

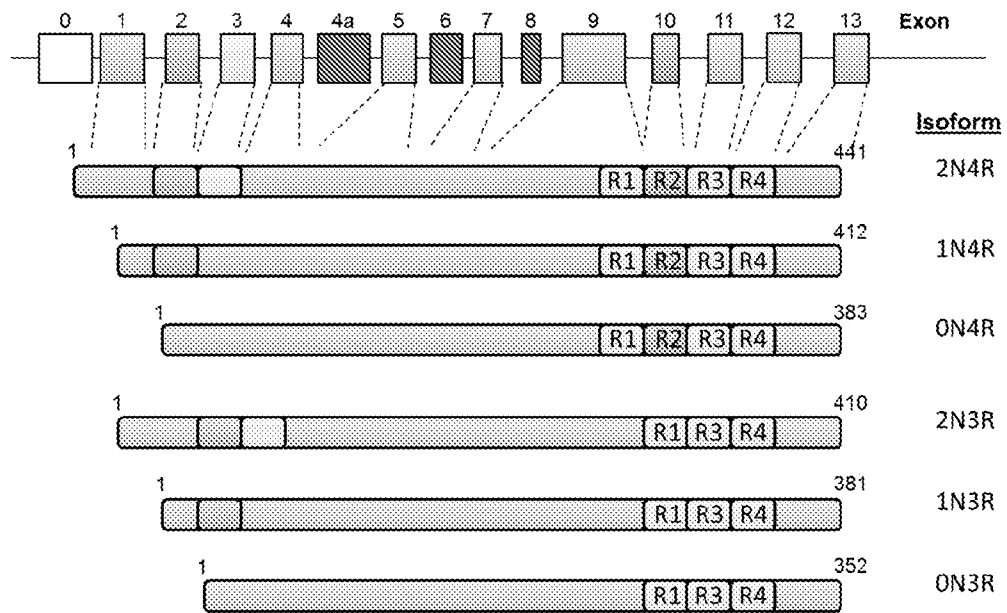
Figure 1

Figure 2

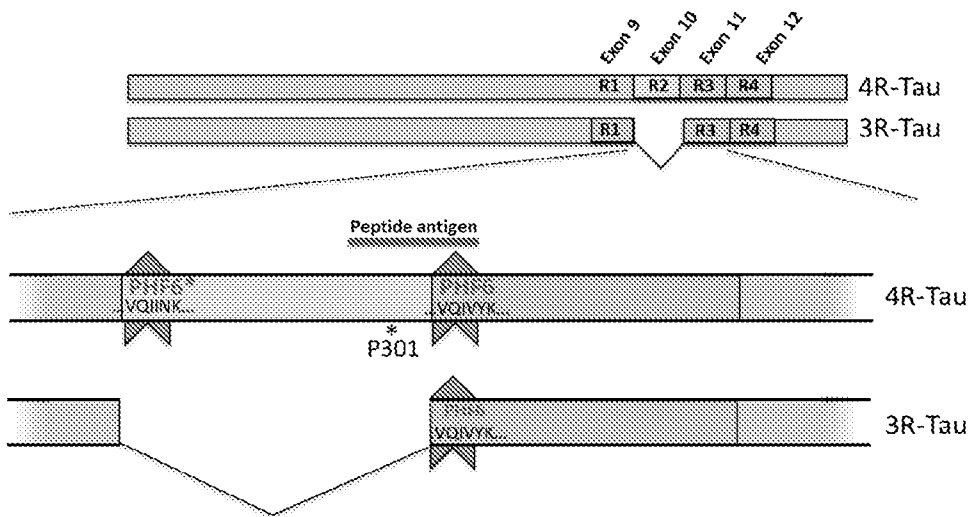


Figure 3A

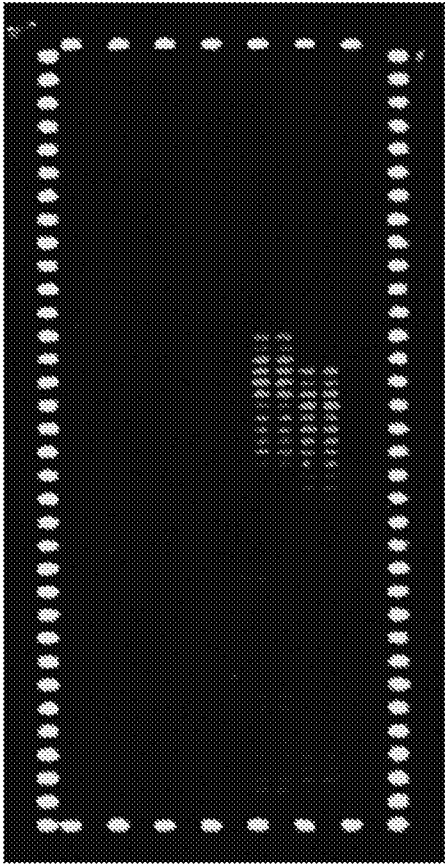


Figure 3B

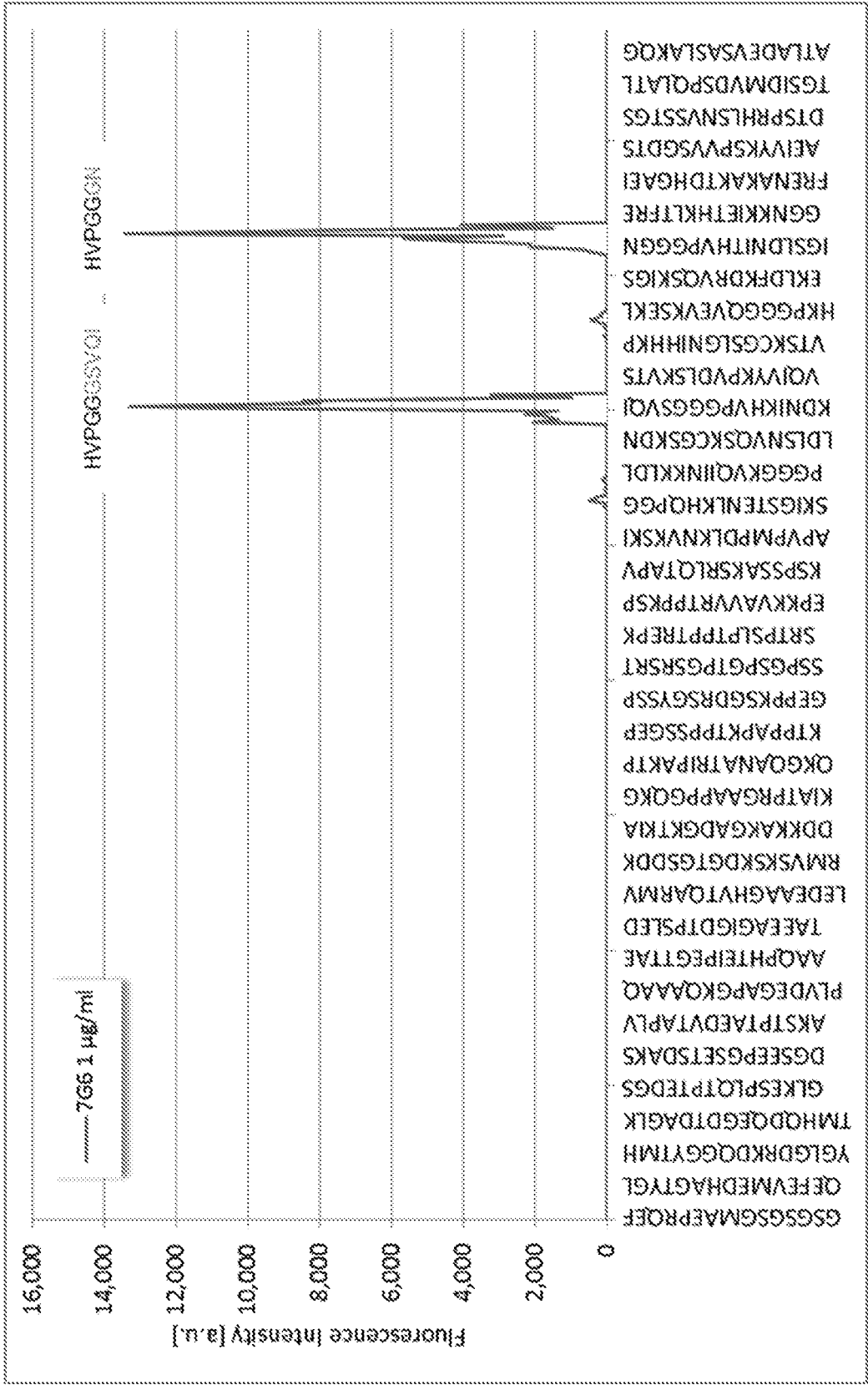


Figure 5A

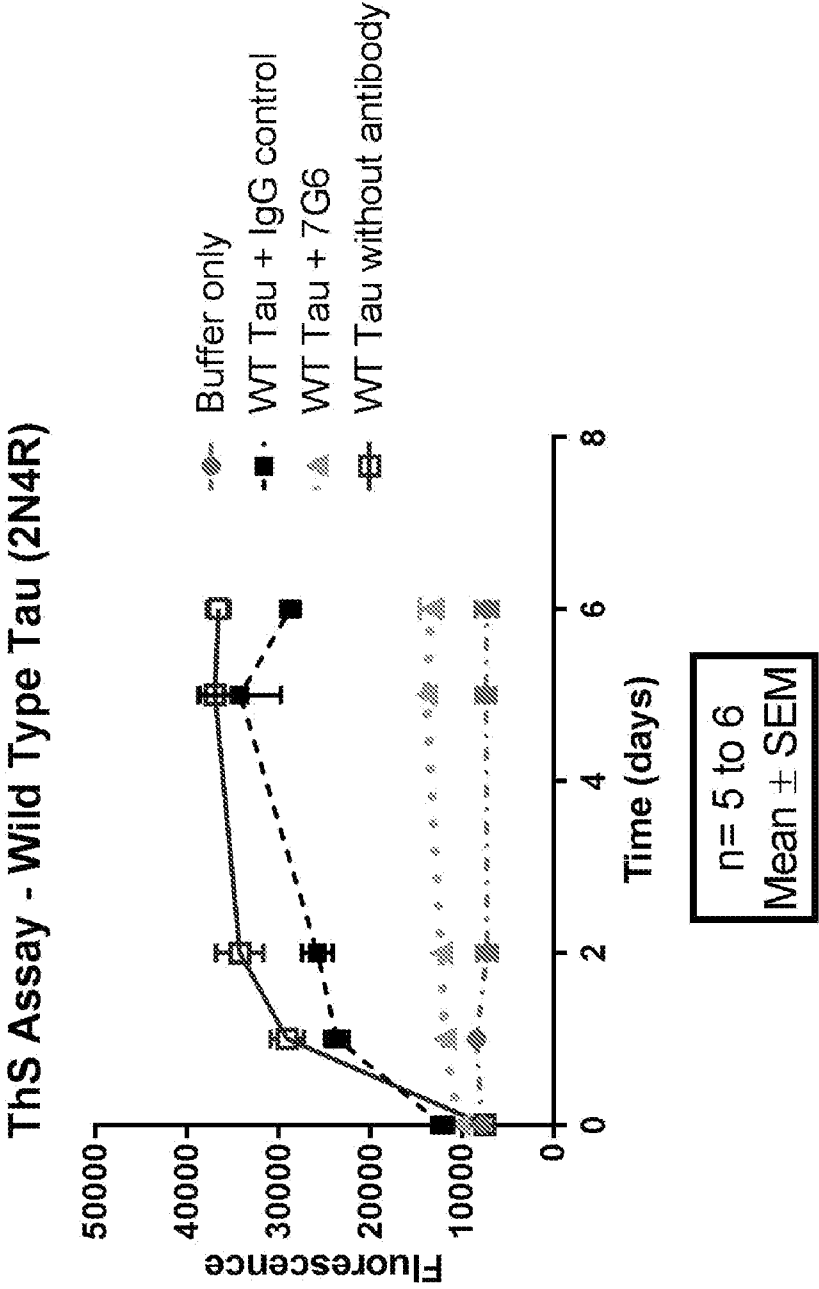


Figure 5B

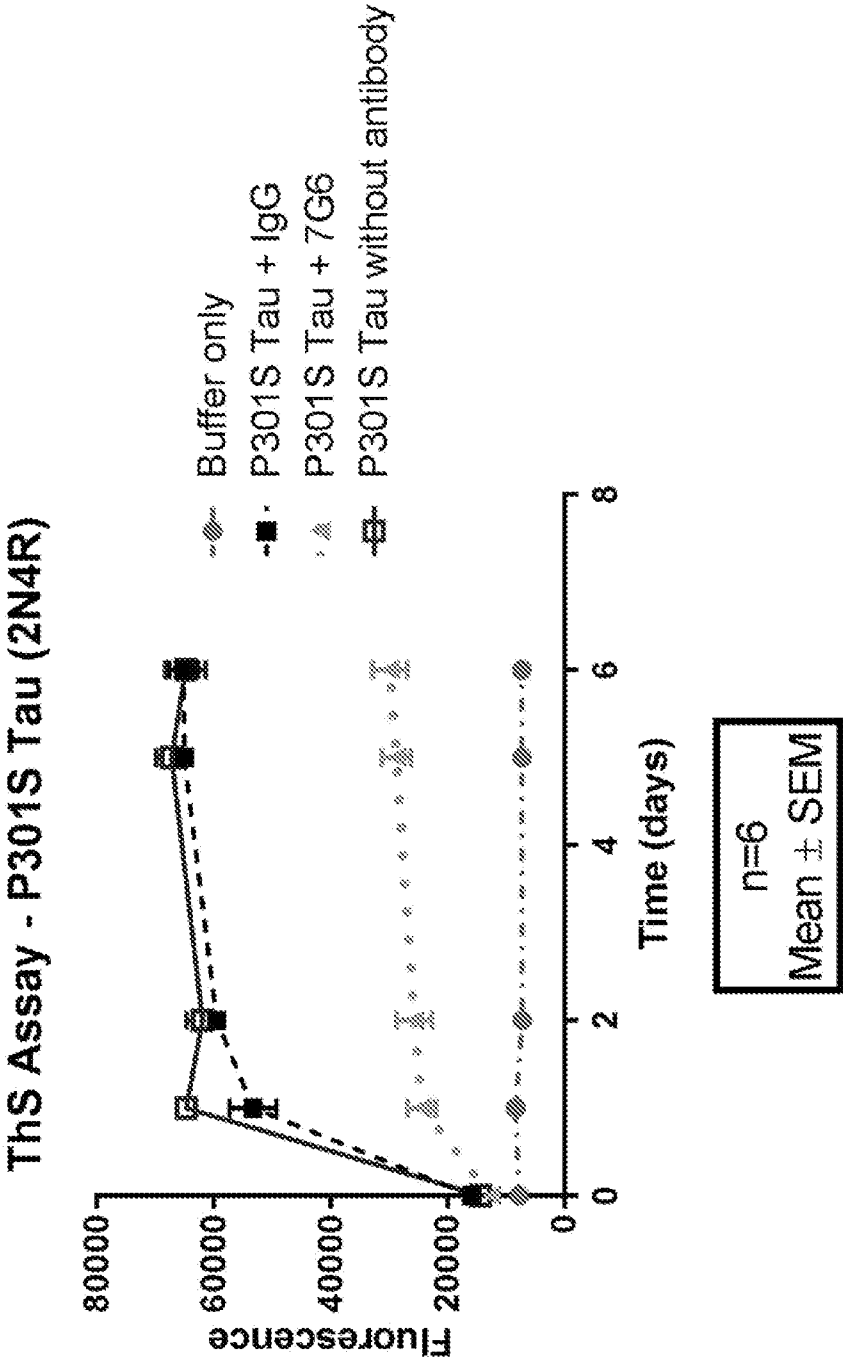


Figure 6A

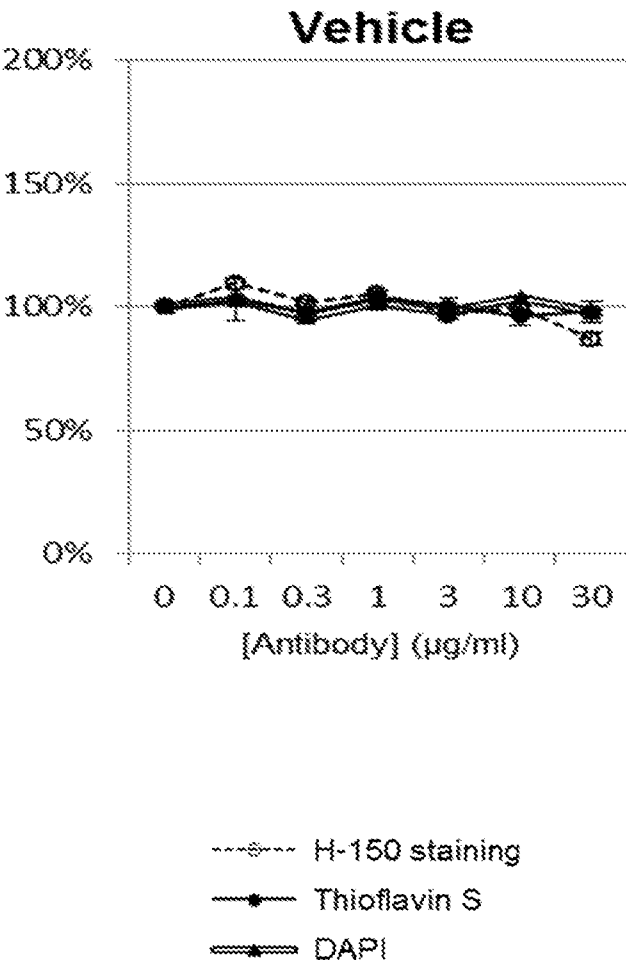
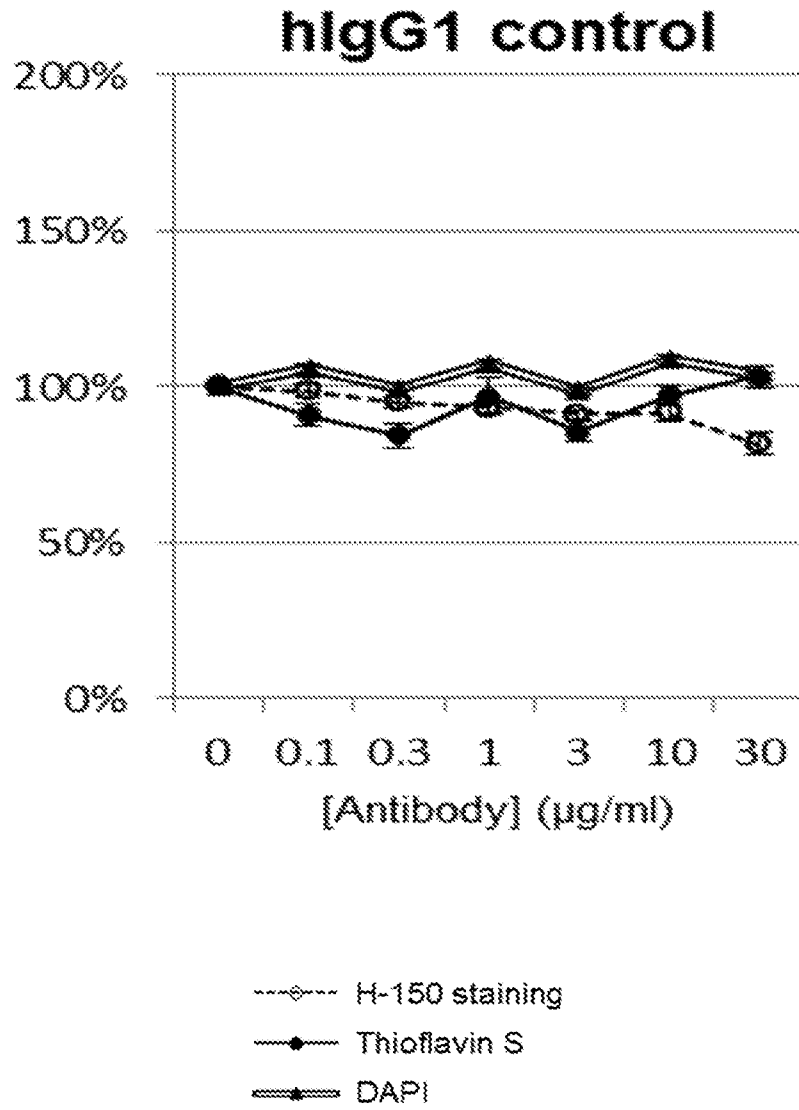


