QPSVYVLPSPSREEL-SKNTVSLTCLIKDFFPPDIDVEWQSNQGQPEPESEKYRTTTPPQLDED
Canine.IgG.C	QPNVYVLPSPSRDEM-SKNTVTTLTCLVKDFFPPEIDVEWQSNQGQPEPESEKYRMTTPPQLDED
	:* . ***** *:*.**:***:***:***:***** ** **: *.*****
Canine.IgG.A	GSYFLYSKLSVDKSRWQQGDPFTCAVMHETLQNHYTDLSLSHSPGK
Canine.IgG.D	GSYFLYSKLSVDKSRWQQGDTFTCAVMHEALQNHYTDLSLSHSPGK
Canine.IgG.B	GSYFLYSKLSVDKSRWQRGDTFICAVMHEALHNHYTQESLSHSPGK
Canine.IgG.C	GSYFLYSKLSVDKSRWQRGDTFICAVMHEALHNHYTQISLSHSPGK
	*****:***.* ******:***:*****: *****

Canine. IgG. A	VPEPLGGPSVLIFPPKPKDILRITRTPEVTCVVDLGLREDPEVQISWFVDGKEVHT
Canine. IgG. D	VPESLGGPSVFIFFPKPKDILRITRTPEITCVVDLGLREDPEVQISWFVDGKEVHT
Canine. IgG. B	APEMPLGGPSVFIFFPKPKDITLLIARTPEVTCVVVDLDPEDPEVQISWFVDGKQMOT
Canine. IgG. C	GCGLLGGPSVFIFFPKPKDILVTARTPTVTCVVVDLDPENPEVQISWFVDSKQVQT
	*****:***** * :*** :****:***. *:*****. *:***
Canine. IgG. A	AKTQSQREQFNGTYRVVSVLP ¹ IEHQDWLTGKEFKCRVNHIDLPSPIERTISKARGRAHKP
Canine. IgG. D	AKTQPREQQFNSTYRVVSVLP ¹ IEHQDWLTGKEFKCRVNHIGLPSPIERTISKARGQAHQP
Canine. IgG. B	AKTQPREEQFNGTYRVVSVLP ¹ IGHQDWLGKGQFTCKVNNKALPSPIERTISKARGQAHQP
Canine. IgG. C	ANTQPREEQSQNGTYRVVSVLP ¹ IGHQDWLSGKGQFKCKVNNKALPSPIELISKTPGQAHQP
	*:***:*** *.***** *****.***:***:*** *****. ***: *:***:*
Canine. IgG. A	SVYVLPSPKELSSDTSITCLIKDFYPPDIDVEWQSGNGQOQEPERKHRMTPPOLDEDGS
Canine. IgG. D	SVYVLPSPKELSSDTSVTLTCLIKDFFPPEIDVEWQSGNGQOPEPESKYHTTAPOLDEDGS
Canine. IgG. B	SVYVLPSPSREEL-SKNTVSLTCLIKDFFPPDIDVEWQSGNGQOPEPESKYRTTPPOLDEDGS
Canine. IgG. C	NVYVLPSPSRDEM-SKNTVTTLTCLVKDFFPPEIDVEWQSGNGQOPEPESKYRMTTPPOLDEDGS
	. ***** *: *:***:***:***:***:***** ***** *** *: * *****
Canine. IgG. A	YFLYSKLSVDKSRWQQDPFTCAVMHETLQNH ² YTDLSLSHSPGK
Canine. IgG. D	YFLYSKLSVDKSRWQQDFTTCAVMHEALQNH ² YTDLSLSHSPGK
Canine. IgG. B	YFLYSKLSVDKSRWQRGDTFICAVMHEALHNHY ³ TQESLSHSPGK
Canine. IgG. C	YFLYSKLSVDKSRWQRGDTFICAVMHEALHNHY ³ TQISLSHSPGK
	*****:***. * *****:*. *****: *****: *****

5/28

FIG. 5

CH2 DOMAIN							
	EU	hlgG1	clgG.A	clgG.B	clgG.C	clgG.D	SM
A-strand	237	G	G	G	G	G	
	238	P	P	P	P	P	
	239	S	S	S	S	S	
	240	V	V	V	V	V	
	241	F	L	F	F	F	
	242	L	I	I	I	I	
	243	F	F	F	F	F	
	244	P	P	P	P	P	
	245	P	P	P	P	P	
	246	K	K	K	K	K	
	247	P	P	P	P	P	
	248	K	K	K	K	K	
	249	D	D	D	D	D	
	250	T	I	T	I	I	E or Q
	251	L	L	L	L	L	D or E
AB-turn	252	M	R	L	V	R	Y
	253	I	I	I	T	I	
B-strand	254	S	T	A	A	T	T
	255	R	R	R	R	R	
	256	T	T	T	T	T	D, E, or F
	257	P	P	P	P	P	
	258	E	E	E	T	E	
	259	V	V	V	V	I	
	260	T	T	T	T	T	
	261	C	C	C	C	C	
	262	V	V	V	V	V	
	263	V	V	V	V	V	
	264	V	L	V	V	L	
BC-loop	265	D	D	D	D	D	
	266	V	L	L	L	L	
	267	S	G	D	D	G	
	268	H	R	P	P	R	
	269	E	E	E	E	E	
	270	D	D	D	N	D	
	271	P	P	P	P	P	
	272	E	E	E	E	E	
	273	V	V	V	V	V	

6/28

	274	K	Q	Q	Q	Q	
C-strand	275	F	I	I	I	I	
	276	N	S	S	S	S	
	277	W	W	W	W	W	
	278	Y	F	F	F	F	
	279	V	V	V	V	V	
	280	D	D	D	D	D	
	281	G	G	G	S	G	
CD-loop	282	V	K	K	K	K	
	283	E	E	Q	Q	E	
	284	V	V	M	V	V	
	285	H	H	Q	Q	H	N,D
	-	-	-	-	-	-	
	-	-	-	-	-	-	
	-	-	-	-	-	-	
D-strand	286	N	T	T	T	T	D
	287	A	A	A	A	A	
	288	K	K	K	N	K	
	289	T	T	T	T	T	
	290	K	Q	Q	Q	Q	
	291	P	S	P	P	P	
	292	R	R	R	R	R	
	293	E	E	E	E	E	
DE-turn	294	E	Q	E	E	Q	
	295	Q	Q	Q	Q	Q	
	296	Y	F	F	S	F	
	297	N	N	N	N	N	
	298	S	G	G	G	S	
	299	T	T	T	T	T	
	300	Y	Y	Y	Y	Y	
	301	R	R	R	R	R	
E-strand	302	V	V	V	V	V	
	303	V	V	V	V	V	
	304	S	S	S	S	S	
	305	V	V	V	V	V	
	306	L	L	L	L	L	
	307	T	P	P	P	P	R,Q,A
	308	V	I	I	I	I	P
	309	L	E	G	G	E	P
	310	H	H	H	H	H	
	311	Q	Q	Q	Q	Q	V

7/28

	312	D	D	D	D	D	
	313	W	W	W	W	W	
EF-turn	-	-	-	-	-	-	
	-	-	-	-	-	-	
F-strand	314	L	L	L	L	L	
	315	N	T	K	S	T	D
	316	G	G	G	G	G	
	317	K	K	K	K	K	
	318	E	E	Q	Q	E	
	319	Y	F	F	F	F	
	320	K	K	T	K	K	
	321	C	C	C	C	C	
FG-loop	322	K	R	K	K	R	
	323	V	V	V	V	V	
	324	S	N	N	N	N	
	325	N	H	N	N	H	
	326	K	I	K	K	I	
	327	A	D	A	A	G	
	-	-	-	-	-	-	
	328	L	L	L	L	L	
	329	P	P	P	P	P	
	330	A	S	S	S	S	
	331	P	P	P	P	P	
	332	I	I	I	I	I	
G-strand	333	E	E	E	E	E	
	334	K	R	R	E	R	
	335	T	T	T	I	T	
	336	I	I	I	I	I	
	337	S	S	S	S	S	
	338	K	K	K	K	K	
	339	A	A	A	T	A	
	340	K	R	R	P	R	

hlgG1 = human IgG1; clgGA = canine IgG.A; clgGB = canine IgG.B; clgGC = canine IgG.C; clgGD = canine IgG.D; SM= mutations that can extent antibody half-life

