

Figure 1

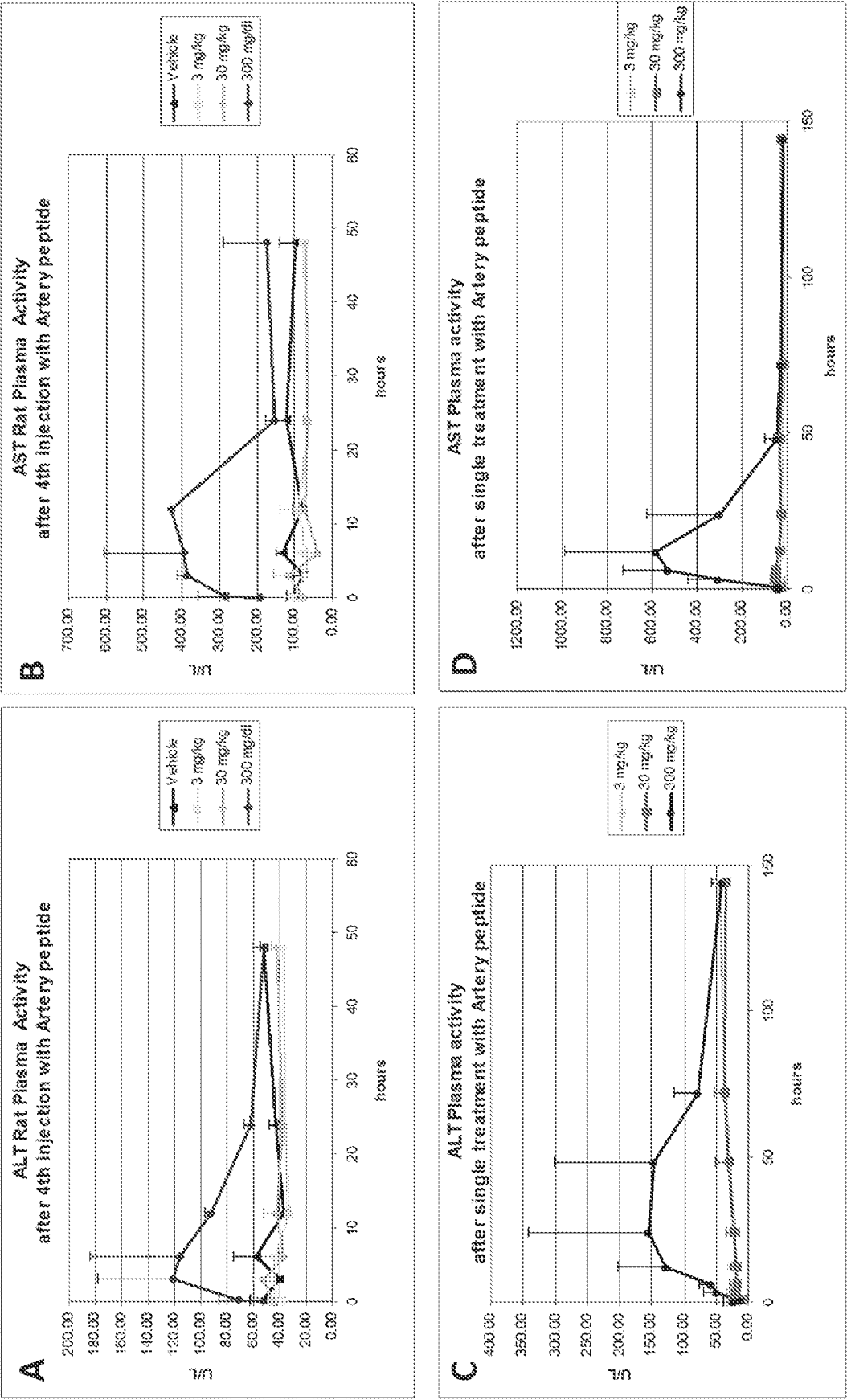
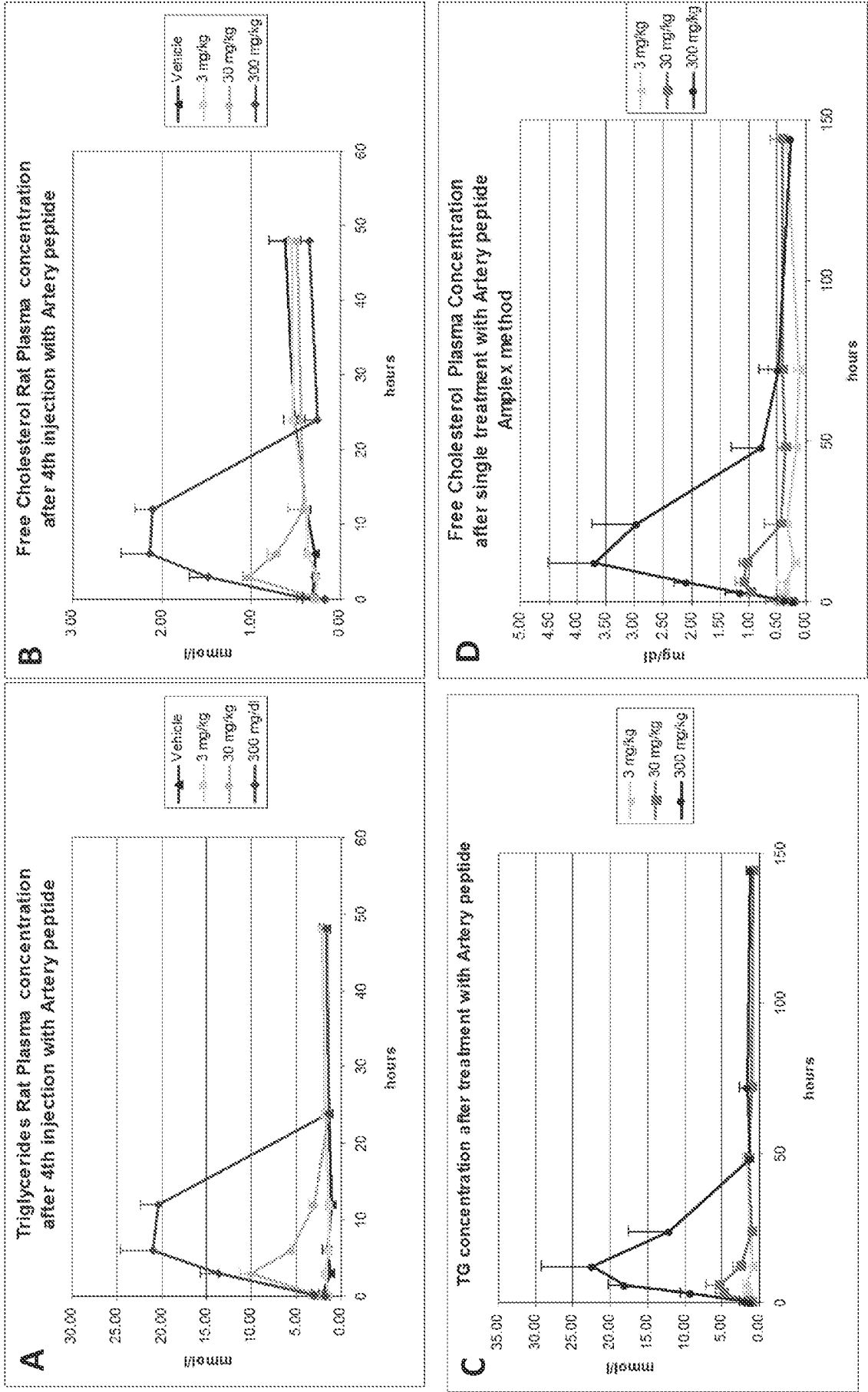


Figure 2



3 June 2004

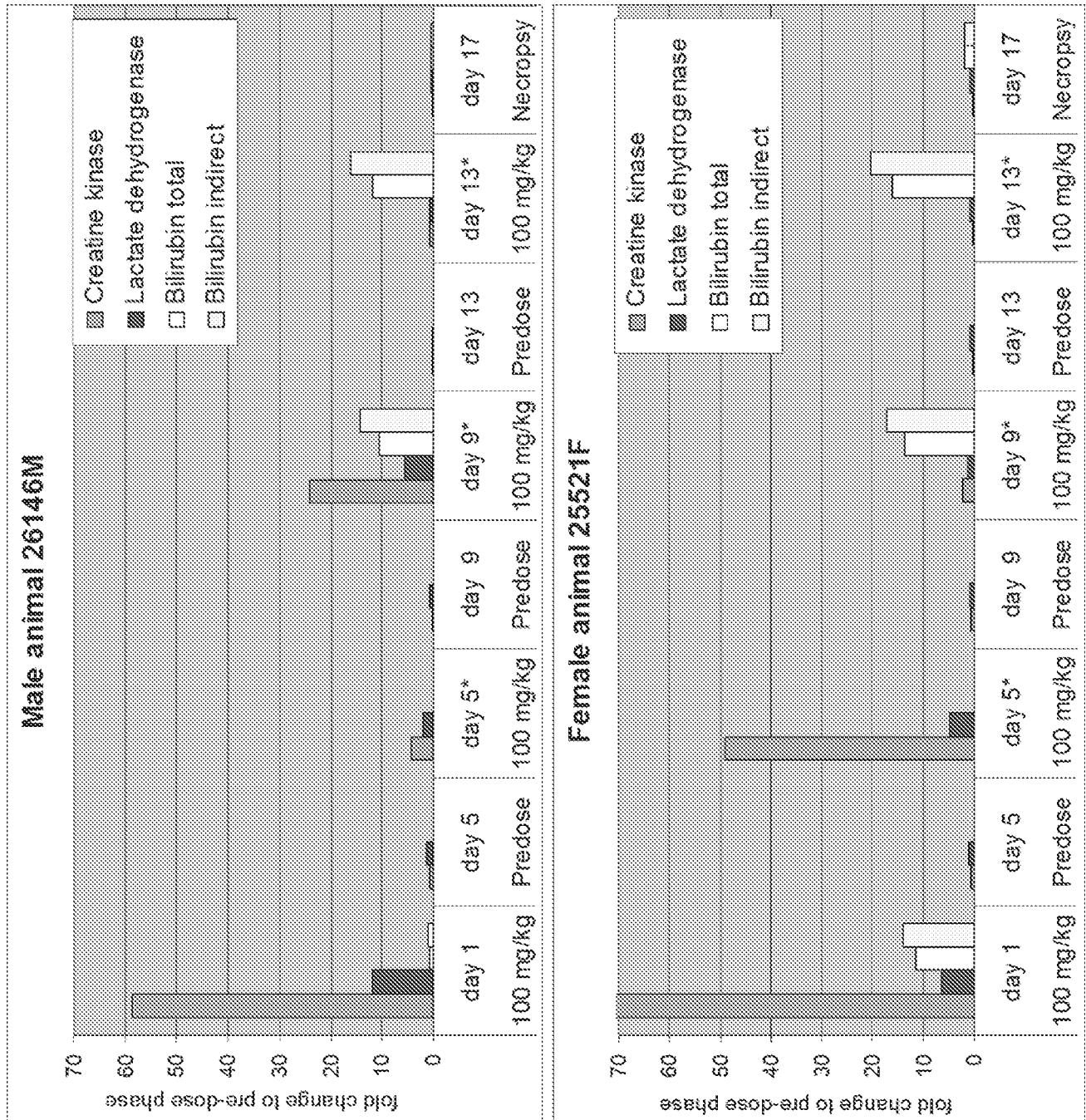


Figure 4

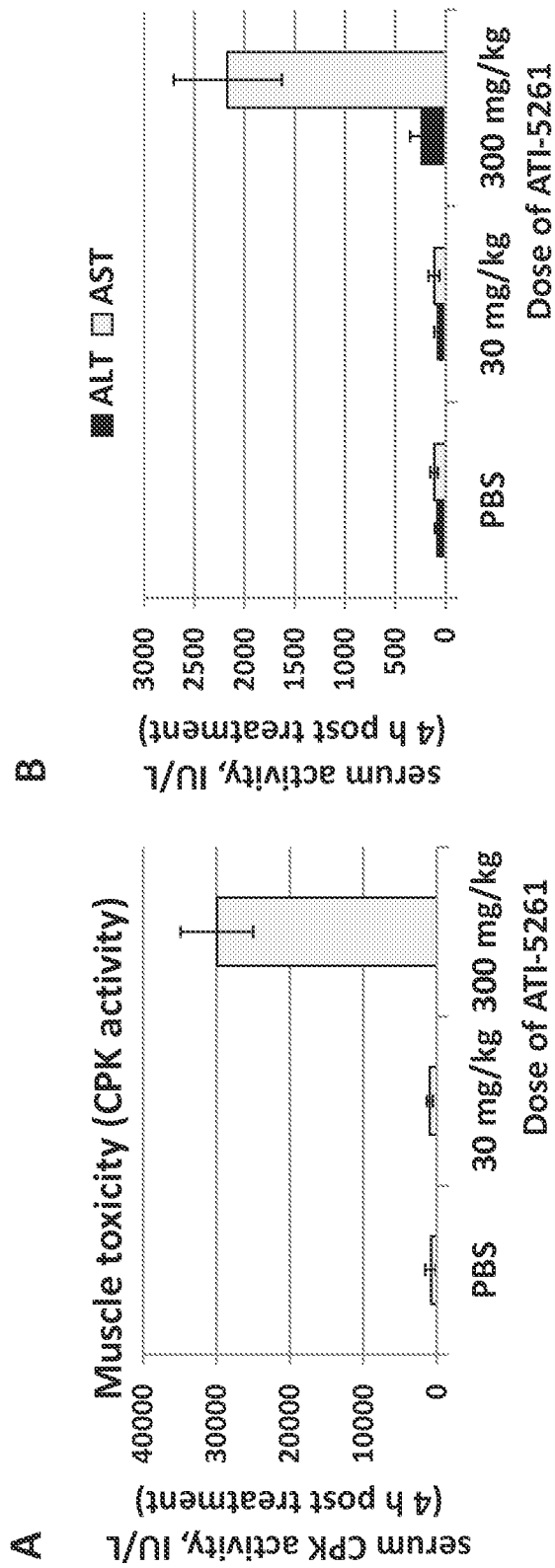


Figure 5

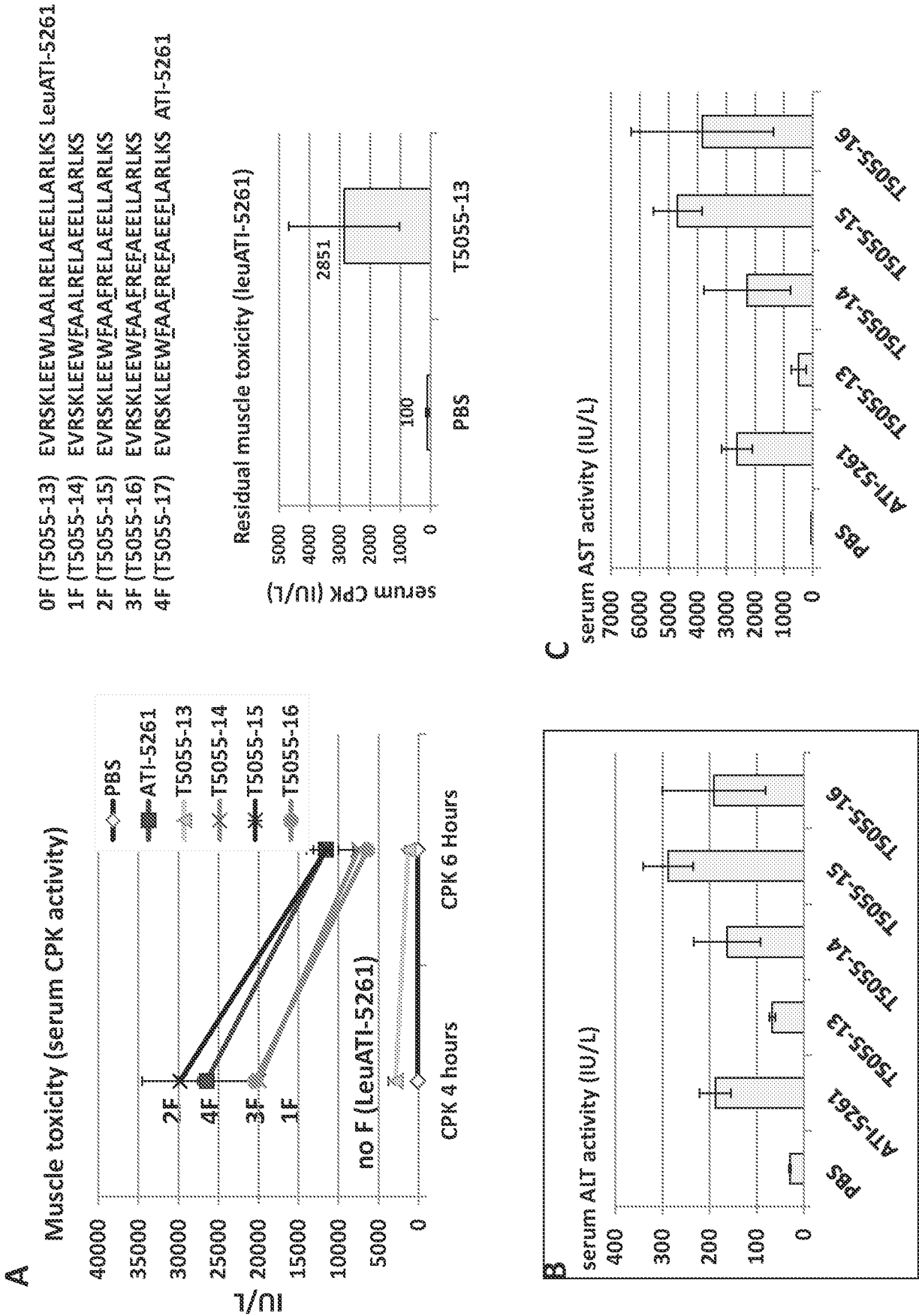


Figure 6

Serum lipid concentrations (mg/dl) following treatment (4 versus 6 hours) with peptides									
	triglyceride		total cholesterol		free cholesterol		cholesteryl ester		
	4 h	6 h	4 h	6 h	4 h	6 h	4 h	6 h	
PBS	37±7	29±6	71±21	66±4	11±2	12±4	60±21	54±5	
ATI-5261	1951±117	1358±161	172±25	174±18	43±15	44±8	128±36	130±15	
T5055-13	757±500	455±28	125±39	112±32	36±19	44±29	88±23	67±18	
T5055-14	1153±755	821±574	140±45	109±55	47±27	58±34	93±19	61±7	
T5055-15	1393±123	1009±64	129±24	131±11	56±16	80±6	74±25	51±14	
T5055-16	1390±453	1011±277	103±18	130±17	52±17	65±27	51±27	66±15	

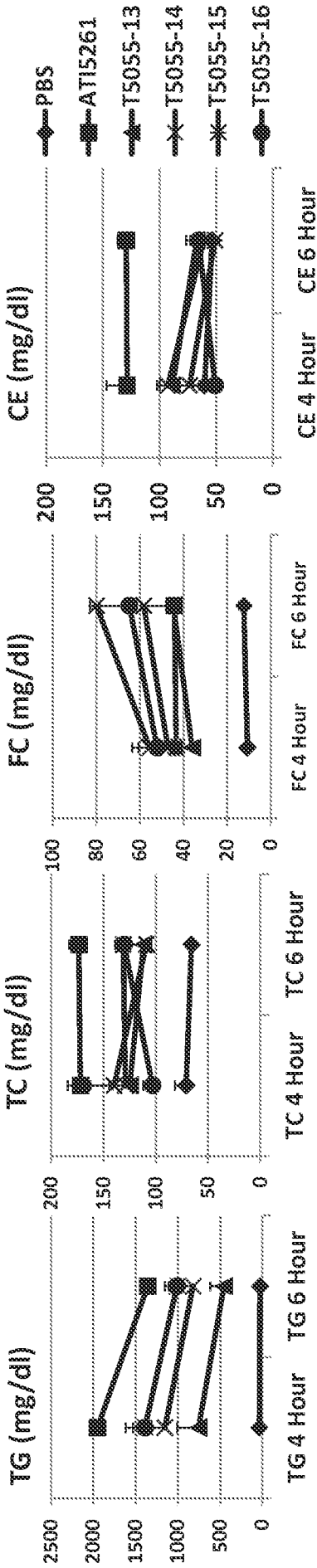


Figure 7

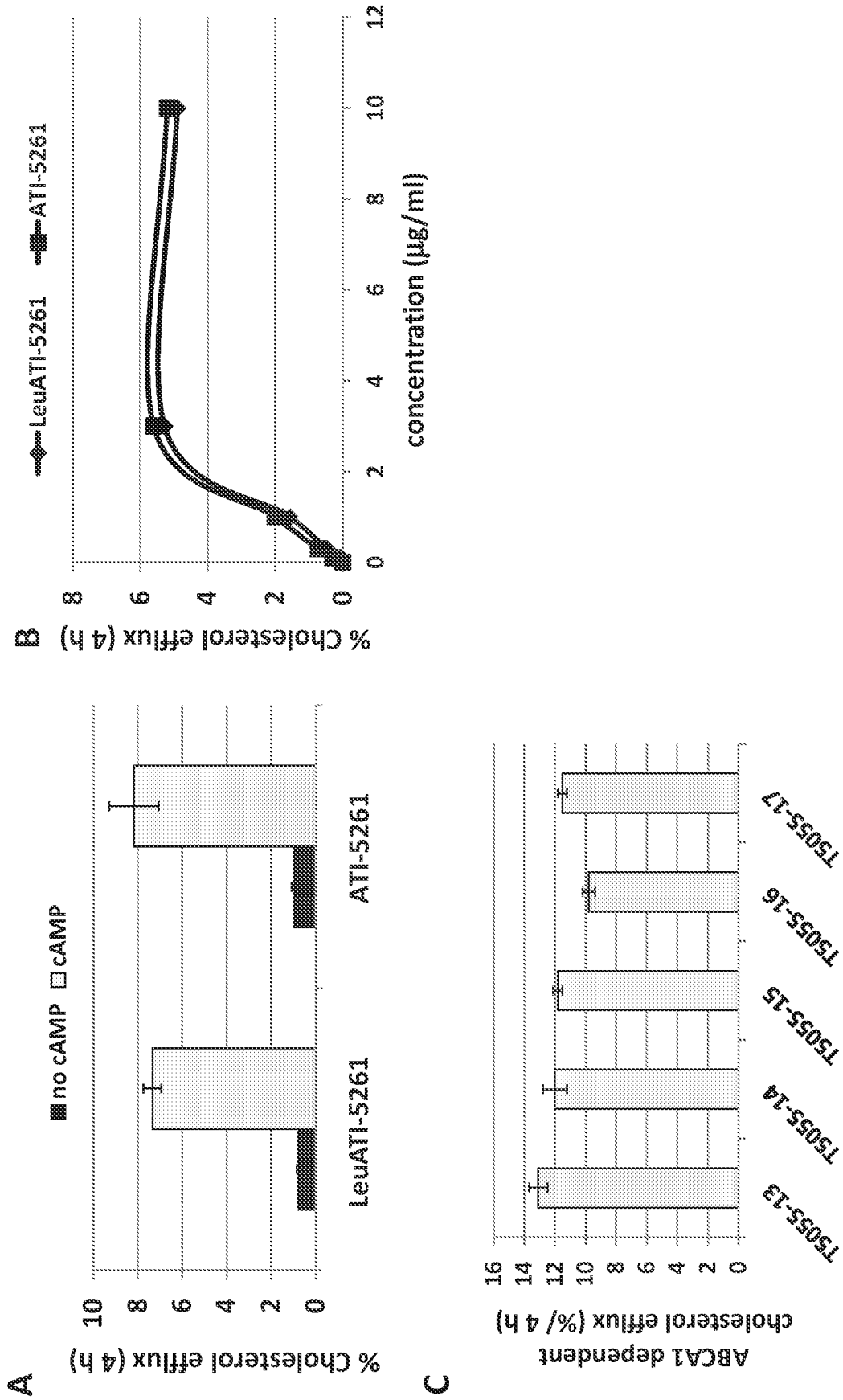
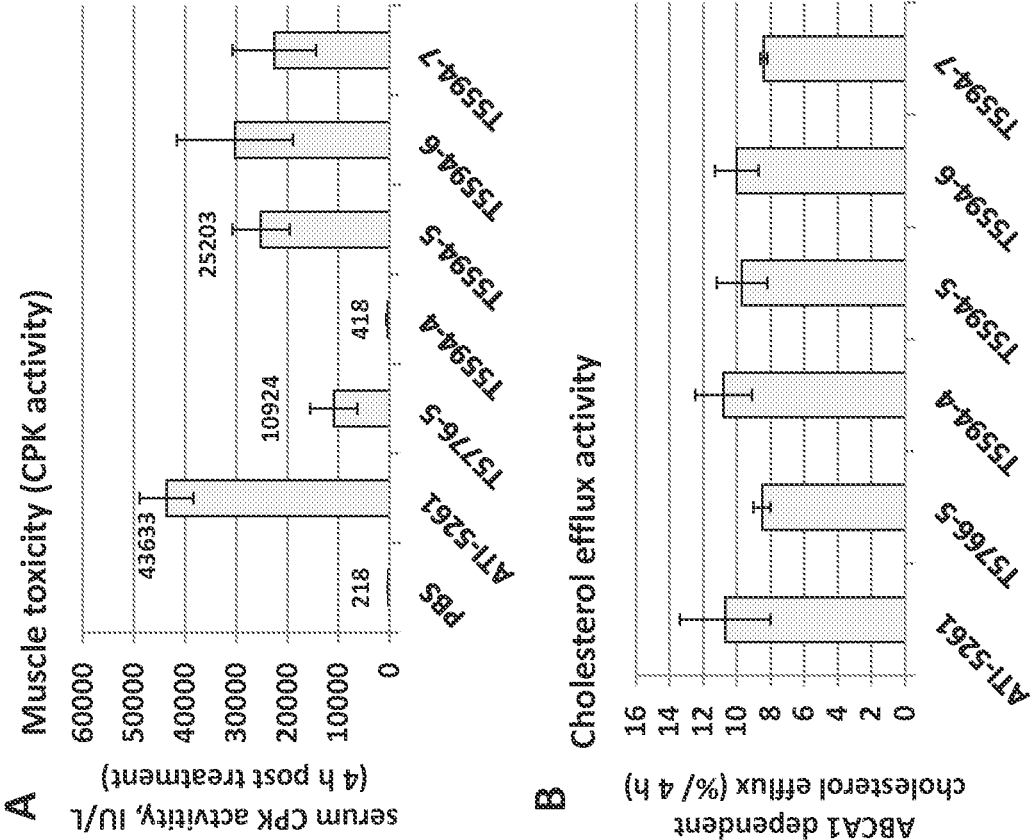