Figure 6B



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Figure 6C

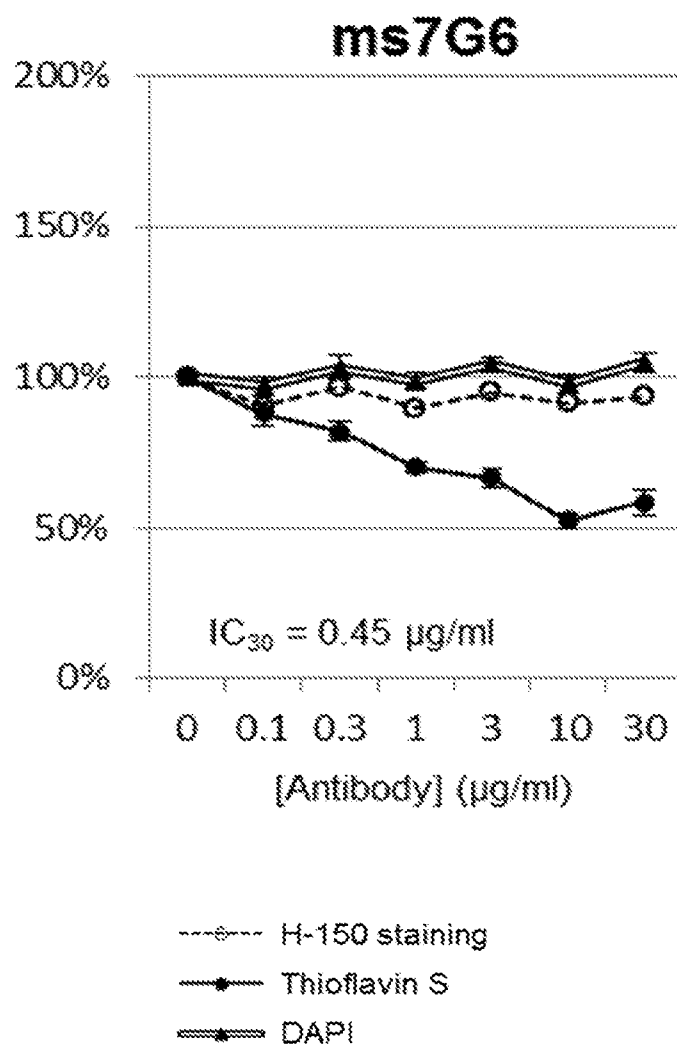


Figure 6D

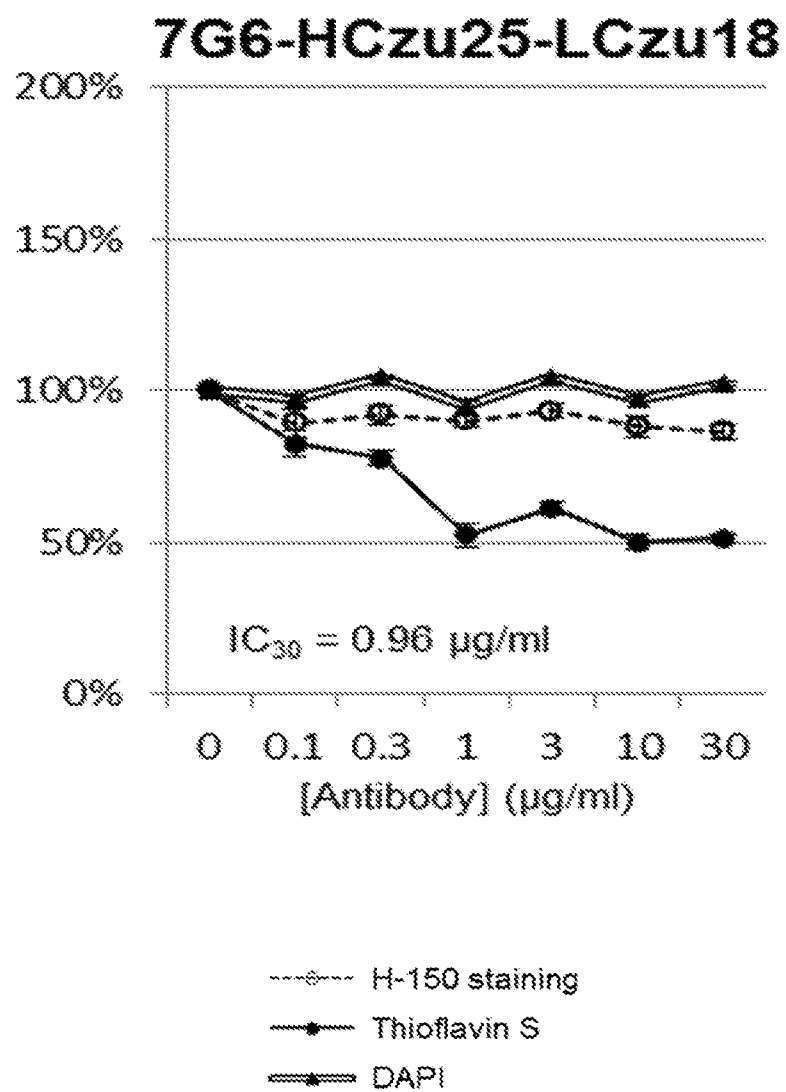


Figure 7

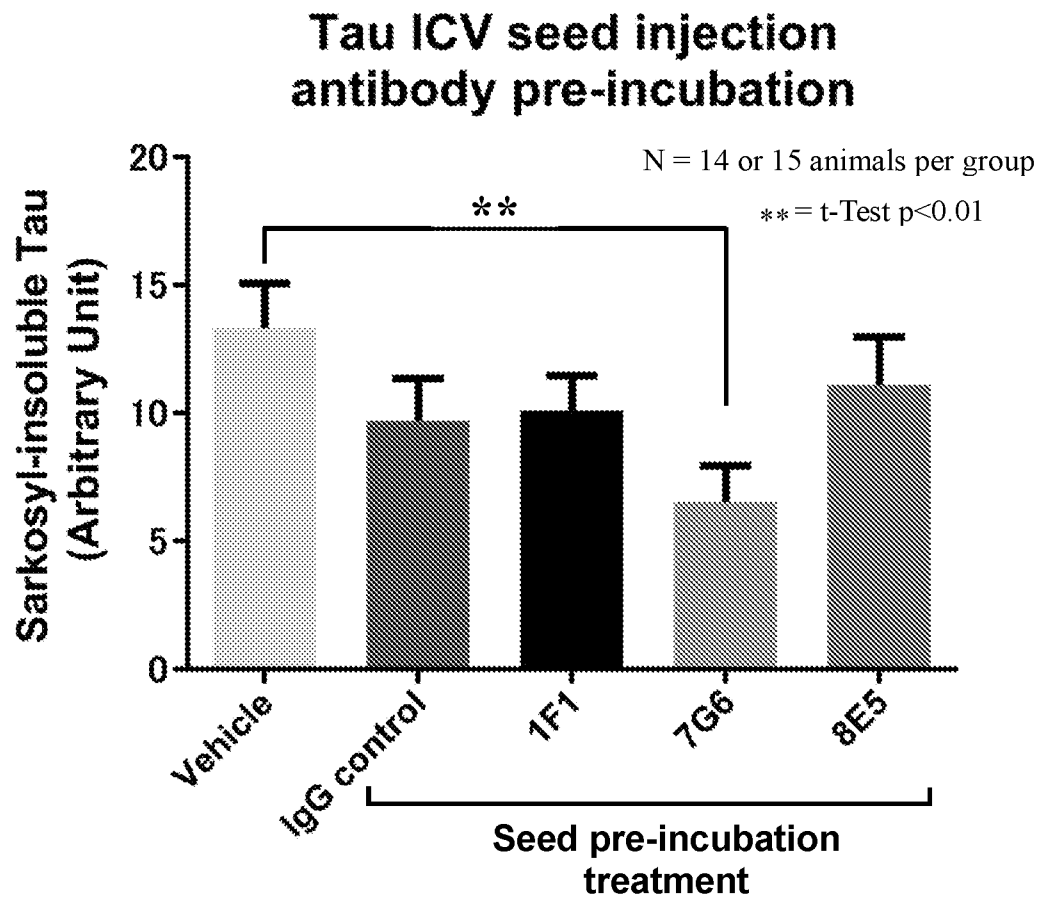
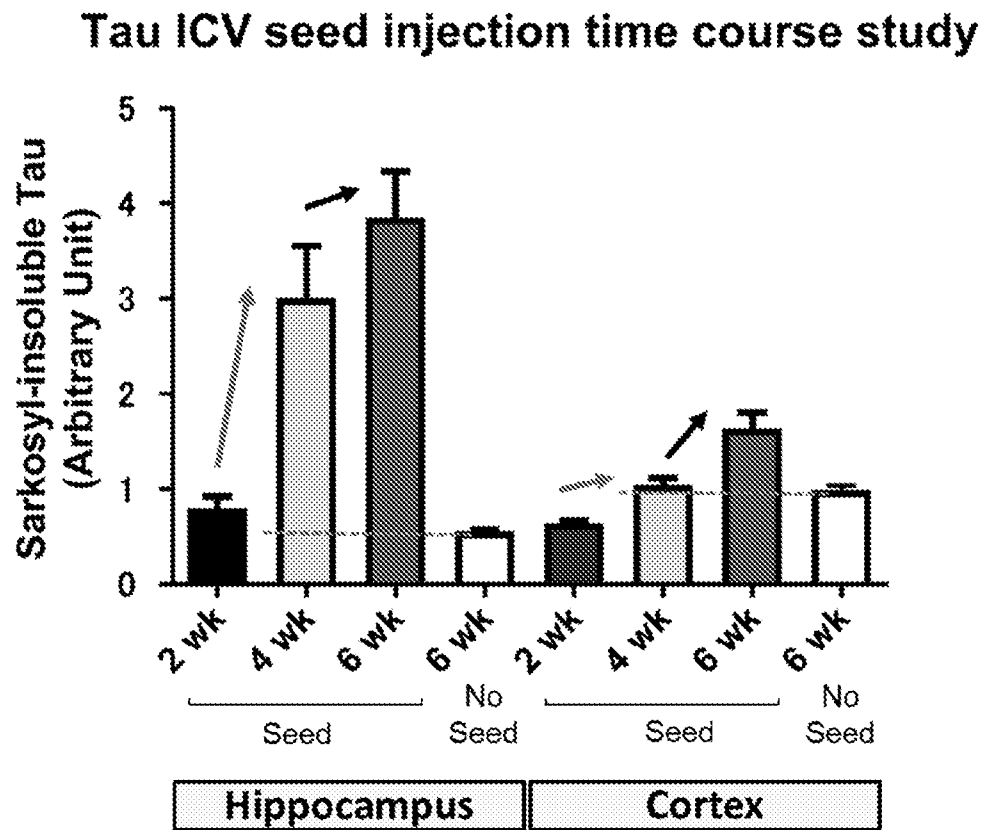


Figure 8

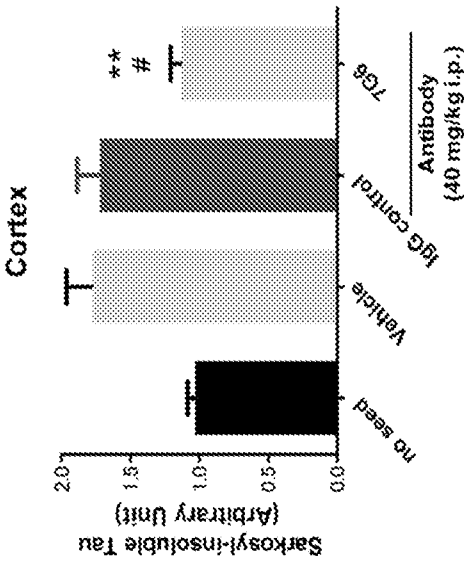
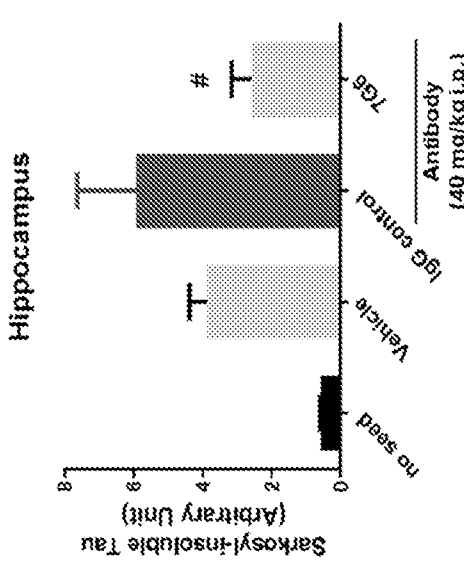


Mean $\pm$ SEM. N=10 (2 wk and 4 wk). N=16 or 17 (6 wk).

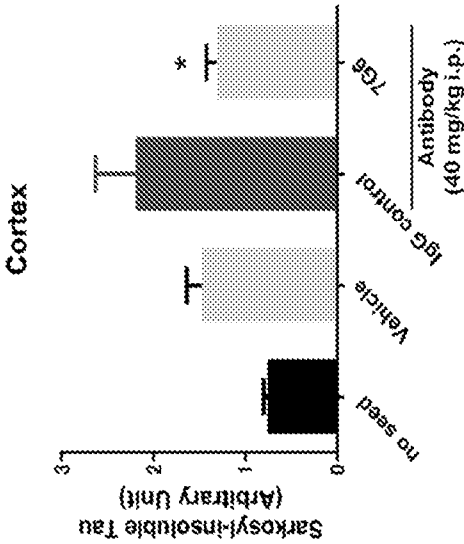
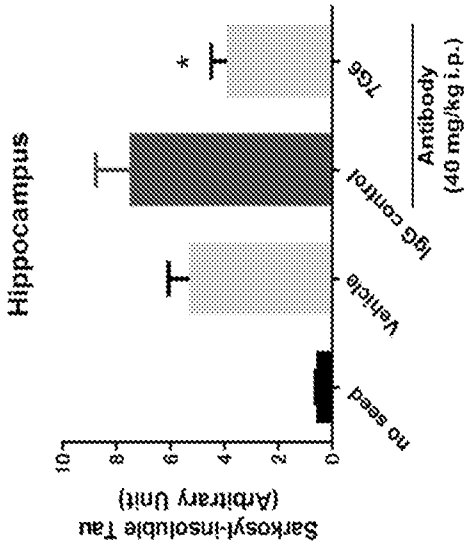
Figure 9

Experiment 1

Experiment 2



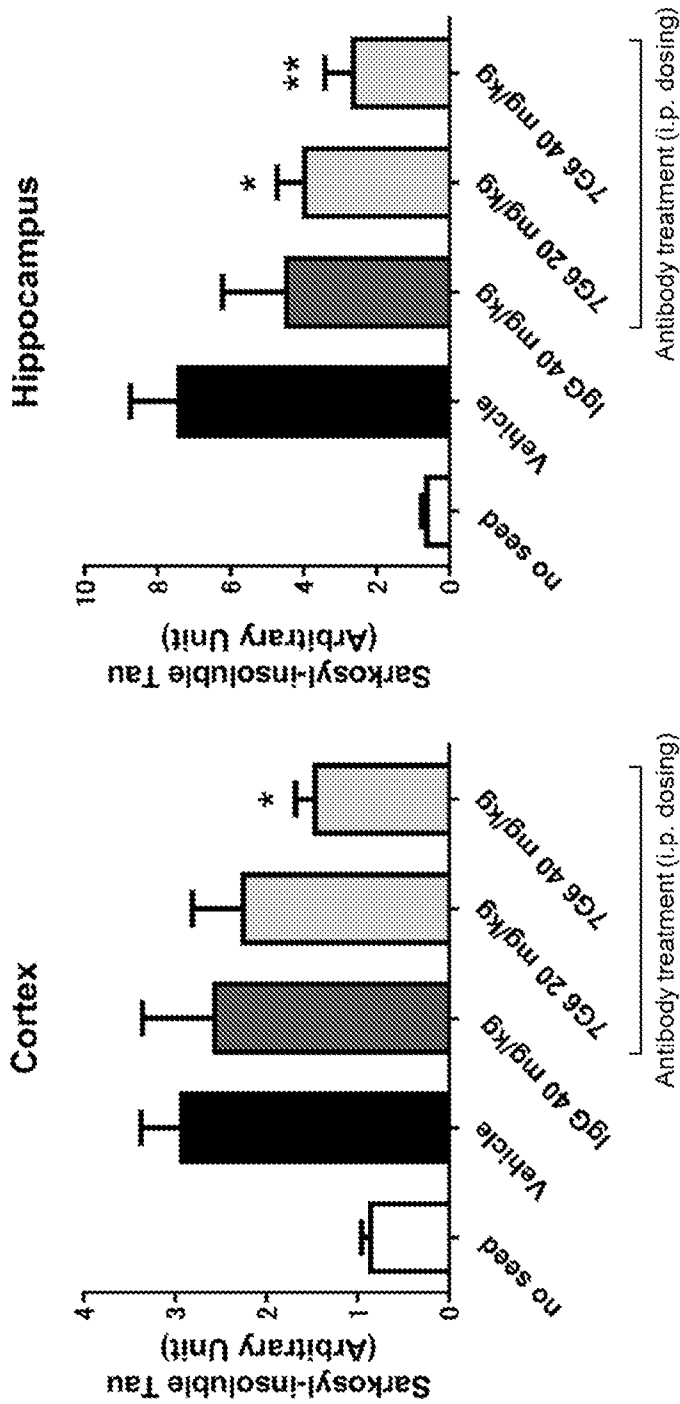
Mean $\pm$ SEM. N=16-17 (Vehicle, IgG, and TG6) N=5 (no seed).
*, p<0.01 versus buffer; #, p<0.05 versus IgG.
(One way ANOVA followed by Dunnett's test)



Mean $\pm$ SEM. N=22 (Vehicle, IgG, and TG6) N=6 (no seed).
*, p<0.05 versus IgG (One way ANOVA followed by Dunnett's test)

Figure 10

Experiment 3



Mean $\pm$ SEM. N=17 (Vehicle, 7G6 40 mg/kg). N=19 (IgG 40 mg/kg). N=20 (7G6 20 mg/kg). N=7 (no seed). **; $p < 0.01$ vs buffer, *; $p < 0.05$ vs buffer (One way ANOVA followed by Dunnett's test).

Figure 11

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IMGT      <-----FR1-IMGT-----><CDR1-I><-----FR2-IMGT-----><CDR2-I><-----FR3-IMGT-----><-----FR4----->
Kabat     <-----FR1-----><CDR><-----FR2-----><-----CDR2-----><-----FR3-----><-----CDR3-----><-----FR4----->
mouse 7G6  QVQLLPGAELVKPGASVIMSCKASGYTFITWVKQRPQGQLEWIGDIYPGSSICNYNNEKFKSKALTITVDITSSSTAMQINSLTSEDSAVYICAREDDGYDAWFAYWGQGTIVTVSA
IGHV1-46*03  ...V.S...VK.....KV.....S.YMH...R.A.....M.I.N.SGGSTS.AQ..QGRV.M.R...T.V..E.S..R...T.....S
IGHV1-46*01  ...V.S...VK.....KV.....S.YMH...R.A.....M.I.N.SGGSTS.AQ..QGRV.M.R...T.V..E.S..R...T.....S
IGHV1-2*02  ...V.S...VK.....KV.....G.YMH...R.A.....M.W.N.N.GGT..AQ..QGRV.M.R...I.....E.SR.R.D.T.....S

IMGT      <-----FR1-IMGT-----><CDR1-IMGT><-----FR2-IMGT-----><C><-----FR3-IMGT-----><-----FR4----->
Kabat     <-----FR1-----><-----CDR1-----><-----FR2-----><-----CDR2-----><-----FR3-----><-----CDR3-----><-----FR4----->
mouse 7G6  DVIMTQTPLSLPVSLGDAQSISCRSSQSIILHSGNNTYLEWYLQKPGQSPKLLICKVSNRFSGVDPDRFSGSGSGTDFTLKISRVEAEDLGVYYCFQGHVFTFGSGTKLEIK
IGKV2-30*02  .V...S.....T..QP.....LV..D...N.FQ.R....RR..Y....D.....D.....V....M..T.W.  ..Q.....
IGKV2-29*02  .IV.....S..TP..QP.....K...L...D.K...Y.....Q...YE..S.....Q.....V....M..I.L.  ..Q.....
IGKV2-29*03  .IV.....S..TP..QP.....K...L...D.K...Y.....Q...YE..S.....Q.....V....M..I.L.  ..Q.....

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Figure 12 – Humanized 7G6Vh1/Vk2 variants

IMGT	<-----FR1-IMGT-----><CDR1-I><-----FR2-IMGT-----><CDR2-I><-----FR3-IMGT-----><-----CDR3-----><-----FR4----->
Kabat	<-----FR1-IMGT-----><CDR><-----FR2-----><-----CDR2-----><-----FR3-----><-----CDR3-----><-----FR4----->
mouse	QVQLVQSGAEVKKPKGASVIMSCKASGYTFTTYWIITWVRQAPQGGLWIGDIYPGSSICNYNEKFKSRATLTVDTSSTAYMQLNSLTSEDSAVYYCAREDDGDAWFAYWGQGTILVTVSA
HCzu1	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSICNYNEKFKSRVTMTVDTSSTVYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu2	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSICNYNEKFKSRVTMTVDTSSTVYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu3	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSICNYNEKFKSRVTMTVDTSSTVYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu4	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSICNYAQKFQGRVTMTVDTSSTAYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu5	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSISNYNEKFKSRVTMTVDTSSTAYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu6	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSISNYNEKFKSRVTMTVDTSSTVYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu7	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSISNYAQKFQGRVTMTVDTSSTVYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu8	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSISNYAQKFQGRVTMTVDTSSTVYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu9	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSICNYAQKFQGRVTMTVDTSSTVYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
HCzu10	QVQLVQSGAEVKKPKGASVKVSCKASGYTFTTYWIITWVRQAPQGGLWMDIYPGSSICNYAQKFQGRVTMTVDTSSTVYMELSSLRSEDTAVYYCAREDDGDAWFAYWGQGTILVTVSS
IMGT	<-----FR1-IMGT-----><CDR1-IMGT><-----FR2-IMGT-----><C><-----FR3-IMGT-----><-----CDR3-----><-----FR4----->
Kabat	<-----FR1-----><-----CDR1-----><-----FR2-----><-----FR3-----><-----CDR3-----><-----FR4----->
mouse	DVLMQTPLSLPVLIGDQASISCRSSQSIILHSGNTYLEWYLQKPGQSPKLLICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDLGVYYCFQGSHPVPTFGSGTKLEIK
LCzu1	DVMTQSPSLPVLIGQPASISCRSSQSIILHSGNTYLEWYFQQRPGQSPRLIYKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu2	DVMTQSPSLPVLIGQPASISCRSSQSIILHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu3	DVMTQSPSLPVLIGQPASISCRSSQSIILHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu4	DVMTQSPSLPVLIGQPASISCRSSQSIILHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu5	DVMTQSPSLPVLIGQPASISCRSSQSIILHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu6	DVMTQSPSLPVLIGQPASISCRSSQSIILHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu7	DVMTQSPSLPVLIGQPASISCRSSQSIIVHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu8	DVMTQSPSLPVLIGQPASISCRSSQSIIVHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu9	DVMTQSPSLPVLIGQPASISCRSSQSIIVHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu10	DVMTQSPSLPVLIGQPASISCRSSQSIIVHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu21	DVMTQSPSLPVLIGQPASISCRSSQSIILHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK
LCzu22	DVMTQSPSLPVLIGQPASISCRSSQSIILHSGNTYLEWYFQQRPGQSPRLIICKVSNRFGVDPDRFSGSGGTDTFLIKISRVEAEDVGVYYCFQGSHPVPTFGQGTLEIK