8/28

FIG. 6

CH3 DOMAIN							
	EU	hlgG1	clgG.A	clgG.B	clgG.C	clgG.D	SM
A-strand	345	E	K	Q	Q	Q	
	346	P	P	P	P	P	
	347	Q	S	S	N	S	
	348	V	V	V	V	V	
	349	Y	Y	Y	Y	Y	
	350	T	V	V	V	V	
	351	L	L	L	L	L	
	352	P	P	P	P	P	
	353	P	P	P	P	P	
	354	S	S	S	S	S	
	355	R	P	R	R	P	
	356	D	K	E	D	K	
	357	E	E	E	E	E	
	358	L	L	L	M	L	
	359	T	S	S	S	S	
AB-turn	-	-	-	-	-	-	
	-	-	S	-	-	S	
B-strand	360	K	S	K	K	S	
	361	N	D	N	N	D	
	362	Q	T	T	T	T	
	363	V	V	V	V	V	
	364	S	S	S	T	T	
	365	L	I	L	L	L	
	366	T	T	T	T	T	
	367	C	C	C	C	C	
	368	L	L	L	L	L	
	369	V	I	I	V	I	
	370	K	K	K	K	K	
BC-loop	371	G	D	D	D	D	
	372	F	F	F	F	F	
	373	Y	Y	F	F	F	
	374	P	P	P	P	P	
	-	-	-	-	-	-	
	-	-	-	-	-	-	
	375	S	P	P	P	P	
	376	D	D	D	E	E	
	377	I	I	I	I	I	

9/28

	378	A	D	D	D	D	V
C-strand	379	V	V	V	V	V	
	380	E	E	E	E	E	A
	381	W	W	W	W	W	
	382	E	Q	Q	Q	Q	
	383	S	S	S	S	S	
	384	N	N	N	N	N	
	385	G	G	G	G	G	
CD-loop	386	Q	Q	Q	Q	Q	
	387	P	Q	Q	Q	P	
	388	E	E	E	E	E	
	389	N	P	P	P	P	
	-	-	E	E	E	E	
	-	-	R	S	S	S	
D-strand	390	N	K	K	K	K	
	391	Y	H	Y	Y	Y	
	392	K	R	R	R	H	
	393	T	M	T	M	T	
	394	T	T	T	T	T	
	395	P	P	P	P	A	
	396	P	P	P	P	P	
	397	V	Q	Q	Q	Q	
DE-turn	398	L	L	L	L	L	
	399	D	D	D	D	D	
	400	S	E	E	E	E	
	401	D	D	D	D	D	
	402	G	G	G	G	G	
	403	S	S	S	S	S	
	404	F	Y	Y	Y	Y	
	405	F	F	F	F	F	
E-strand	406	L	L	L	L	L	
	407	Y	Y	Y	Y	Y	
	408	S	S	S	S	S	
	409	K	K	K	K	K	
	410	L	L	L	L	L	
	411	T	S	S	S	S	
	412	V	V	V	V	V	
	413	D	D	D	D	D	
	414	K	K	K	K	K	
	415	S	S	S	S	S	

10/28

	416	R	R	R	R	R	
	417	W	W	W	W	W	
EF-turn	-	-	-	-	-	-	
	-	-	-	-	-	-	
F-strand	418	Q	Q	Q	Q	Q	
	419	Q	Q	R	R	Q	
	420	G	G	G	G	G	
	421	N	D	D	D	D	
	422	V	P	T	T	T	
	423	F	F	F	F	F	
	424	S	T	I	I	T	
	425	C	C	C	C	C	
FG-loop	426	S	A	A	A	A	
	427	V	V	V	V	V	
	428	M	M	M	M	M	L
	429	H	H	H	H	H	
	430	E	E	E	E	E	A, K
	431	A	T	A	A	A	
	432	L	L	L	L	L	
	433	H	Q	H	H	Q	K
	434	N	N	N	N	N	S, A, F
	435	H	H	H	H	H	Y
	436	Y	Y	Y	Y	Y	H
	437	T	T	T	T	T	
G-strand	438	Q	D	Q	Q	D	
	439	K	L	E	I	L	
	440	S	S	S	S	S	
	441	L	L	L	L	L	
	442	S	S	S	S	S	
	443	L	H	H	H	H	
	444	S	S	S	S	S	
	445	P	P	P	P	P	
tail	446	G	G	G	G	G	
	447	K	K	K	K	K	

hIgG1 = human IgG1; clgGA = canine IgG.A; clgGB = canine IgG.B; clgGC = canine IgG.C; clgGD = canine IgG.D; SM= mutations that can extent antibody half-life

FIG. 7A

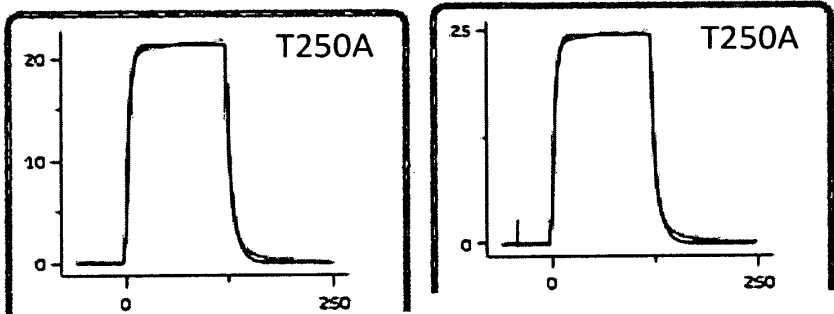


FIG. 7B

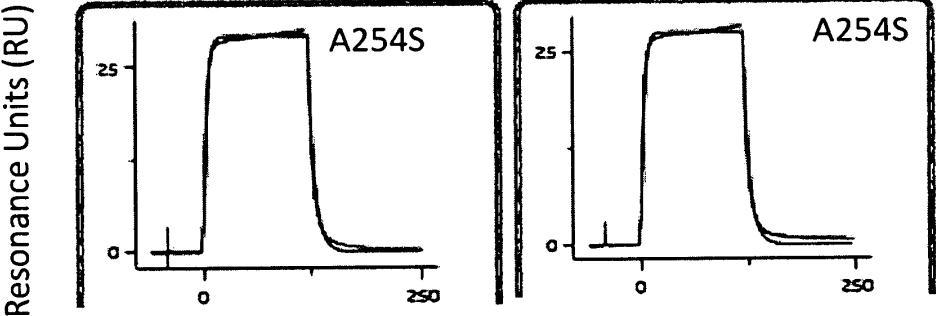
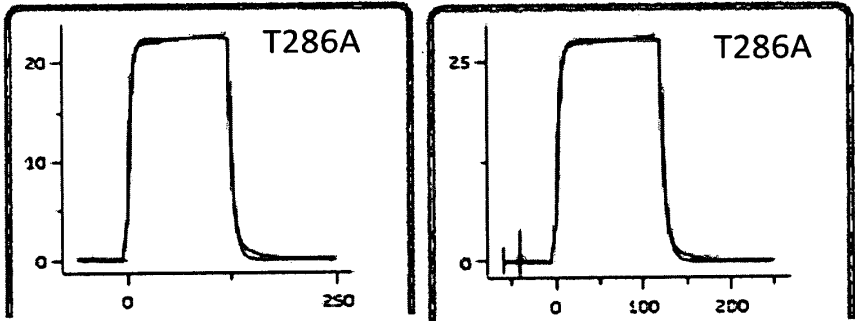