Figure 8

ATI-5261 analogs (lysine substitution or deletion)
T5766-5 EVRSKLEEWFAAFREFAEEFLARL 24-mer ATI-5261 (no KS)
T5594-4 EVRSKLEEWFAAFREFAEEFLARLNS K25→N
T5594-5 EVRSKLEEWFAAFKEFAEEFLAKLS R3,14,23→K



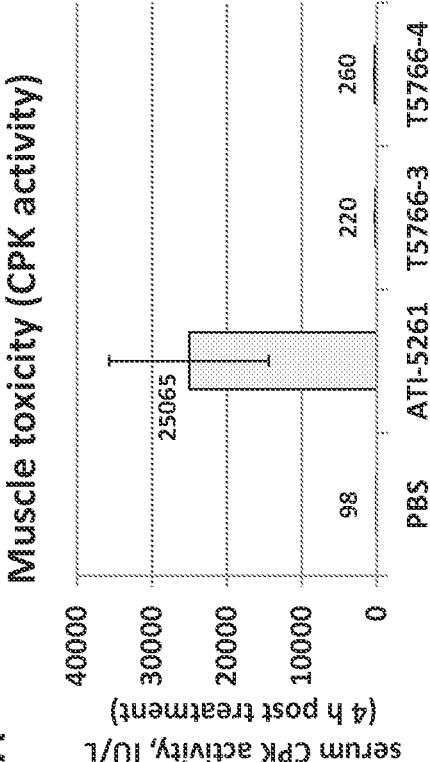
Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	57±3	80±8	37±1	21±3	0.69±0.05
ATI-5261	242±76	3391±1165	1671±1092	105±8	0.77±0.25
T5766-5	158±43	2065±772	1682±180	95±5	0.59±0.14
T5594-4	47±7	280±44	1642±383	163±16	0.76±0.27
T5594-5	130±12	1858±187	1876±400	95±4	0.63±0.16

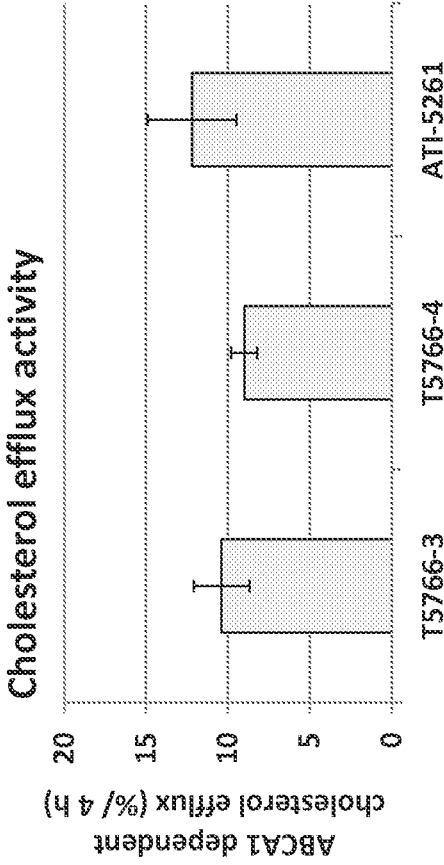
Figure 9

LeuATI-5261 analogs
T5766-3 EVQSKLEEWLAALQELAEELLARKS (R3,14→Q)
T5766-4 EVNSKLEEWLAALNELAEELLARKS (R3,14→N)

A



B



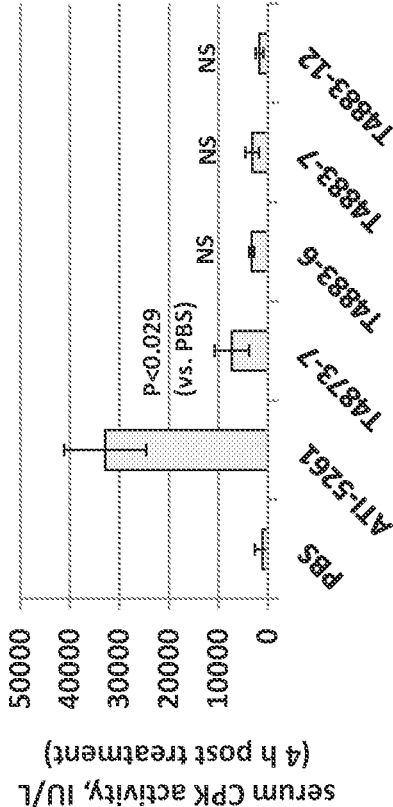
Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	23±2	47±8	48±4	33±3	0.63±0.05
ATI-5261	208±57	2610±1011	7688±554	170±7	0.68±0.23
T5766-3	44±12	87±35	954±317	44±47	0.92±0.07
T7766-4	38±4	83±25	414±326	69±42	1.04±0.24

Figure 10

Leu.ATI-5261--- hydrophobic analogs
T4873-7 EVRSKLEEWLAALRELAEEELLARLKS LeuATI-5261
T4883-6 EVRSKLEEWLAALRELAEEELLARAKS L24A
T4883-7 EVRSKLEEWLAALRELAEEELLARLKS L21A
T4883-12 EVRSKLEEWLAALREAAEEELAAARAKS L24,21,16A

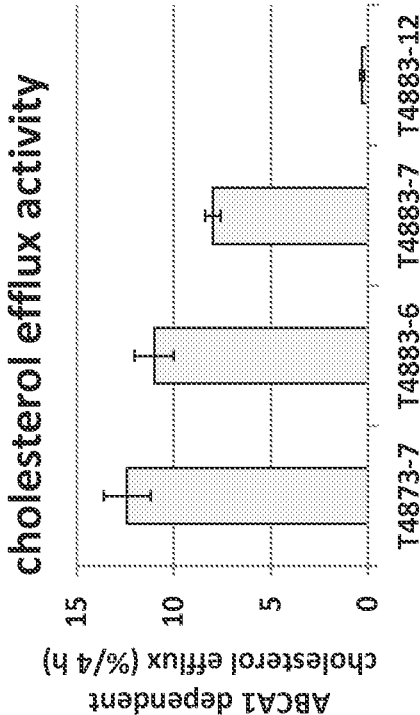
A Muscle toxicity (CPK activity)



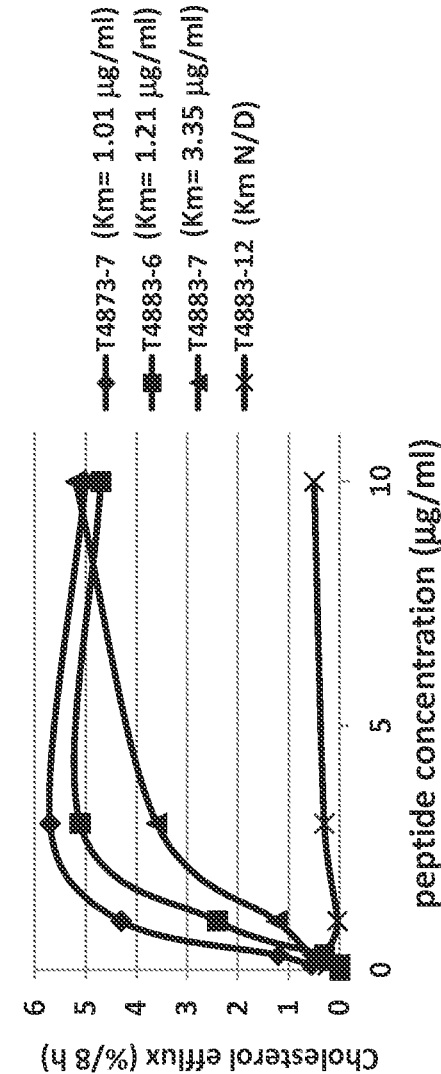
Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	43±22	106±52	4236±6		1.2
ATI-5261	247±50	3368±480	1860162±15		1
T4873-7	85±3	656±183	1266137±23		1.9
T4883-6	51±9	308±28	561111±53		1.7
T4883-7	73±47	293±56	835156±22		2.7
T4883-12	53±12	216±74	11752±32		1.3

B

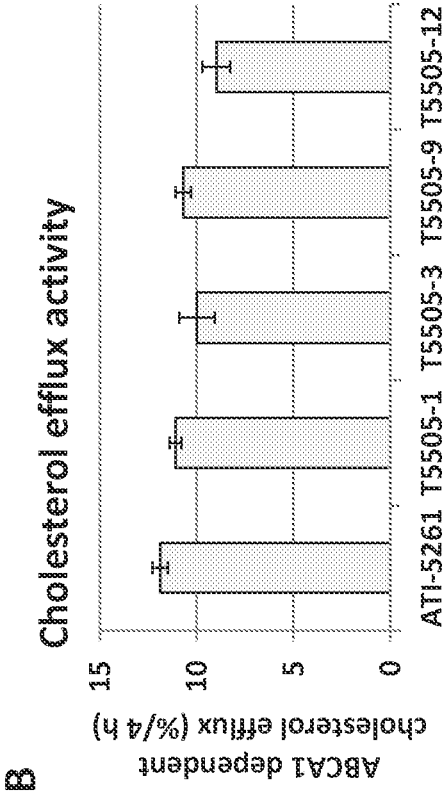
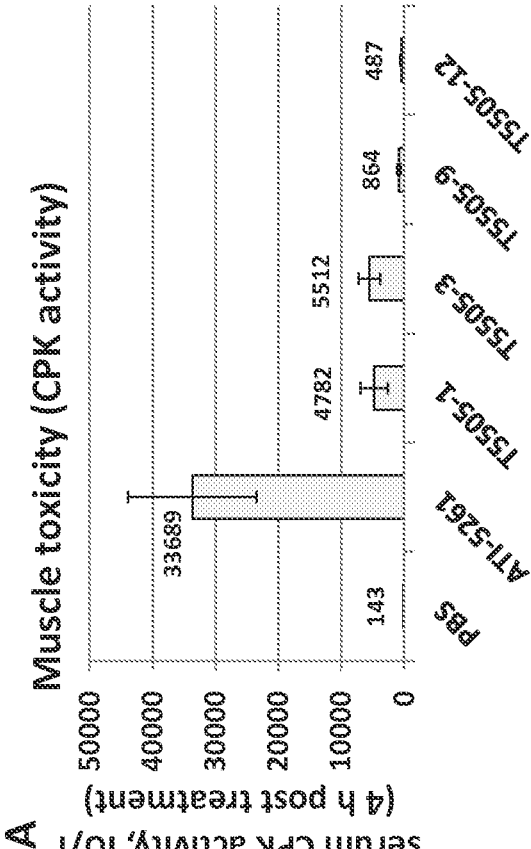


C



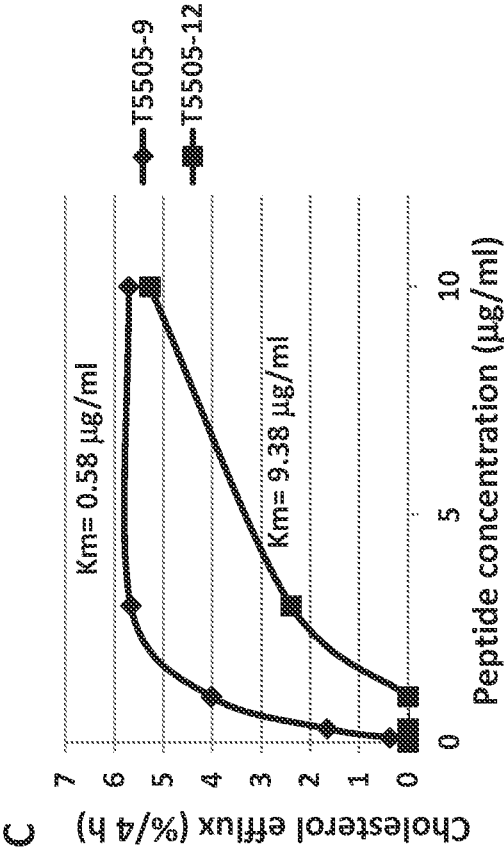
Leu.ATI-5261----- hydrophobic analogs continued
T5505-1 EARSKLEEWLAALRELAELLARLKS V2>A
T5505-3 EVRSKLEEWAAALRELAELLARLKS L10>A
T5505-9 EVRSKLEELLAALRELAELLARAKS L24>A; W9>L
T5505-12 EARSKAEEWLAALRELAELLARAKS V2, L6, L24>A

Figure 11



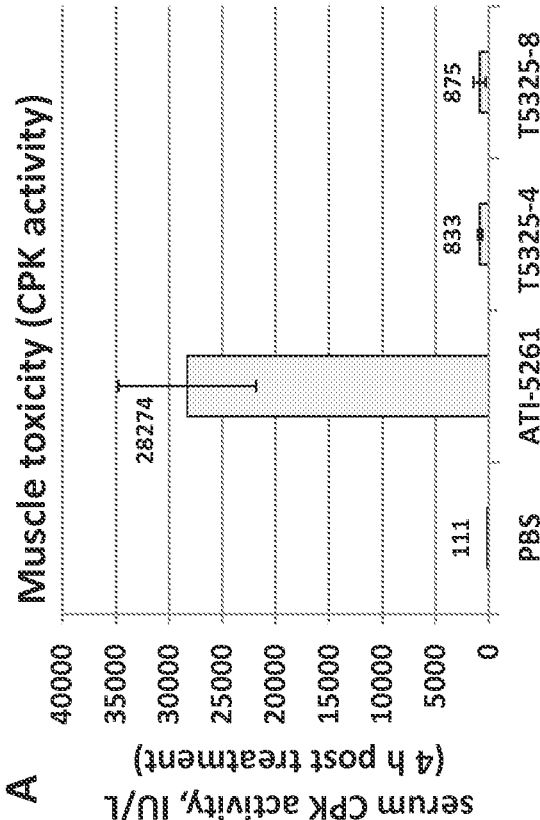
Serum clinical markers- 4 hour post treatment

	ALT (IU/l)	AST (IU/l)	TG (mg/dl)	NEFA (mg/dl)
PBS	33±5	56±4	45±5	0.55±0.07
ATI-5261	316±79	4183±1099	1950±616	0.58±0.18
T5505-1	70±9	518±111	1657±165	1.25±0.23
T5505-3	60±11	412±123	1868±294	1.07±0.14
T5505-9	57±8	190±40	136±43	0.55±0.11
T5505-12	44±7	108±26	172±45	0.88±0.14



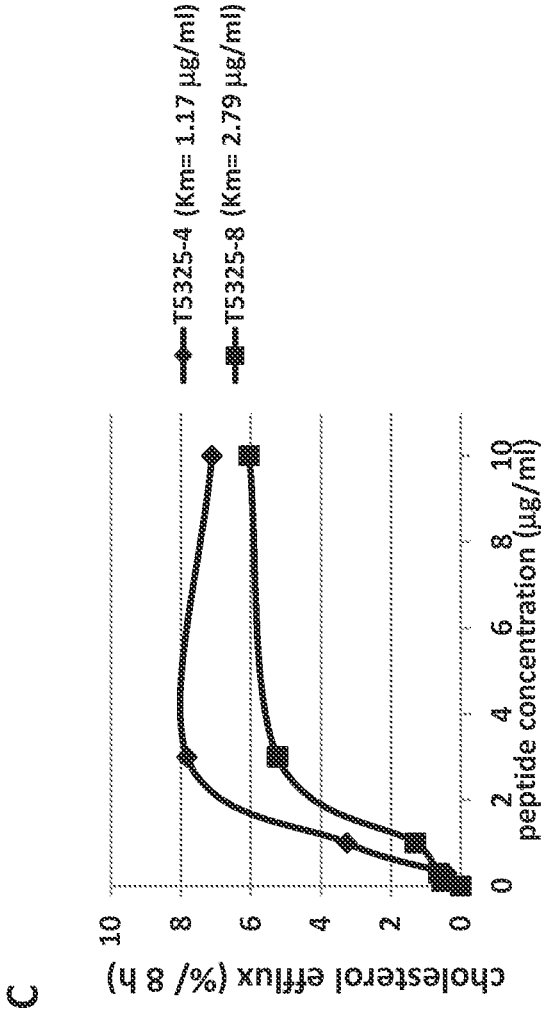
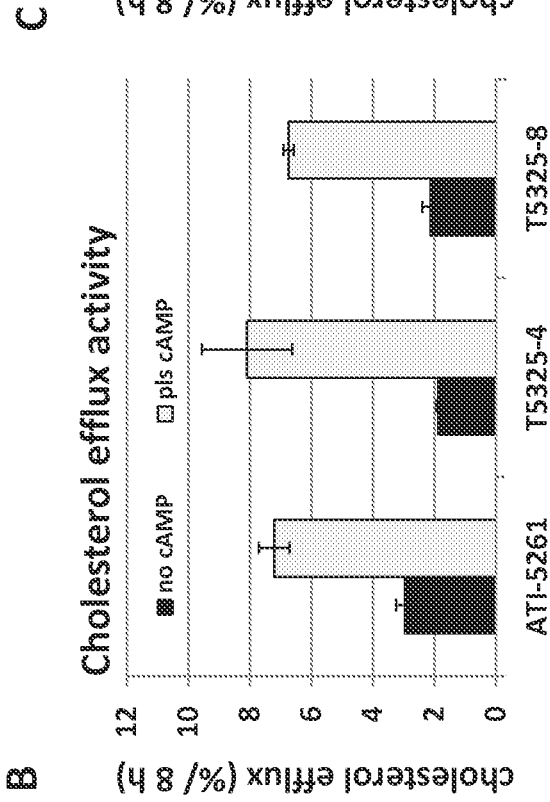
Leu.ATI-5261----- hydrophobic analogs continued
T5325-4 EVRSKLEELAAALRELAELLARLKS W9>A
T5325-8 EVRSKLEEVLAALRELAELLARAKS L24>A; W9V

Figure 12



Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	37±11	63±11	45±6	47±11	0.43±0.03
ATI-5261	226±22	3554±629	2272±244	145±10	0.48±0.05
T5325-4	39±5	149±52	429±158	88±21	0.70±0.14
T5325-8	42±8	168±64	153±81	49±11	0.46±0.09