Figure 13A

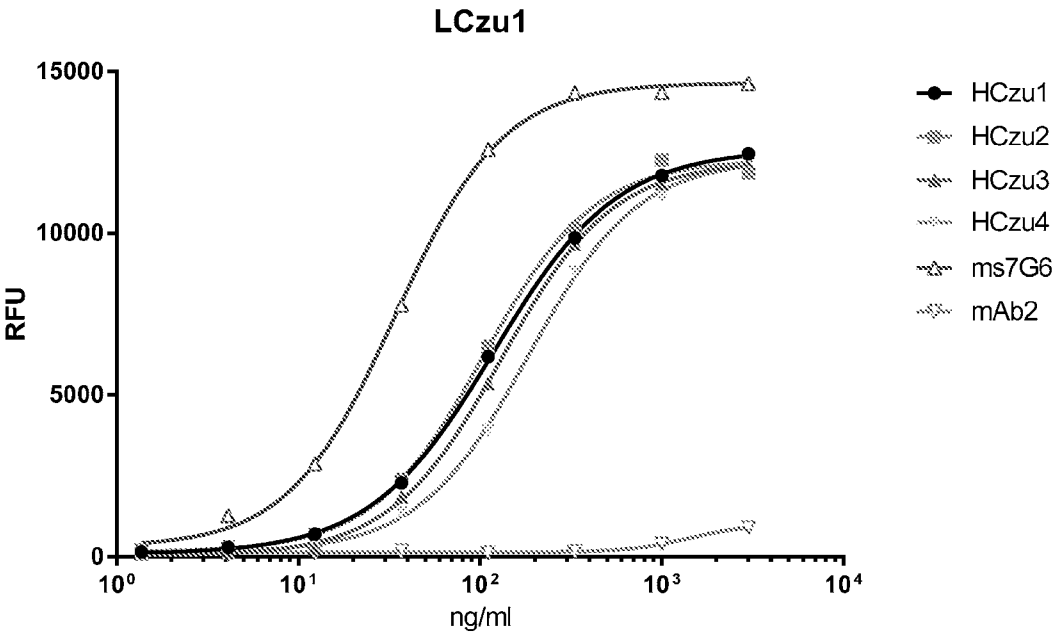


Figure 13B

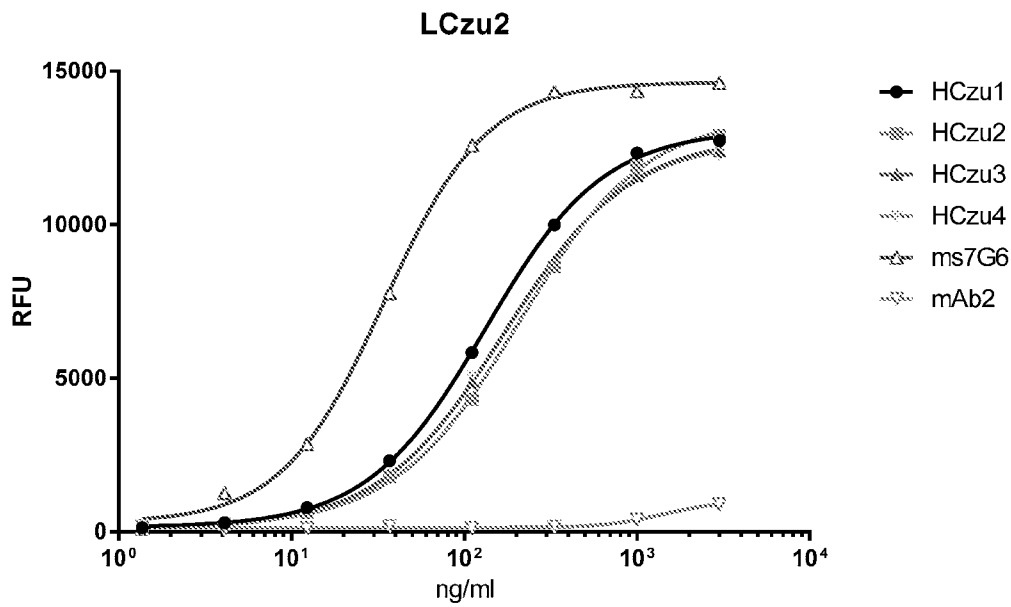


Figure 13C

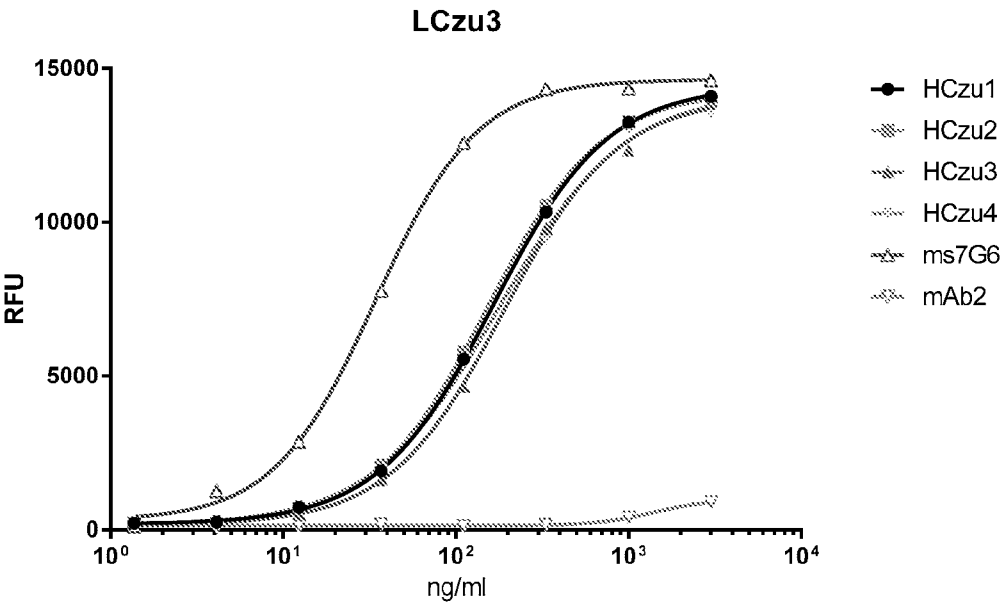


Figure 13D

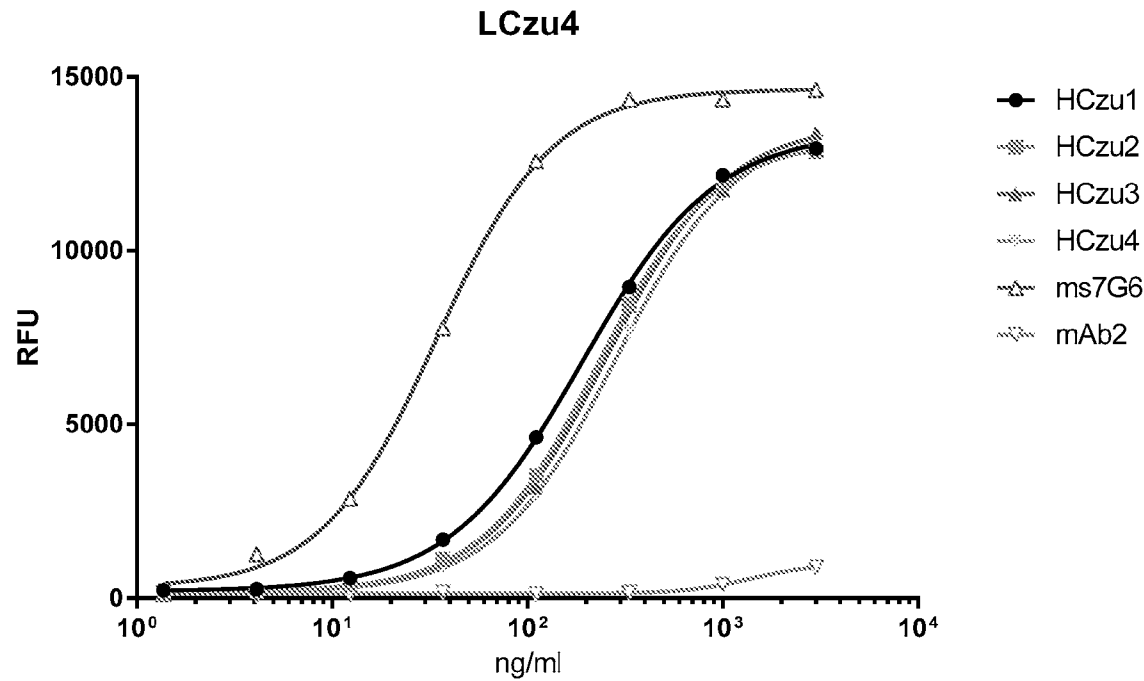


Figure 13E

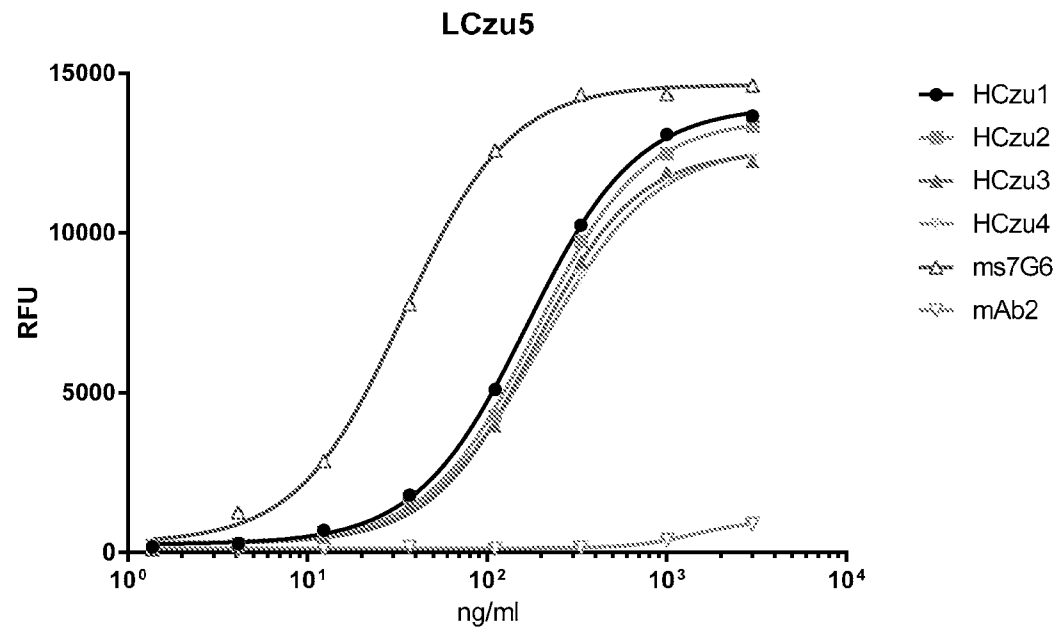


Figure 13F

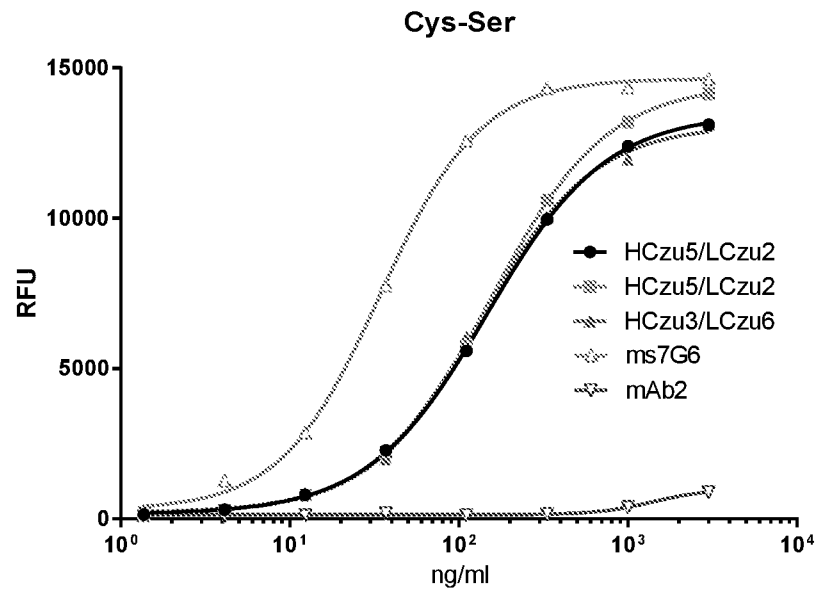


Figure 14

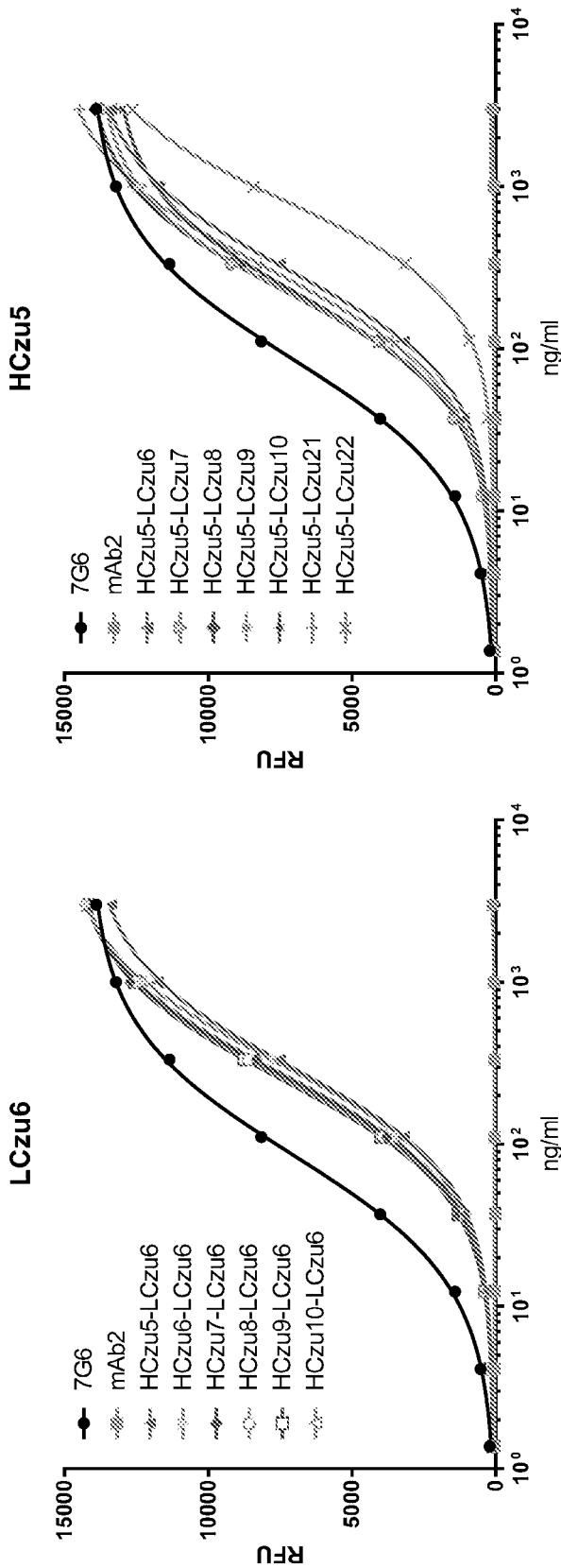


Figure 15

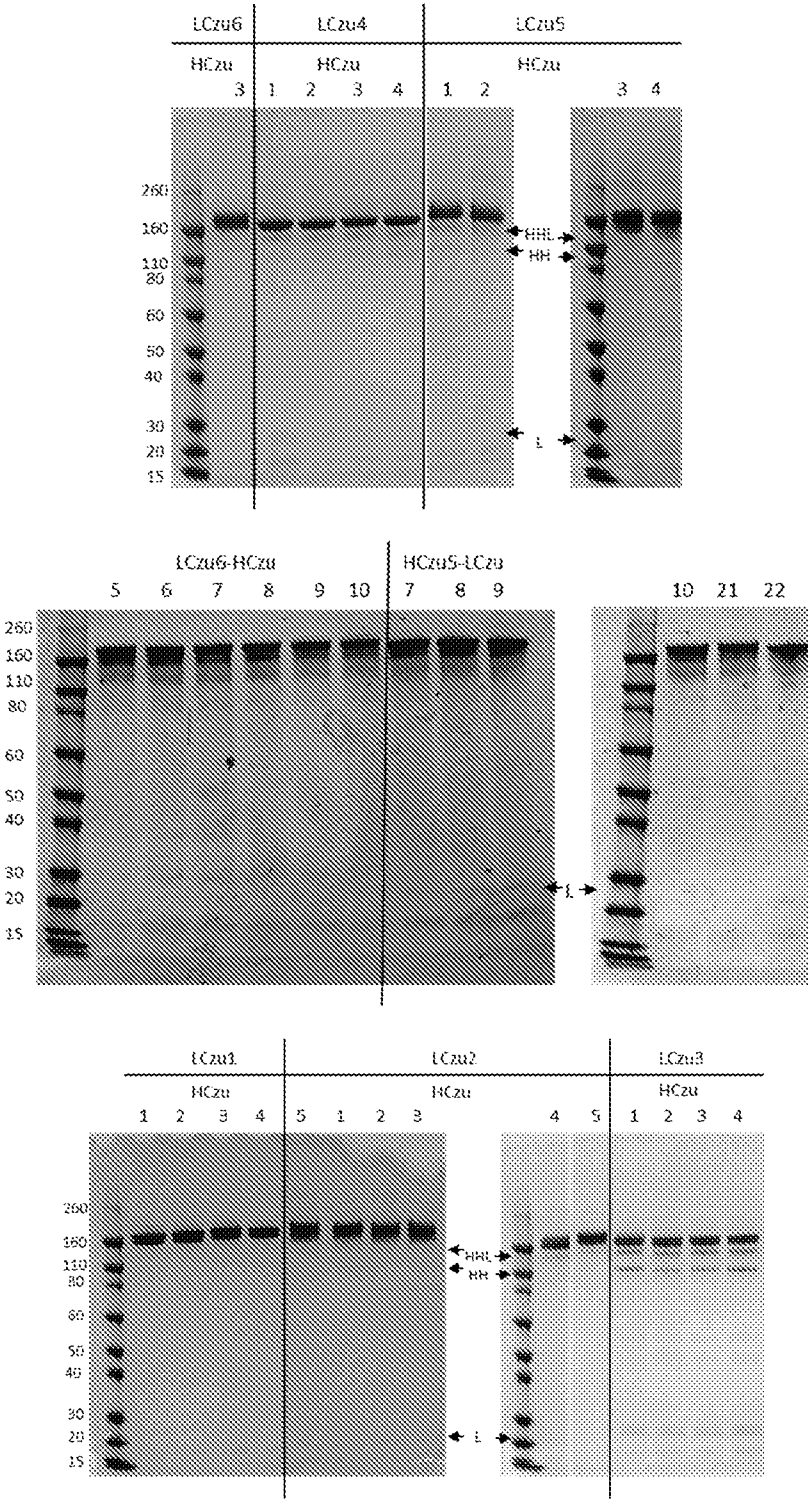


Figure 16

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IMGT numbering  <-----FR1-IMGT-----><CDR1-I><-----FR2-IMGT-----><CDR2-I><-----FR3-IMGT-----><-----FR4----->
Kabat numbering  <-----FR1-----><CDR><-----FR2-----><-----CDR2-----><-----FR3-----><-----FR4----->
7G6-VH          QVQLLPQGAELVKPGASVIMSCKASGYTFTTWTWVKQRPQGLEWIGDIYPGSSICNYNEKFKSKATLTVTSSTAYMQLNSLTSEDSAVYICAREDGVDWAFYWGQGLTVTVSA
IGHV3-23*03     E....ES.GG..Q..G..LRL..A...F..SS.AMS..R.A..K....VSV..S.G.STY.ADSV.GRF.ISR.N.KN..L.I.M..R.A..T.....K.....S
IGHV3-30*02     ....VES.GGV.Q..G..LRL..A...F..SS.GMH..R.A..K....VAF.RYDG.NKY.ADSV.GRF.ISR.N.KN..L.I.M..R.A..T.....K.....S

HCzu11          EVQLLESGGGLVQPGGSLRLSCAASGYTFTTWTWVRQAPGKLEWVSDIYPGSSICNYNEKFKSRFTISRDNKNTLYIQMNSLRAEDTAVYICAREDGVDWAFYWGQGLTVTVSS

IMGT numbering  <-----FR1-IMGT-----><CDR1-IMGT><-----FR2-IMGT-----><C><-----FR3-IMGT-----><-----FR4----->
Kabat numbering  <-----FR1-----><-----CDR1-----><-----FR2-----><-----FR3-----><-----FR4----->
7G6-VL          DVLMTQTPLSLPVSLIGDQASISCRSSQSIILHSNGNTYLEWYLQKPGQSPKLLICKVSNRFSGVDPDRFSGSGGTDFTLKISRVEAEDIGVYCFQGSHPVFTFGSGTKLEIK
IGKV1-39*01     .IQ...S..S..SA.V..RVT..T..A...-----SS..N..Q....KA....YAA.SLQ....S.....T..SLQP..FAT...Q..SYST..Q.....
IGKV1-17*01     .IQ...S..S..SA.V..RVT..T..A..G.-----RND.G..Q....KA..R..YAA.SLQ....S.....E...T..SLQP..FAT...L.HNSY..Q.....