FIG. 7C



Time - sec

12/28

FIG. 7D

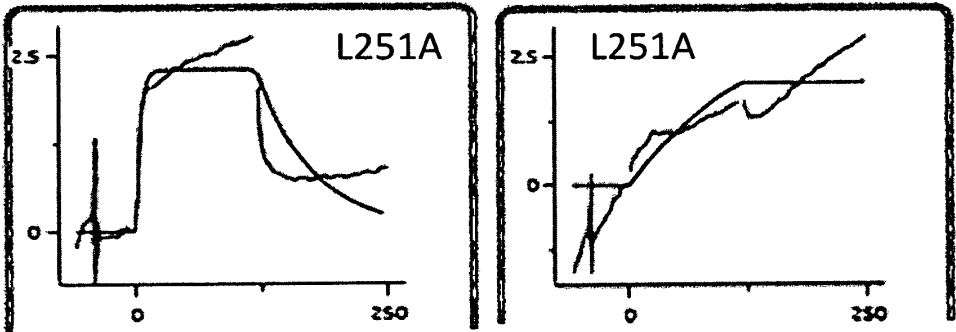


FIG. 7E

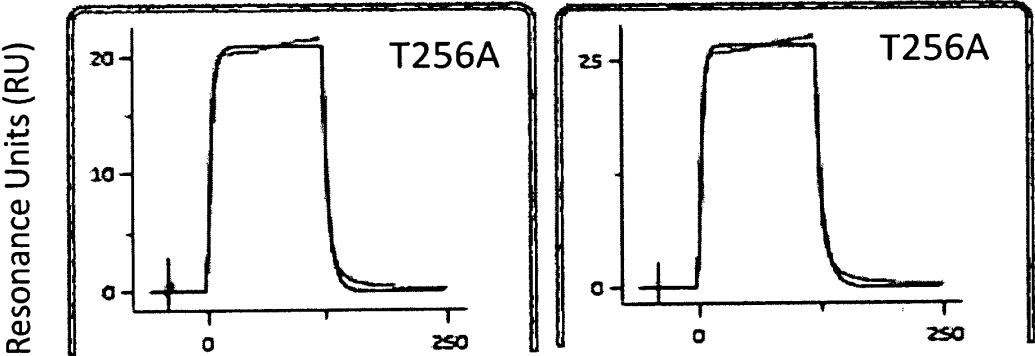
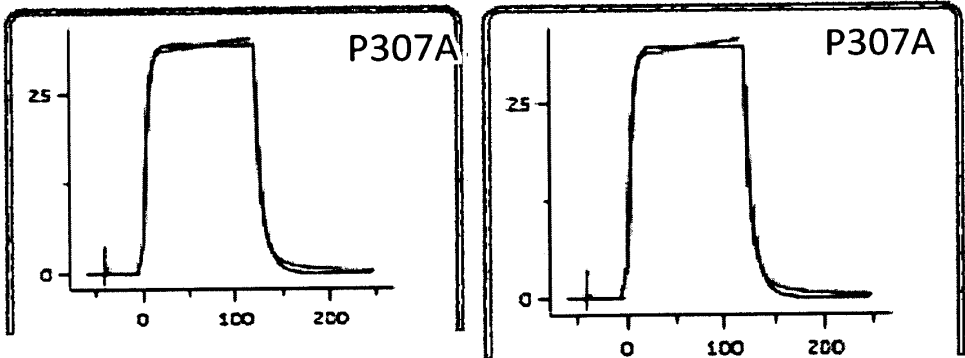


FIG. 7F



Time - sec

FIG. 7G

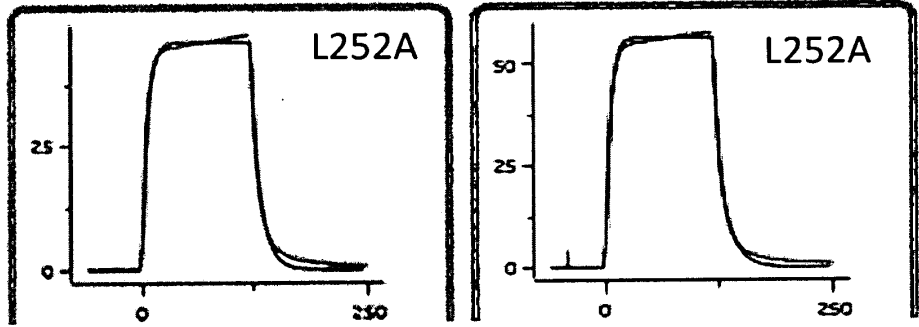


FIG. 7H

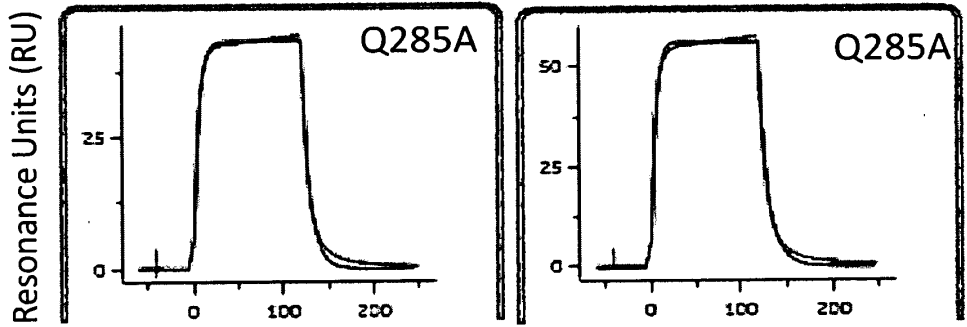
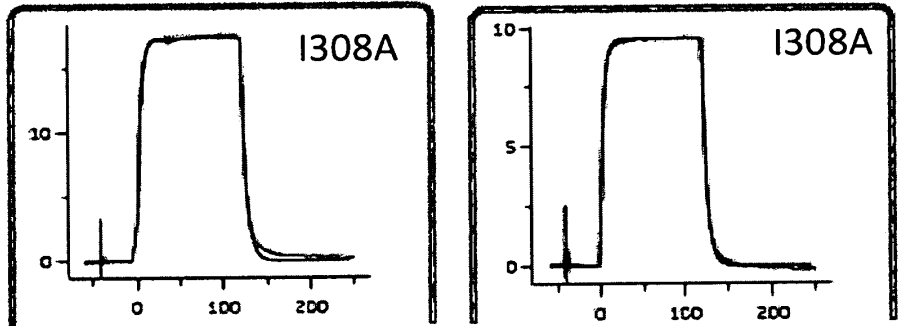


FIG. 7I



Time - sec

FIG. 7J

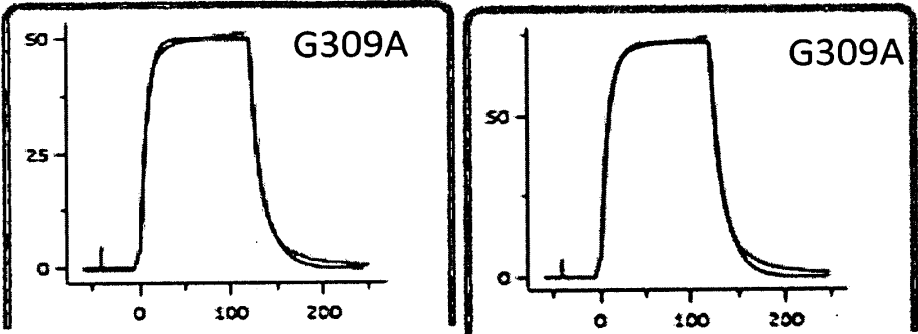


FIG. 7K

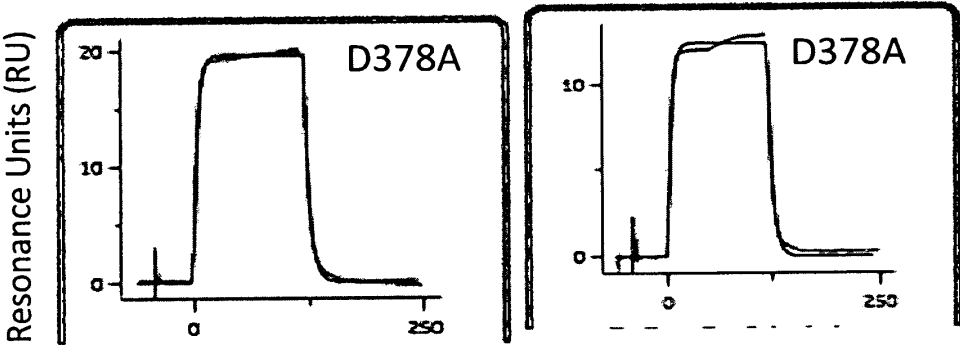
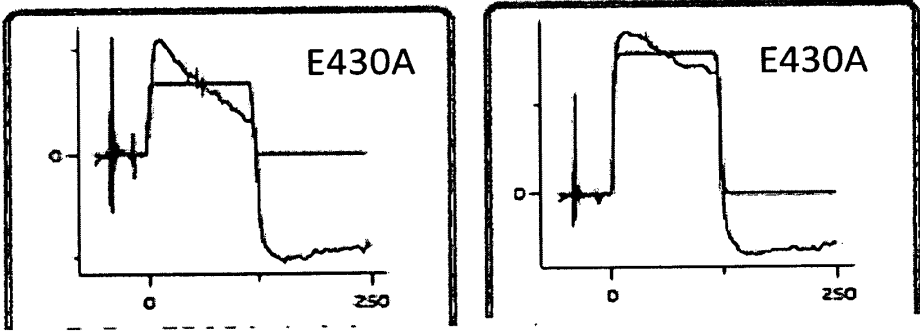