LeuATI-5261 analogs, R14 del, R14L, or R14A in T5505-12

T5211-1

EARSKAEEWLAAAL_ELAEEELLARAKS

T5505-12 with R14 deletion

T5211-2

EARSKAEEWLAAALLELAEEELLARAKS

T5505-12 with R14L

T5211-3

EVRSKLEEWFAAF_EFAEEFLARLKS

ATI-5261 with R14 deletion

T5211-4

EVRSKLEEWFAAFLEFAEEFLARLKS

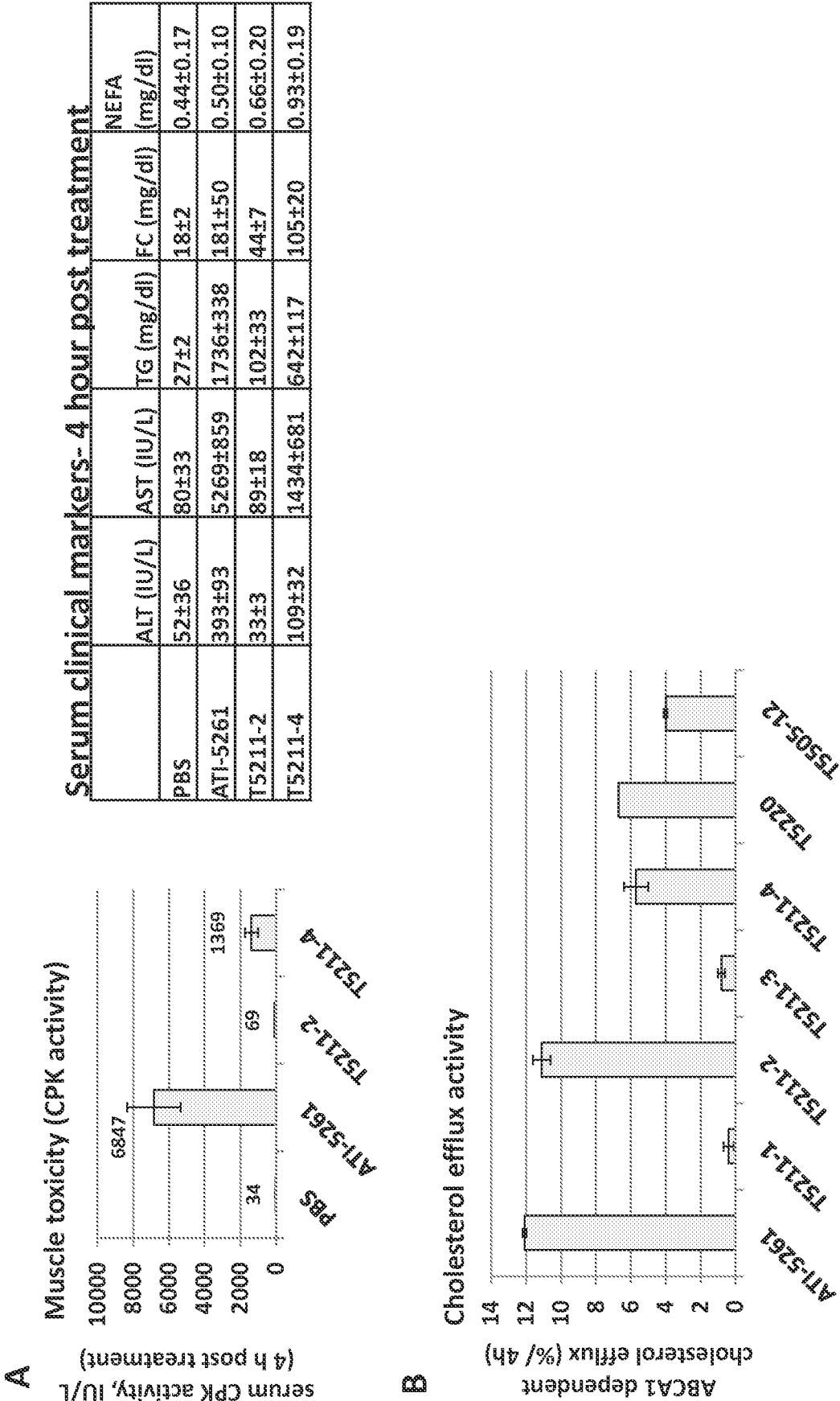
ATI-5261 with R14L

T5220

EARSKAEEWLAAALAEELAEELLARAKS

T5505-12 with R14A

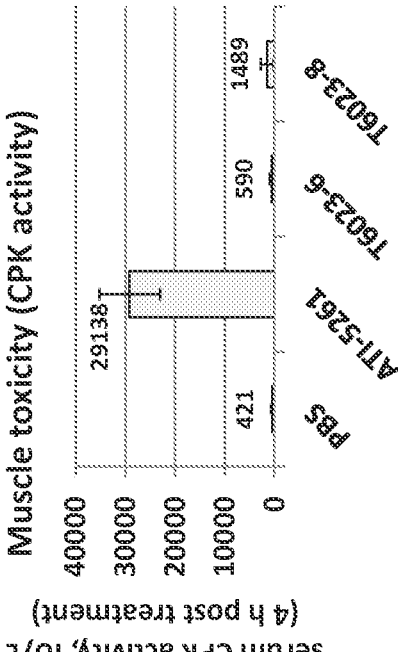
Figure 13



R14L analogs of Leu.ATI-5261 (i.e. T5211-2 analogs) Figure 14

T6023-3 EARSKAEEWLAALLEAEELLARAKS T5211-2
T6023-4 EARSKAEEWLAALLEAEELLARA T5211-2, (24-mer; no KS)
T6023-6 EVRSKAEEWLAALLEAEELLARA T5211-2, with A2V (24-mer; no KS)
T6023-8 EVRSKVEEWLAALLEAEELLARA T5211-2, with A2,6→V(24-mer; no KS)

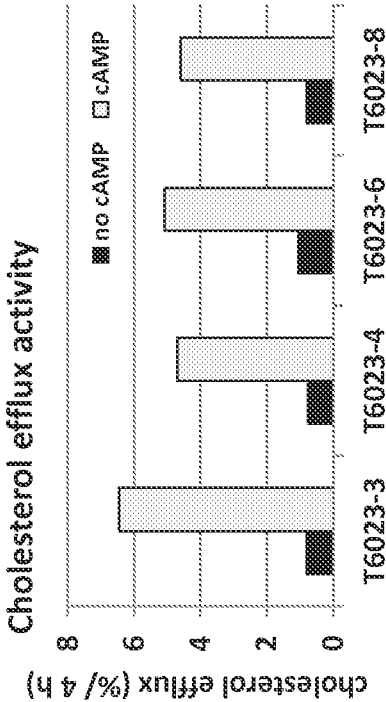
A



Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	TC (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	31±8	76±27	54±9	78±9	43±1	0.94±0.04
ATI-5261	210±31	2865±725	1885±627	163±18	132±11	0.83±0.27
T6023-6	76±48	170±83	1344±429	216±24	170±16	1.85±0.41
T6023-8	53±20	270±67	1317±256	176±29	152±14	1.09±0.44

B



C

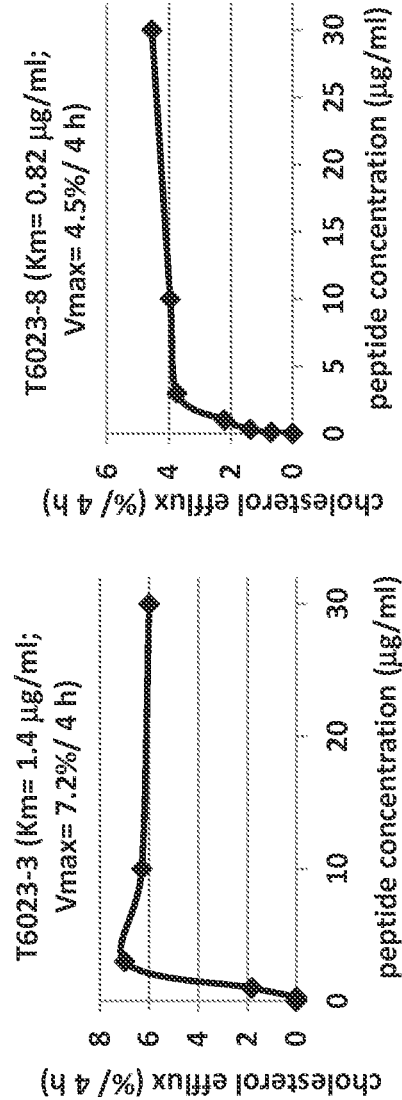
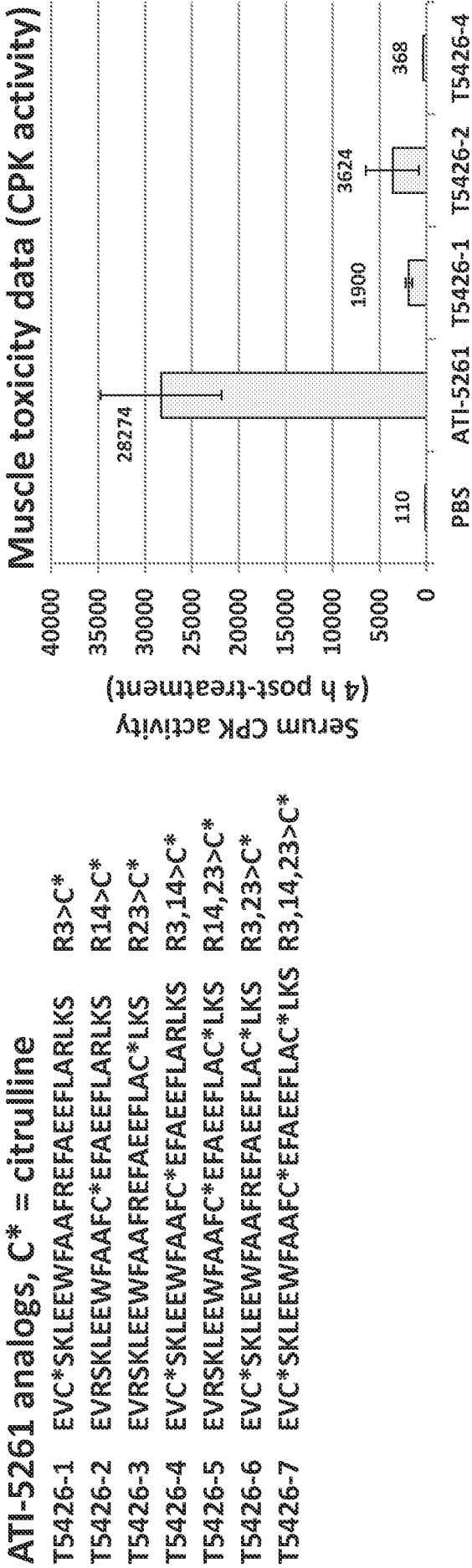


Figure 15



Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	37±11	63±11	45±6	47±11	0.43±0.03
ATI-5261	226±22	3554±629	2272±244	145±10	0.48±0.05
T5426-1	49±5	241±41	1620±150	143±10	0.62±0.14
T5426-2	55±11	453±173	1434±190	138±15	0.58±0.03
T5426-4	44±12	119±18	1054±248	136±12	0.60±0.11

Figure 16

Cholesterol efflux activity-- ATI-5261 citrulline analogs

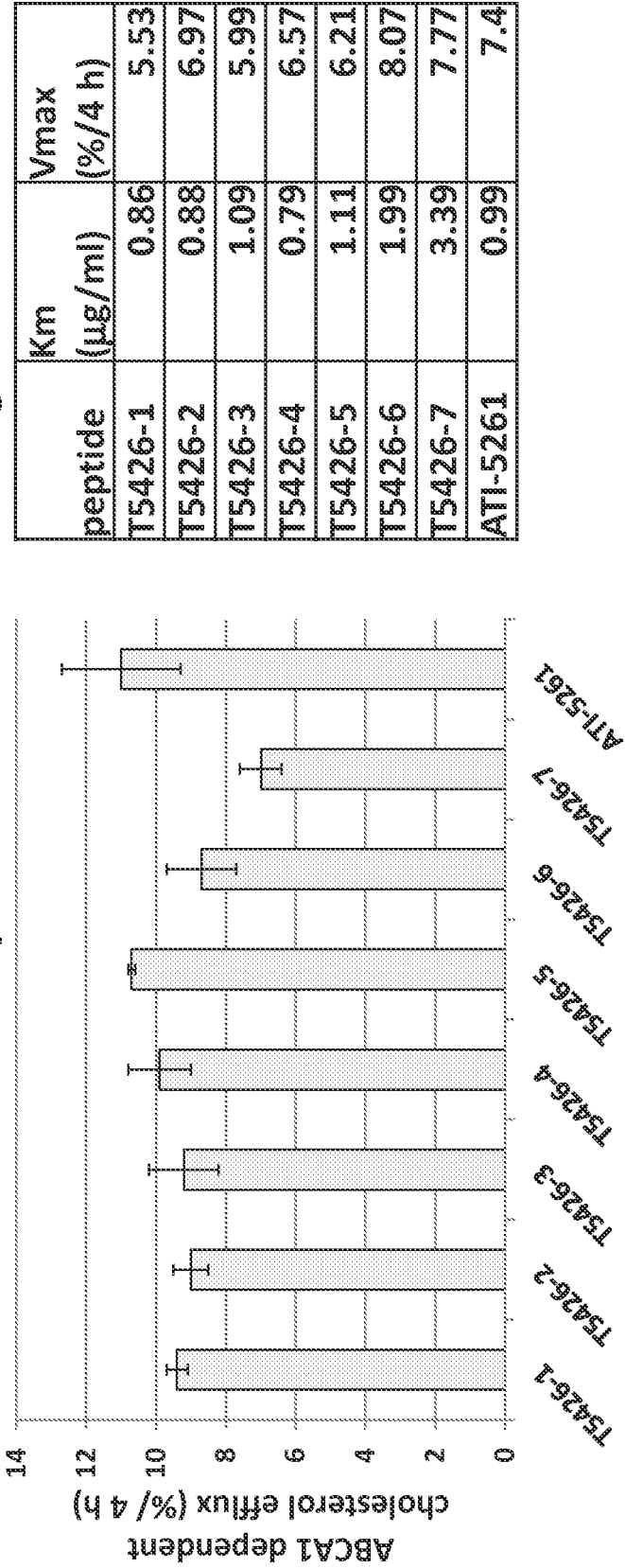


Figure 17

Citrulline analogs of ATI-5261; W9→L, A, or V (C* = citrulline)

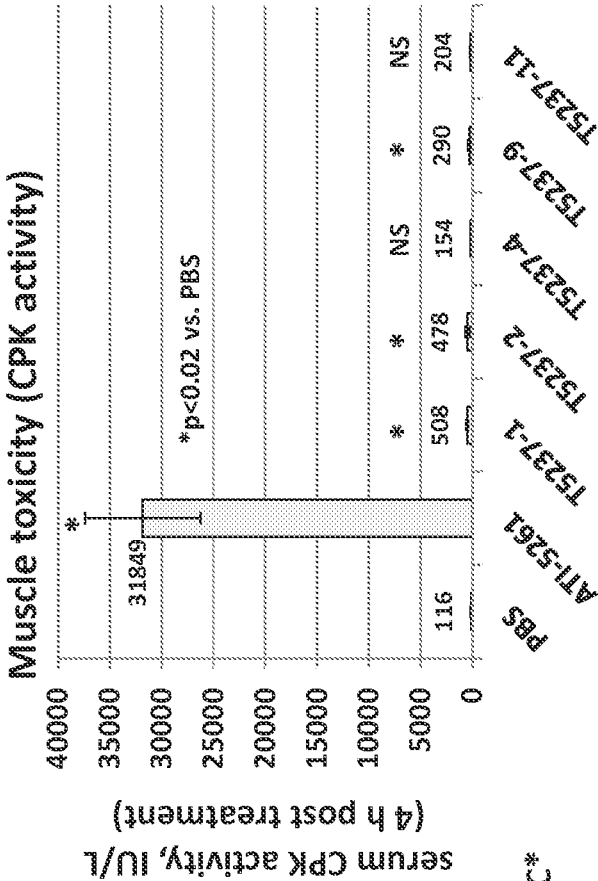
- T5594-1
- EVC*SKLEELFAAFC*EFAEEFLARLKS
- W9L
- T5594-2
- EVC*SKLEEAFAAFC*EFAEEFLARLKS
- W9A
- T5594-3
- EVC*SKLEEVFAAFC*EFAEEFLARLKS
- W9V



Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	52±36	80±33	27±2	18±2	0.44±0.17
ATI-5261	393±93	5269±859	1736±338	181±50	0.50±0.10
T5594-1	42±7	120±38	377±126	78±17	0.99±0.32
T5594-2	32±6	89±25	150±83	40±15	0.75±0.24
T5594-3	41±13	108±17	231±114	52±19	0.87±0.48

Figure 18



LeuATI-5261 analogs, C* = citrulline

T5237-1 EVC*SKLEEWLAALRELAELLARLKS R3>C*
T5237-2 EVRSKLEEWLAALC*ELAEELLARLKS R14>C*
T5237-3 EVRSKLEEWFAAFREFAEEFLAC*LKS R23>C*
T5237-4 EVC*SKLEEWLAALC*ELAEELLARLKS R3,14>C*
T5237-5 EVC*SKLEEWFAAFREFAEEFLAC*LKS R3,23>C*
T5237-6 EVRSKLEEWFAAFC*EFAEEFLAC*LKS R14,23>C*
T5237-7 EVC*SKLEEWFAAFC*EFAEEFLAC*LKS R3,14,23>C*
T5237-9 EVRSKLEELLAALC*ELAEELLARAKS T5505-9 R14>C*
T5237-11 EVC*SKLEELLAALC*ELAEELLARAKS T5505-9 R3,14>C*

Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	TC (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	58±8	53±9	57±8	81±18	21±2	0.51±0.1
ATI-5261	240±54	3640±959	3202±168	212±22	87±26	0.80±0.14
T5237-1	38±3	100±20	1539±469	176±20	93±24	0.89±0.11
T5237-2	47±11	147±59	447±372	138±68	57±31	0.81±0.21
T5237-4	36±4	68±4	321±79	79±15	32±3	0.78±0.09
T5237-9	43±7	99±10	51±8	41±15	18±2	0.49±0.05
T5237-11	36±5	76±14	40±13	34±22	17±4	0.50±0.02

Figure 19

Cholesterol efflux activity- LeuATI-5261 citrulline analogs

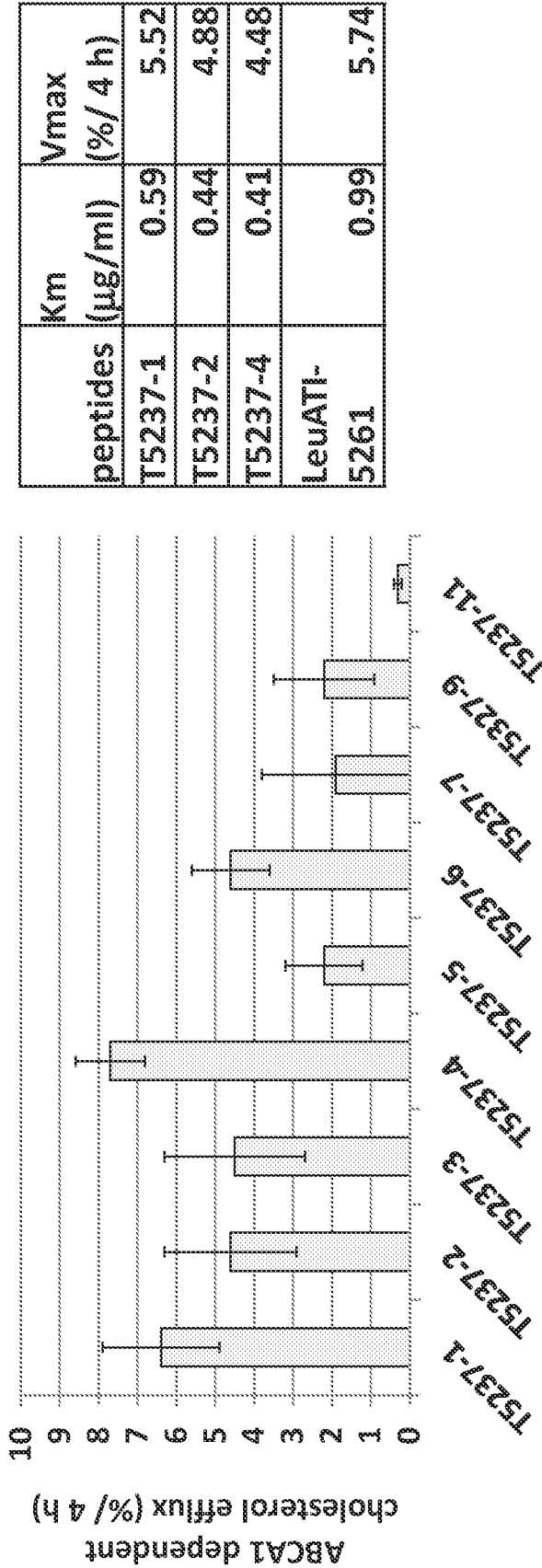


Figure 20

Acidic residue substitutions(E→Q); C*= citrulline

T5554-1 EVRSKLQEWFAAFREFAQEFLARLKS E7,18→Q

T5554-2 EVRSKLQEWFAAFREFAEEFLARLKS E7→Q

T5554-3 EVRSKLEEWFAAFREFAQEFLARLKS E18→Q

T5554-4 EVC*SKLQEWFAAFREFAEEFLARLKS E7→Q; R3→C*

T5554-5 EVC*SKLQEWFAAFC*EFAQEFLARLKS E7,18→Q; R3,14→C*

T5554-6 EVC*SKLQEWFAAFC*EFAQQFLAC*LKS E7,18,19→Q; R3,14,23→C*

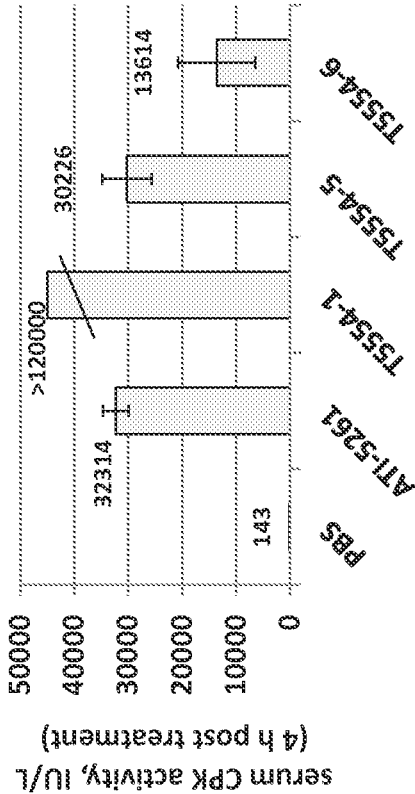
T5554-7 EVC*SKLQEWFAAFC*EFAEEFLARLKS E7→Q; R3,14→C*

T5554-8 EVC*SKLEEWFAAFC*EFAQEFLARLKS E18→Q; R3,14→C*

T5554-9 EVRSKLQEWLAALRELAEEELLARLKS E7→Q in LeuATI-5261

T5554-10 EVC*SKLQEWLAALRELAEEELLARLKS E7→Q; R3→C* in LeuATI-5261

Muscle toxicity (CPK activity)



Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	26±6	84±21	26±5	36±3	0.49±0.05
ATI-5261	233±10	4595±933	1787±175	173±42	0.94±0.28
T5554-1	1573±226	14194±1454	726±101	128±5	0.67±0.06
T5554-5	185±47	3330±1003	1752±380	201±97	0.36±0.13
T5554-6	154±22	2095±187	1760±174	166±31	0.56±0.14

Figure 21

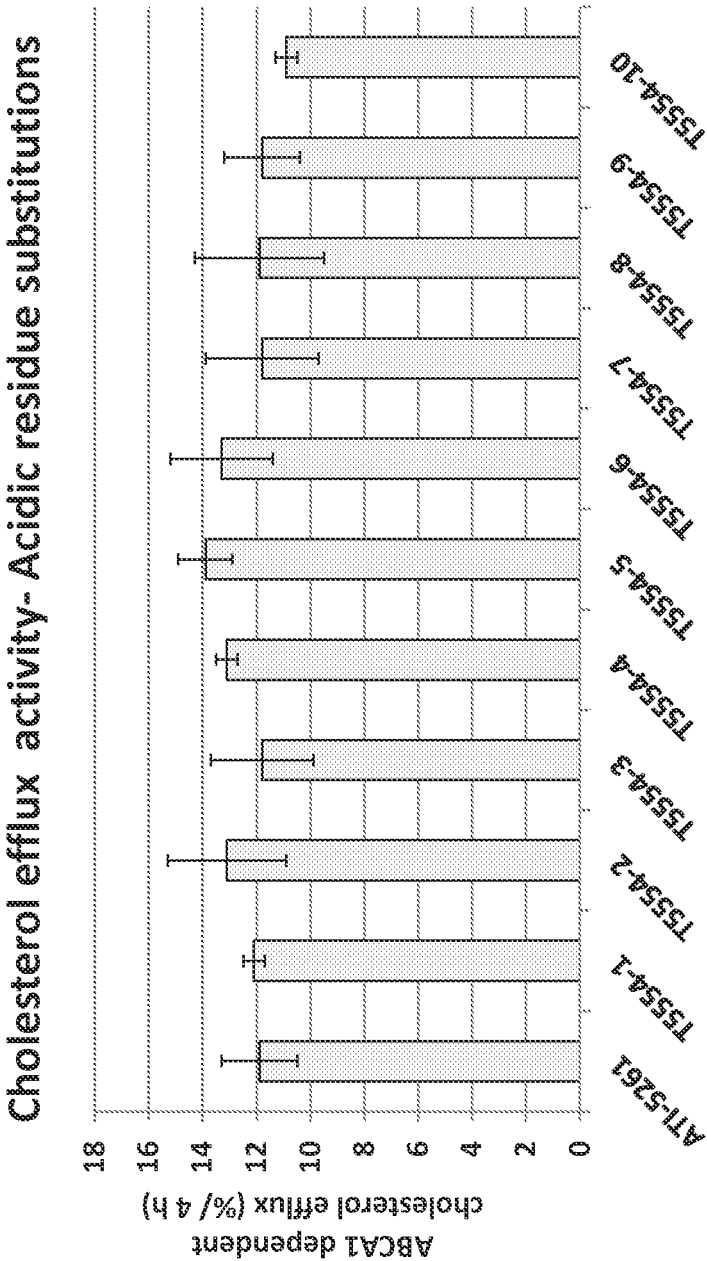
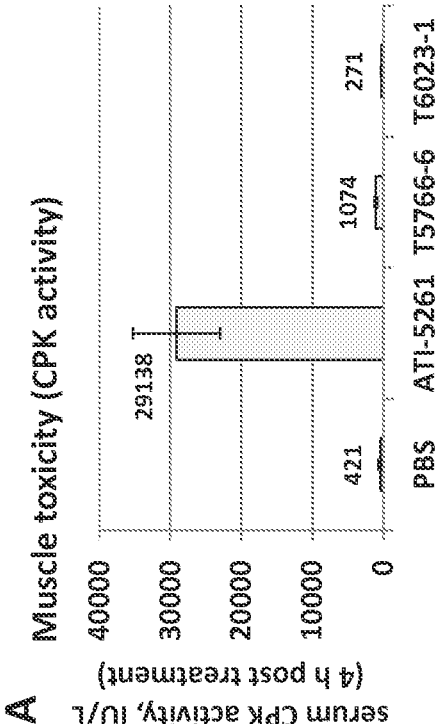