LCzu11          DIQMTQSPSSLSASVGDRVTITCRSSQSIILHSNGNTYLEWYQKPKAPKLLIYKVSNRFSGVPSRFSGSGGTDFTLTISLQPEDFATYYCFQGSHPVFTFGSGTKLEIK

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Figure 17

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IMGT  <-----FR1-IMGT-----><CDR1-I><---FR2-IMGT-----><CDR2-I><-----FR3-IMGT-----><---CDR3---><---FR4--->
Kabat  <-----FR1-----><CDR1-I><---FR2-IMGT-----><CDR2-----><-----FR3-----><---CDR3---><---FR4--->
mouse  QVQLLQPGAELVPGASVIMSCKASGYTFITYWITWVQKPGQGLEWIGDIYPGSSICNYNEKFKSKATITVDTSSTAYMQLNLSITSESAVYYCAREDDYDAWFAYWGQGTLVTVSSA
HCzu11 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYNEKFKSRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKEDGYDAWFAYWGQGTLVTVSS
HCzu12 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYNEKFKSRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu13 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYADSVKGRFTISVDNSKSTAYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu14 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYADKFKGRFTISVDNSKSTAYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu15 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYNEKFKSRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu16 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYNEKFKSRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu17 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYNEKFKSRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu18 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYNEKFKSRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu19 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu20 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKEDGYDAWFAYWGQGTLVTVSS
HCzu21 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSICNYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu23 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSISNYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu24 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSISNYNEKFKSRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS
HCzu25 EVQLLEGGGLVQPGGSLRLSCAASGYTFITYWITWVRQAPGRGLEWVSDIYPGSSISNYNEKFKSRFTISRDNKNTLYLQMNSLRAEDTAVYYCAREDDYDAWFAYWGQGTLVTVSS

IMGT  <-----FR1-IMGT-----><CDR1-IMGT><---FR2-IMGT-----><C><-----FR3-IMGT-----><---CDR3---><---FR4--->
Kabat  <-----FR1-----><---CDR1-----><---FR2-----><CDR2-><-----FR3-----><---CDR3---><---FR4--->
mouse  DVLMQTPLSLPVSLGDAQASISCRSSQSIILHSNGNTYLEWYLQKPGQSPKLLICKVSNRFGSVPDRFSGSGSGTDFTLKISRVEAEDLGVYCFQGSHVPTFTFGSGTKLEIK
LCzu11 DIQMTQSPSSLSASVGRVTITCRSSQSIILHSNGNTYLEWYQOKPGKAPKLLIYKVSNRFGSVPDRFSGSGSGTDFTLTISIQPEDFATYYCFQGSHPVPTFTFGQTKLEIK
LCzu12 DVQMTQSPSSLSASVGRVTITCRSSQSIILHSNGNTYLEWYQOKPGKAPKLLICKVSNRFGSVPDRFSGSGSGTDFTLTISIQPEDFATYYCFQGSHPVPTFTFGQTKLEIK
LCzu13 DVQMTQSPSSLSASVGRVTITCRSSQSIILHSNGNTYLEWYQOKPGKAPKLLICKVSNRFGSVPDRFSGSGSGTDFTLTISIQPEDFATYYCFQGSHPVPTFTFGQTKLEIK
LCzu14 DIQMTQSPSSLSASVGRVTITCRSSQSIILHSNGNTYLEWYQOKPGKAPKLLICKVSNRFGSVPDRFSGSGSGTDFTLTISIQPEDFATYYCFQGSHPVPTFTFGQTKLEIK
LCzu15 DVQMTQSPSSLSASVGRVTITCRSSQSIILHSNGNTYLEWYQOKPGKAPKLLISKVSNRFGSVPDRFSGSGSGTDFTLTISIQPEDFATYYCFQGSHPVPTFTFGQTKLEIK
LCzu16 DVQMTQSPSSLSASVGRVTITCRSSQSIIVHSNGNTYLEWYQOKPGKAPKLLISKVSNRFGSVPDRFSGSGSGTDFTLTISIQPEDFATYYCFQGSHPVPTFTFGQTKLEIK
LCzu17 DVQMTQSPSSLSASVGRVTITCRSSQSIIVHSNGNTYLEWYQOKPGKAPKLLISKVSNRFGSVPDRFSGSGSGTDFTLTISIQPEDFATYYCFQGSHPVPTFTFGQTKLEIK
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Figure 18