FIG. 7L



Time - sec

FIG. 7M

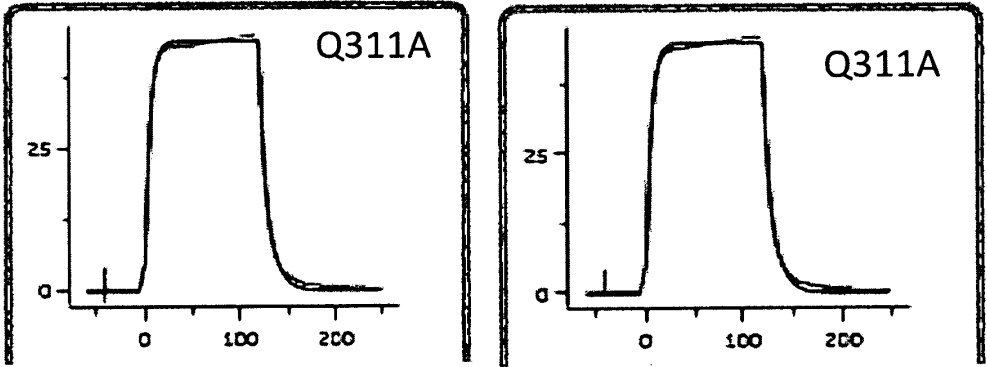


FIG. 7N

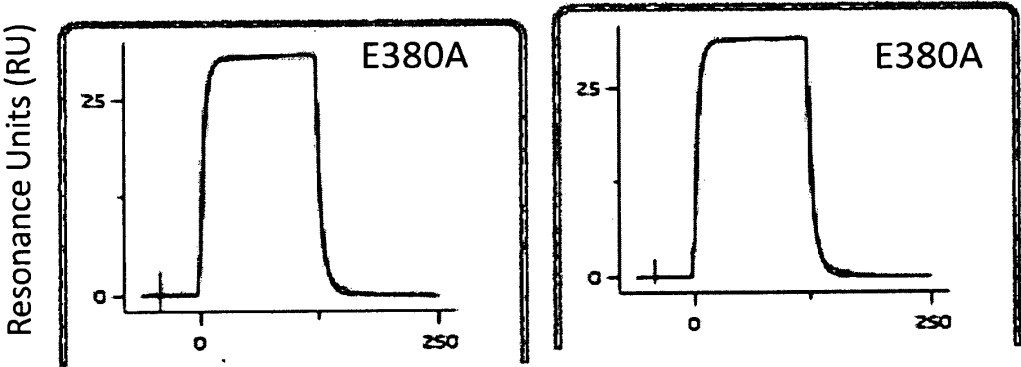
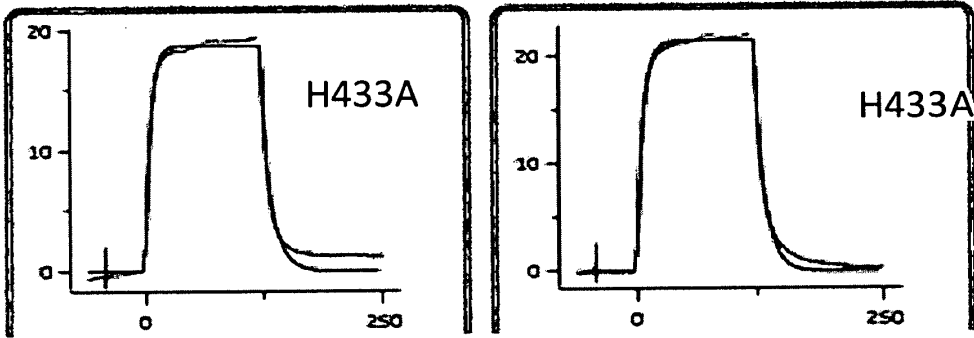


FIG. 7O



Time - sec

FIG. 7P

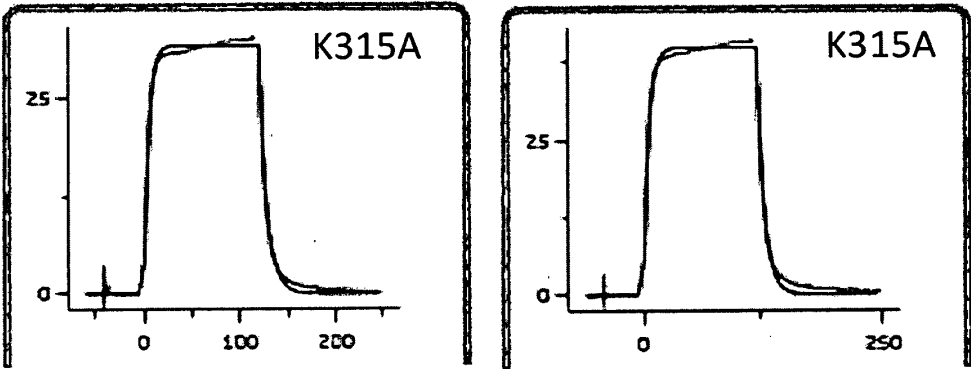


FIG. 7Q

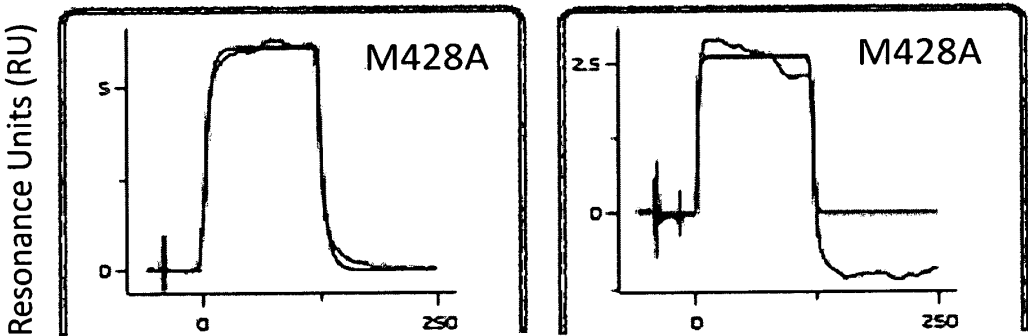
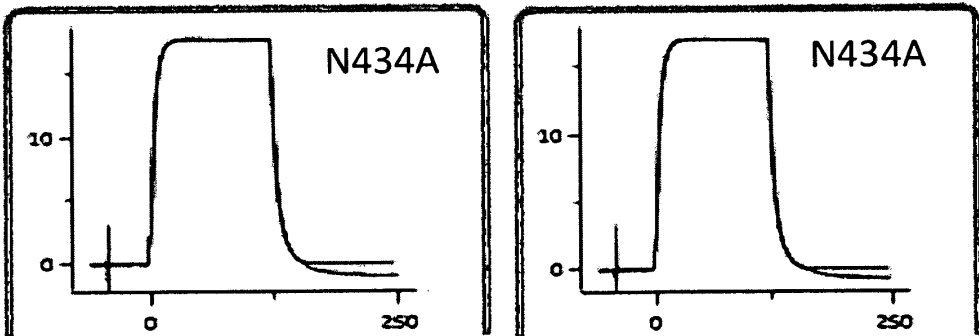