Figure 22

Cit.LeuATI-5261 analogs, 24-mers, C* = citrulline
T5766-6 EVRSKLEEWLAALRELAEEELLARKS
T6023-1 EVC*SKLEEWLAALC*ELAEELLARL
Leu.ATI-5261 (no KS)
Cit.LeuATI-5261 (no KS)



Serum clinical markers- 4 hour post treatment

	ALT (IU/L)	AST (IU/L)	TG (mg/dl)	TC (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	31±8	76±27	54±9	78±9	43±1	0.94±0.04
ATI-5261	210±31	2865±725	1885±627	163±18	132±11	0.83±0.27
T5766-6	45±11	242±30	1711±239	201±32	145±12	0.90±0.05
T6023-1	37±5	84±10	1561±756	174±27	159±19	1.74±0.24

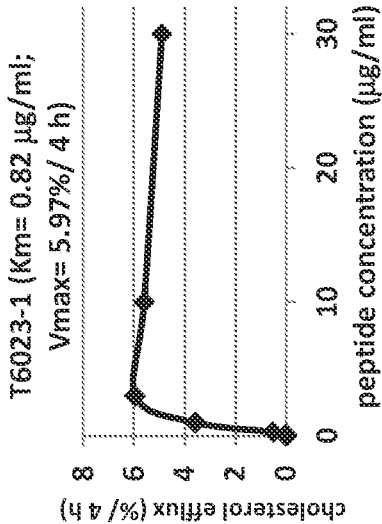
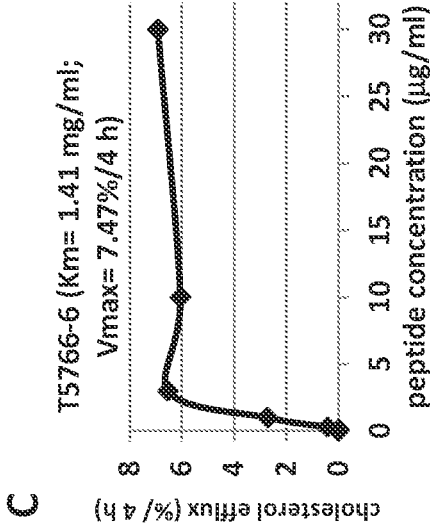
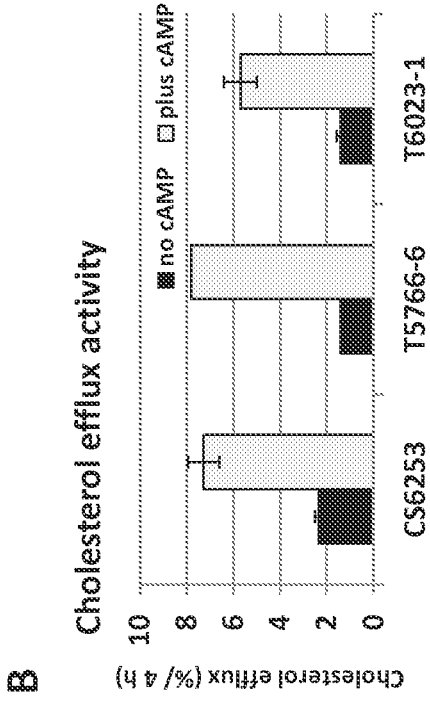


Figure 23

Cit.LeuATl-5261 analogs, C* = citrulline
T6623-2 EVLSKLEEWLAALC*ELAEELLARIKS C*3→L
T6275-3 ELC*SKLEEWLAALC*ELAEELLARIKS V2→L

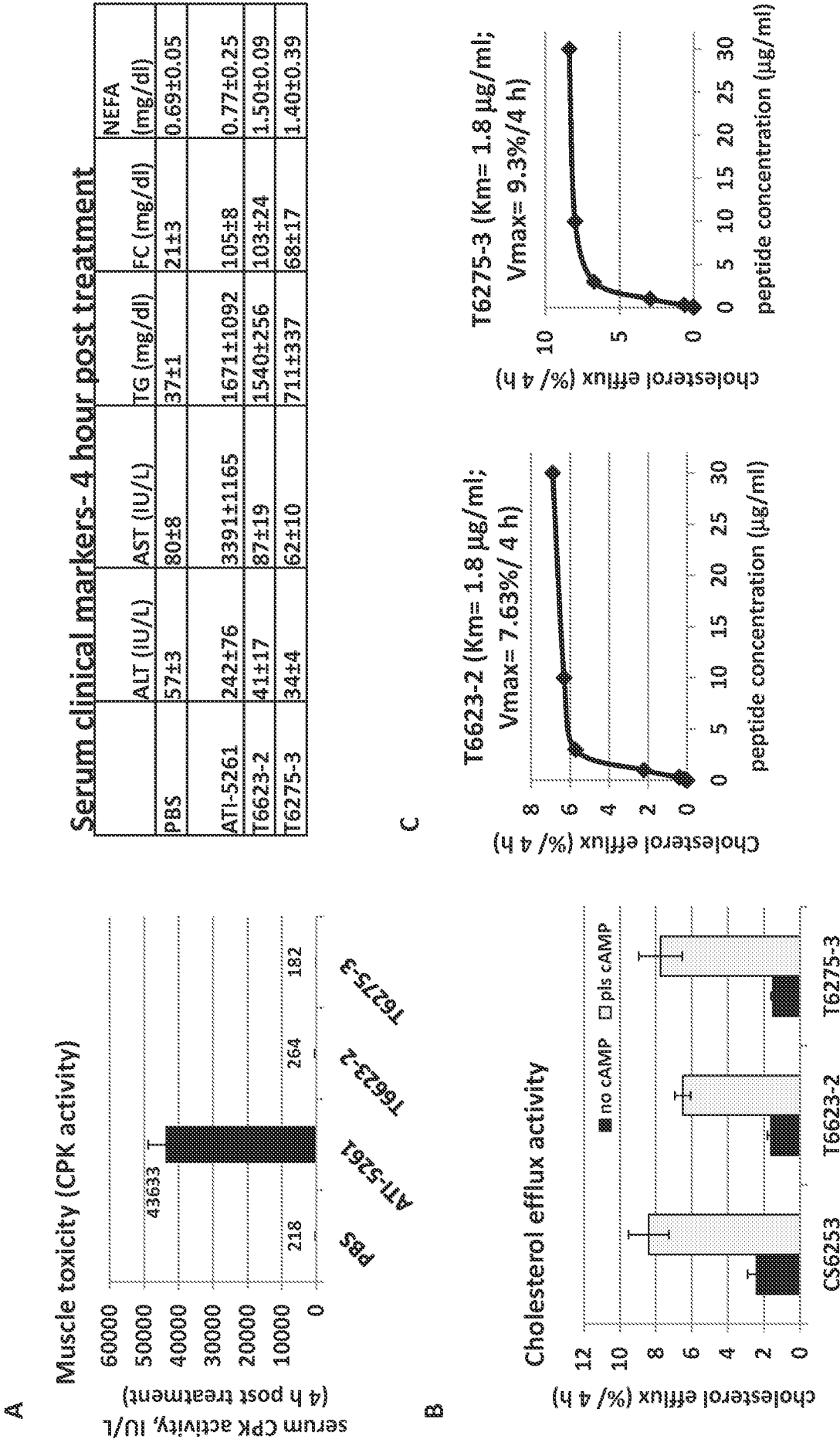
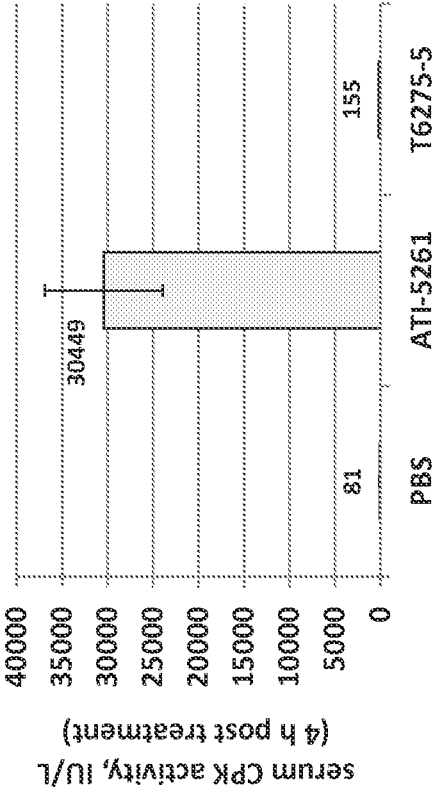


Figure 24

Cit.LeuATI-5261 analogs, C* = citrulline

T6275-5	EVC*SKLEEWLAALLEAEELLARLKS	C*14L
T6623-1	ELC*SKLEEWLAALLEAEELLARLKS	V2L & C*14L
T6623-2	EVL SKLEEWLAALC*ELAEELLARLKS	C*3L
T6623-3	ELLSKLEEWLAALC*ELAEELLARLKS	V2L & C*3L
T6623-4	EVL SKLEEWLAALLEAEELLARLKS	C*3, 14L
T6623-5	ELLSKLEEWLAALLEAEELLARLKS	V2L & C*3, 14L
T6623-6	ELC*SKLEEWLAALLEAEELLARL	V2L & C*14L, no KS
T6623-7	EVL SKLEEWLAALC*ELAEELLARL	C*3L, no KS
T6623-8	ELLSKLEEWLAALC*ELAEELLARL	V2L & C*3L, no KS
T6623-9	EVL SKLEEWLAALLEAEELLARL	C3, 14L, no KS
T6623-10	ELLSKLEEWLAALLEAEELLARL	V2L & C*3, 14L, no KS
T6623-11	ELRSKLEEWLAALLEAEELLARL	V2L & C*14L, with R3 and no KS
T6623-12	ELLSKLEEWLAALRELAEEELLARL	V2L & C*3L, with R14 and no KS

Muscle toxicity (CPK activity)



Serum clinical markers- 4 hour post treatment

	ALT (IU/l)	AST (IU//l)	TG (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	33±11	49±10	51±9	29±1	0.91±0.15
ATI-5261	190±31	2611±355	2130±37	132±23	0.68±0.18
T6275-5	40±25	79±23	1232±262	135±27	1.27±0.22

Figure 25

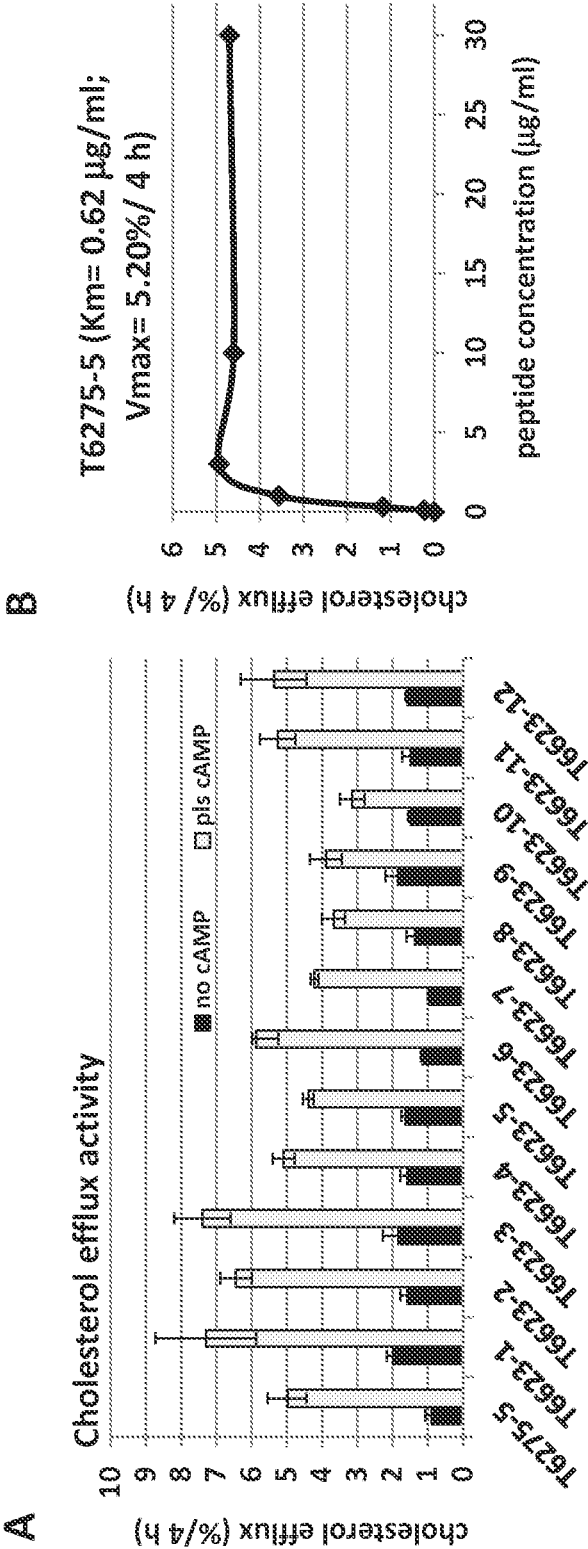
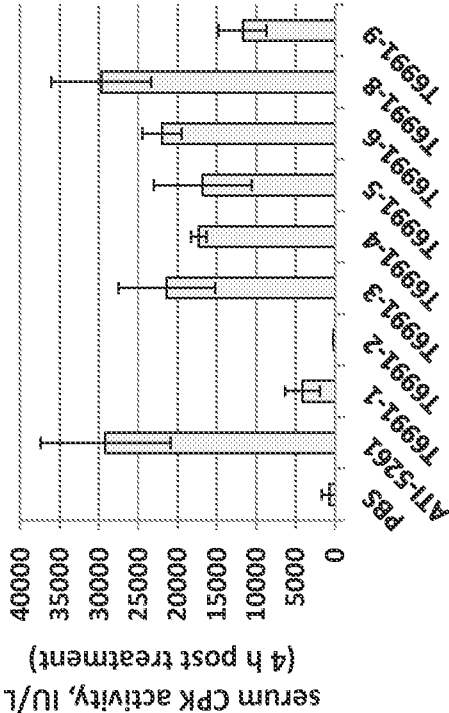


Figure 26

ATI-5261 analogs with citrulline, C* = citrulline

T6991-1	EVRSKLEEWIAAIREIAEEILARLKS	F10,13,16,20→I (F to isoleucine in ATI-5261)
T6991-2	EVC*SKLEEWIAAIC*EIAEEILARLKS	R3, 14→ C* in isoleucine form of ATI-5261
T6991-3	EVRAKLEEWFAAFREFSEEFARLKS	S4/A17 swap
T6991-4	EVRSKLEEWFAAFREFSEEFARLKA	S26/A17 swap
T6991-5	EVRSKLEEWFAAFREFSEEFARLKS	A17→S
T6991-6	EVRSKLEEWFAAFREFYEEFARLKS	A17→Y
T6991-7	EVRSKLEEVFAAFREFAEFARLKS	W9→Y
T6991-8	EVRSKLEEWFAAFREFAEFLARSKL	S26/L24 swap
T6991-9	EVRSKLEEWFAAFREFYEEFLARSKL	S26/L24 swap with A17→Y

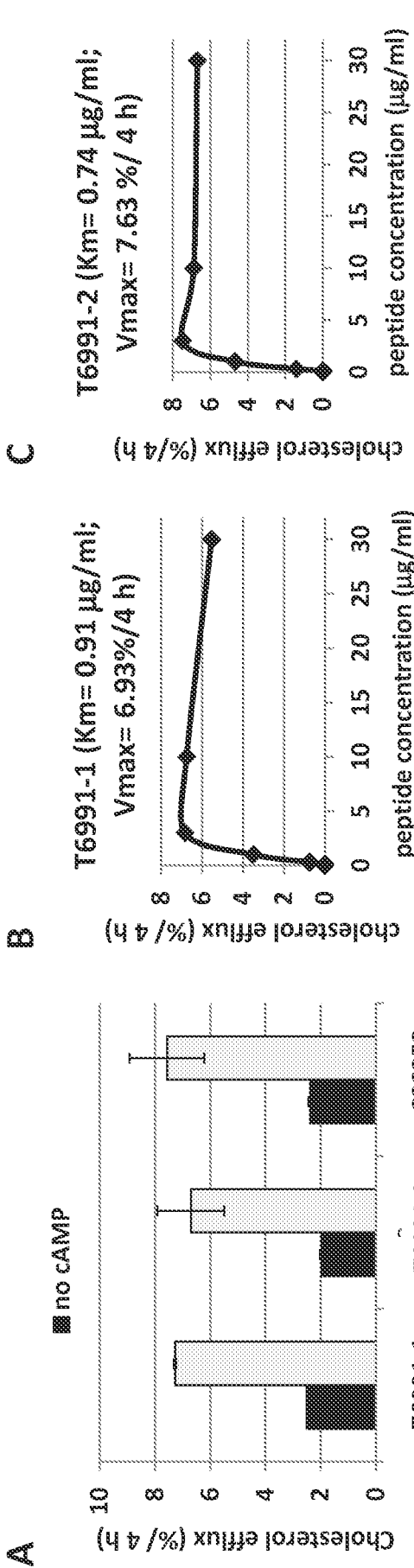
Muscle toxicity (CPK activity)



Serum clinical markers- 4 hour post treatment

	ALT (IU/l)	AST (IU/l)	TG (mg/dl)	TC (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	18±7	50±29	63±13	70±2	20±3	0.69±0.10
ATI-5261	143±42	2645±1071	2397±288	176±3	99±11	0.77±0.28
T6991-1	61±4	875±198	1462±278	146±25	96±14	2.43±0.26
T6991-2	19±4	54±12	220±158	69±12	30±8	0.87±0.13
T6991-3	93±17	1350±294	2245±434	154±10	88±21	1.47±0.59
T6991-4	88±6	1213±36	2566±174	167±10	101±7	1.26±0.07
T6991-5	111±24	1572±285	1938±438	147±23	101±14	1.53±0.23
T6991-6	170±26	2923±649	2049±493	150±16	97±13	0.98±0.17
T6991-8	141±11	2530±212	1758±534	138±23	91±21	1.71±0.36
T6991-9	70±13	894±185	1944±296	142±3	100±9	1.95±0.33