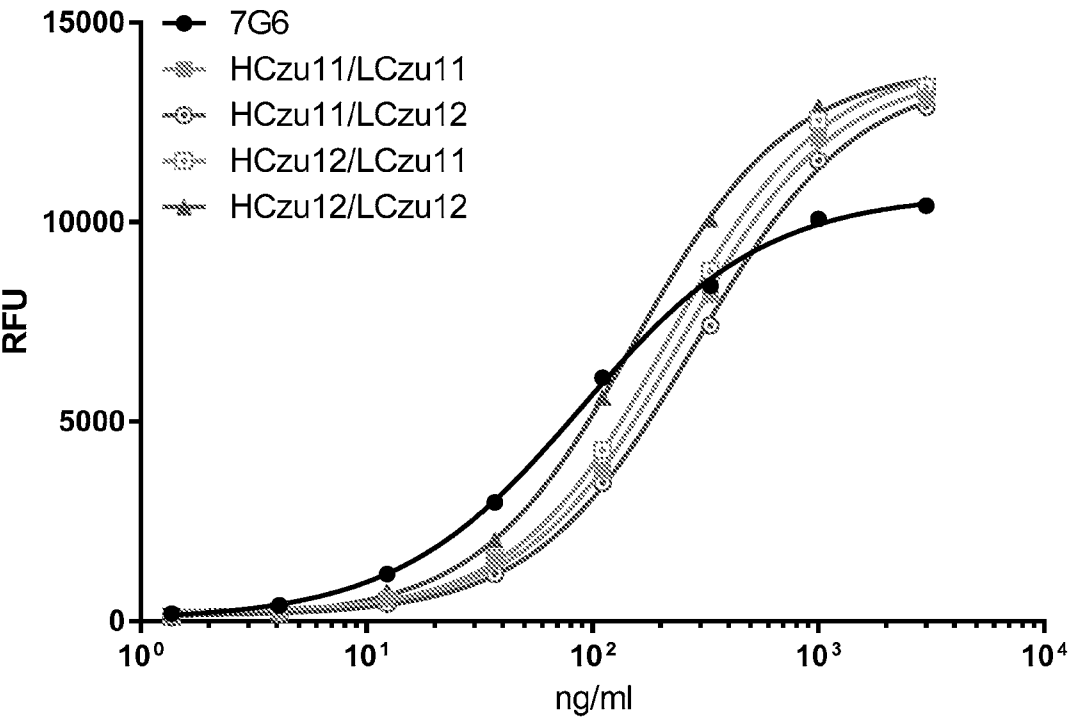


Figure 19A

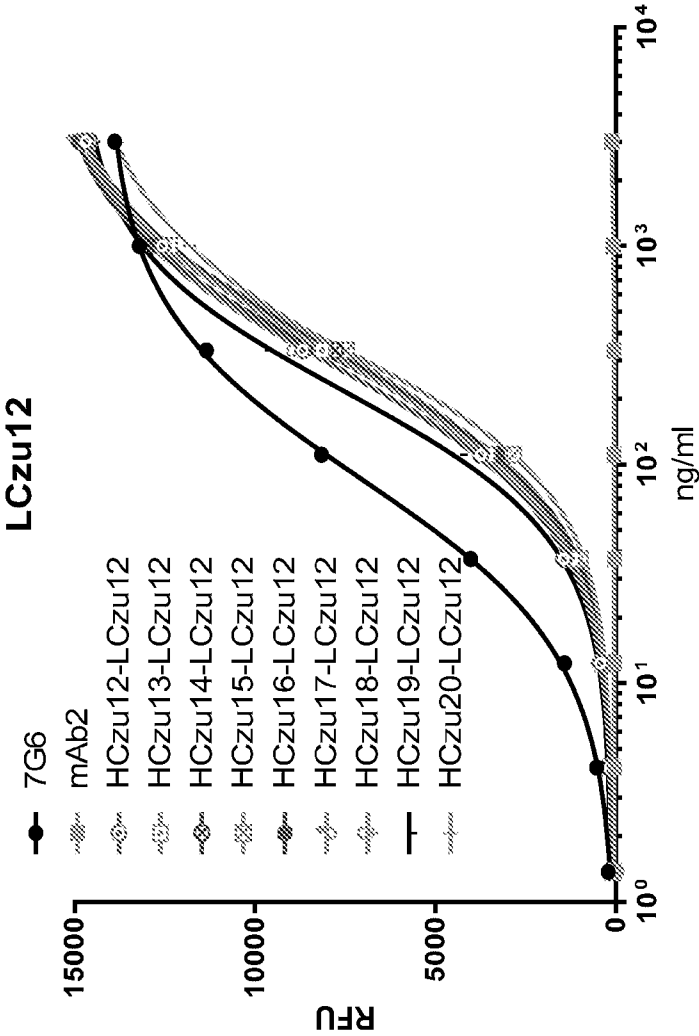


Figure 20A

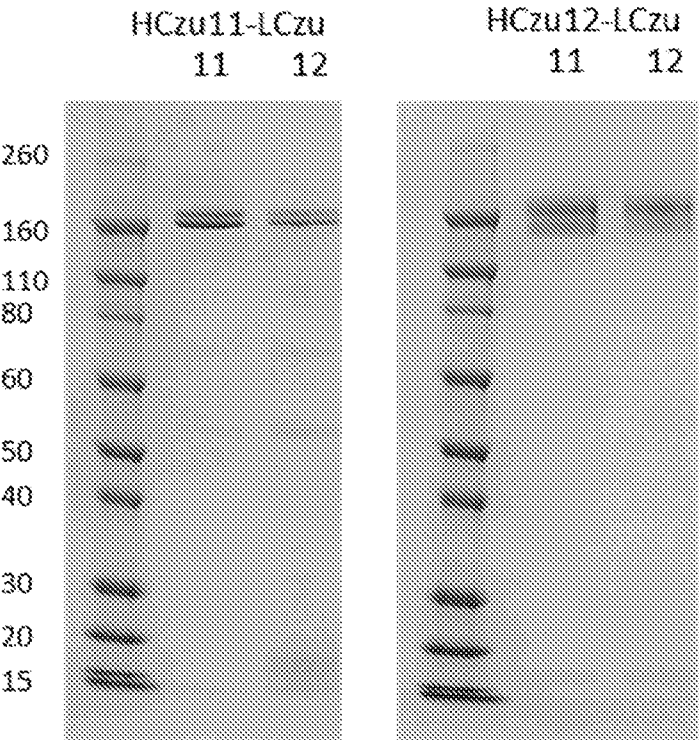


Figure 20C

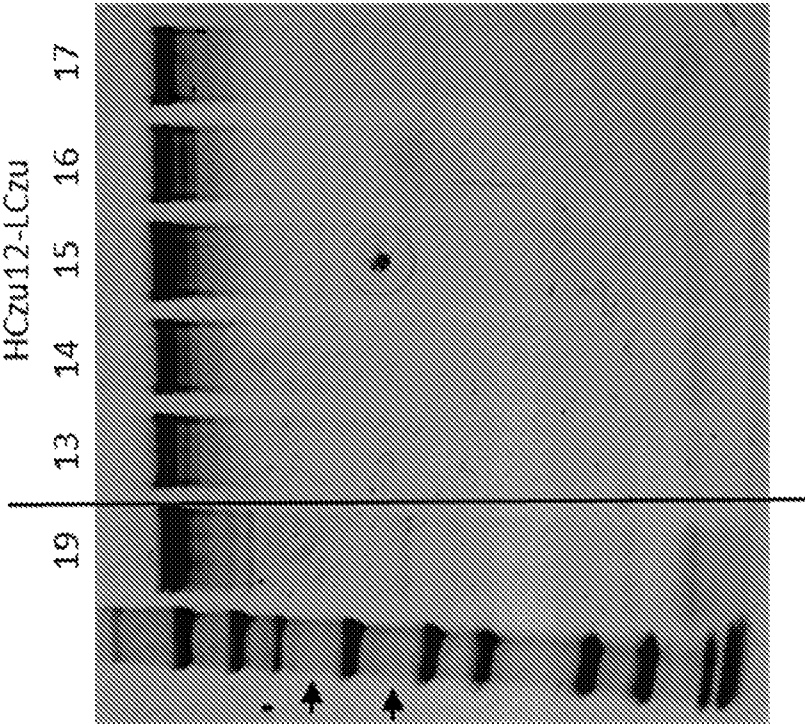


Figure 20B

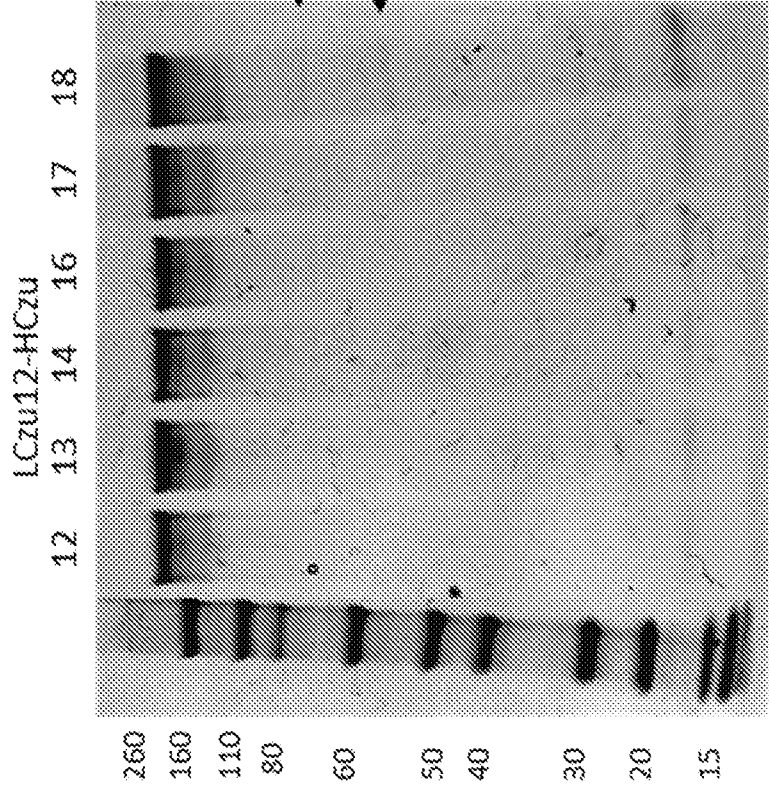


Figure 21A

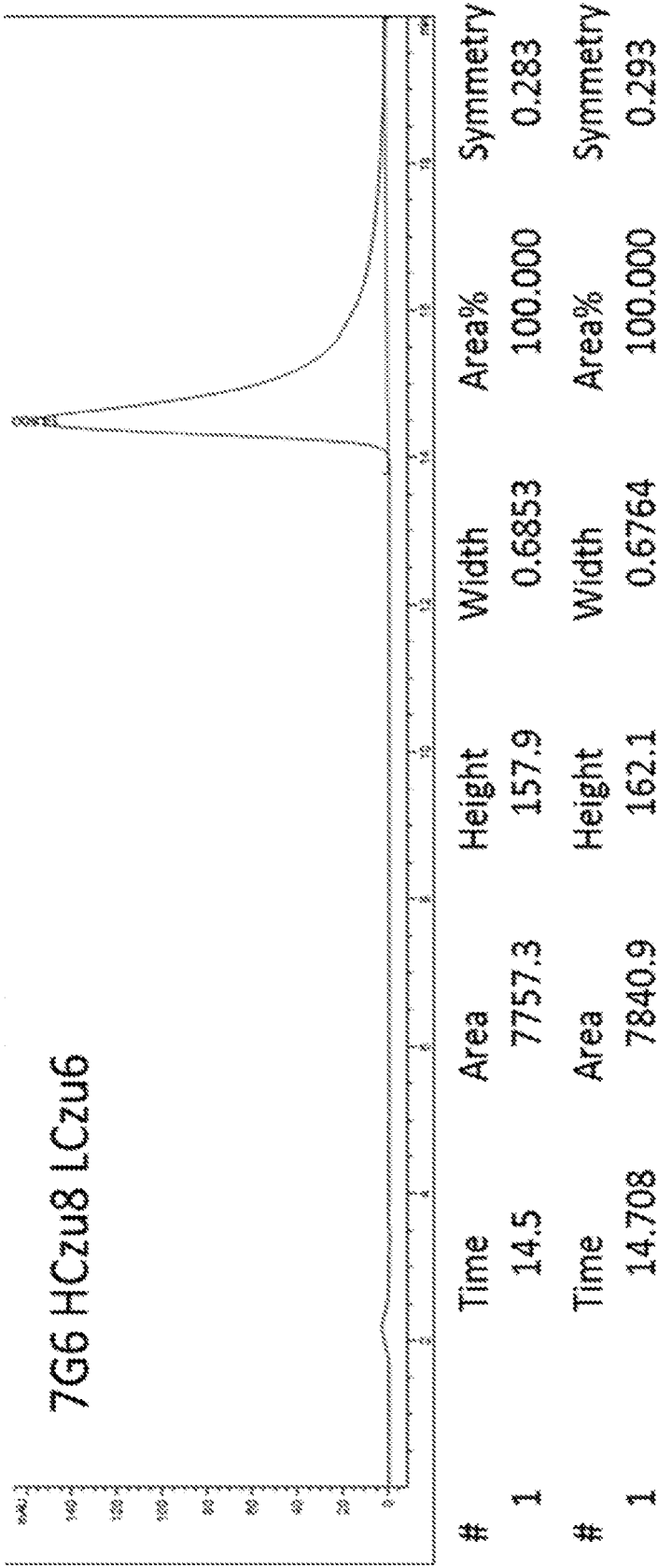


Figure 21B

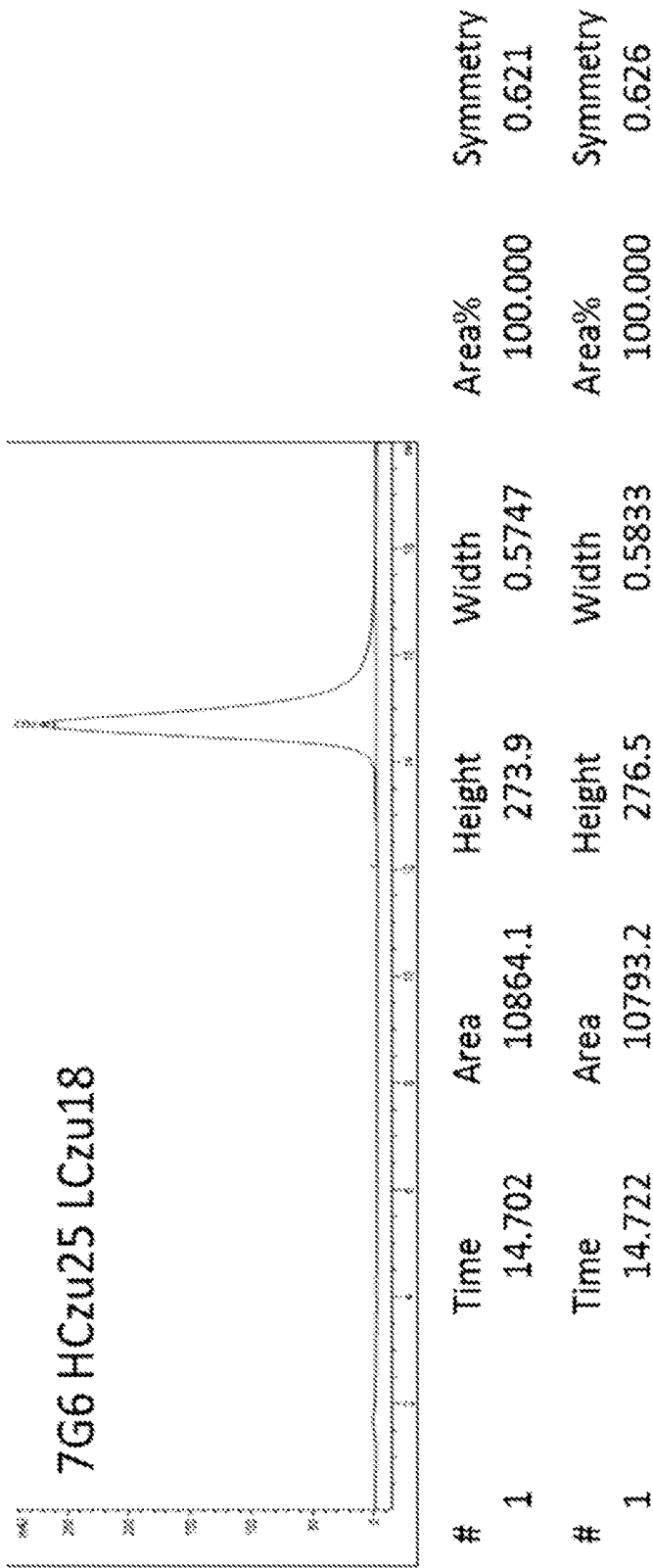


Figure 22A

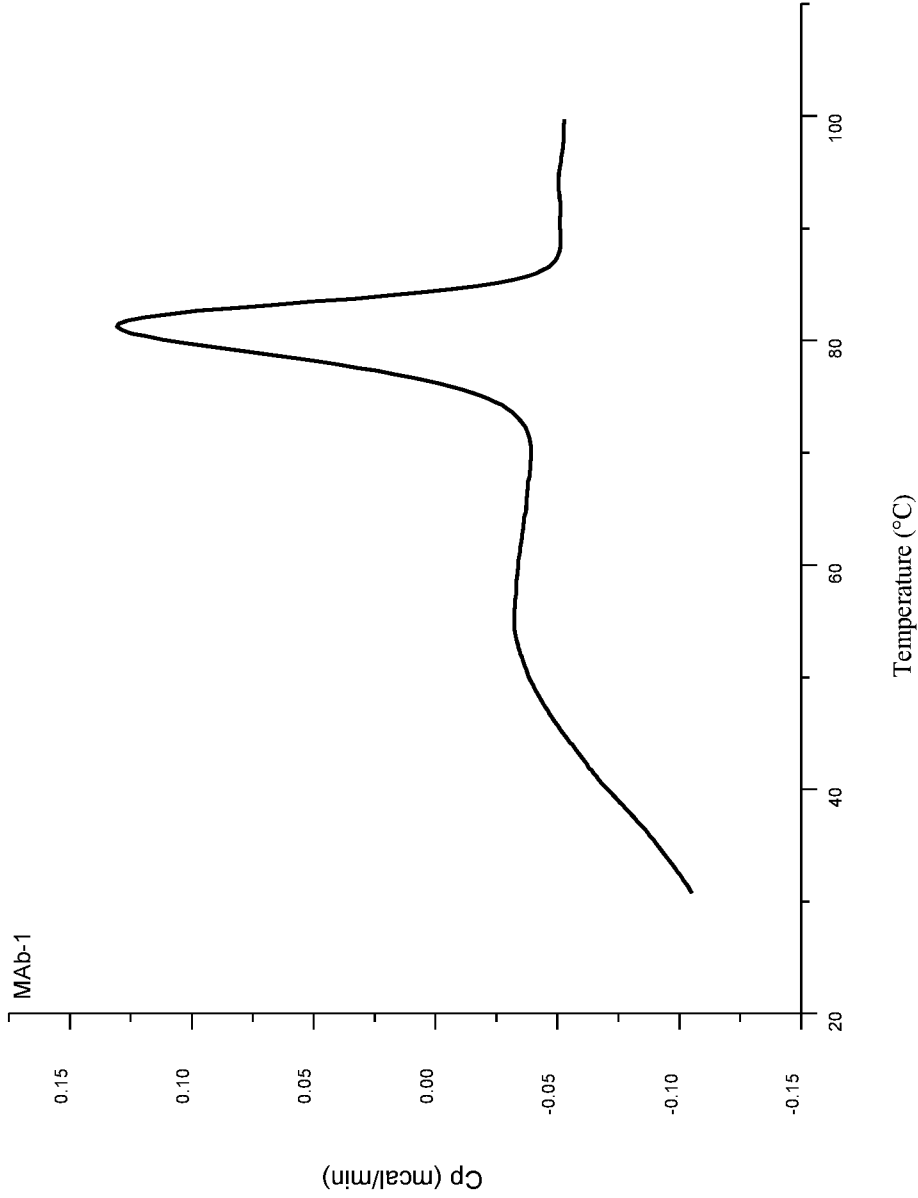


Figure 22B

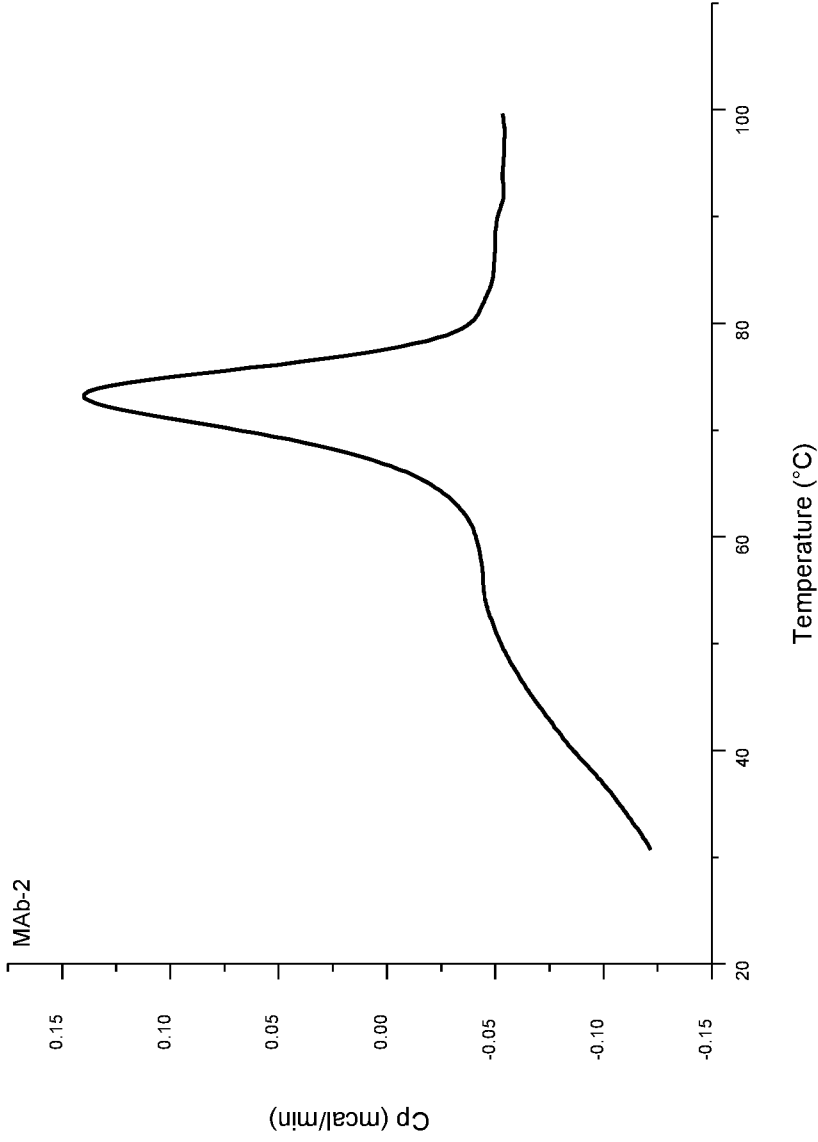


Figure 22C

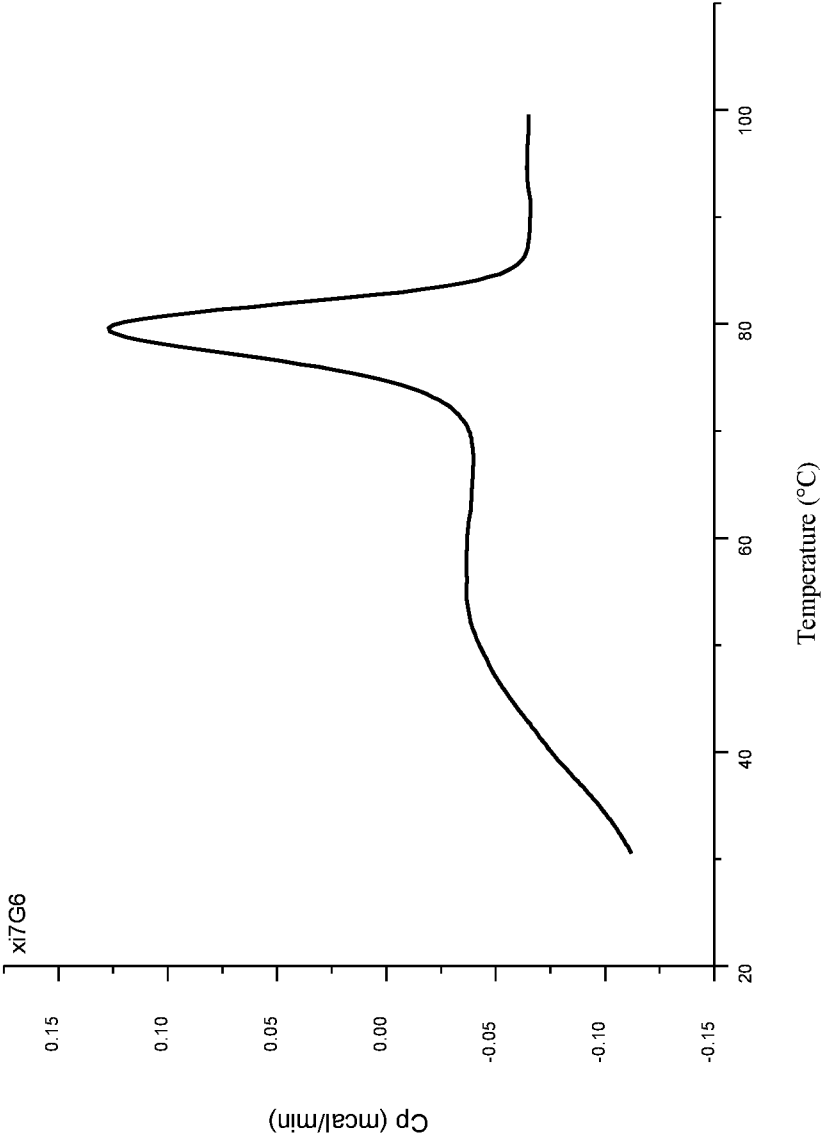


Figure 22D

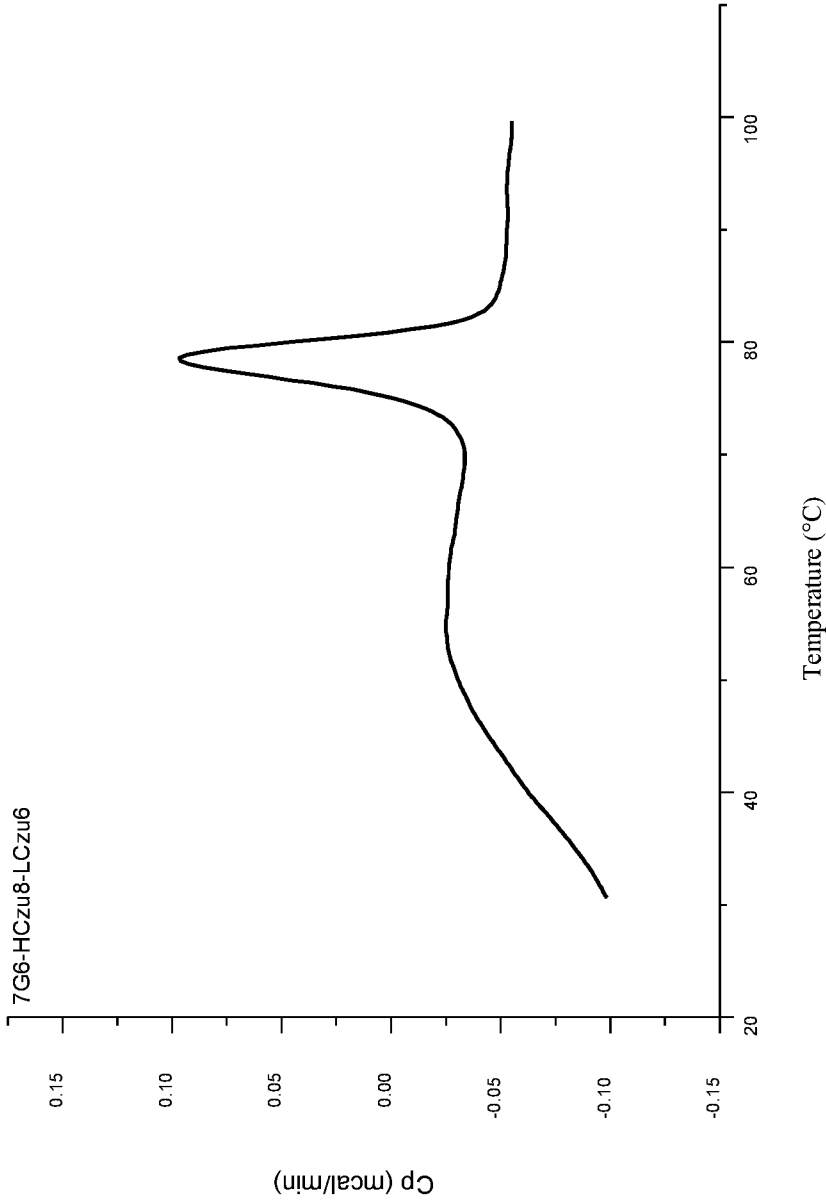


Figure 22E

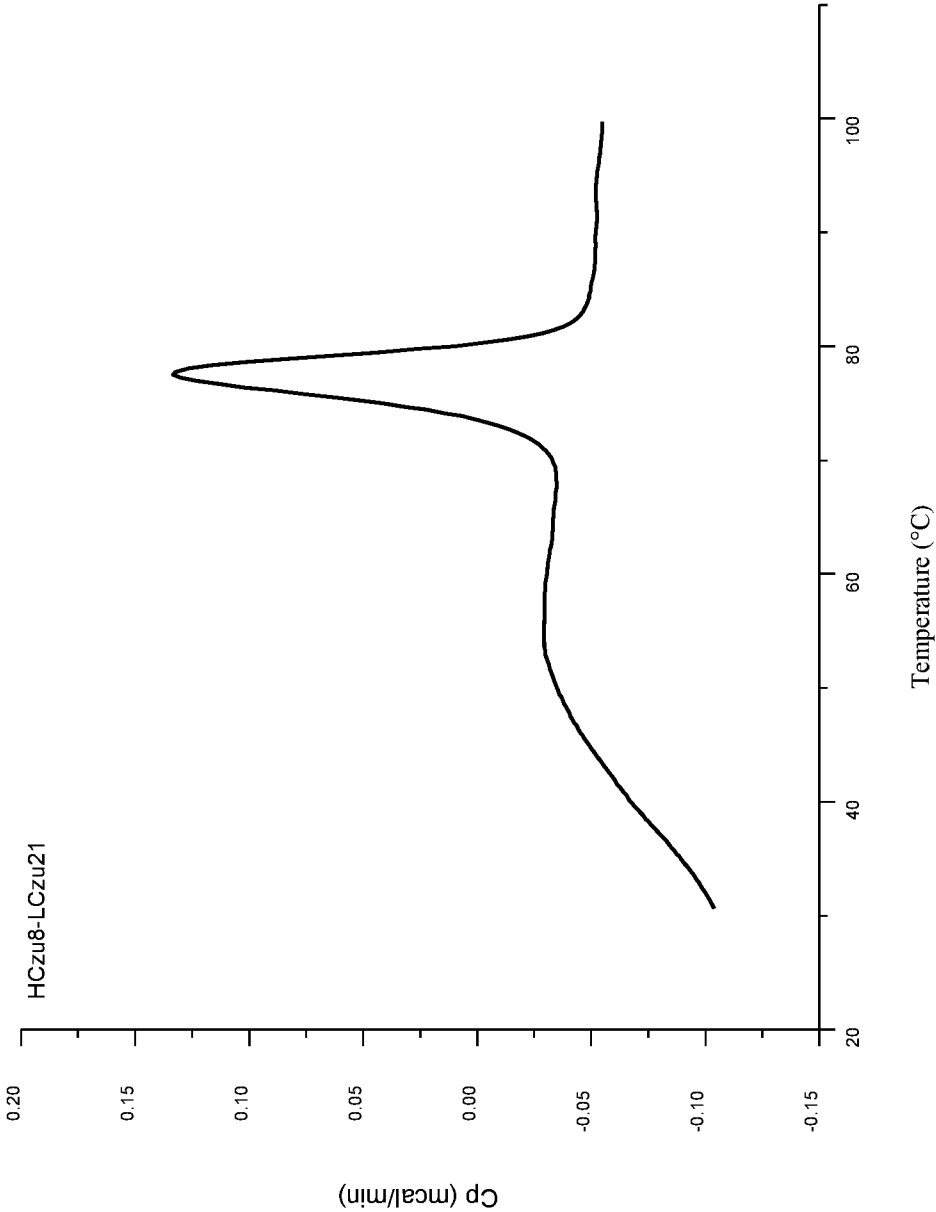


Figure 22F

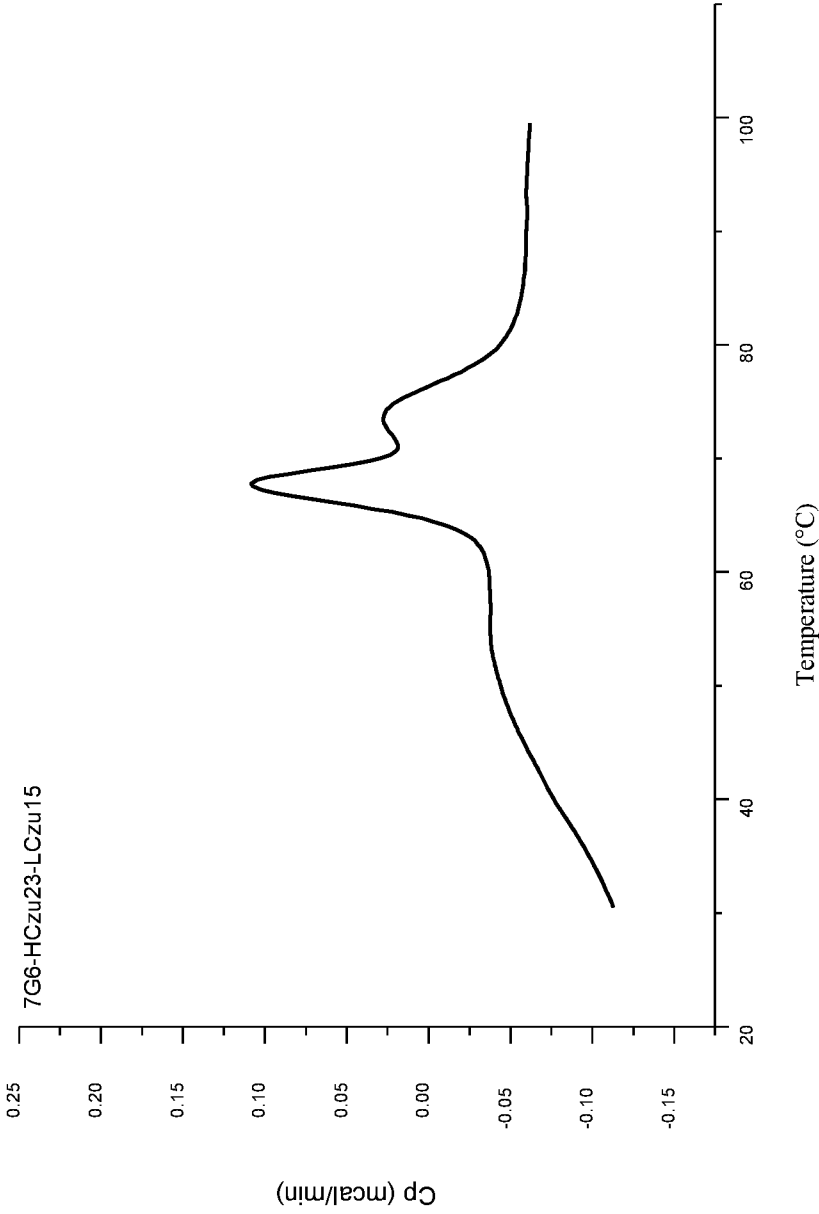


Figure 22G

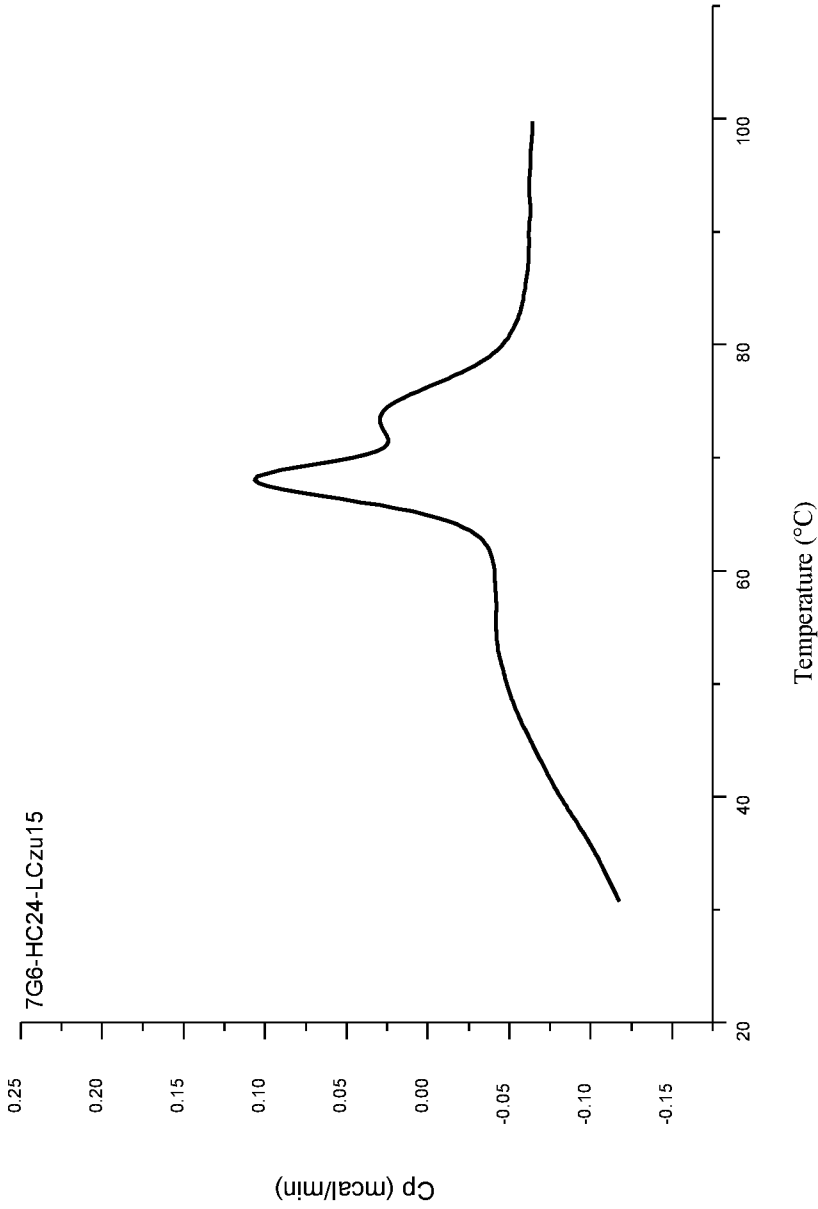


Figure 22H

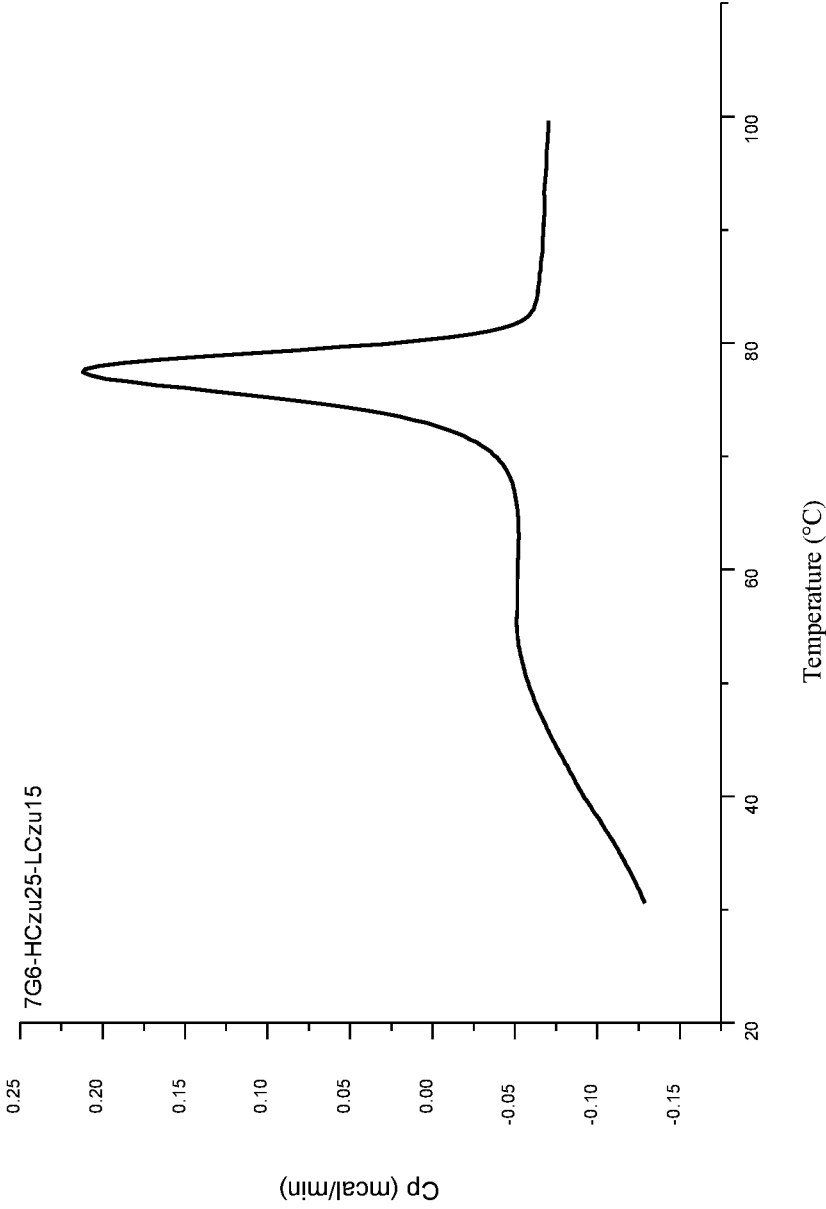


Figure 22I

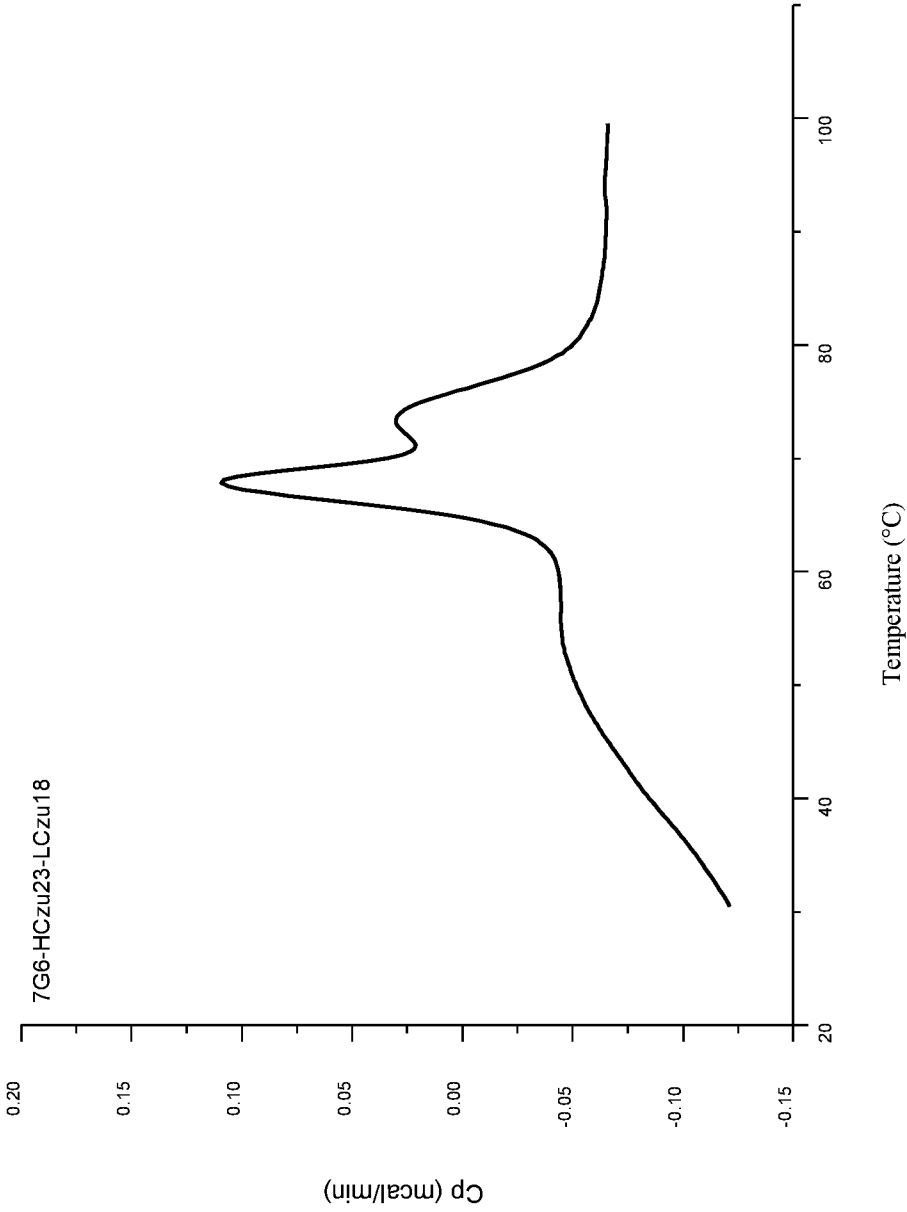


Figure 22J

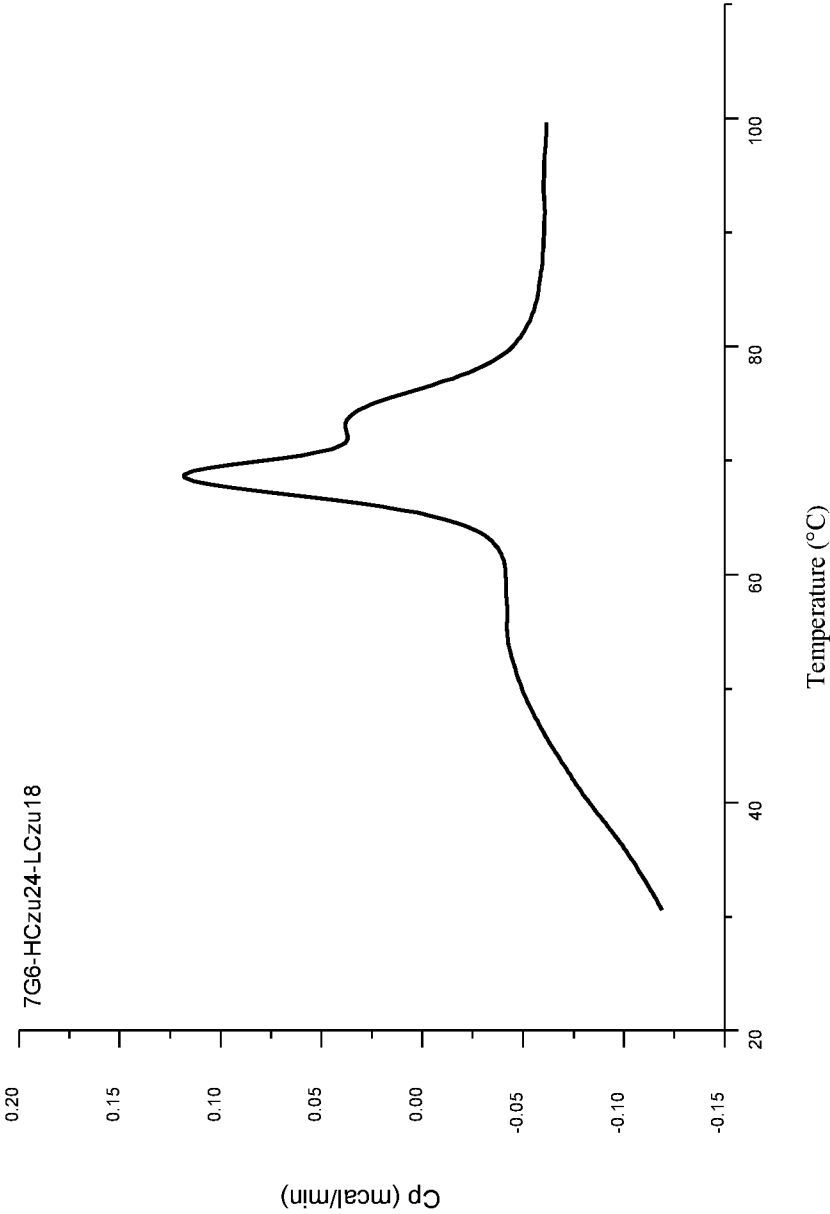


Figure 22K

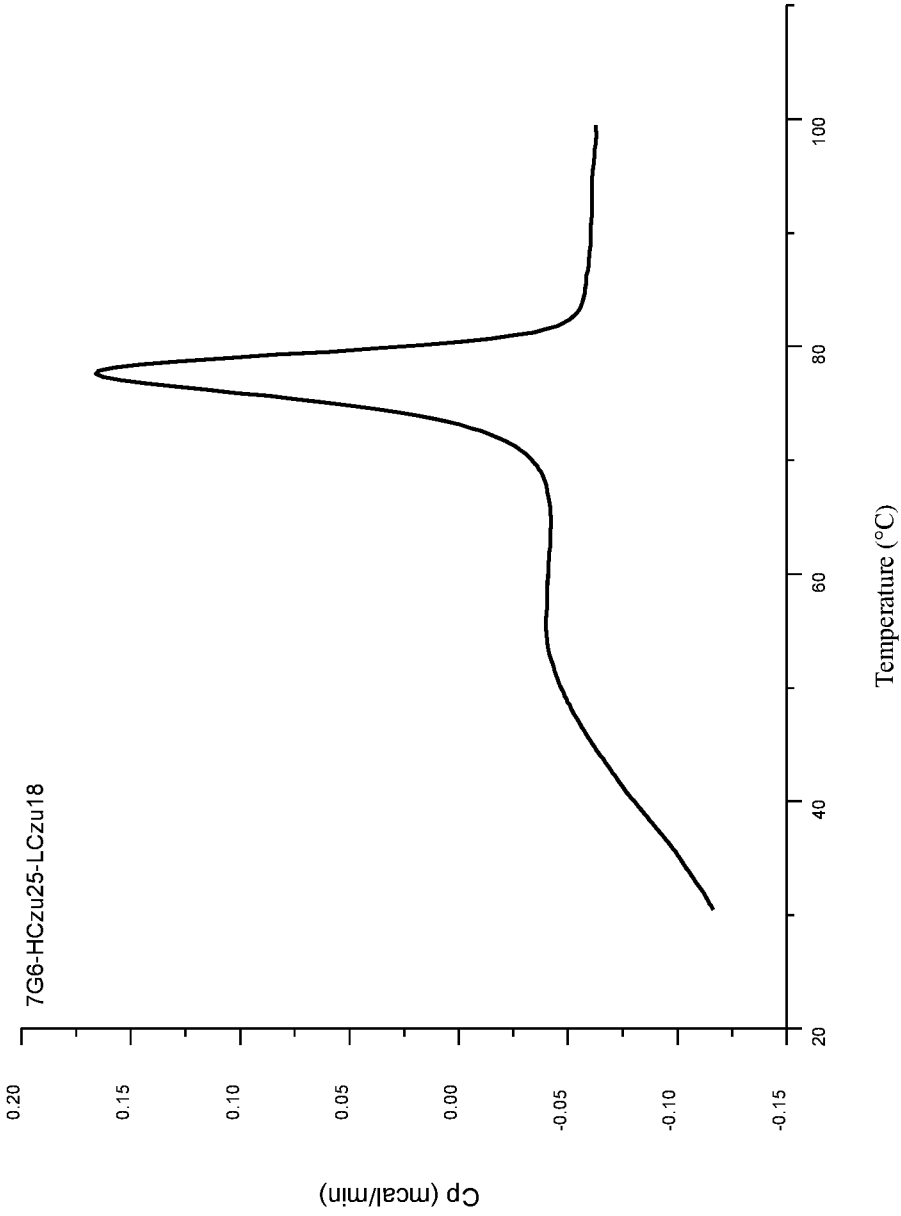


Figure 22L

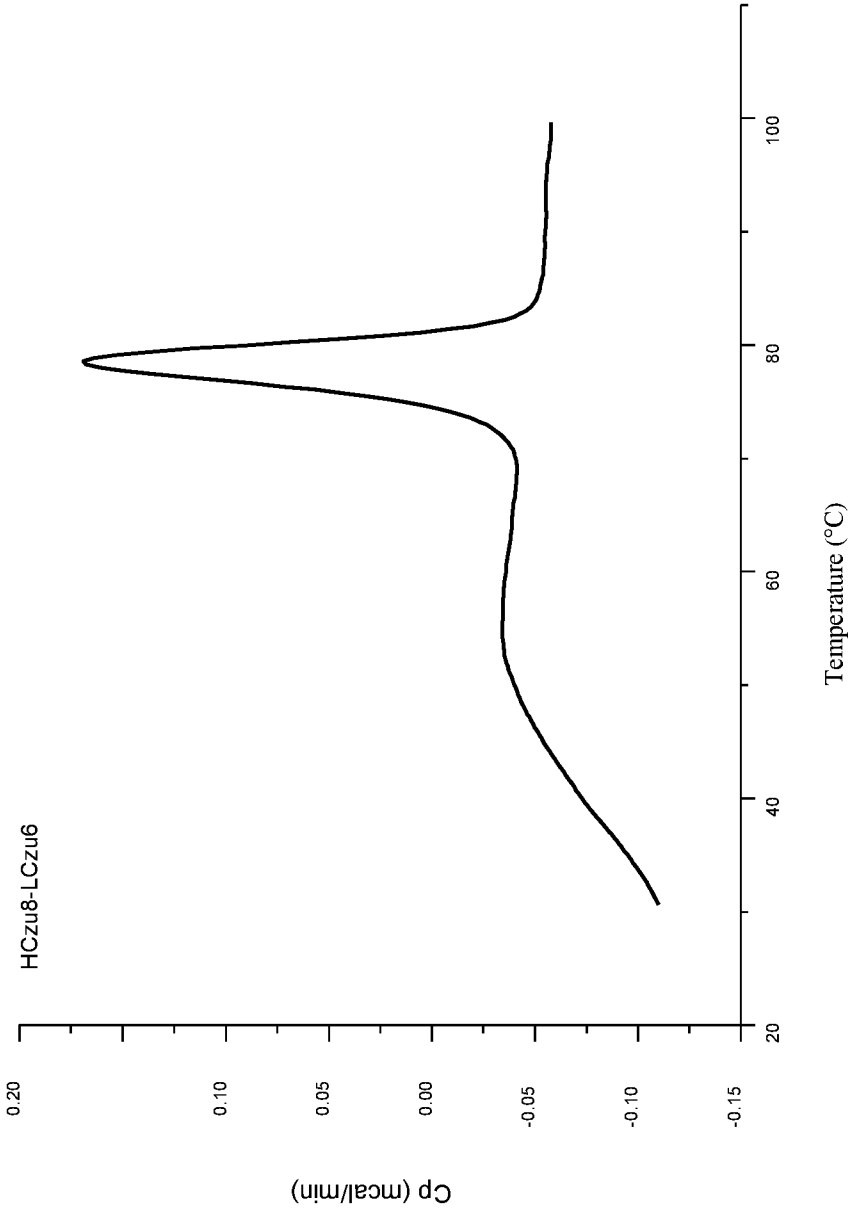


Figure 23A

HCzu8 Epitope Predictions

Start	Peptide Sequence	#Binding Alleles	Max Residue Identity to Any Germline	% Germline 9/9 Identity	% Germline 8/9 Identity	DRB1* 0101	DRB1* 0301	DRB1* 0401	DRB1* 0701	DRB1* 0801	DRB1* 1101	DRB1* 1301	DRB1* 1501
2	VQLVSGAE	1	9	14.37	18.48					3			
4	LVQSGAEVK	1	9	15.25	17.89			3					
18	VKVSCKASG	3	9	16.42	17.01		2			5		3	
32	YWTWVRQA	3	7	0	0			3	5		2		
36	WVRQAPGQG	5	9	9.09	41.94	2	4	4		3	3		
37	VRQAPGQGL	3	9	9.09	43.7	1			2				4
47	WMGDYPGS	2	8	0	1.76		3	4					
57	ISNVAQKFQ	1	8	0	1.17					4			
64	FQGRVIMTR	3	9	3.52	7.04			4		1	2		
70	MTKDTIST	1	9	1.76	5.28			5					
79	VMELSSLR	1	9	0.88	10.85			2					
80	VMELSLRS	3	9	10.85	16.13	3		1			1		
86	LRSEDYAV	4	9	7.92	35.19		5	1		5		4	
93	VWYCARVDG	2	6	0	0		4						5
108	VWGGTILVT	2	0	0	0			2			4		

3-allele binder with no identity to representative germlines

3-allele binder with identity to ~3.5% of representative germlines (including the source for humanization), lower relative risk but worth noting

Figure 23B

HCu25 Epitope Predictions

Start	Peptide Sequence	#Binding Alleles	Max Residue Identity to Any Germline	% Germline 9/9 identity	% Germline 8/9 identity	DRB1* 0101	DRB1* 0301	DRB1* 0401	DRB1* 0701	DRB1* 0801	DRB1* 1101	DRB1* 1301	DRB1* 1501
2	VQLLESQGG	5	9	2.05	33.43	5	4	5		4	4		
12	VQPGGSLRL	3	9	18.48	38.71	4			1				2
18	LRSCAASG	6	9	32.26	40.47	2	1	2		4	5	2	
32	YMTWVRQA	3	7	0	0			3	5		2		
36	WVRQAPGKG	5	9	28.74	54.55	2	4	4		3	3		
37	VRQAPGKGL	3	9	29.33	55.72	2			3				4
47	WVSDIYPGS	2	7	0	0		2	2					
60	YNEKFSRF	1	5	0	0					3			
64	EKSRETIYSV	3	7	0	0				3	1	3		
68	FTISVDSNK	1	8	0	15.84			3					
79	YLQMNSLR	1	9	24.34	33.72			3					
80	YLQMNSLRA	6	9	24.63	31.67	1		1	5	3	1		3
81	LQMNSLRAE	2	9	24.93	31.67					2		1	
83	MNSLRAEDT	1	9	21.41	29.03	4							
86	LRAEDTAVY	3	9	21.41	38.12			1		5		5	
93	VYVCAREDG	2	6	0	0		4					5	
108	YWGGQTLVT	2	0	0	0			2			4		