FIG. 7R



Time - sec

FIG. 7S

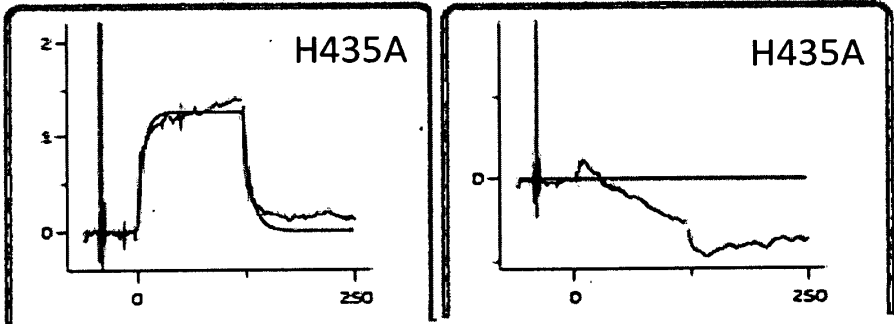


FIG. 7T

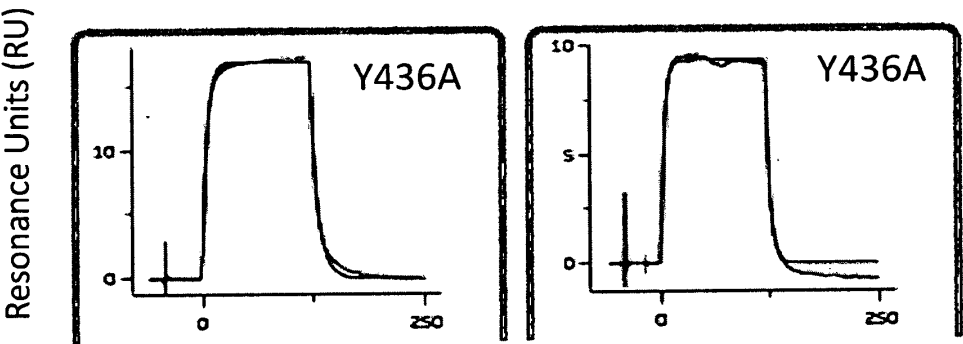


FIG. 7U

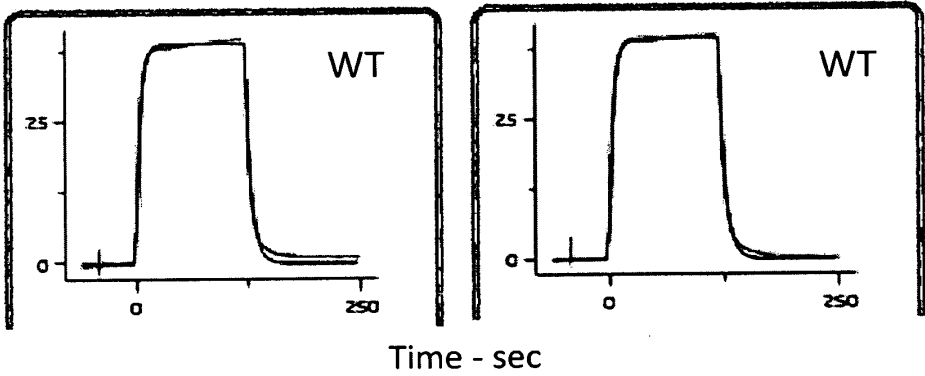


FIG. 8A

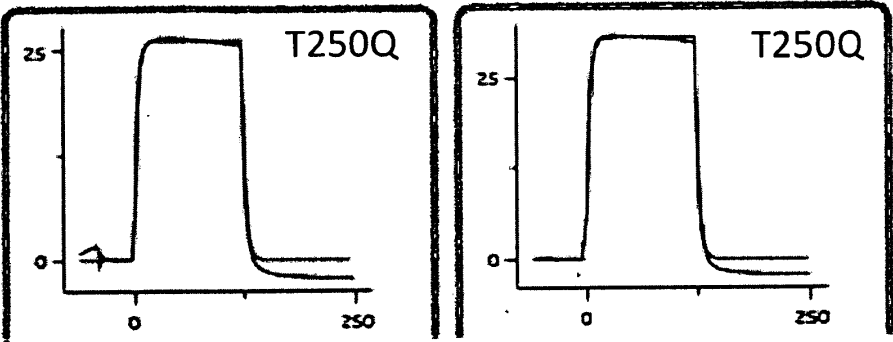


FIG. 8B

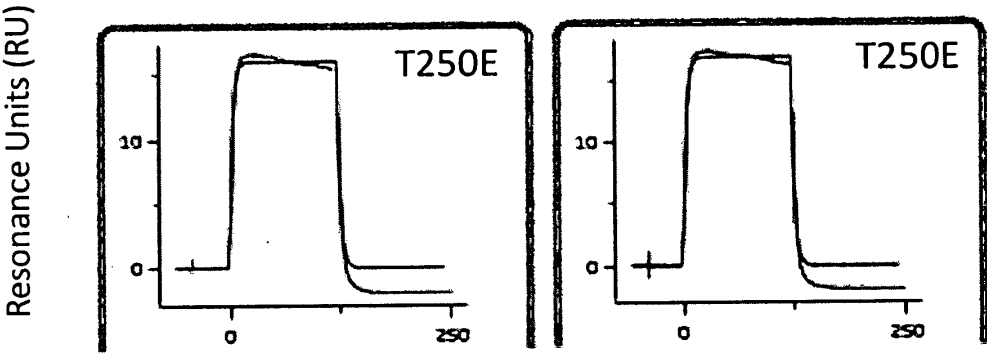
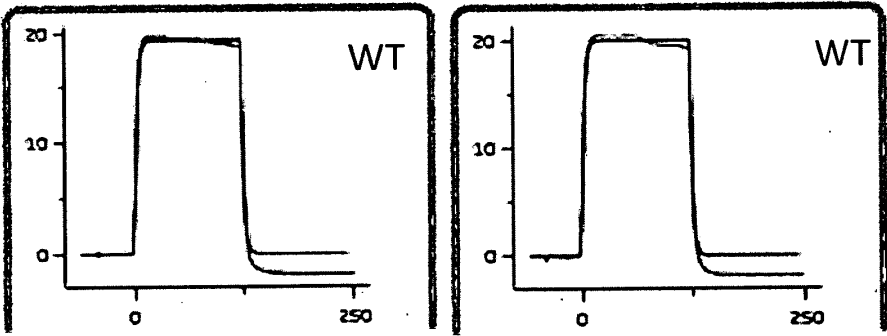


FIG. 8C



Time - sec

FIG. 9A

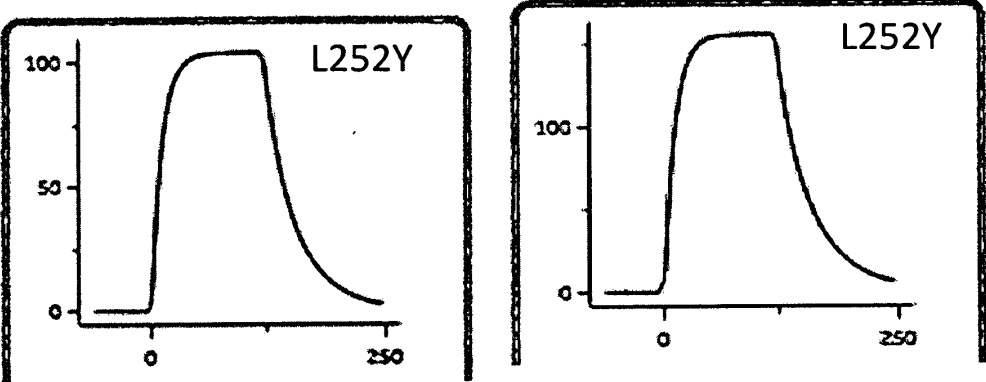


FIG. 9B

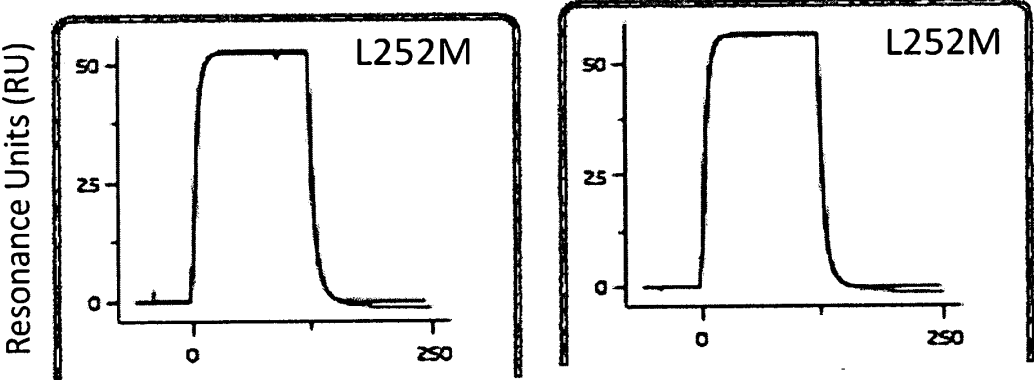
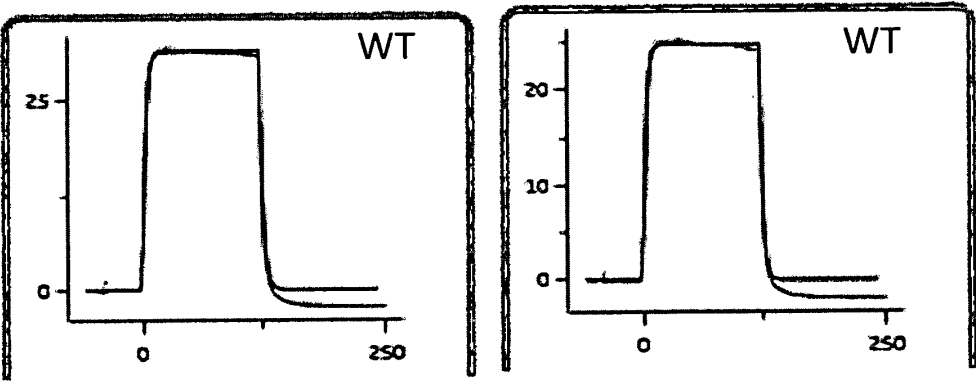