Figure 27



D

E

Efflux kinetics vs. apoA-I

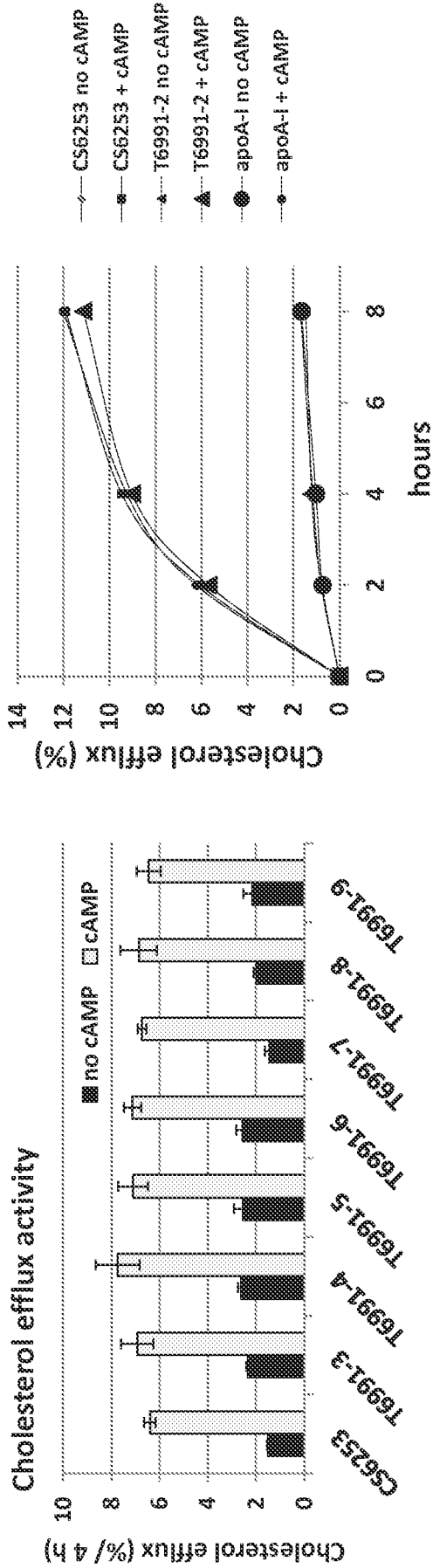


Figure 28

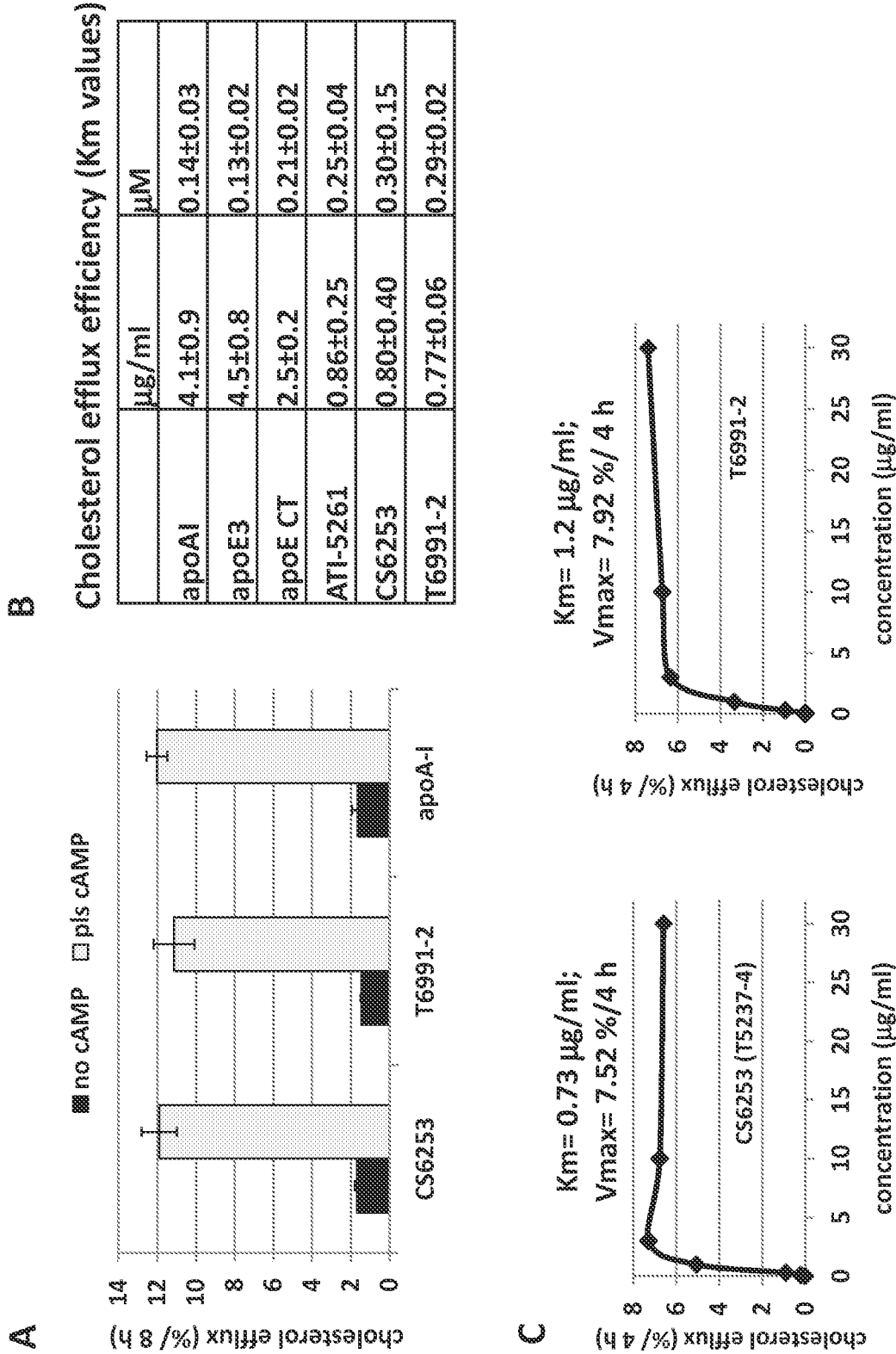


Figure 29

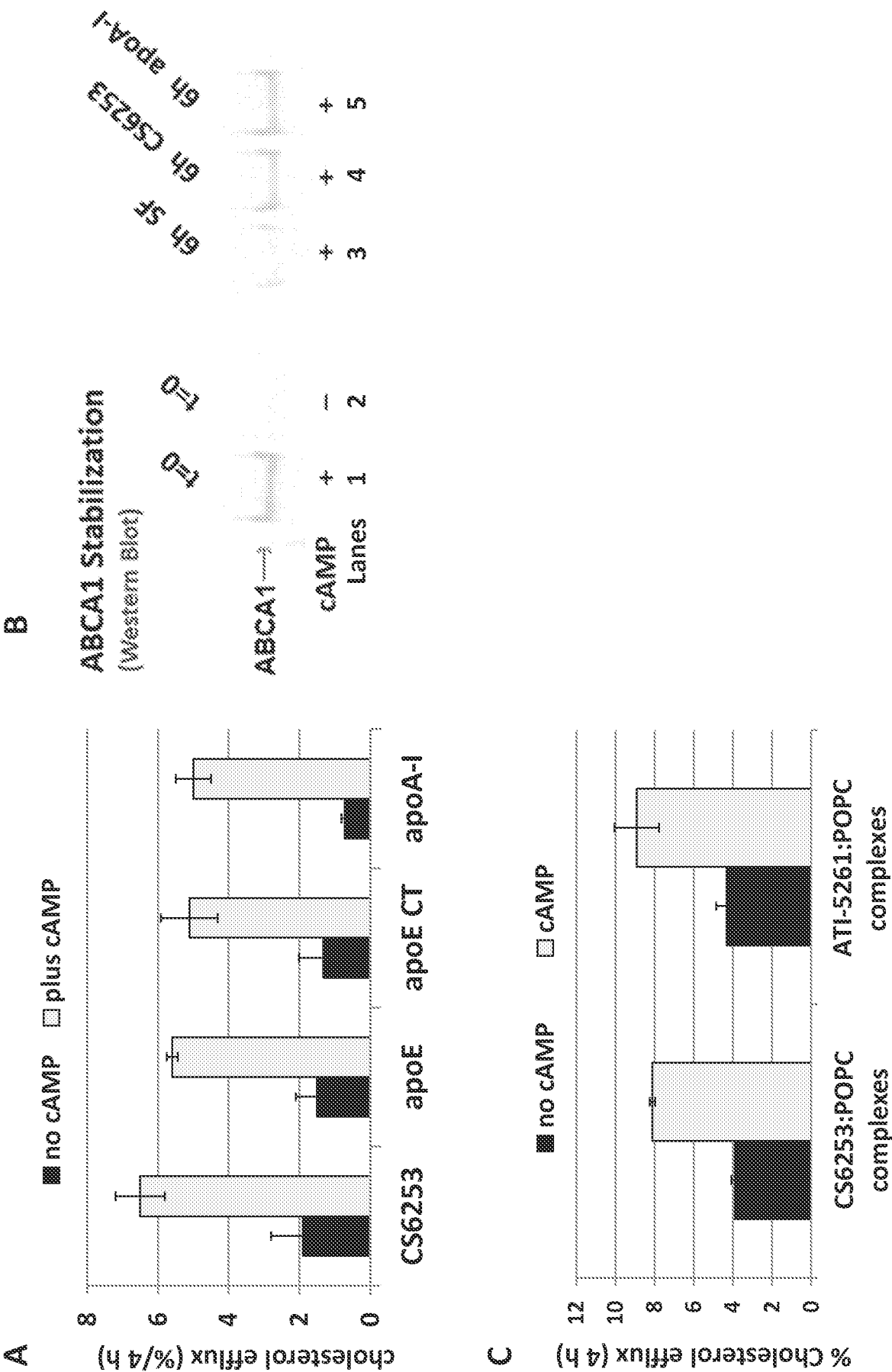


Figure 30

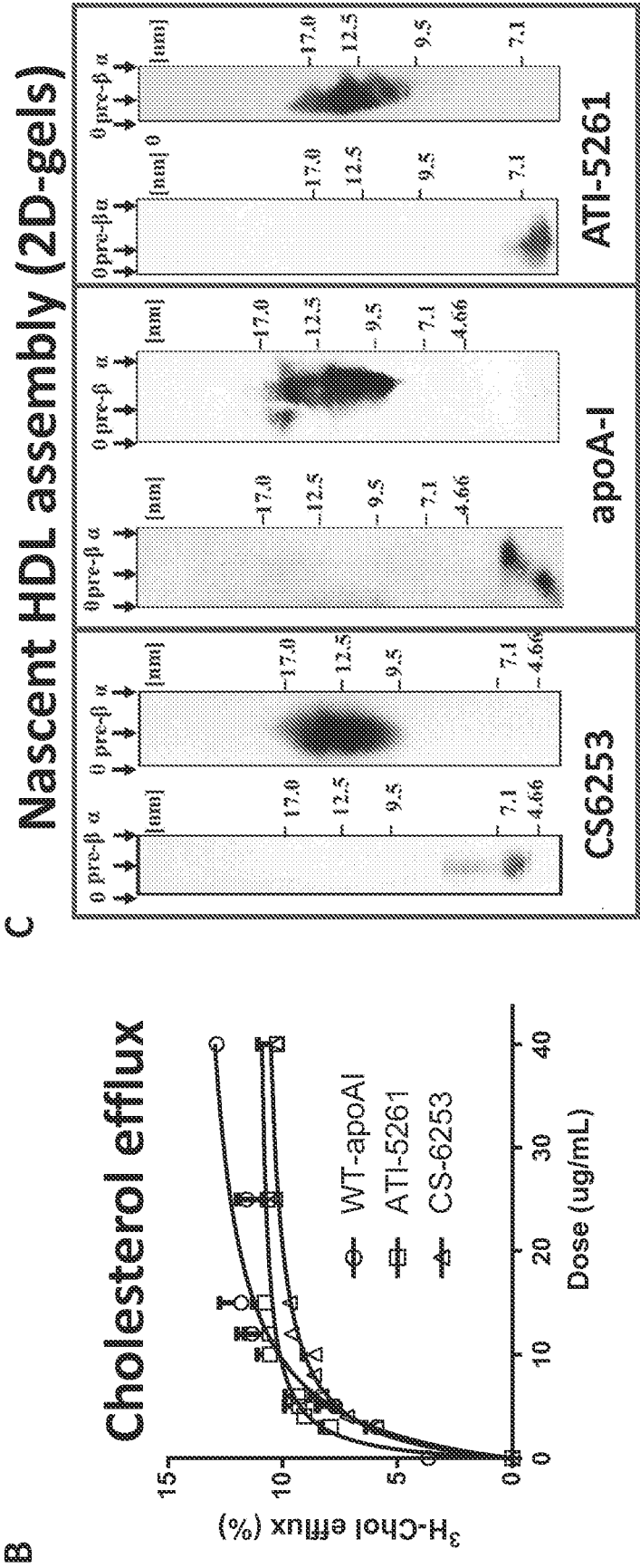
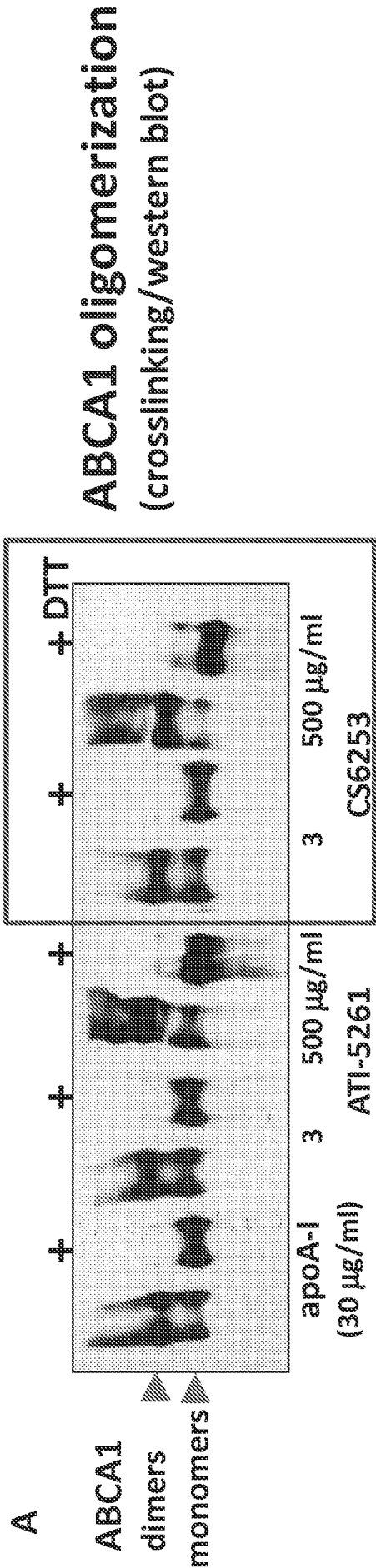