5-allele binder with identity to ~2% of representative germlines (including the source for humanization) – lower relative risk but worth noting

3-allele binder with no identity to representative germlines

3-allele binder with identity to no representative germlines

*Entries in HLA allele columns indicate % threshold at which binding was predicted for the given allele. Lower thresholds are more stringent.

Figure 24A

LCzu6 Epitope Predictions

Start	Peptide Sequence	#Binding Alleles	Max Residue Identity to Any Germline	% Germline 9/9 Identity	% Germline 8/9 Identity	DRB1* 0101	DRB1* 0301	DRB1* 0401	DRB1* 0701	DRB1* 0801	DRB1* 1101	DRB1* 1301	DRB1* 1501
2	WMTQSPIS	7	9	2.97	4.95	2	1	1	4		1	3	2
3	WMTQSPISL	4	9	4.95	15.84	2			4		4	4	
9	LSPVTIGQ	2	9	2.97	4.95			4			4		
13	VTIGQPASI	2	9	4.95	9.9	4	4						
29	LHSNGNTY	1	8	0	0.99				5				
30	LHSNGNTYL	2	9	0.99	3.96	5		4					
40	WYQQRPGQS	2	8	0	2.97			4			3		
51	LISKYSNR	3	8	0	0.99		1	3				3	
52	LISKYSNRF	1	8	0	1.98							2	
76	FTLKSIVE	1	9	17.82	20.79					1			
78	LKSRVAE	3	9	16.83	19.8		2	3	4				
80	LSRVAEDV	1	9	14.85	19.8				5				
88	GVWYCFQG	3	8	0	4.95					4	4	4	2
90	WYCFQGS	1	7	0	0					5			
91	WYCFQGS	2	6	0	0	2							3
92	YCFQGSHP	1	6	0	0			4					
94	FGGSHVPET	3	5	0	0		5	4			5		
101	FTFGQGTKL	2	0	0	0	3			5				
103	FGQGTKLEI	2	0	0	0				4		3		

overlapping 7-allele and 4-allele binders with identity to ~3% and ~5% of representative germlines (including the source for humanization), respectively – both lower relative risk but worth noting

more risky, relative to our database, than matched peptide in LCzu6 overlapping 3 and 1-allele binders with identity to no representative germlines

five overlapping binders of 1-3 alleles each having no identity to representative germlines – note each nonamer peptide extends into CDR3, for which there is only partial germline alignment

Figure 24B

LCzu21 Epitope Predictions

Start	Peptide Sequence	#Binding Alleles	Max Residue Identity to Any Germline	% Germline 9/9 Identity	% Germline 8/9 Identity	DRB1* 0101	DRB1* 0301	DRB1* 0401	DRB1* 0701	DRB1* 0801	DRB1* 1101	DRB1* 1301	DRB1* 1501
2	VWMTQSPIS	7	9	2.97	4.95	2	1	1	4		1	3	2
3	VMTQSPISL	4	9	4.95	15.84	2			4		4	4	
9	ISIPVTLGQ	2	9	2.97	4.95			4			4		
13	VTLGQPASI	2	9	4.95	9.9	4	4						
29	ILHSNGNTY	1	8	0	0.99				5				
30	LHSNGNTYL	2	9	0.99	3.96	5		4					
38	LEWFCQRPQ	1	8	0	2.97							5	
40	WFQORPGQS	2	9	2.97	2.97			5			3		
51	ILISKVSNR	3	8	0	0.99		1	3				3	
52	ILSKVSNRF	1	8	0	1.98							2	
76	FTLKSIRVE	1	9	17.82	20.79				1				
78	LKISRVEAE	3	9	16.83	19.8		2	3	4				
80	ISRVEADV	1	9	14.85	19.8				5				
88	VGWYCFQGG	3	8	0	4.95					4		4	2
90	VYCFQGS	1	7	0	0					5			
91	WCFQGS	2	6	0	0	2							3
92	WCFQGSHP	1	6	0	0			4					
94	WCFQGSHPPT	3	5	0	0		5	4			5		
101	FTFGQTKL	2	0	0	0	3			5				
103	FGQGTKEI	2	0	0	0				4		3		

overlapping 7-allele and 4-allele binders with identity to ~3% and ~5% of representative germlines (including the source for humanization), respectively – both lower relative risk but worth noting

Not present in LCzu6, but low risk epitope.