FIG. 9C



Time - sec

FIG. 10A

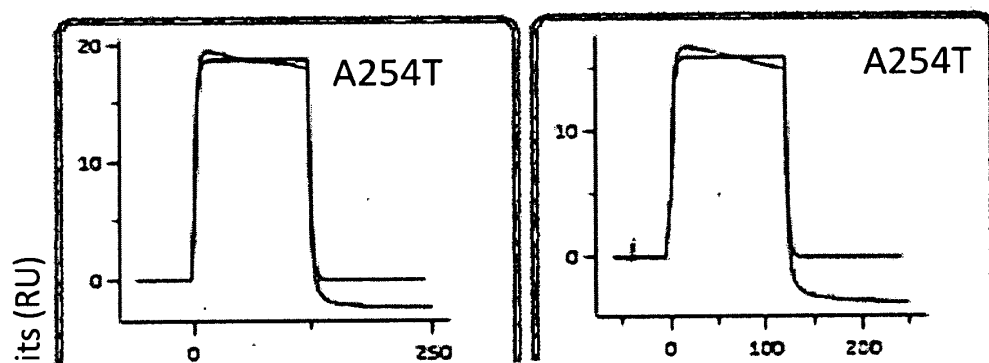
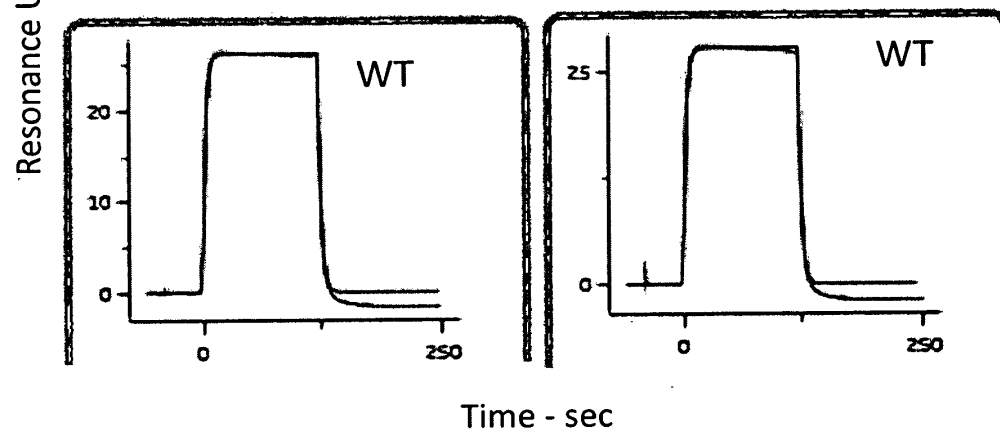


FIG. 10B



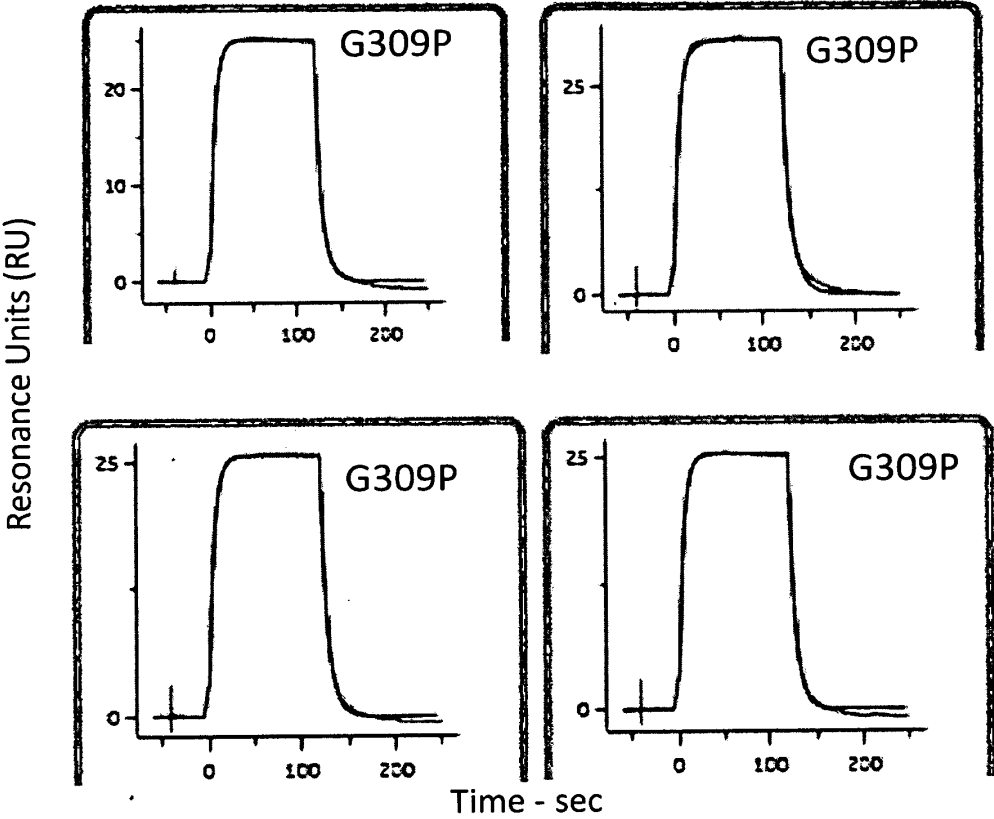


FIG. 11A

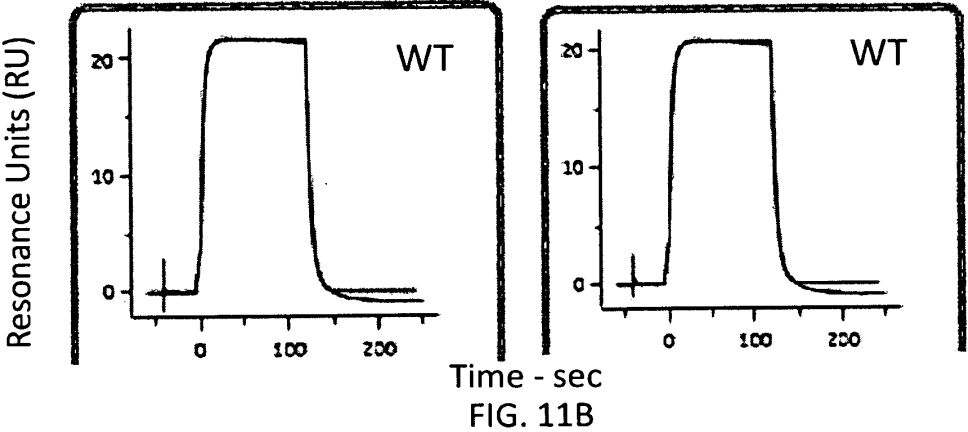


FIG. 11B

FIG. 12A

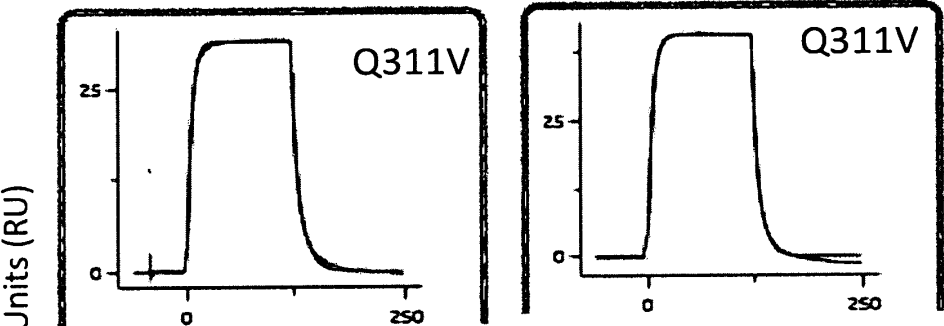
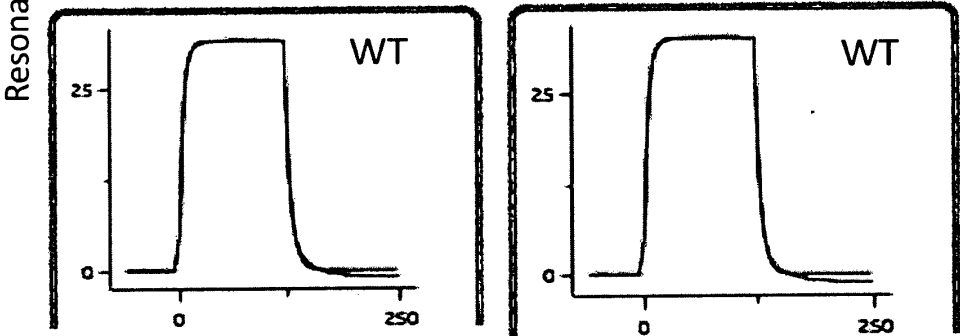