Figure 31

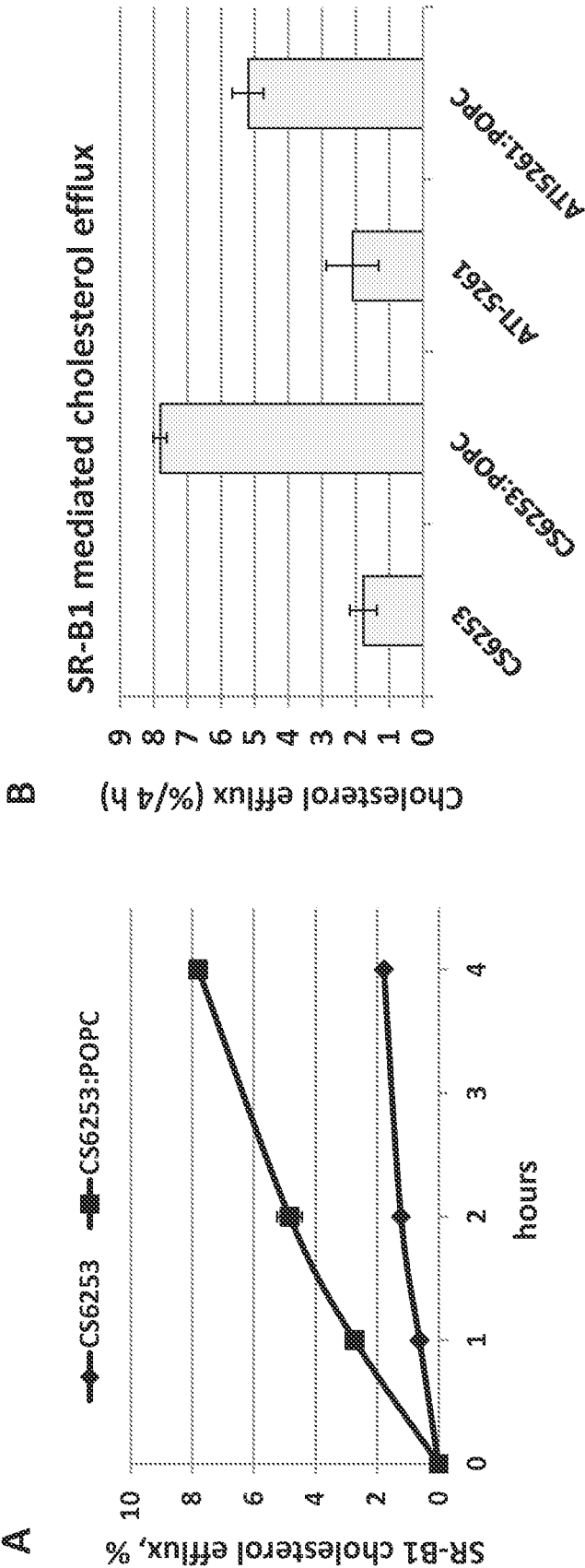


Figure 32

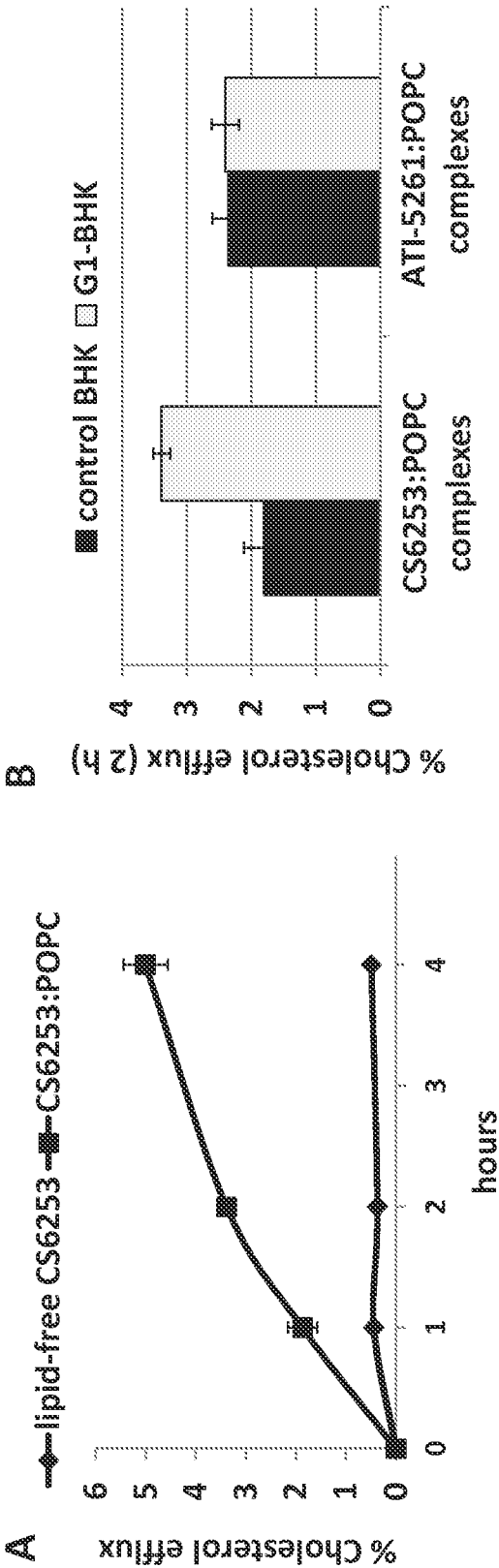


Figure 33

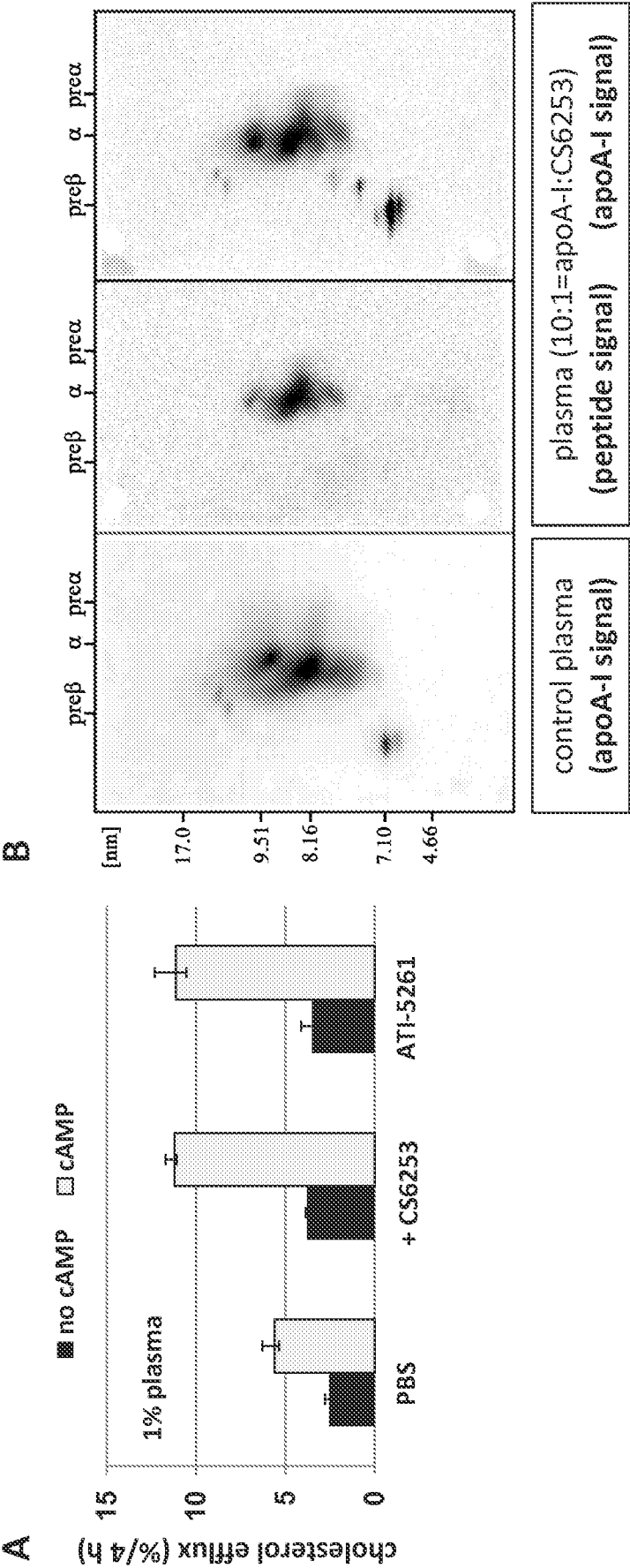


Figure 34

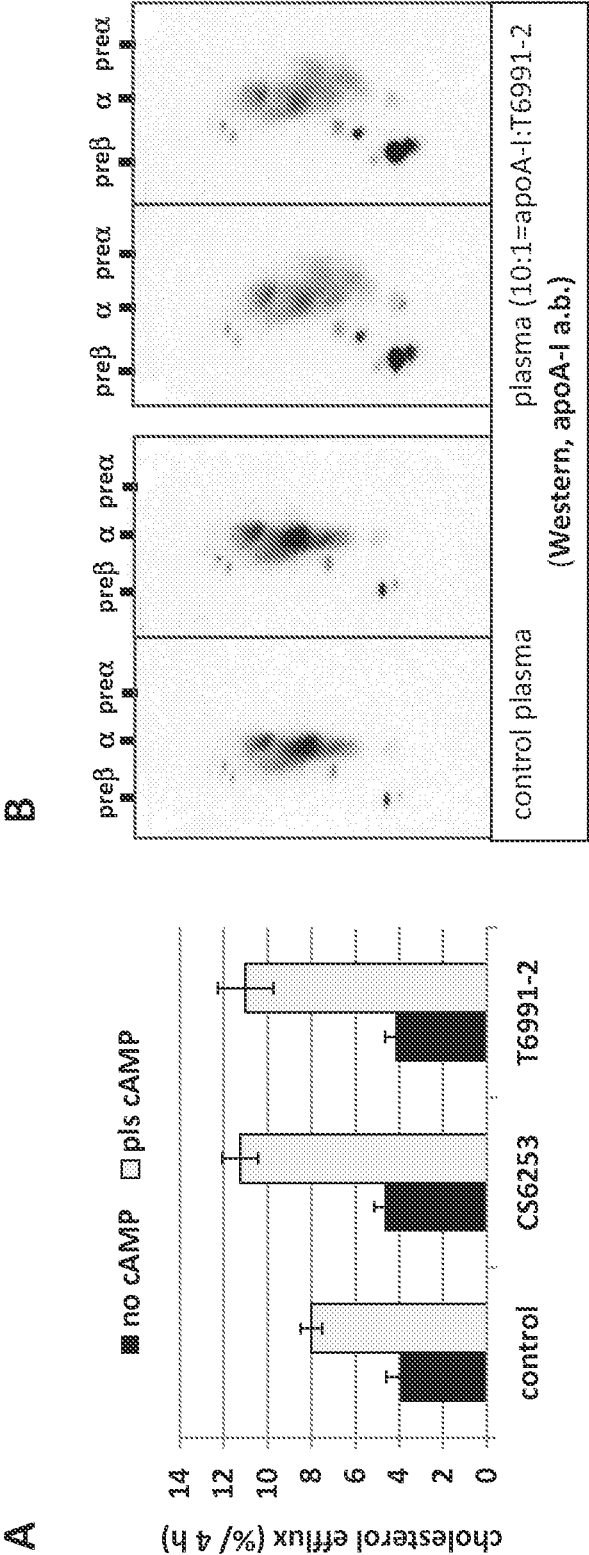


Figure 35

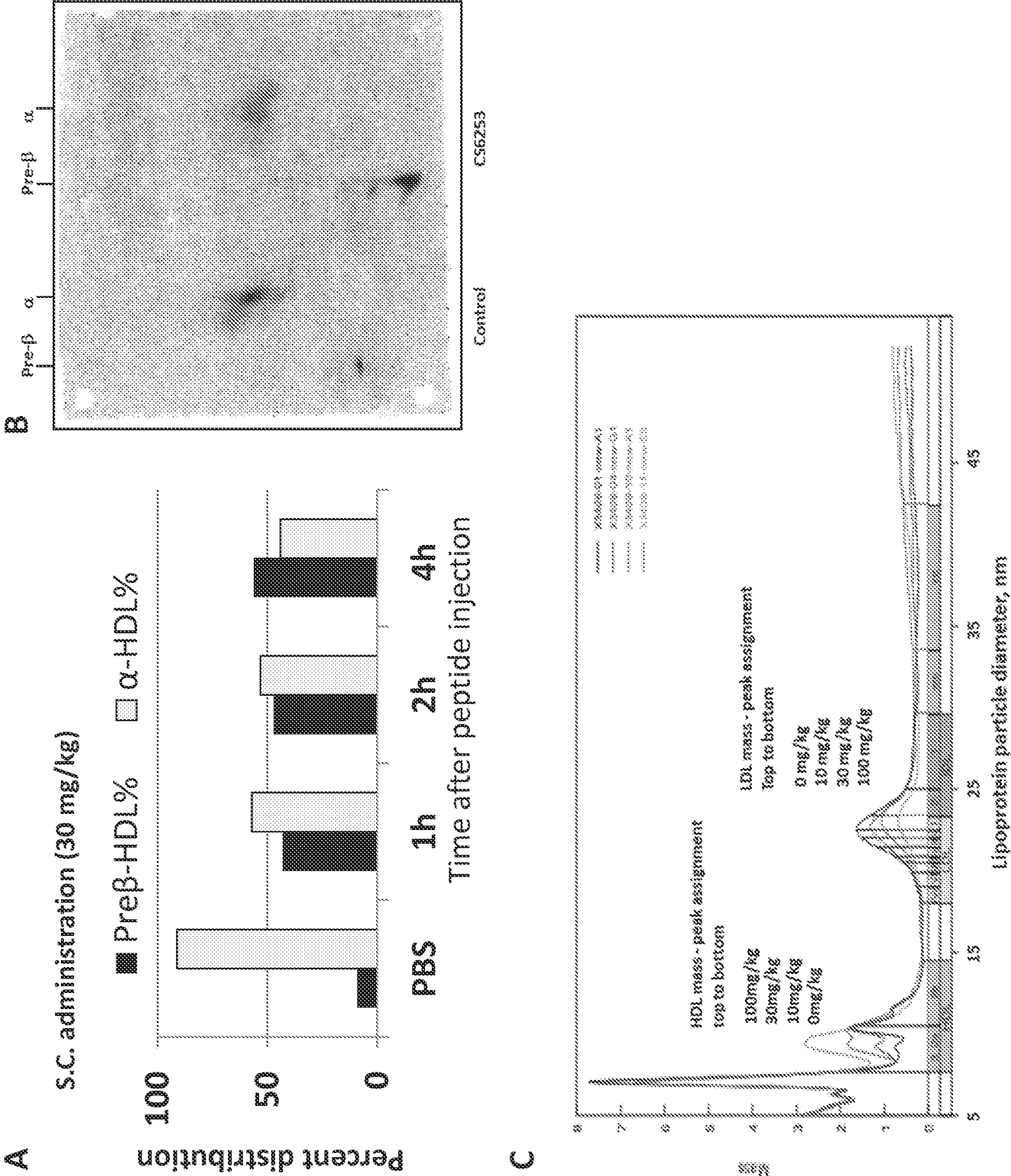
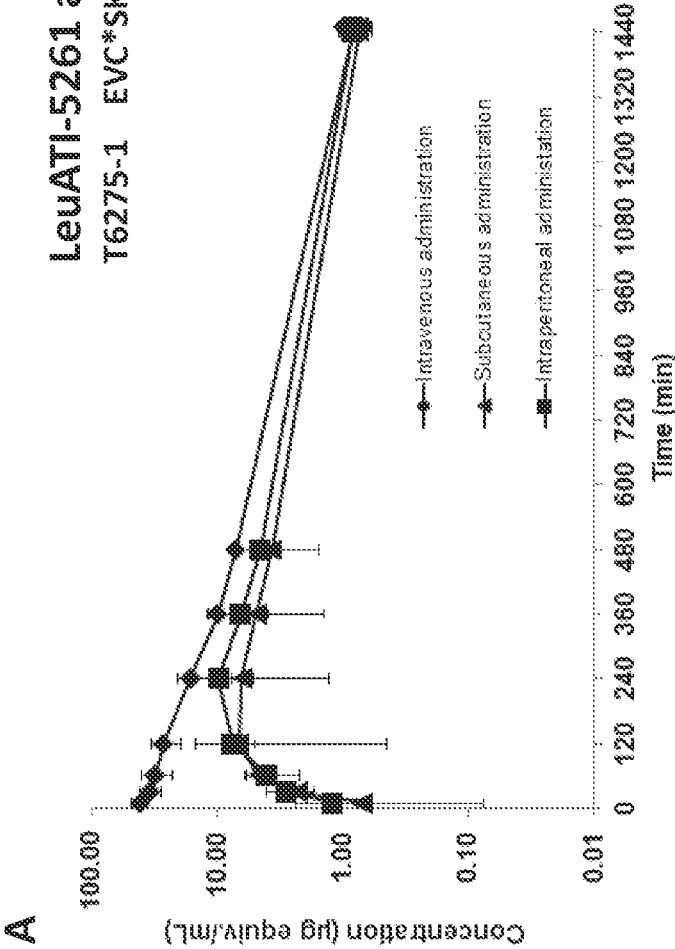


Figure 36

LeuATI-5261 analog, C* = citrulline
T6275-1 EVC*SKLEWLALC*ELAEELLARKY Y26



	t 1/2 (h)	F% (bioavall)
SC	7.01±0.62	33.5
IP	8.33±3.73	41.9
IV	5.85±0.40	NA

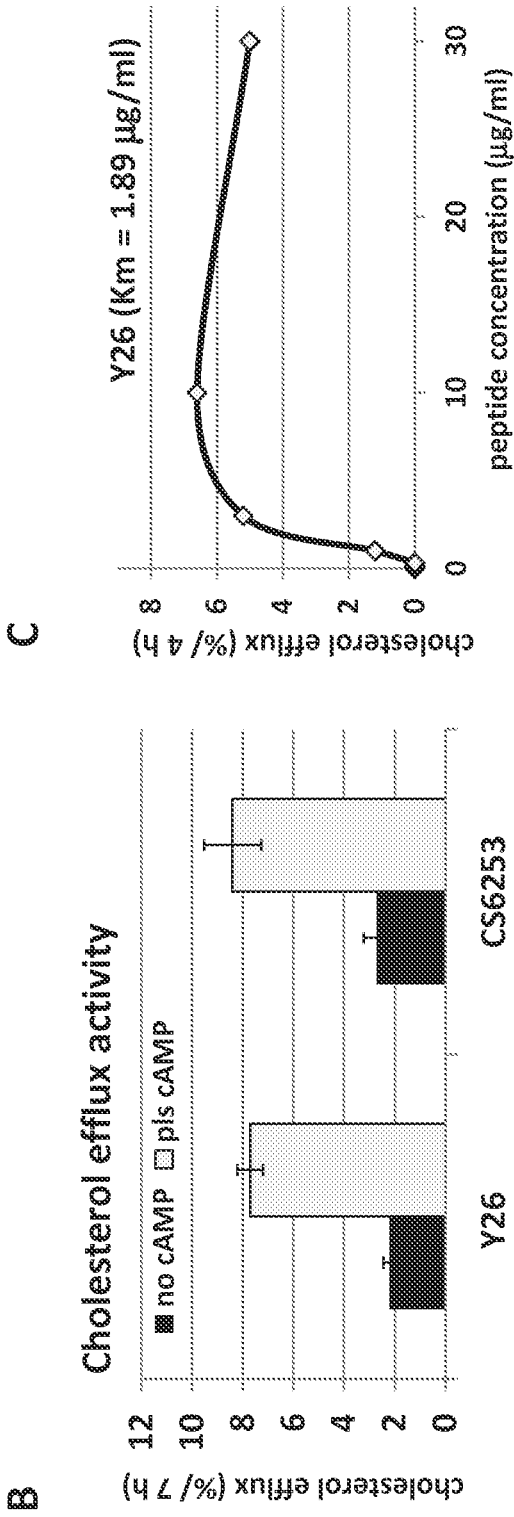


Figure 37

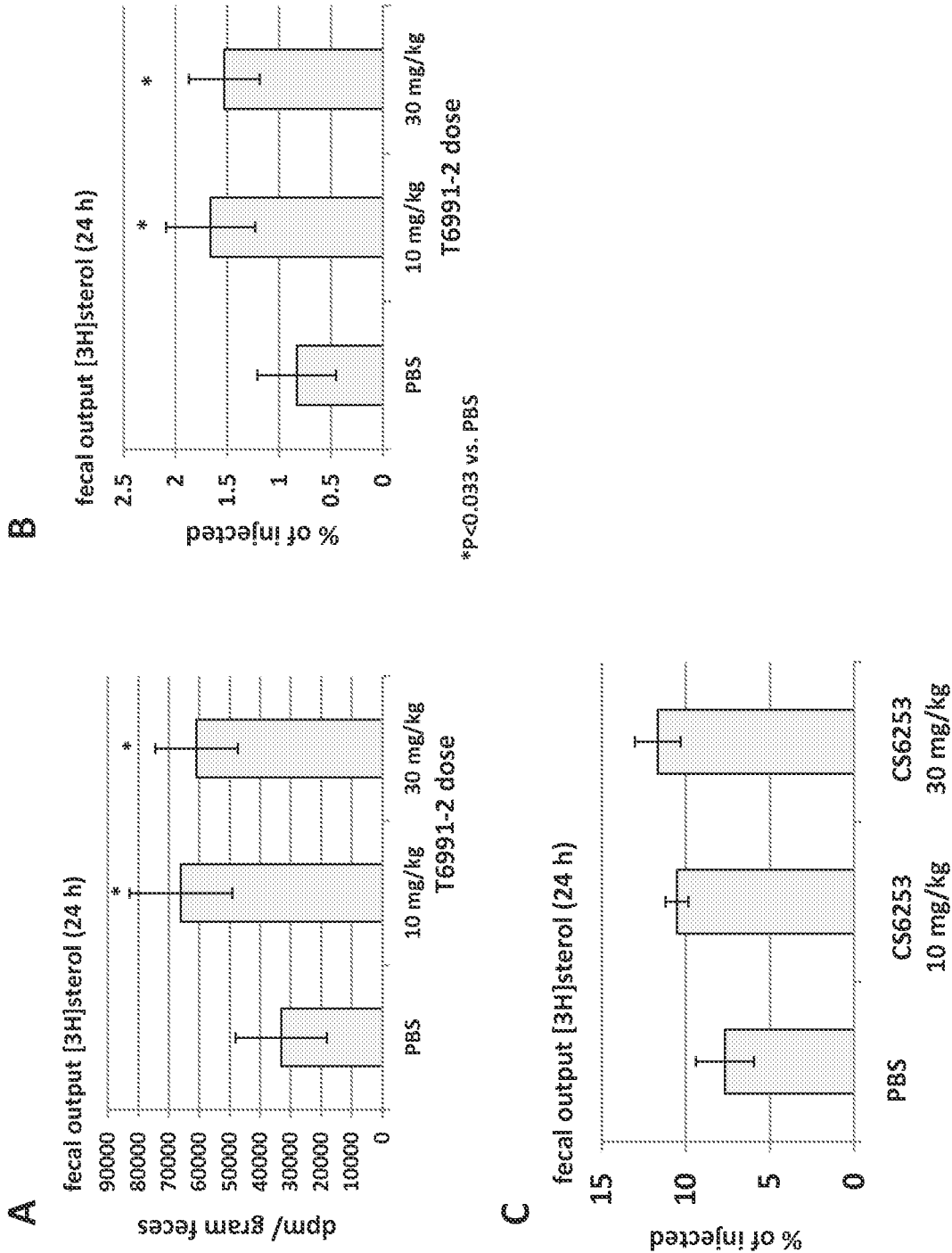


Figure 38

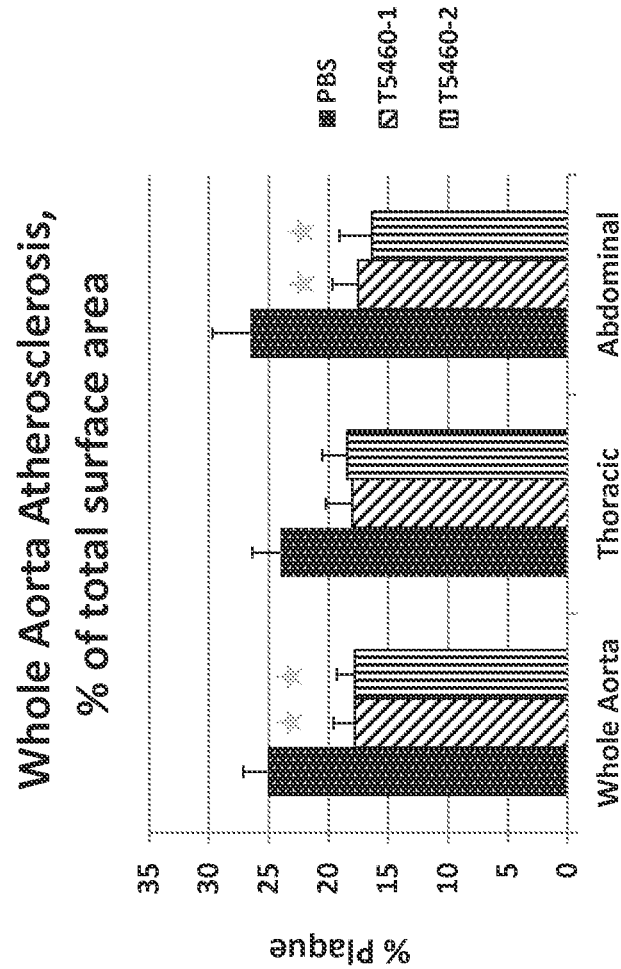


Figure 39

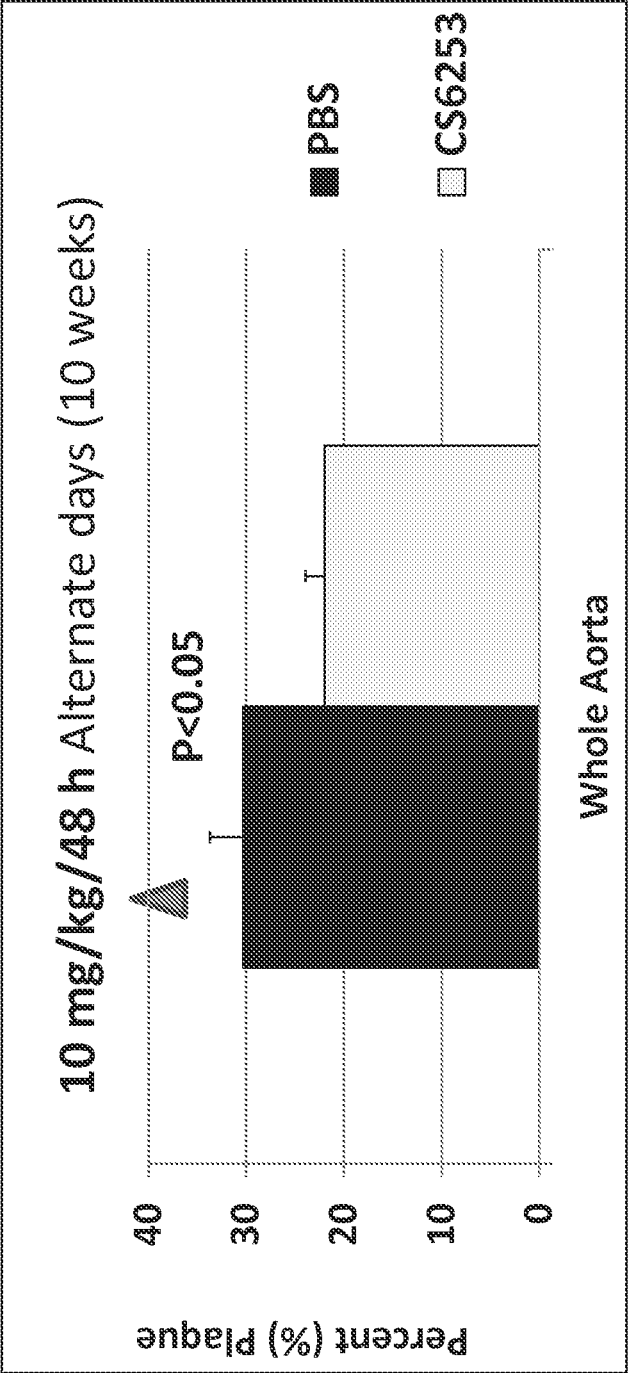
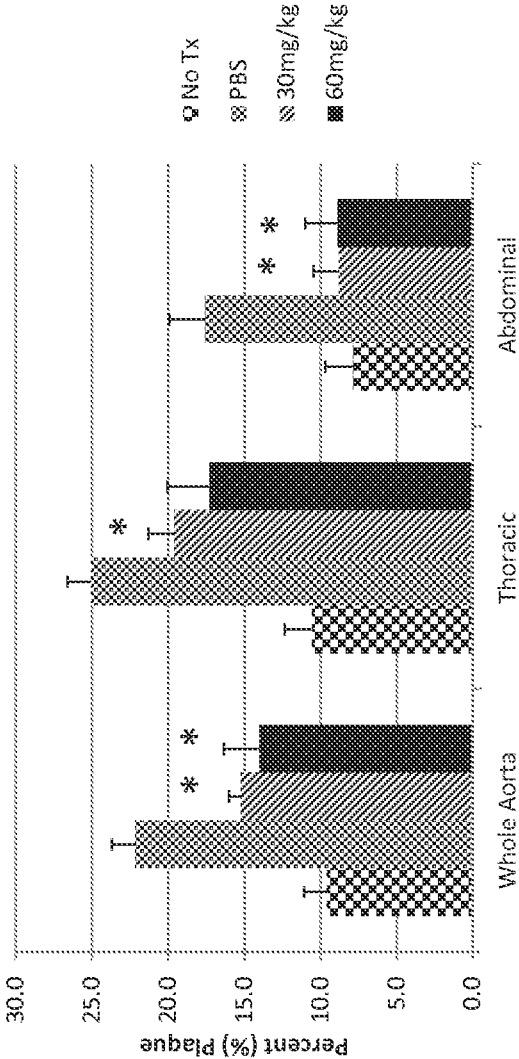


Figure 40

SC administration of CS6253 reduce
atherosclerosis in apoE KO mice



* p<0.05 by active treatment vs. PBS treatment

Figure 41

Stapled peptides can be designed to mediate ABCA1 mediated cholesterol efflux from J774 cells

CS6257 (ATI-5261, R3,23→A with staple at positions 14 and 21 [S5-R8])
EVASKLEEWFAAF(S5)EFAEEF(R8)AALKS

CS6259 (LeuATI-5261, R3,23→Q with staple at positions 14 and 21 [S5-R8])
EVQSKLEEWLAAL(R8)ELAEEL(S5)AQLKS

% efflux 4 h (10 ug/ml peptides)		SD values	
CS6257	CS6259	ATI-5261	
no cAMP	0.45	0.67	1.4
pls cAMP	3.06	3.28	7.81

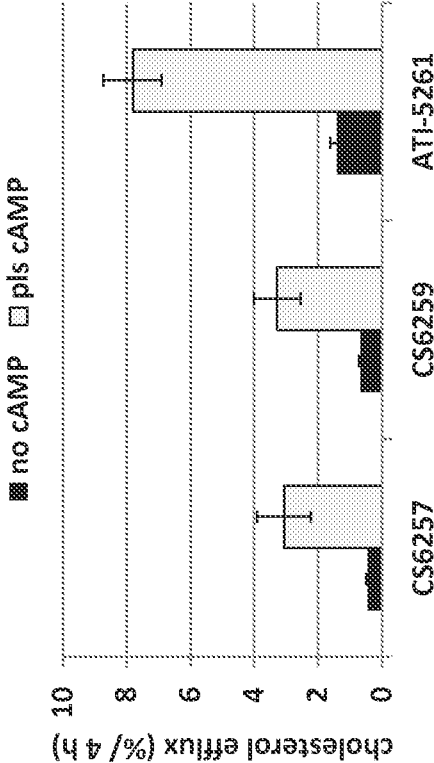


Figure 42

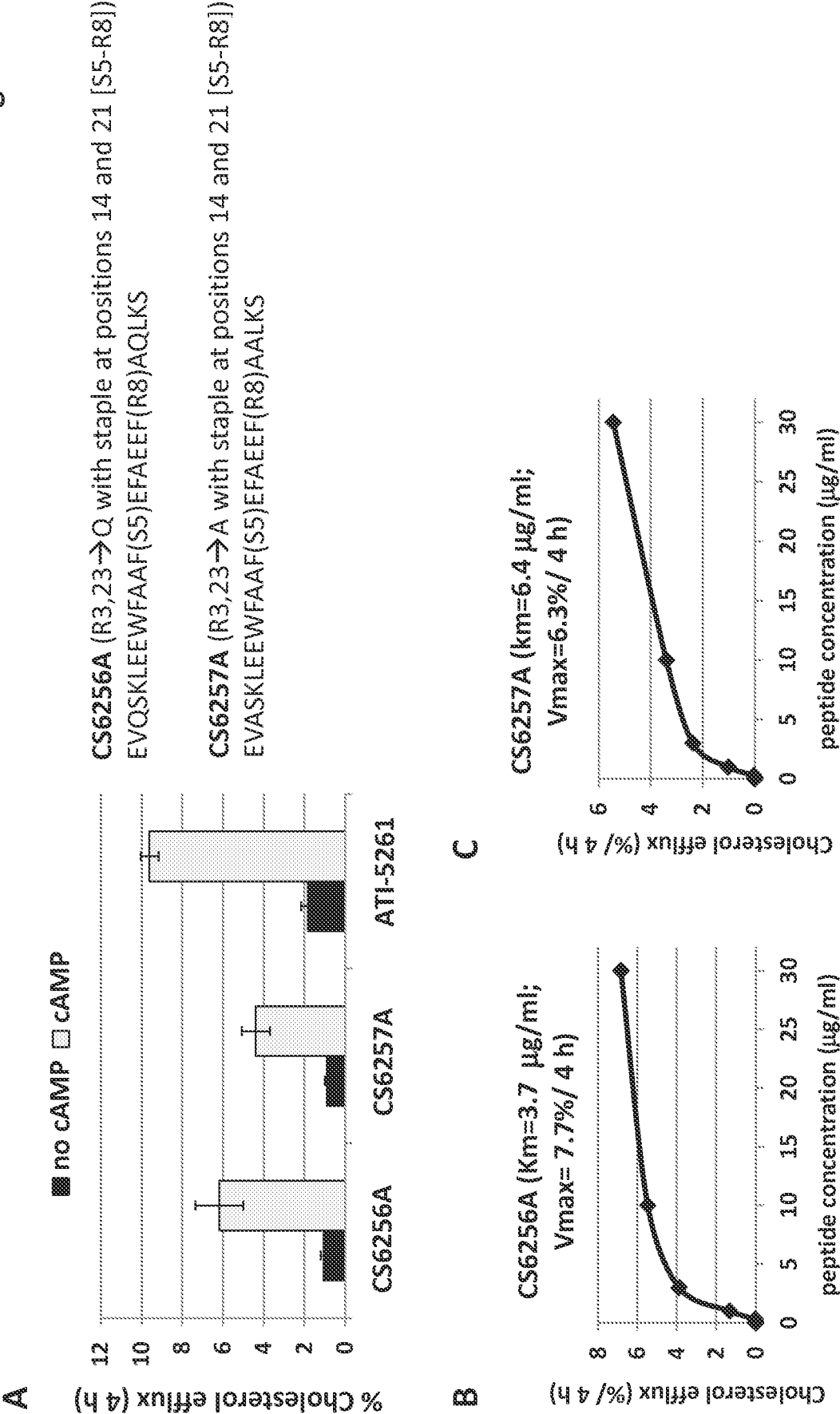
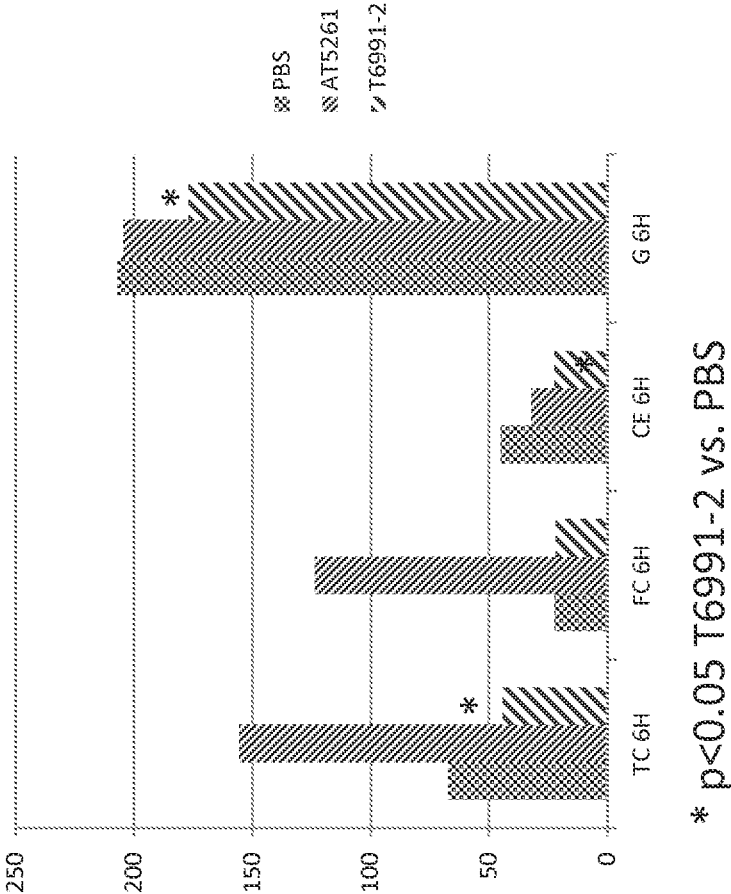