Less risky, relative to our database, than matched peptide in LCzu6 overlapping 3 and 1-allele binders with identity to no representative germlines

Five overlapping binders of 1-3 alleles each having no identity to representative germlines – note each nonamer peptide extends into CDR3, for which there is only partial germline alignment

Figure 24C

LCzu15 Epitope Predictions

Start	Peptide Sequence	#Binding Alleles	Max Residue Identity to Any Germline	% Germline 9/9 Identity	% Germline 8/9 Identity	DRB1* 0101	DRB1* 0301	DRB1* 0401	DRB1* 0701	DRB1* 0801	DRB1* 1101	DRB1* 1301	DRB1* 1501
2	VQMTQSPSS	5	8	0	31.68	5	3	1			3		4
4	MTQSPSSLS	1	9	27.72	47.52			4					
29	LHSGNTY	1	8	0	0.99				5				
30	LHSGNTYL	2	9	0.99	3.96	5		4					
40	WYQQKPGKA	2	9	23.76	64.36	5					5		
51	LLSKVSNR	3	8	0	0.99		1	3				3	
52	LLSKVSNRF	1	8	0	1.98							2	
60	FSGVPSRFS	1	9	1.98	43.56						5		
76	FLTISSLQ	1	9	37.62	63.37			1					
88	FATYGFQG	1	7	0	0					4			
91	WYCFQGS HV	2	6	0	0	2							3
92	WCFQGSHP	1	6	0	0			4					
94	FQGSHPFT	3	5	0	0		5	4			5		
101	FTGQGTKL	2	0	0	0	3			5				
103	FQGTGLEI	2	0	0	0				4		3		

5-allele binder with no identity to representative germlines

overlapping 4 and 1-allele binders with identity to zero and ~1% of representative germlines, respectively

four overlapping binders of 1-3 alleles each having no identity to representative germlines – note each nonamer peptide extends into CDR3, for which there is only partial germline alignment

Figure 24D

LCzu18 Epitope Predictions

Start	Peptide Sequence	#Binding Alleles	Max Residue Identity to Any Germline	% Germline 9/9 Identity	% Germline 8/9 Identity	DRB1* 0101	DRB1* 0301	DRB1* 0401	DRB1* 0701	DRB1* 0801	DRB1* 1101	DRB1* 1301	DRB1* 1501
2	IQMTQSPSS	5	9	31.68	47.52	5	3	1			3		4
4	MTQSPSSLS	1	9	27.72	47.52			4					
29	ILHSGNTY	1	8	0	0.99				5				
30	LHSGNTYL	2	9	0.99	3.96	5		4					
40	WYQKPGKA	2	9	23.76	64.36	5					5		
51	LLSKVSNR	3	8	0	0.99		1	3				3	
52	LSKVSNR	1	8	0	1.98							2	
60	FSGVPSRFS	1	9	1.98	43.56						5		
76	FLTISSLQ	1	9	37.62	63.37			1					
88	FATYCFQG	1	7	0	0					4			
91	WYCFQGSIV	2	6	0	0	2							3
92	YCFQGSHP	1	6	0	0			4					
94	FQGSHPFT	3	5	0	0		5	4			5		
101	FTFGGQTKL	2	0	0	0	3			5				
103	FQGGTKLEI	2	0	0	0				4		3		

overlapping 4 and 1-allele binders with identity to zero and ~1% of representative germlines, respectively

four overlapping binders of 1-3 alleles each having no identity to representative germlines – note each nonamer peptide extends into CDR3, for which there is only partial germline alignment

*Entries in HLA allele columns indicate % threshold at which binding was predicted for the given allele. Lower thresholds are more stringent.

Figure 25

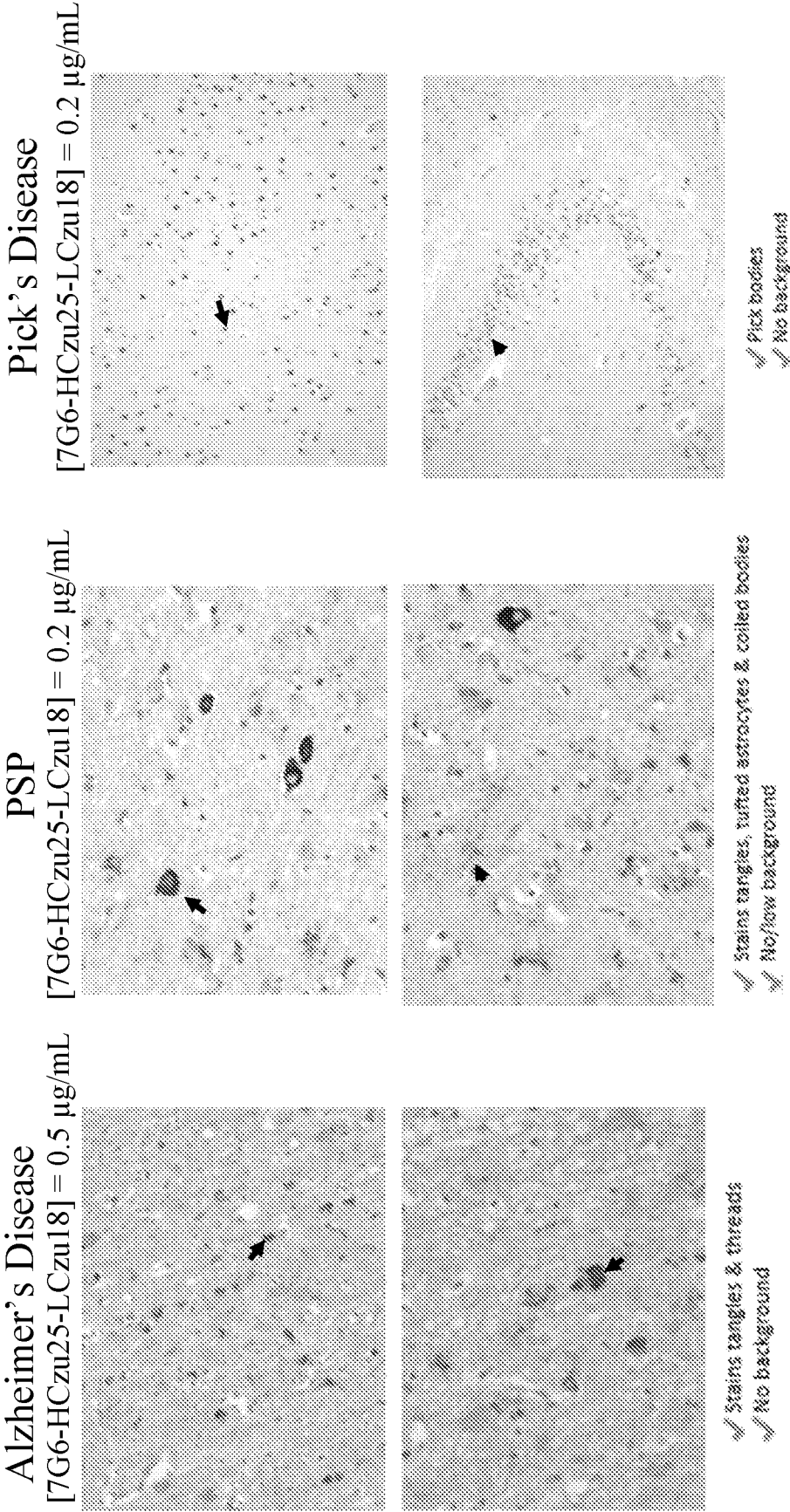


Figure 26A
7G6-HCzu8-LCzu6

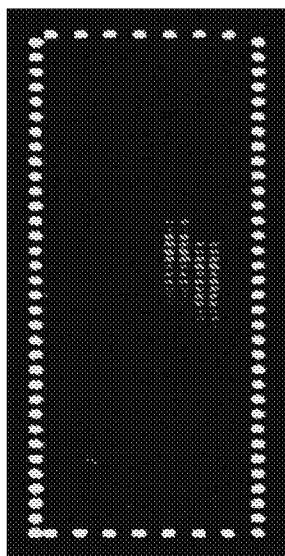
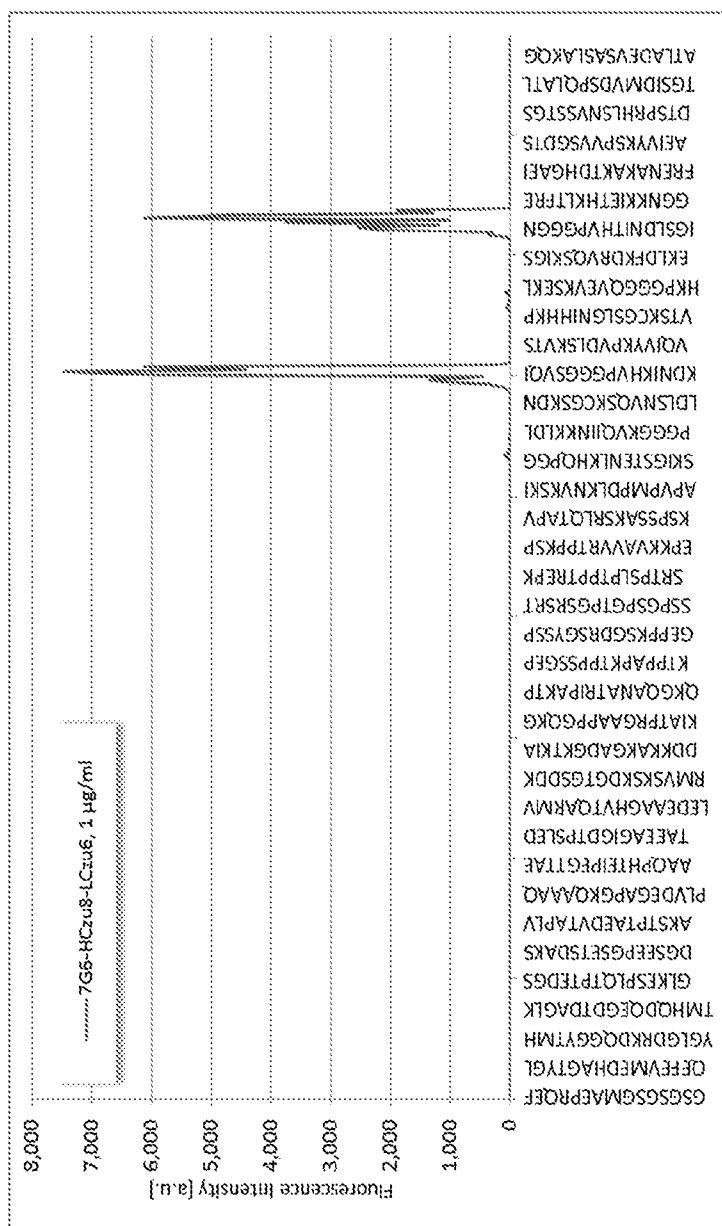


Figure 26B
7G6-HCzu25-LCzu18

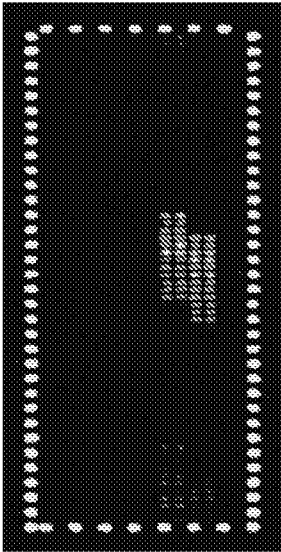
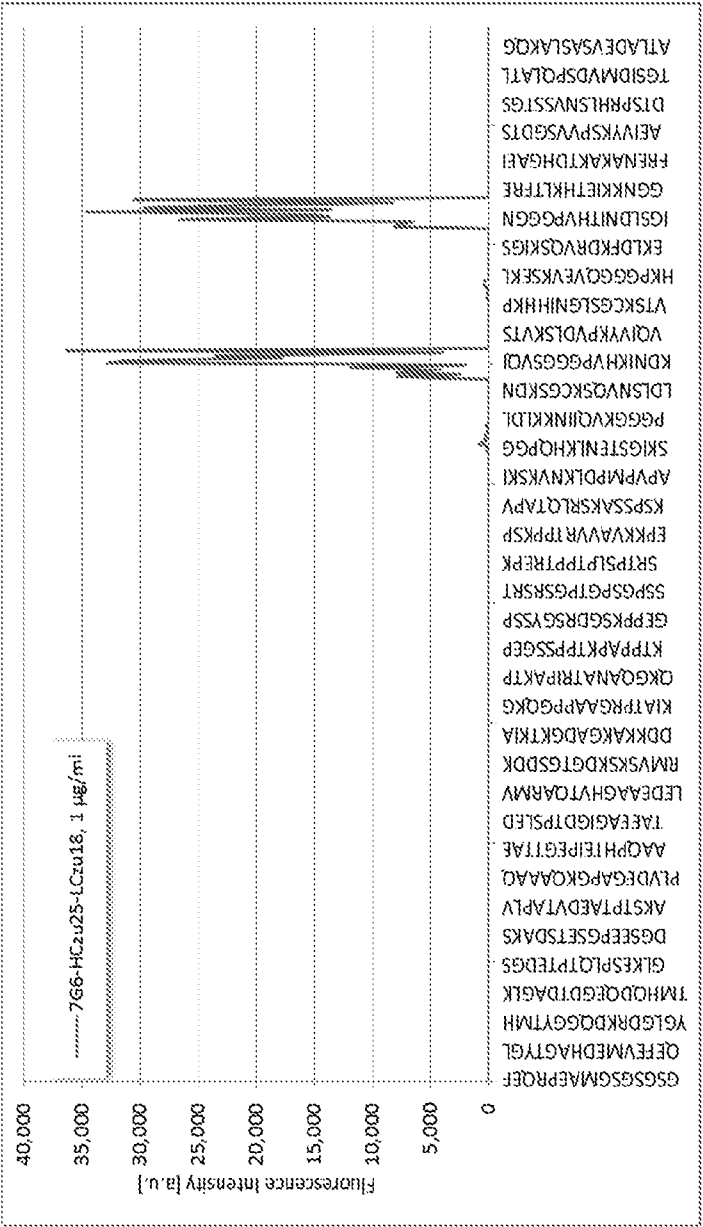


Figure 27

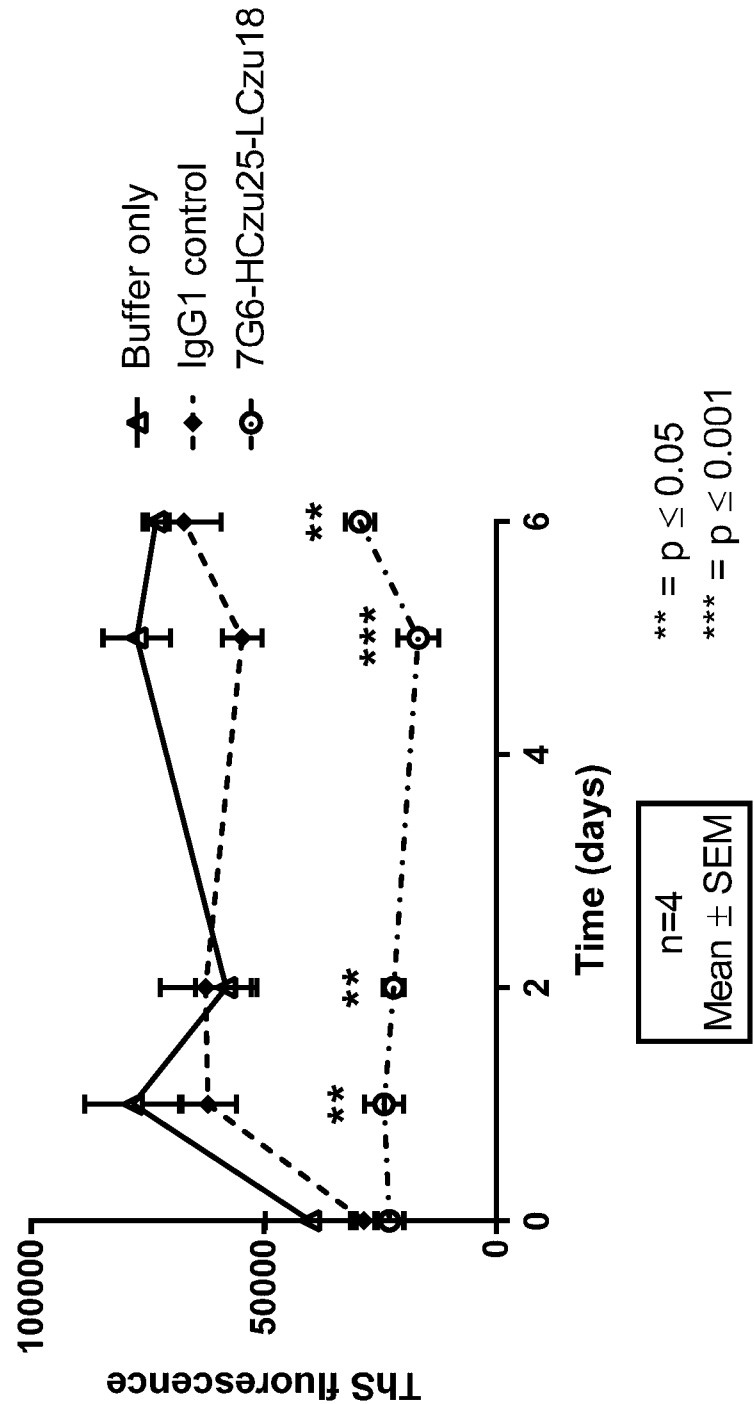


Figure 28

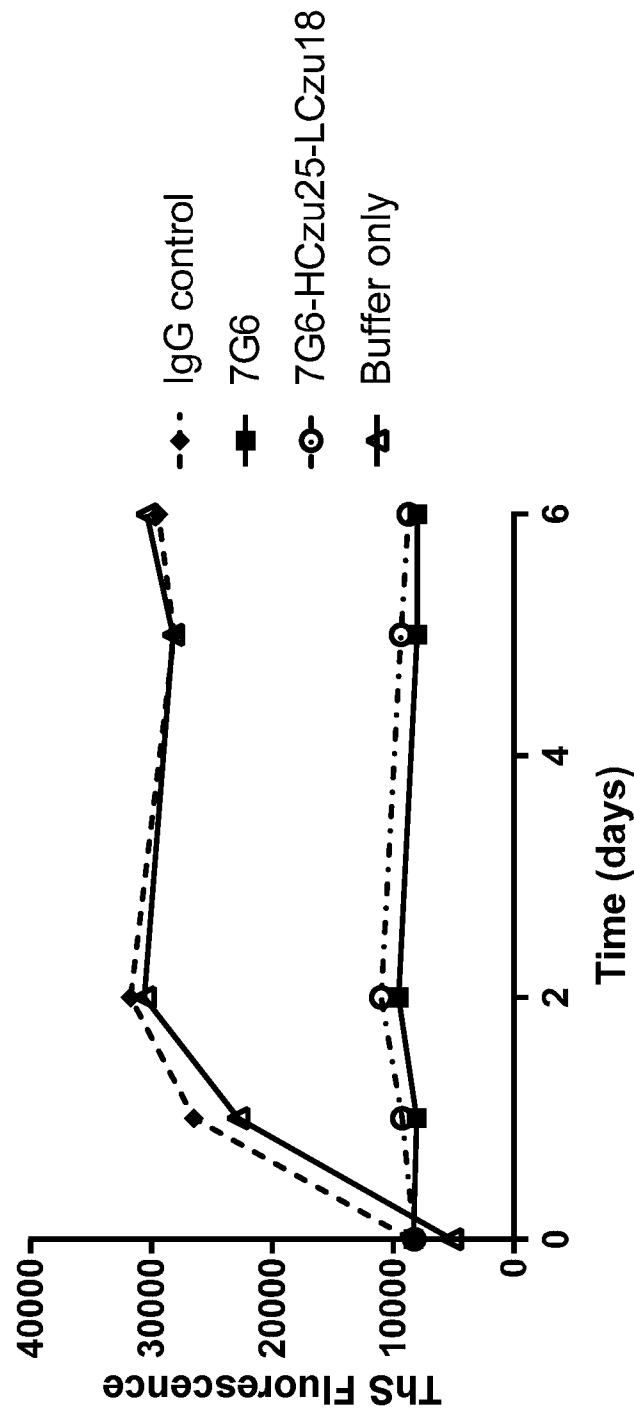
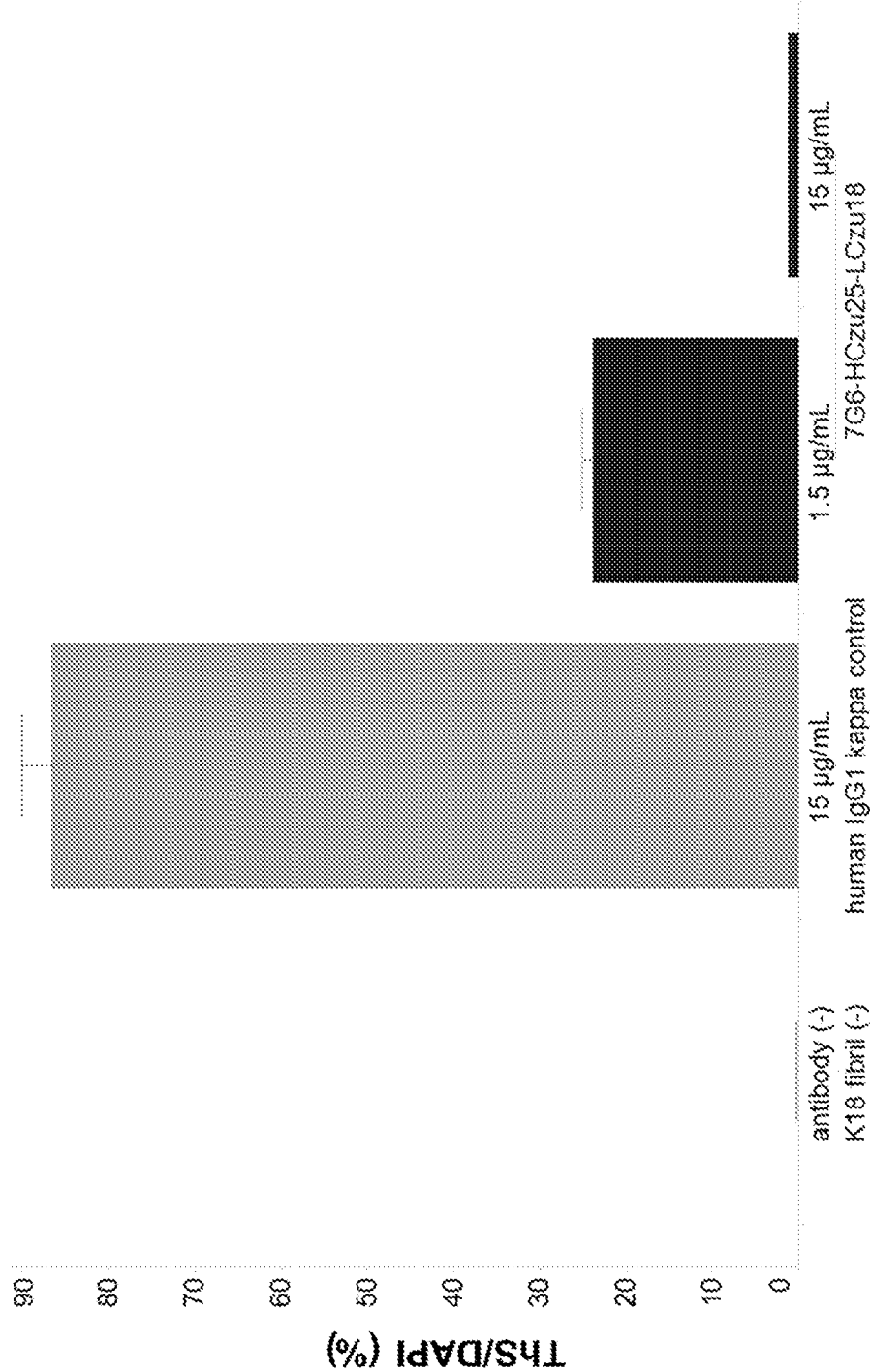