FIG. 12B



Time - sec

FIG. 13A

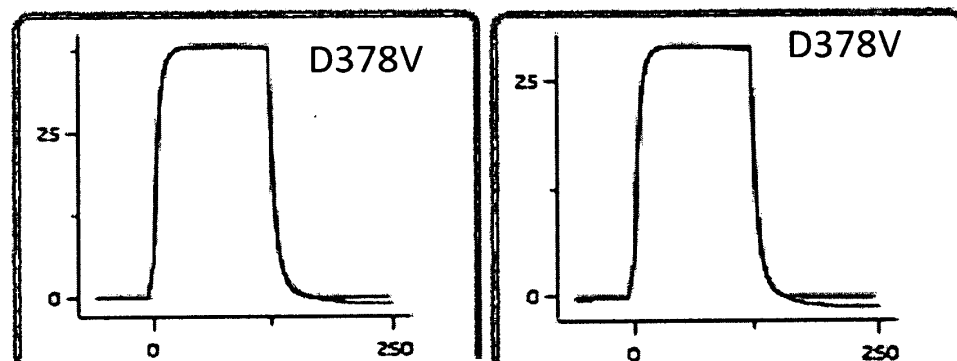


FIG. 13B

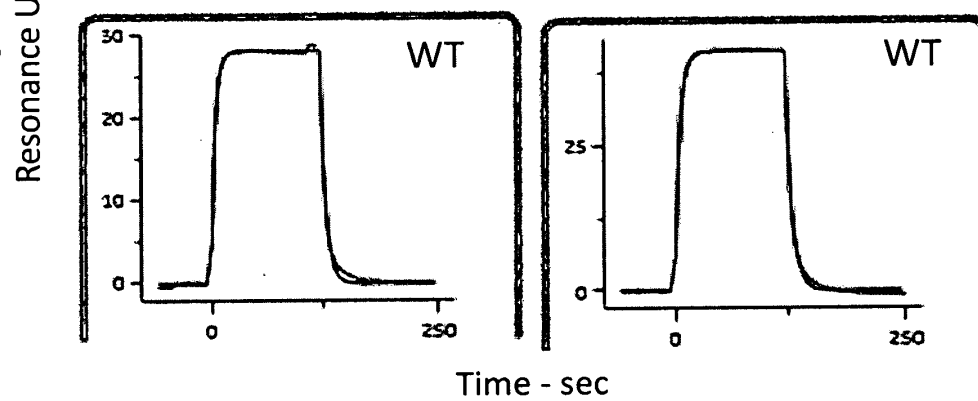


FIG. 14A

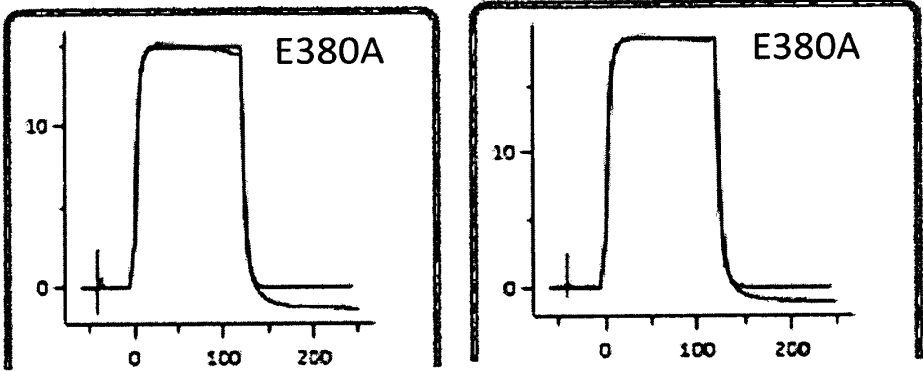
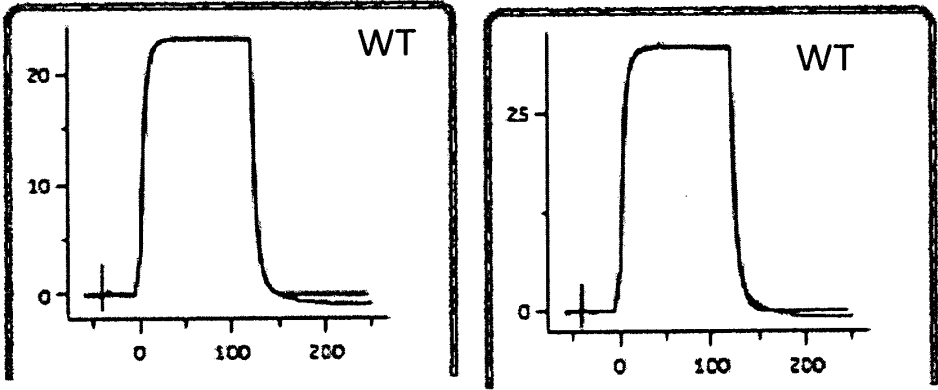