Figure 43

ABCA1 ligand peptides can be designed to have cholesterol lowering and glucose lowering properties



* p<0.05 T6991-2 vs. PBS

Figure 44

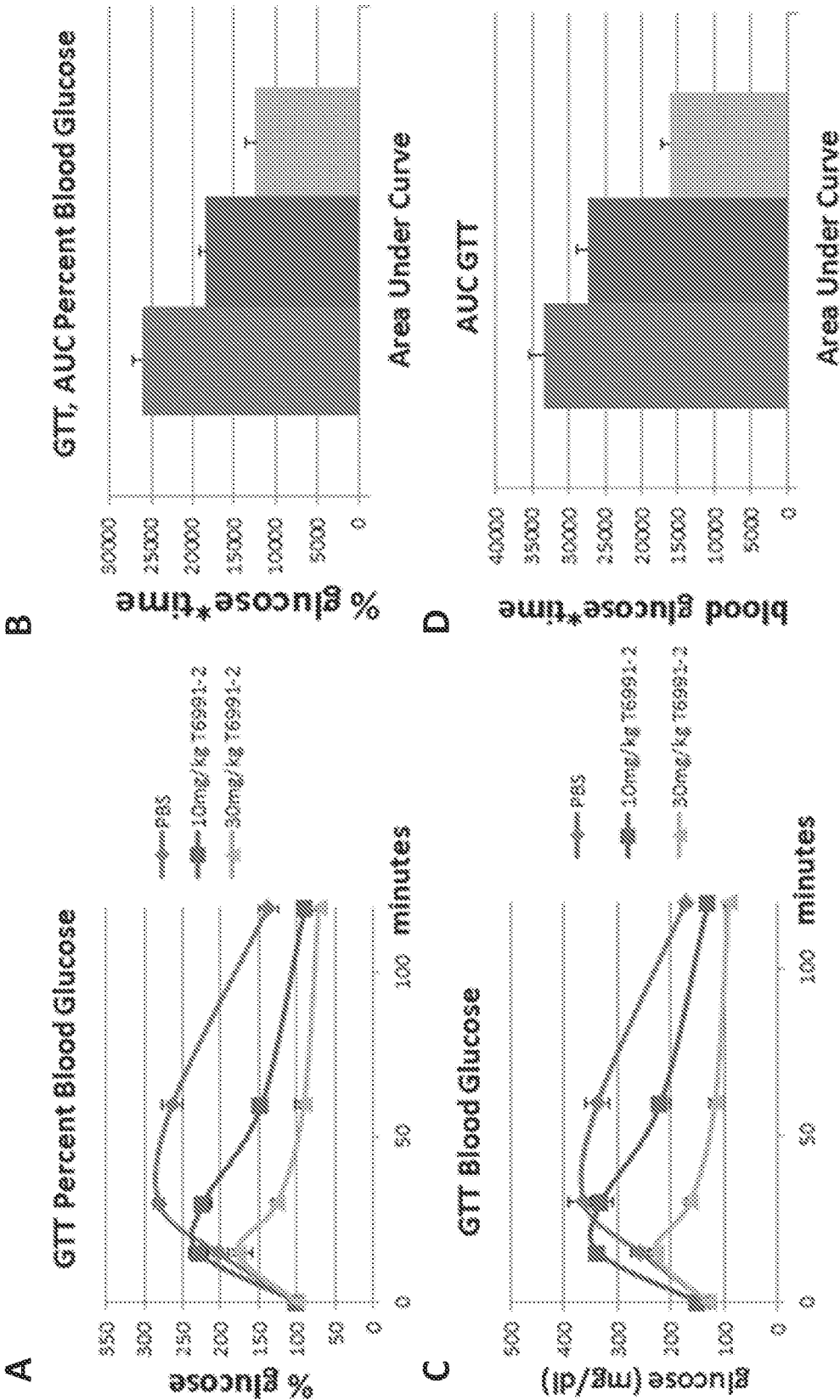


Figure 45

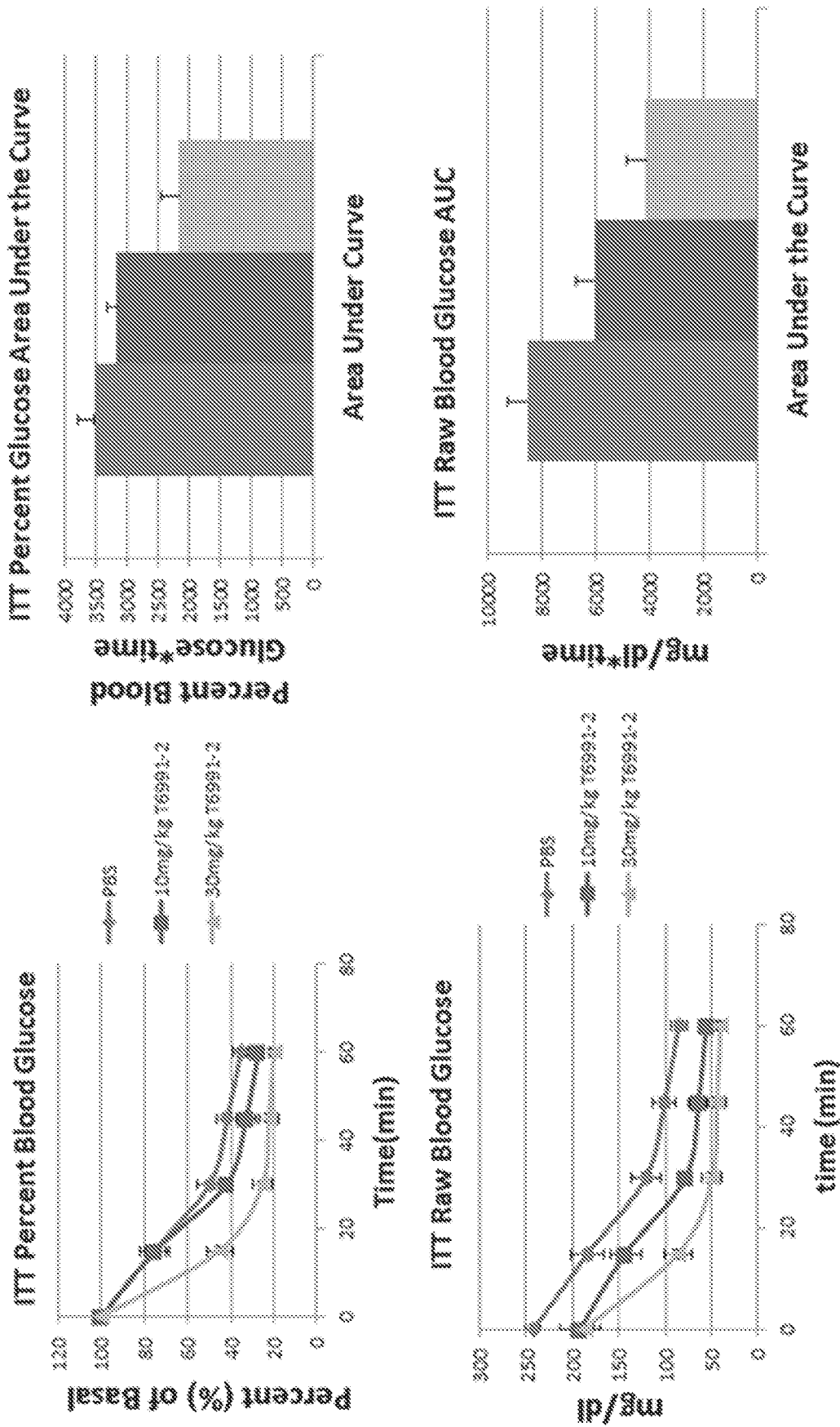


Figure 46

GTT; Ob/Ob mice, 6wks 10mg/kg/48h

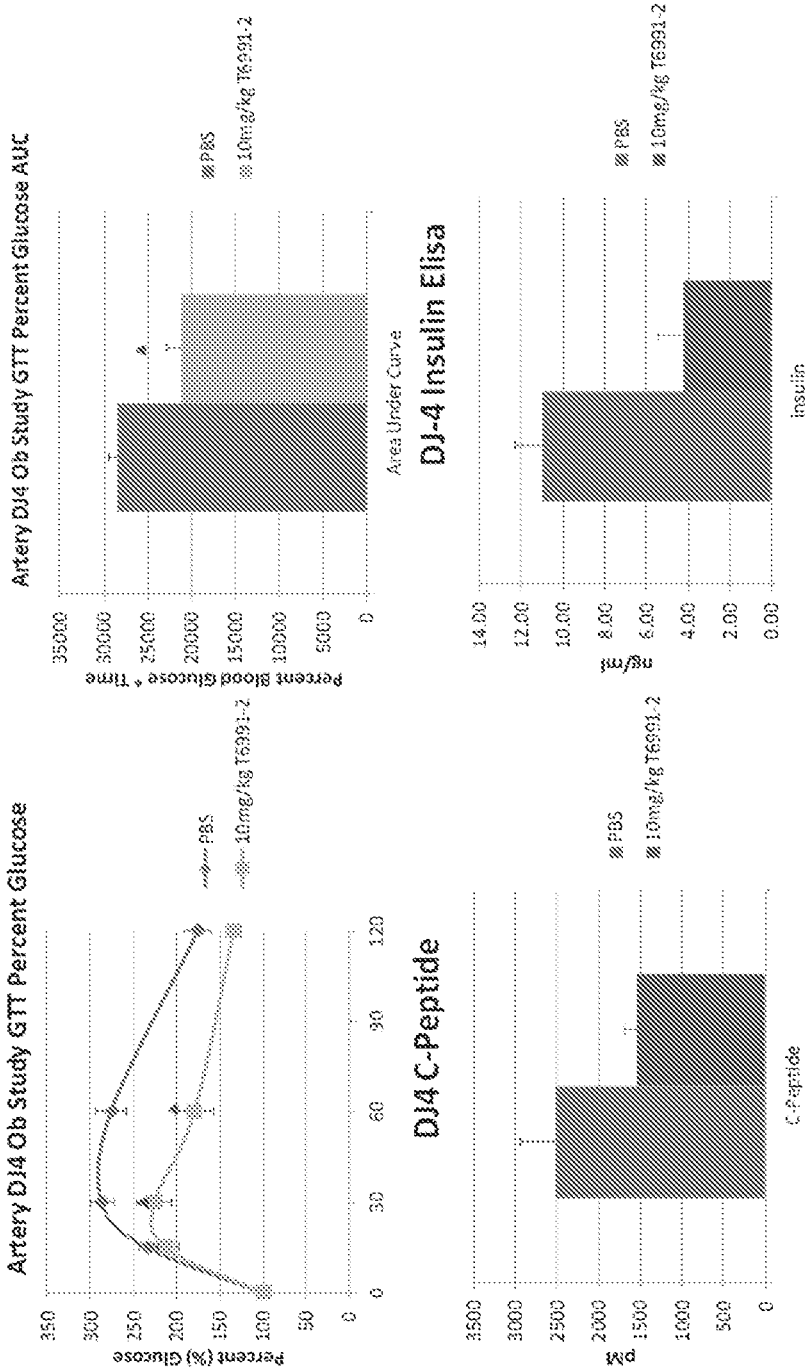
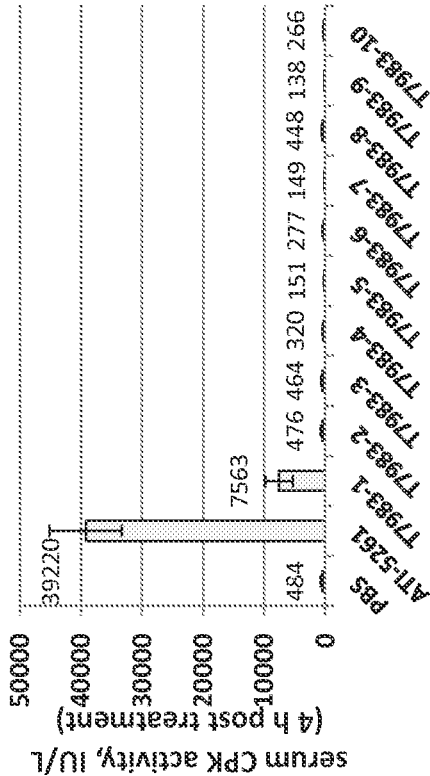


Figure 47

CitLeuATI-5261 (CS6253) analogs with Isoleucine, C* = citrulline

T7983-1	EVRSKLEEWIAAIREIAEEILARL	F10,13,16,20→I (all F to isoleucine in 24 mer of ATI-5261)
T7983-2	EVC*SKLEEWIAAIC*EIAEEILARL	R3, 14→ C* in isoleucine form of 24-mer ATI-5261 (24-mer T6991-2)
T7983-3	EVC*SKLEEWLAALC*ELAEELARLKS	L20→I in CitLeuATI-5261
T7983-4	EVC*SKLEEWIAALC*ELAEELARLKS	L10, 20→I in CitLeuATI-5261
T7983-5	EVC*SKLEEWLAALC*EIAEEELARLKS	L13, 16→I in CitLeuATI-5261
T7983-6	EVC*SKLEEWIAAIC*EIAEEELARLKS	L10,13,16→I in CitLeuATI-5261
T7983-7	EVC*SKLEEWLAALC*EIAEEELARLKS	L13,16,20→I in CitLeuATI-5261
T7983-8	EVISKLEEWLAALC*ELAEELARLKS	R3→I in Cit14_leuATI-5261
T7983-9	EVC*SKLEEWLAALIELAEELARLKS	R14→I in Cit3_leuATI-5261
T7983-10	EVISKLEEWLAALIELAEELARLKS	R3,14→I in LeuATI-5261 (i.e. no citrulline)

Muscle toxicity (CPK activity)



Serum clinical markers- 4 hour post treatment

	ALT (IU/l)	AST (IU/l)	TG (mg/dl)	TC (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	42±6	86±28	59±7	105±20	27±3	0.85±0.22
ATI-5261	230±41	3842±747	1579±185	231±16	118±10	0.46±0.04
T7983-1	115±22	1329±131	941±34	184±20	90±6	1.41±0.32
T7983-2	44±13	113±45	575±273	139±32	75±24	1.78±1.05
T7983-3	54±29	78±14	823±102	167±23	73±18	1.62±0.16
T7983-4	40±7	79±14	627±208	133±15	62±11	2.04±0.57
T7983-5	42±19	66±19	198±118	85±2	29±6	0.98±0.31
T7983-6	38±5	79±19	276±169	88±23	32±14	1.13±0.33
T7983-7	34±3	78±8	201±173	105±6	35±5	1.18±0.52
T7983-8	44±11	88±17	802±101	158±5	75±2	1.21±0.20
T7983-9	30±6	71±9	137±38	58±15	23±7	1.11±0.36
T7983-10	30±3	82±9	249±91	83±25	30±8	1.46±0.73

Figure 48

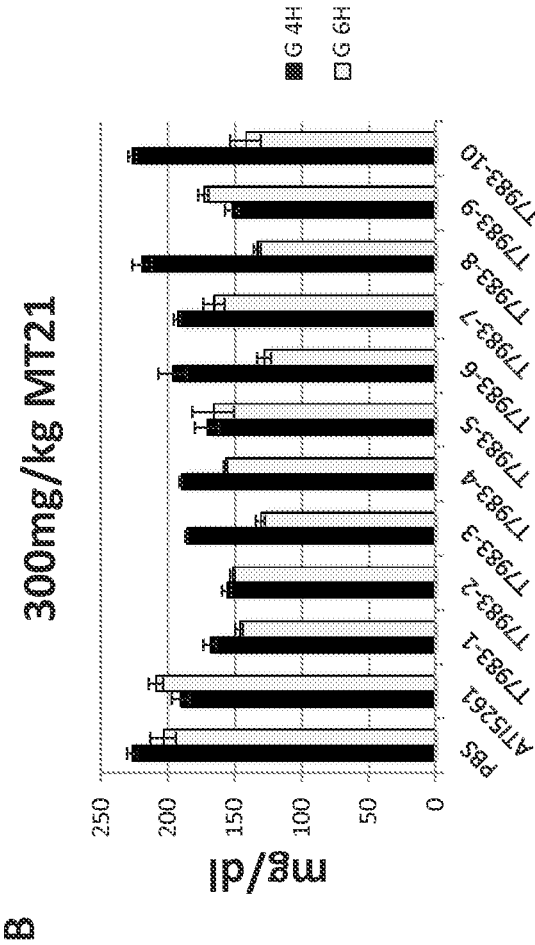
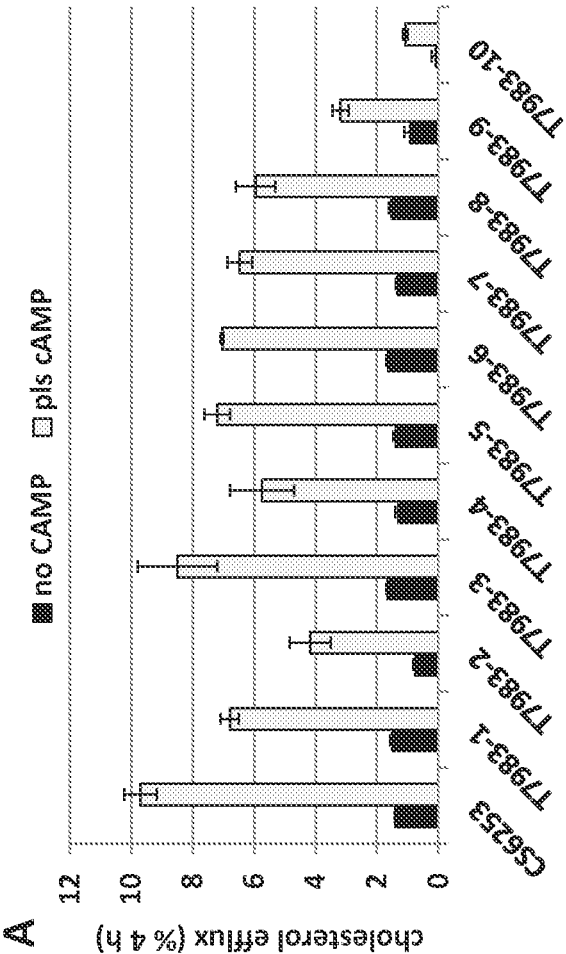
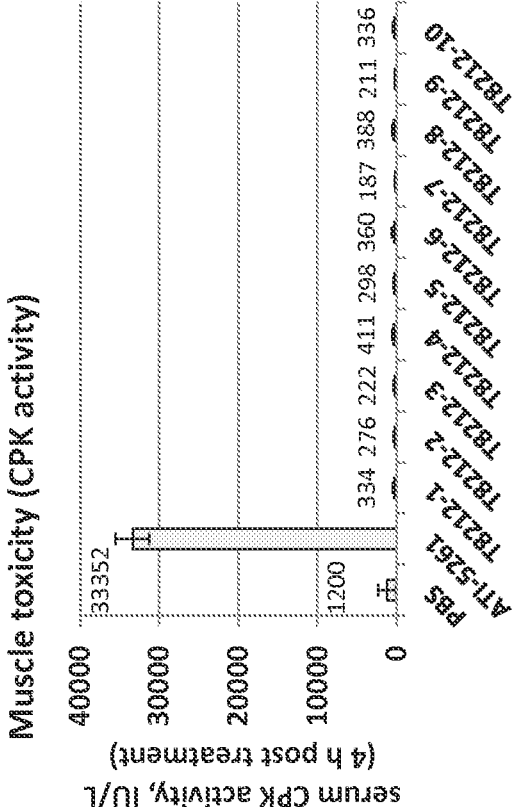