Figure 29
Cell based seeding effects of K18 fibril
after immunodepletion with 7G6-HCzu25-LCzu18



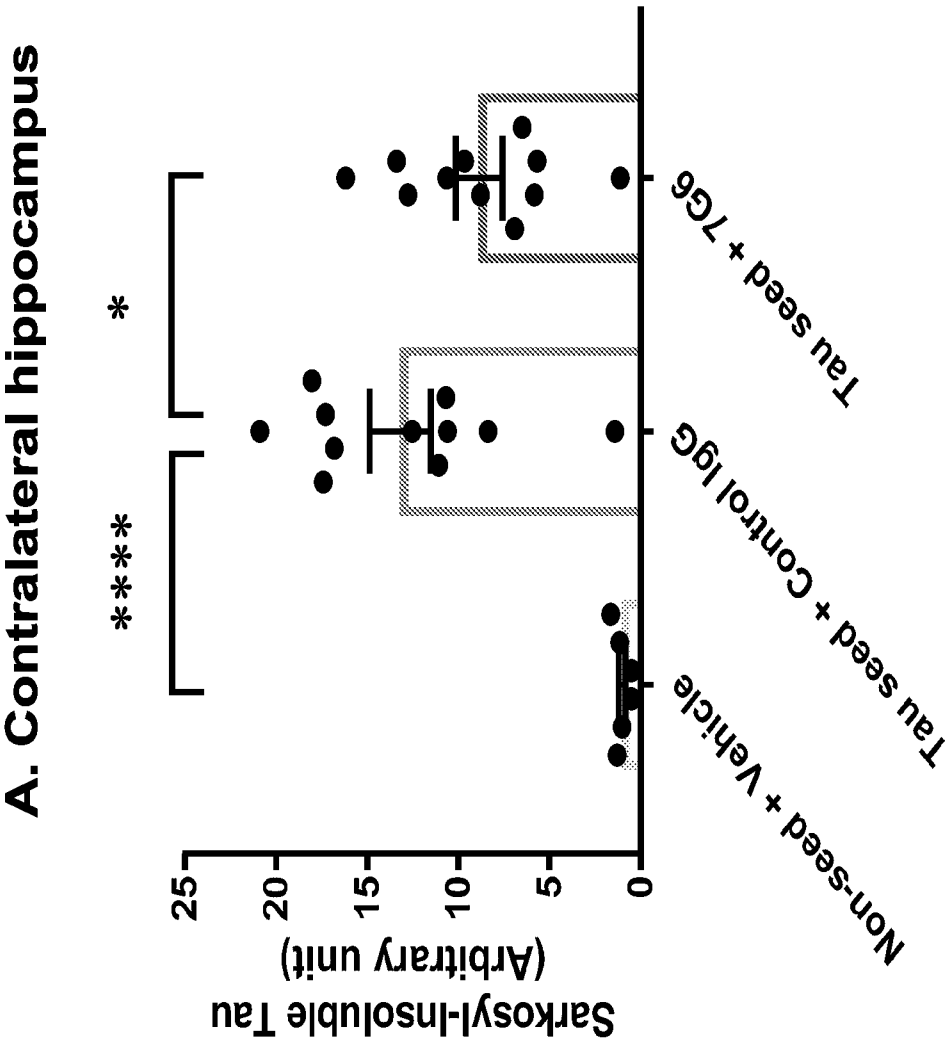


Figure 30A

B. Ipsilateral hippocampus

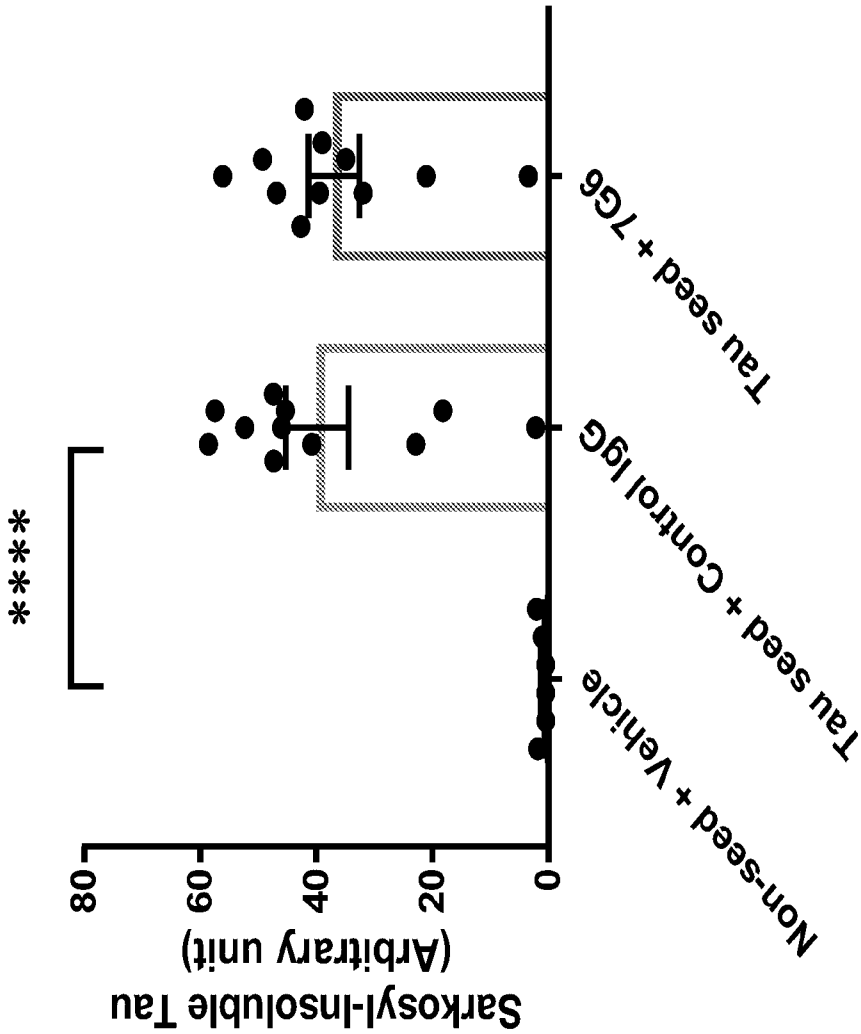


Figure 30B

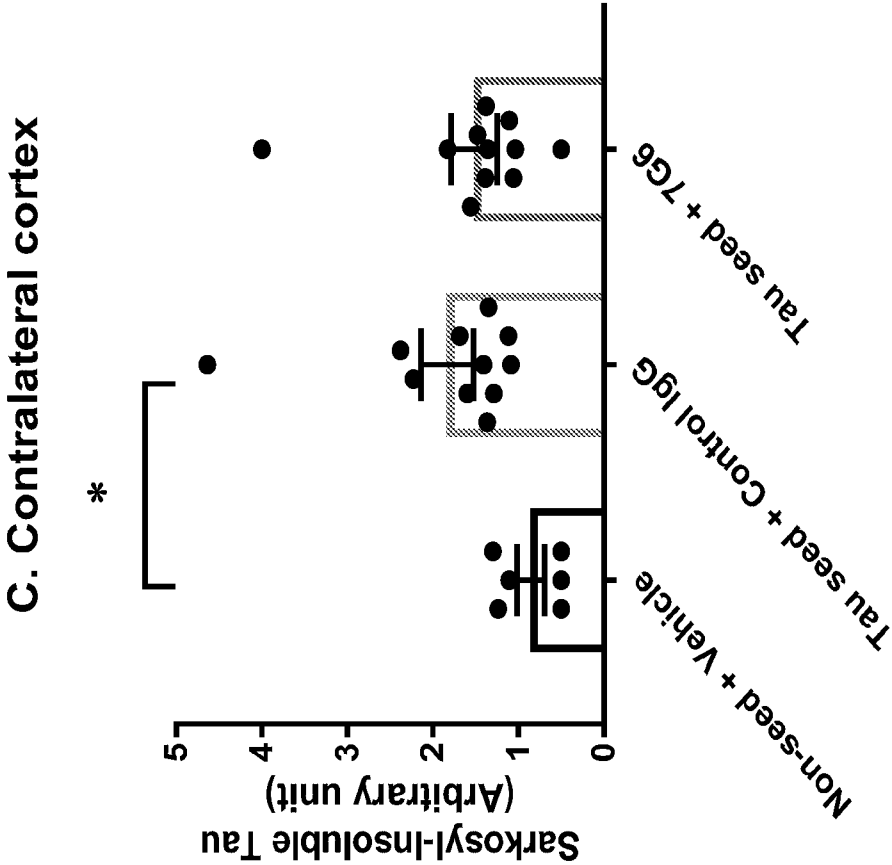


Figure 30C

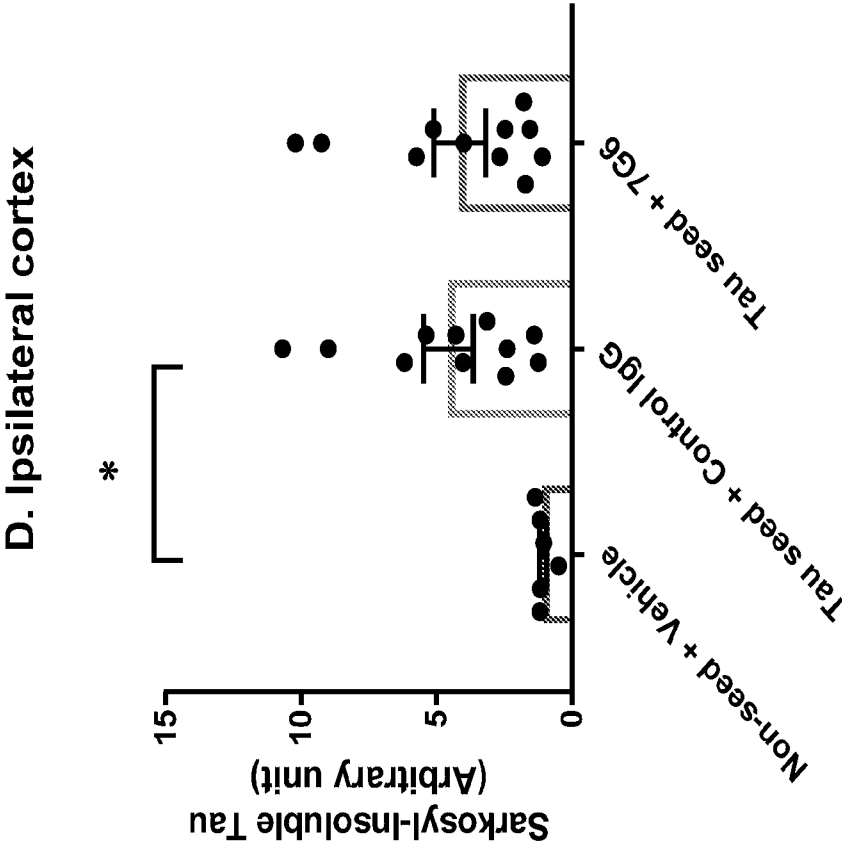
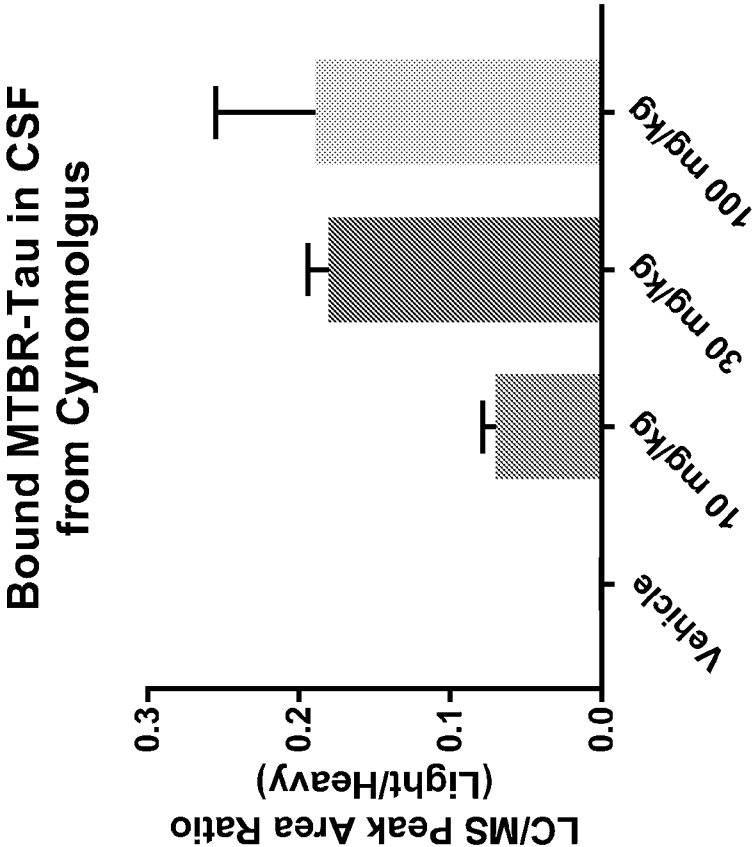


Figure 30D

Figure 31A



Dose, 7G6-HCzu25-LCzu18 (mg/kg)

Figure 31B

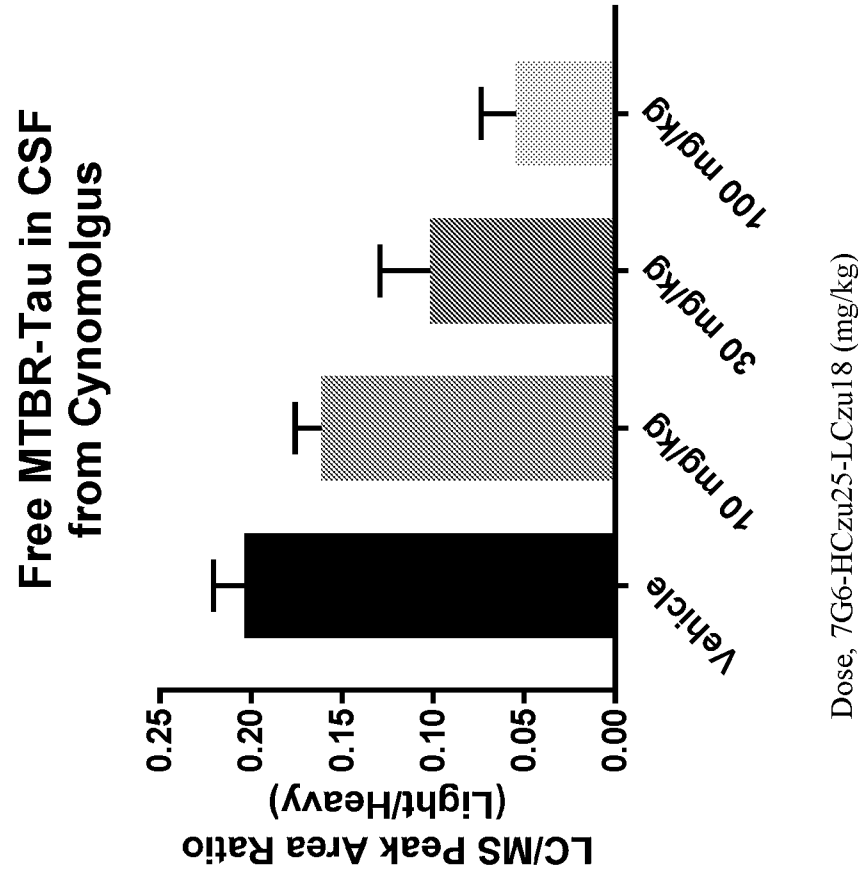


Figure 32

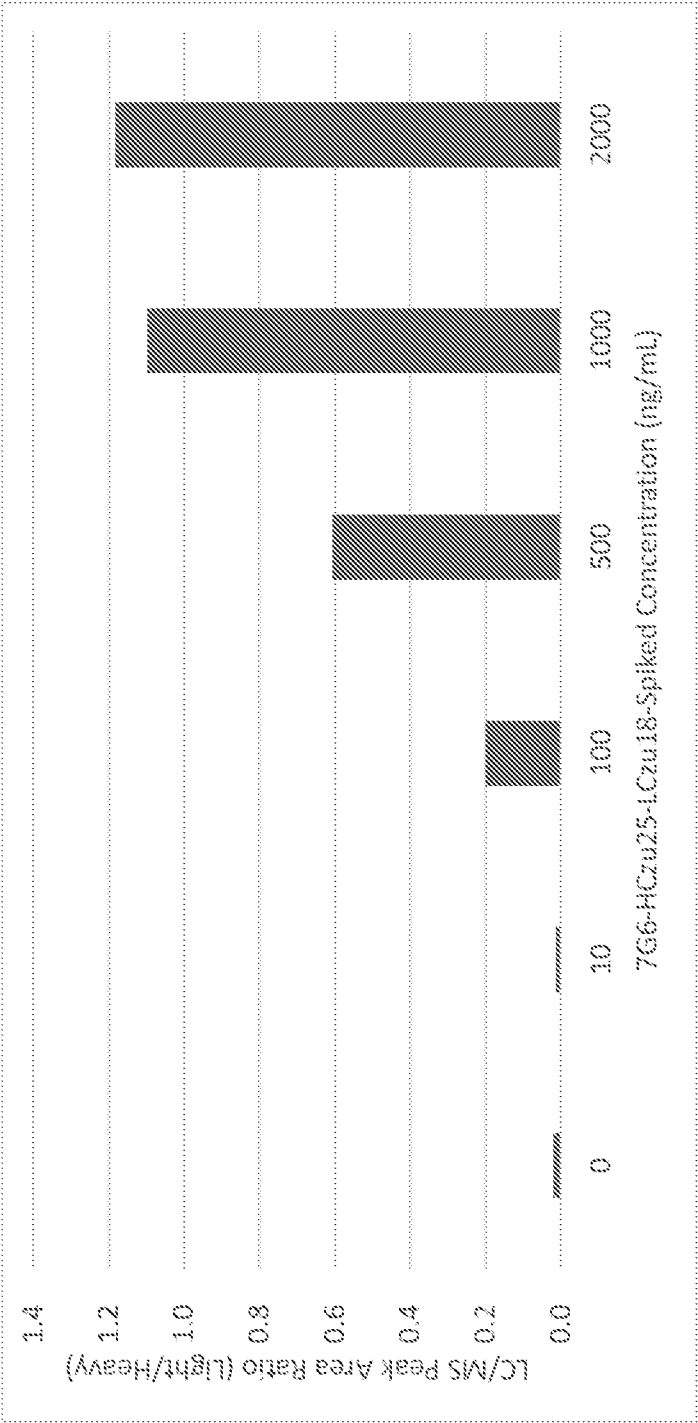


Figure 33A

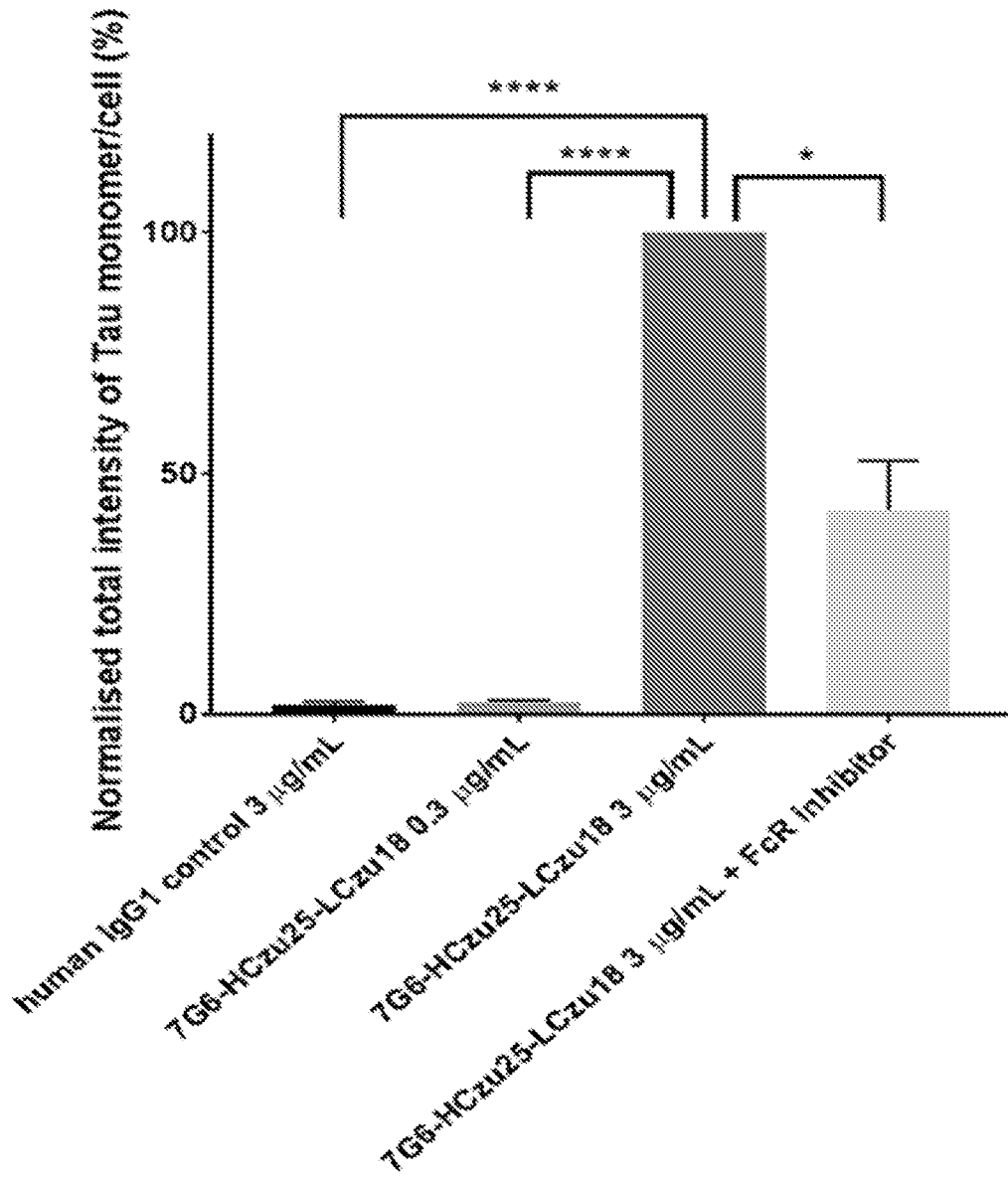


Figure 33B