FIG. 14B



Time - sec

25/28

FIG. 15A

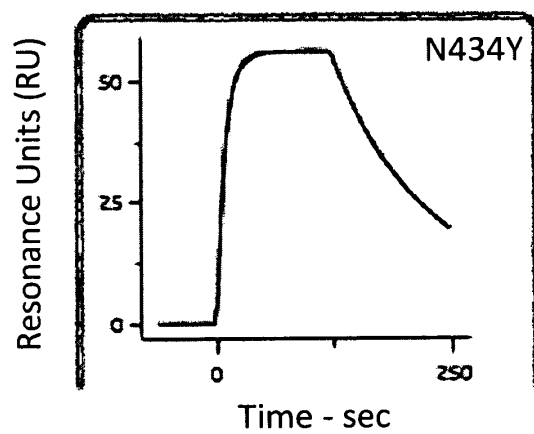


FIG. 15B

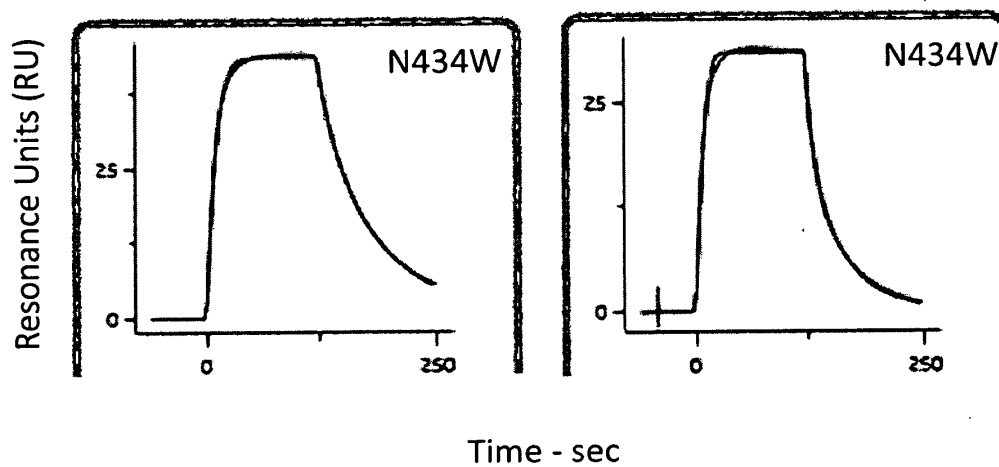


FIG. 15C

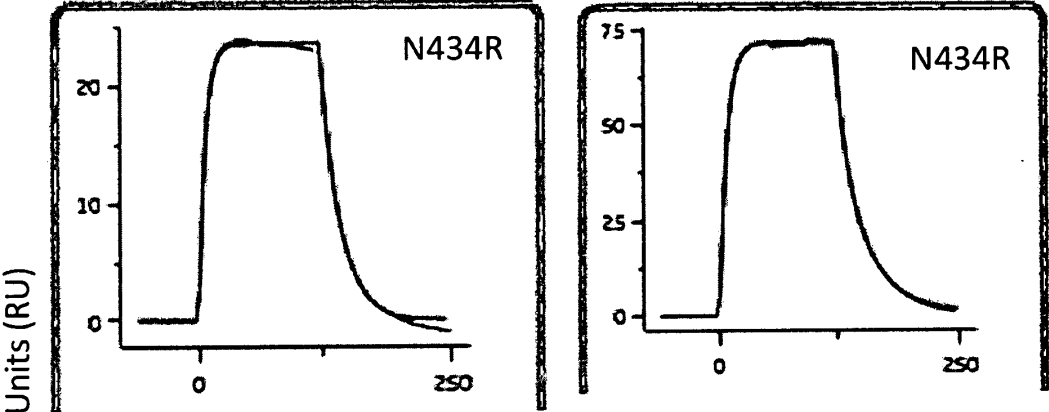
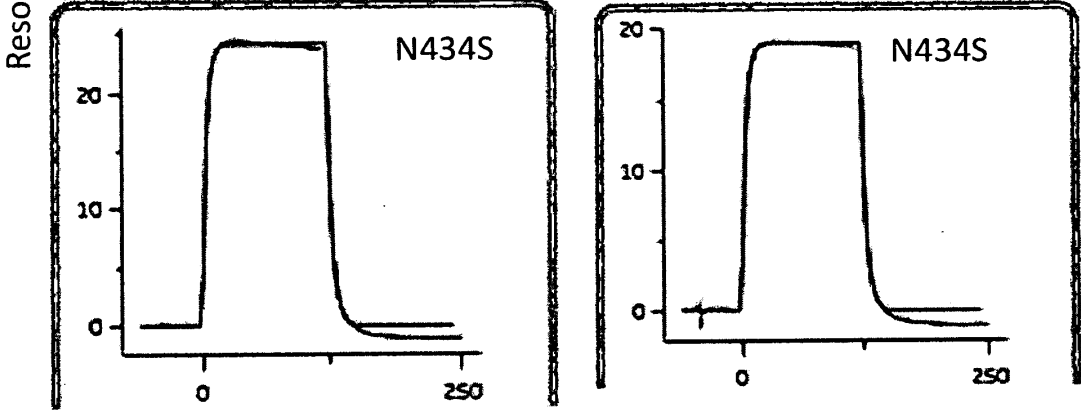


FIG. 15D



Time - sec

FIG. 15E

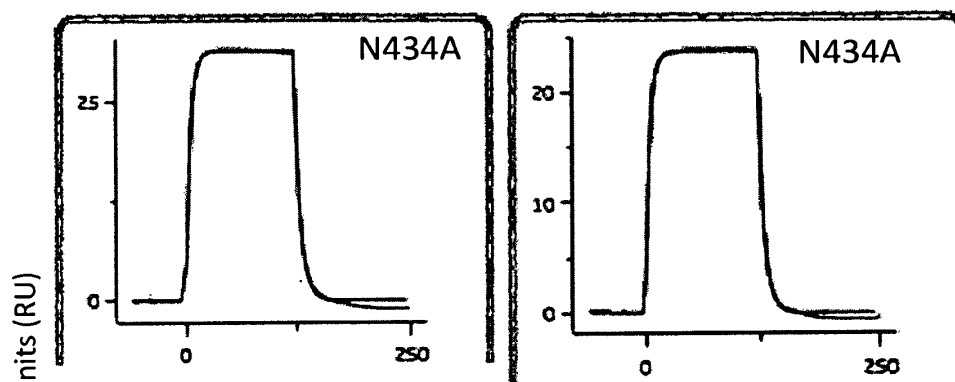
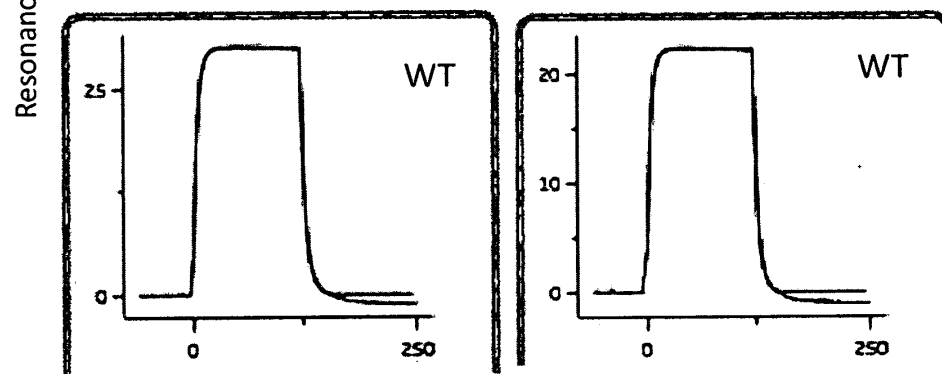


FIG. 15F



Time - sec

FIG.16A

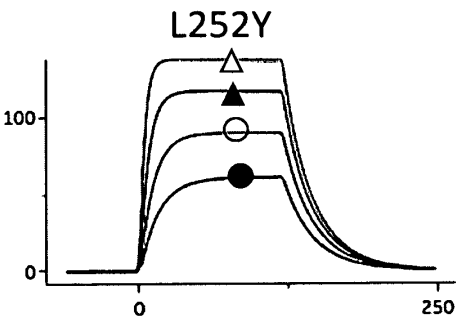


FIG.16B

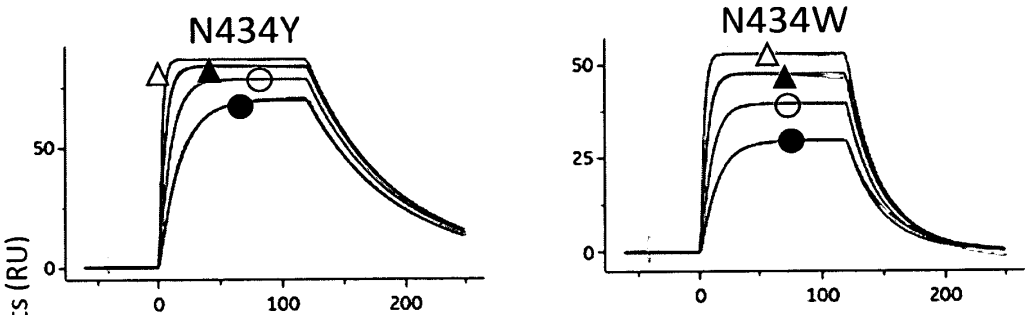


FIG.16C

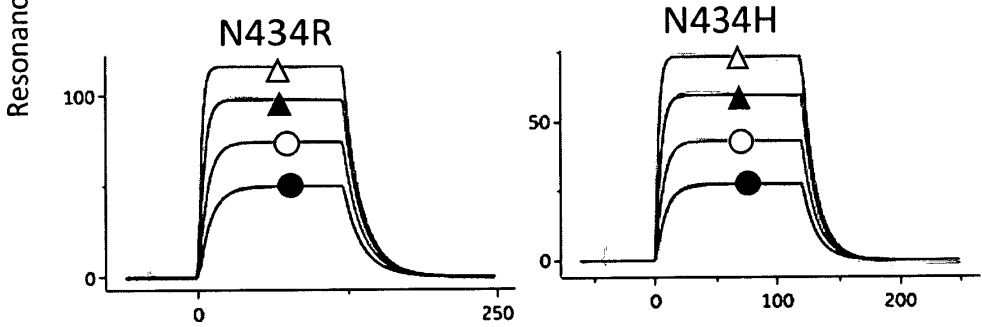


FIG.16D

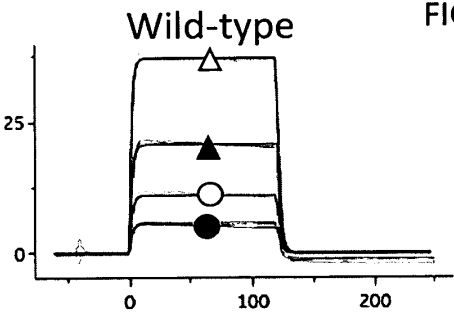
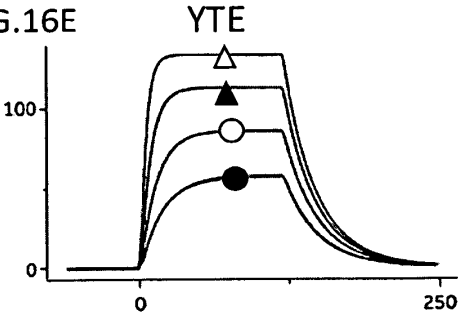


FIG.16E



Time - sec