Figure 49

CitLeuATI-5261 (CS6253) analogs with Isoleucine, C* = citrulline

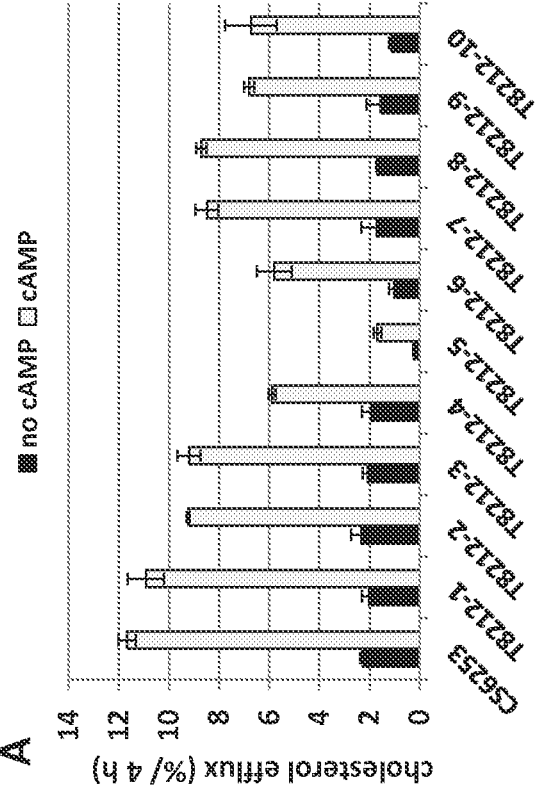
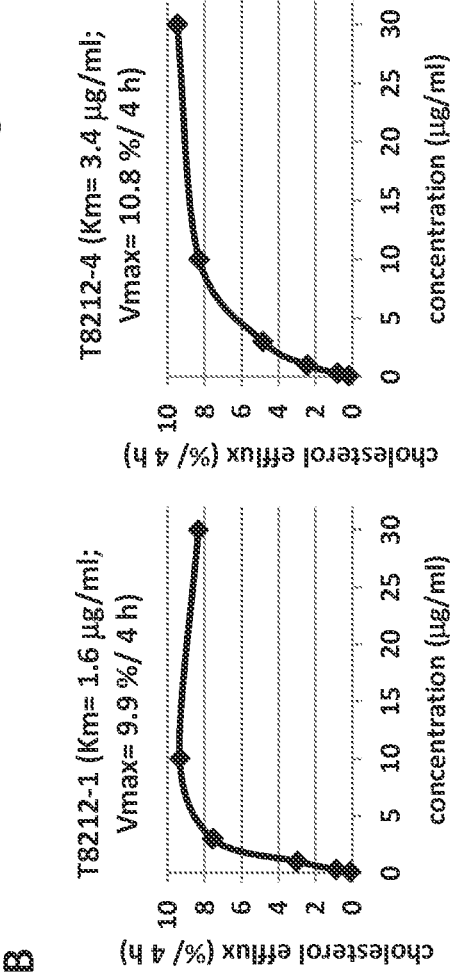
T8212-1	EVC*SKLEEWIAALC*ELAEELLARLKS	L10→I in CitLeuATI-5261
T8212-2	EVC*SKLEEWIAALC*ELAEELLARLKS	L13→I in CitLeuATI-5261
T8212-3	EVC*SKLEEWIAALC*ELAEELLARLKS	L16→I in CitLeuATI-5261
T8212-4	EVC*SKLEEWIAALC*ELAEELLARLKS	L10, 20→I in CitLeuATI-5261
T8212-5	EVC*SKLEEWIAALC*ELAEELLARLKS	L6, 10, 20→I in CitLeuATI-5261
T8212-6	EVC*SKLEEWIAALC*ELAEELLARLKS	L6, 13, 16→I in CitLeuATI-5261
T8212-7	EVC*SKLEEWIAALC*ELAEELLARLKS	L6, 10, 13, 16→I in CitLeuATI-5261
T8212-8	EVC*SKLEEWIAALC*ELAEELLARLKS	L6, 10, 13, 16, 20→I in CitLeuATI-5261
T8212-9	EVC*SKLEEWIAALC*ELAEELLARLKS	L6, 10, 13, 16, 20, 21→I in CitLeuATI-5261
T8212-10	EVC*SKLEEWIAALC*ELAEELLARLKS	L6, 10, 13, 16, 20, 21, 24→I in CitLeuATI-5261 (i.e. all isoleu)



Serum clinical markers- 4 hour post treatment

	ALT(IU/l)	AST(IU/l)	TG (mg/dl)	TC (mg/dl)	FC (mg/dl)	NEFA (mg/dl)
PBS	56±8	185±93	25±16	51±7	17±2	0.80±0.05
ATI-5261	247±26	3279±528	770±225	104±25	59±11	0.46±0.15
T8212-1	40±5	123±10	355±287	72±18	39±21	1.60±0.89
T8212-2	49±20	121±31	373±46	63±13	31±1	1.71±0.19
T8212-3	40±9	98±15	335±30	61±2	40±7	1.72±0.31
T8212-4	44±10	118±19	309±13	67±3	41±3	1.76±0.19
T8212-5	58±2	112±14	252±106	43±4	27±9	1.09±0.05
T8212-6	35±5	117±13	305±168	55±19	36±15	1.15±0.36
T8212-7	45±32	87±14	185±182	68±15	36±16	1.04±0.32
T8212-8	52±8	104±27	384±31	72±7	45±3	1.80±0.11
T8212-9	51±33	95±27	376±289	77±32	44±21	1.57±0.36
T8212-10	42±2	116±28	670±92	110±25	68±8	1.95±0.36

Figure 50



C 300mg/kg MT22

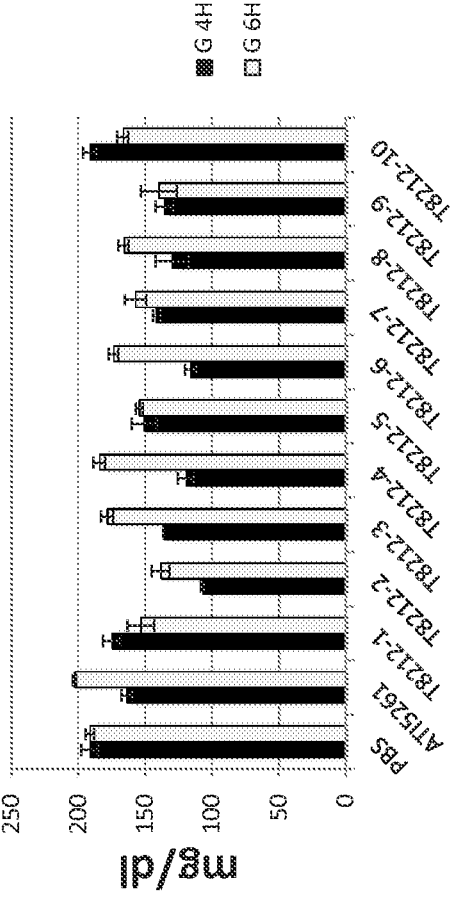


Figure 51

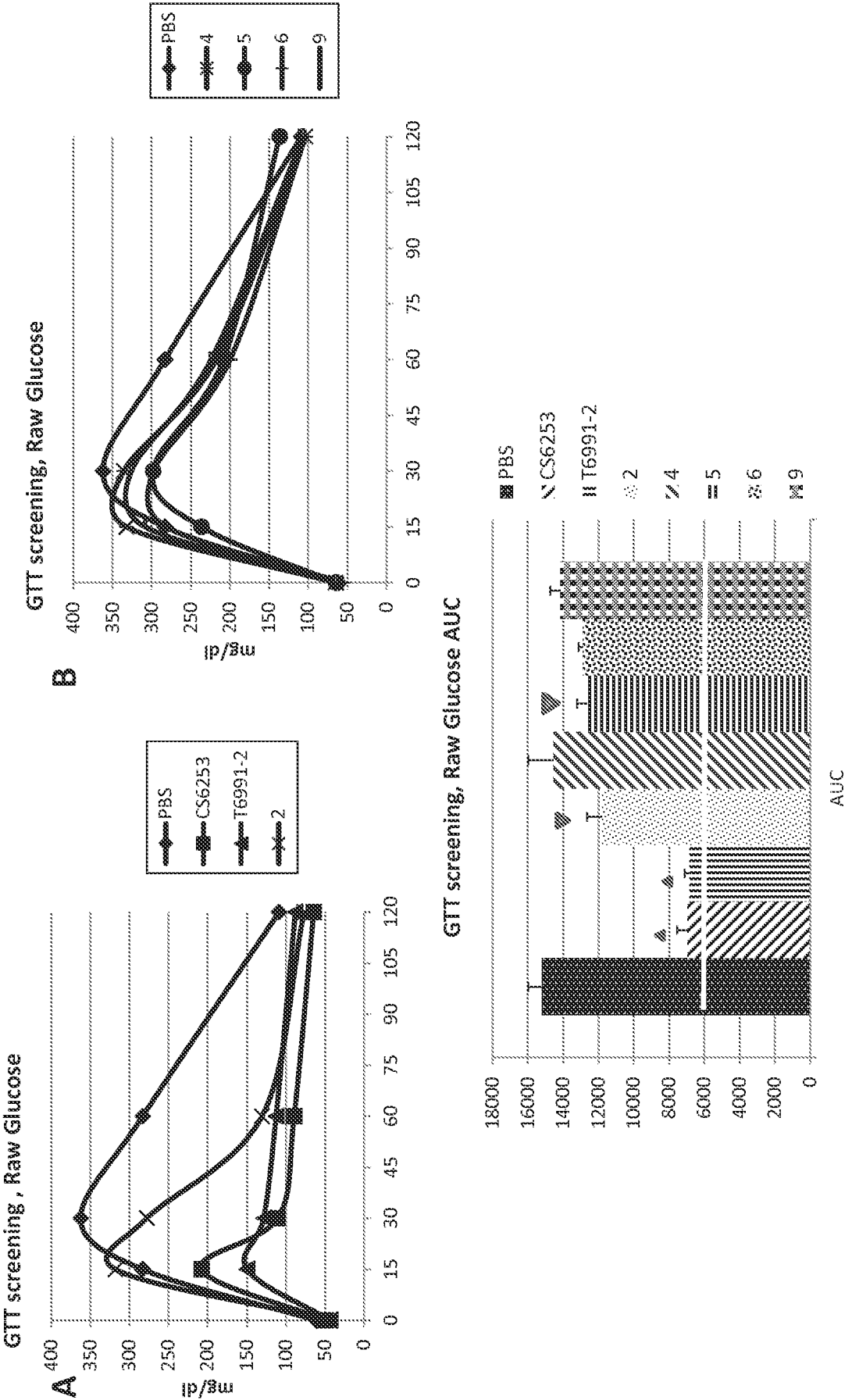


Figure 52

T6991-2 with Y26, C* = citrulline
Batch T7983-11 EVC*SKLEEWIAAIC*EIAEEILARKY

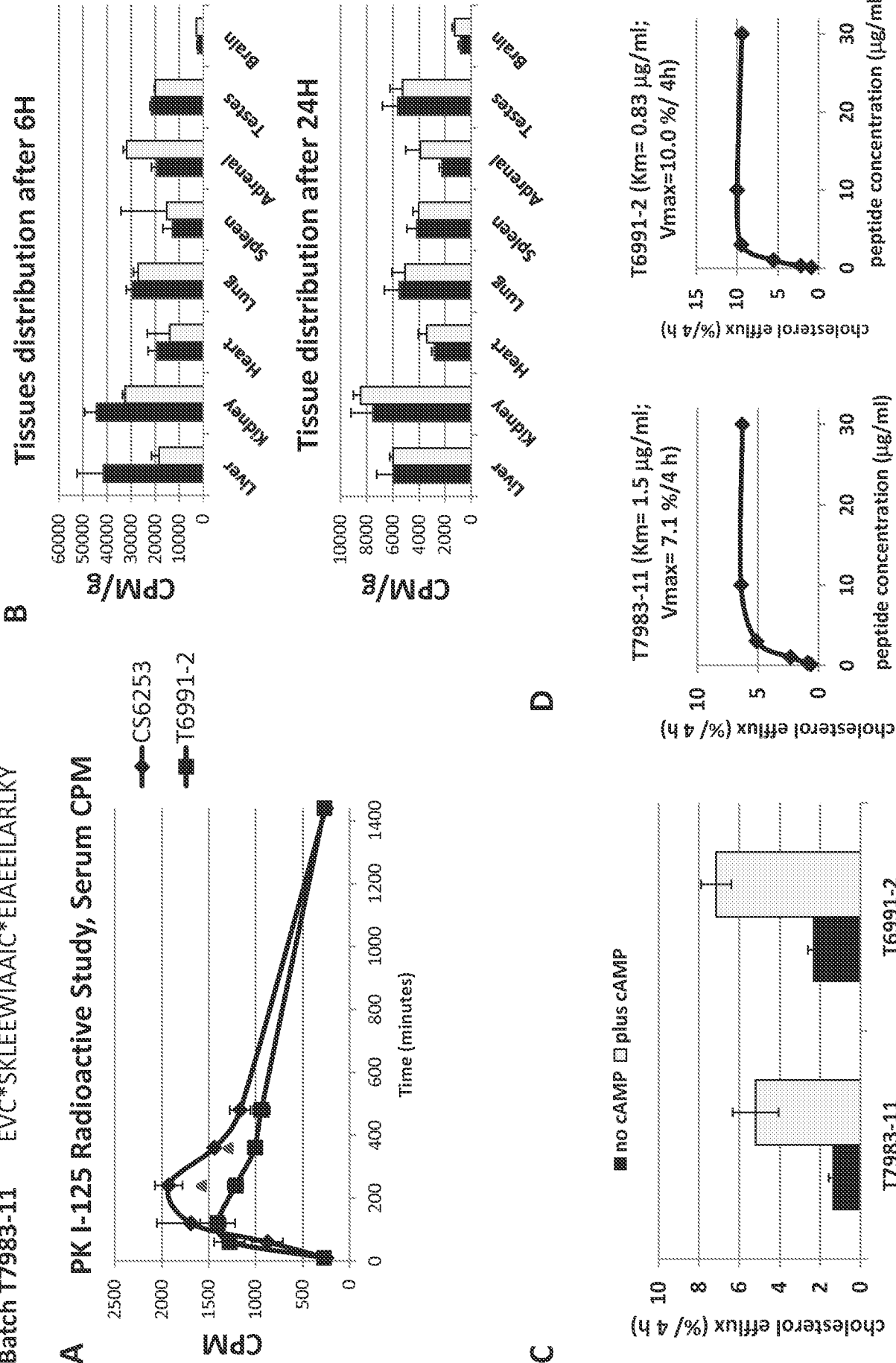


Figure 53

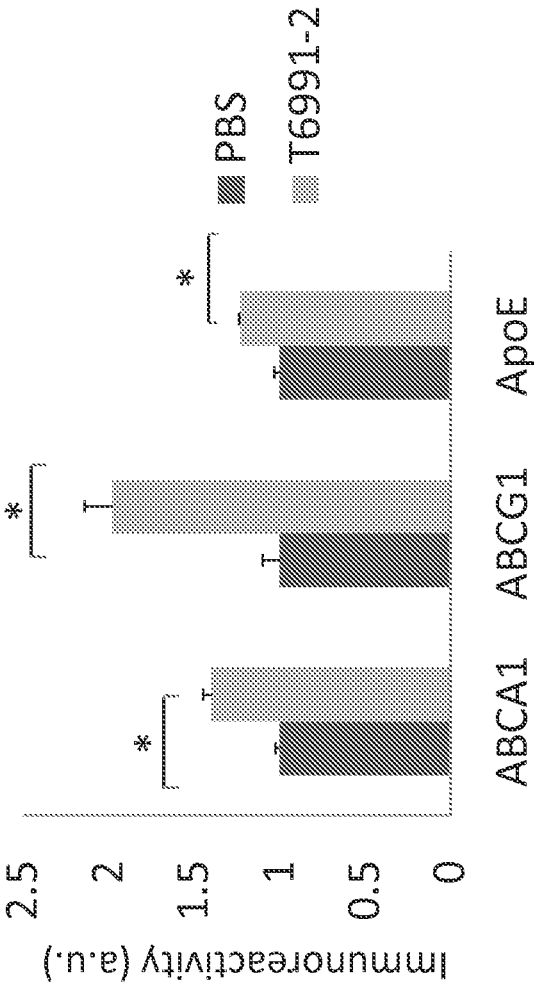
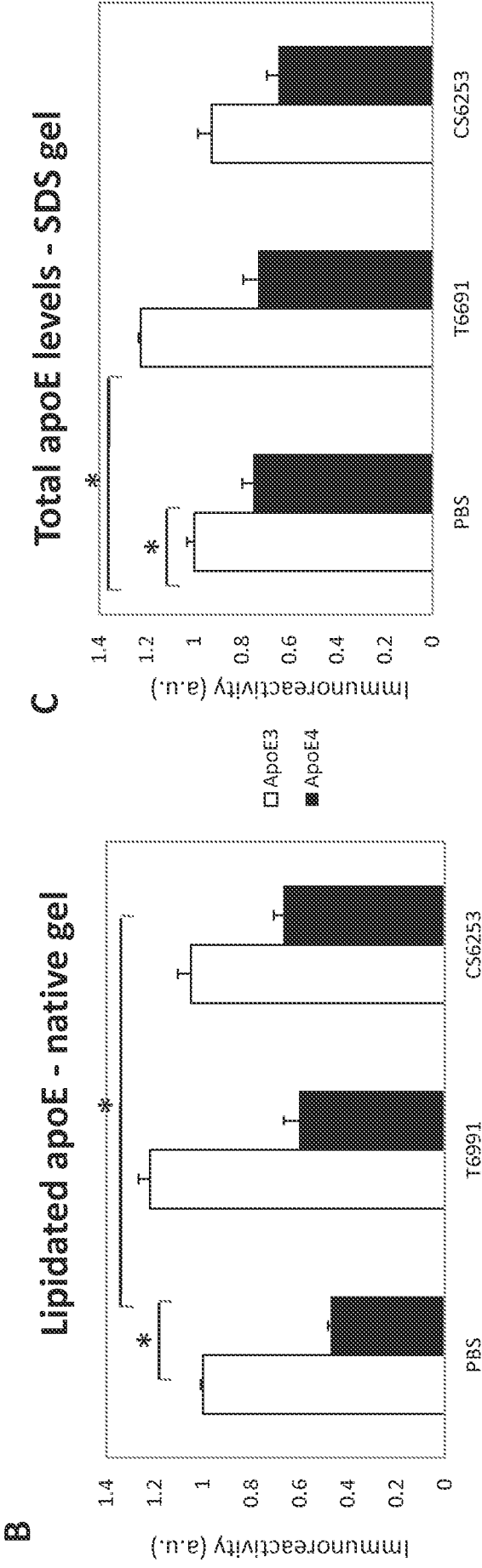
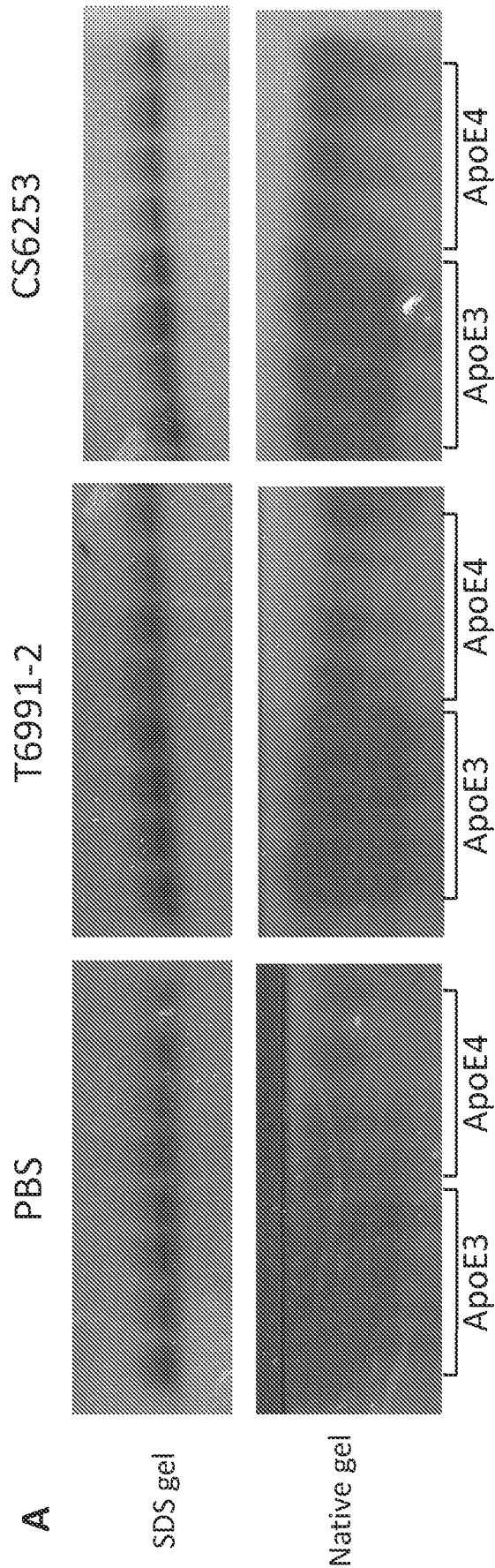


Figure 54



5000

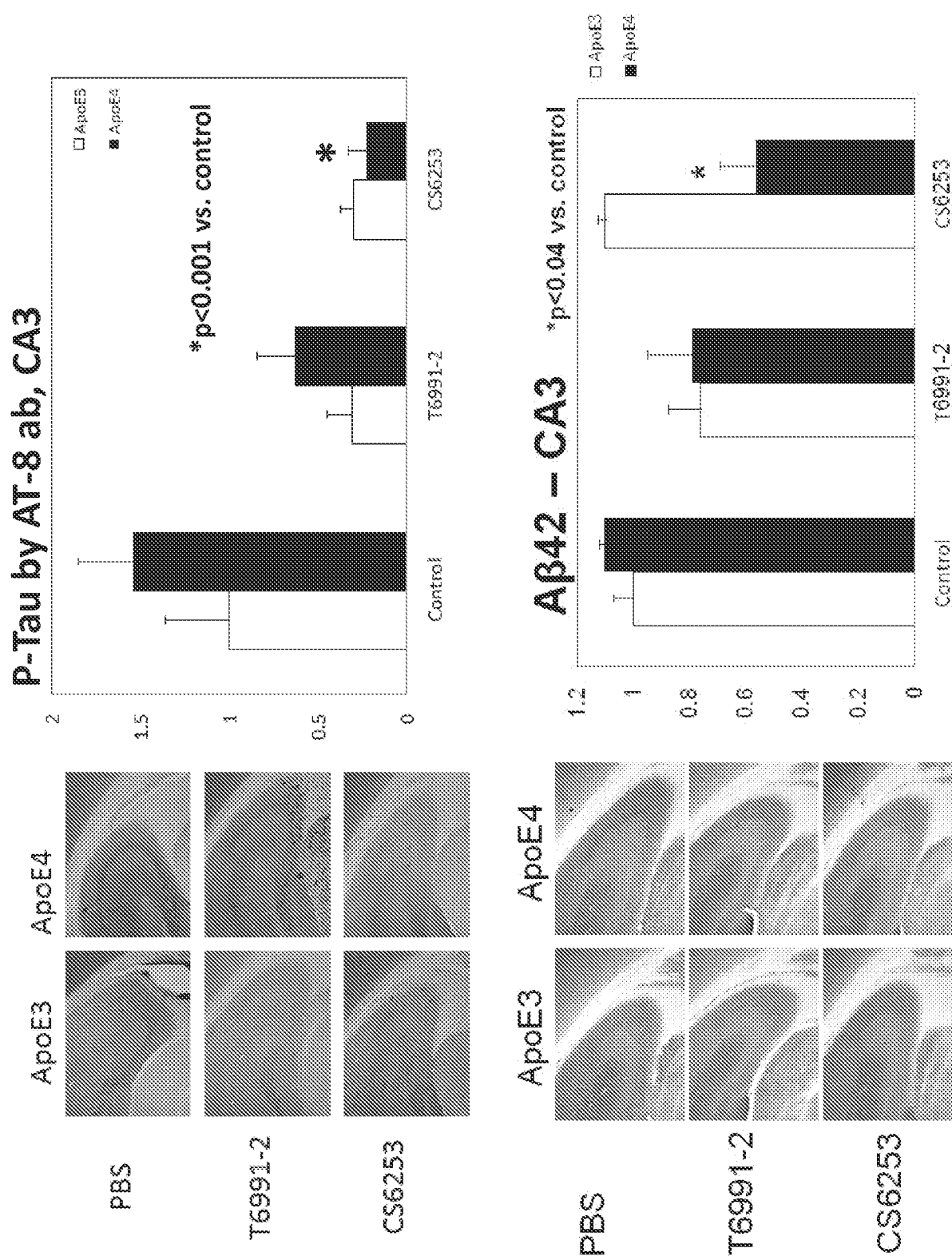


Figure 56

