

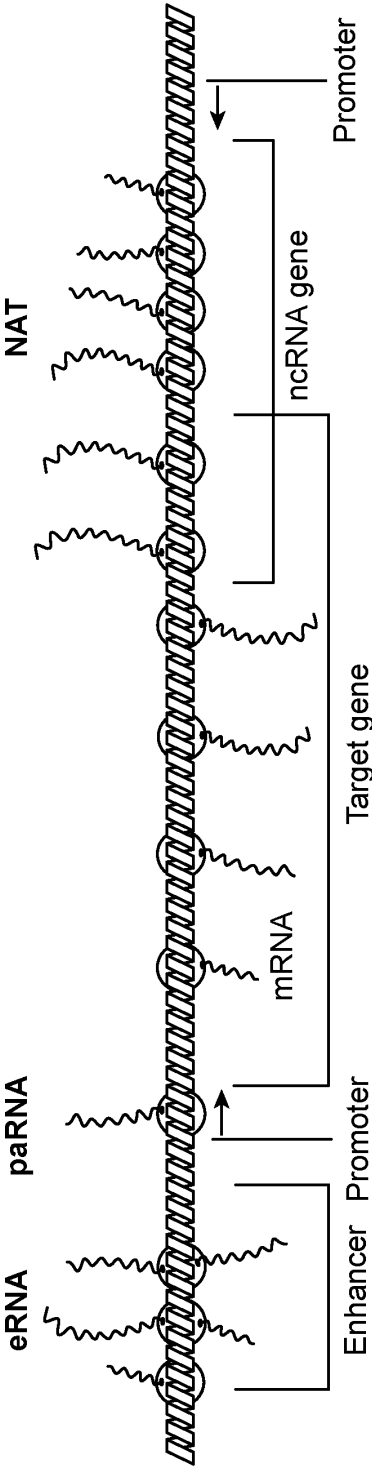


FIG. 1

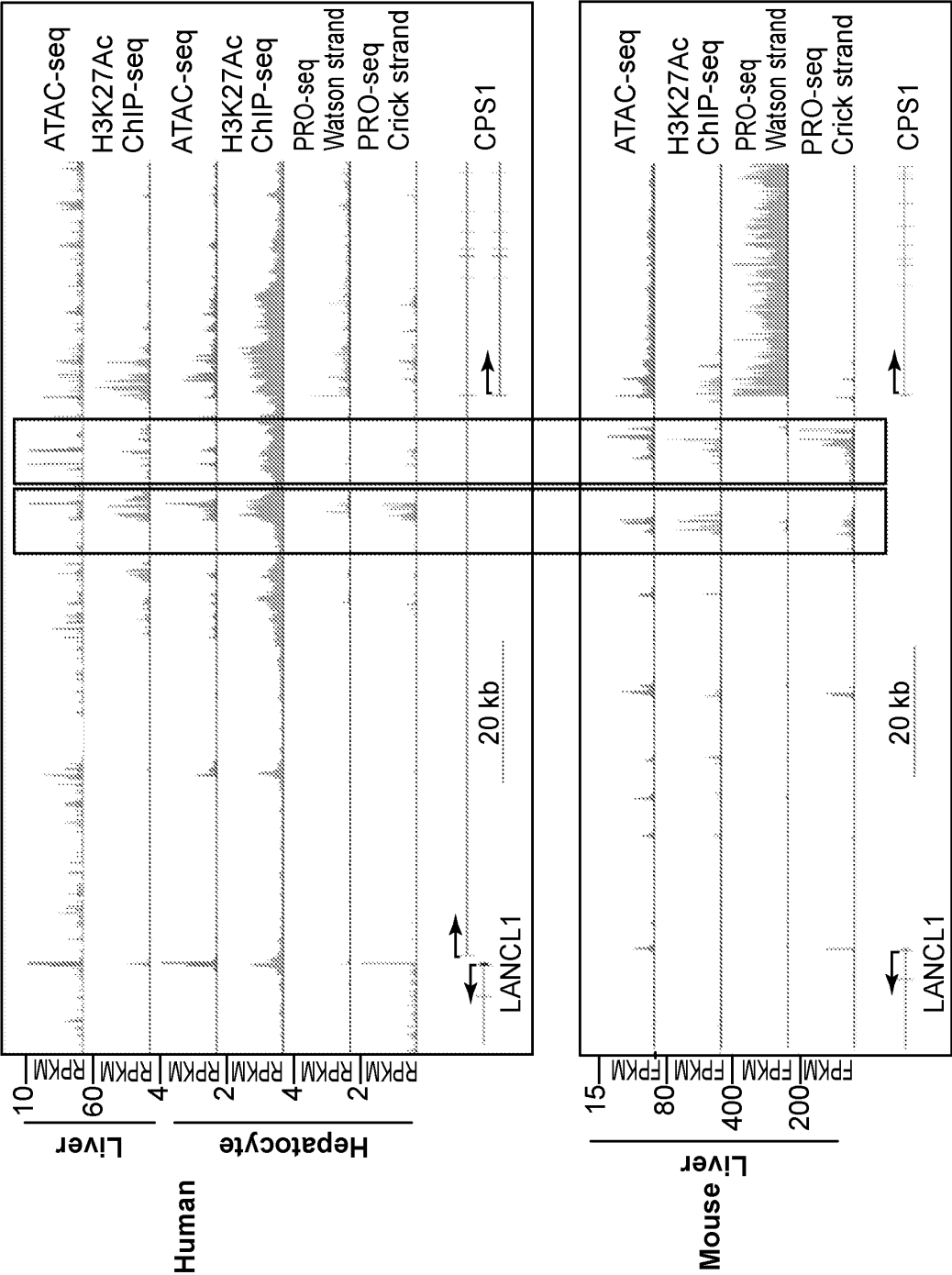


FIG. 2

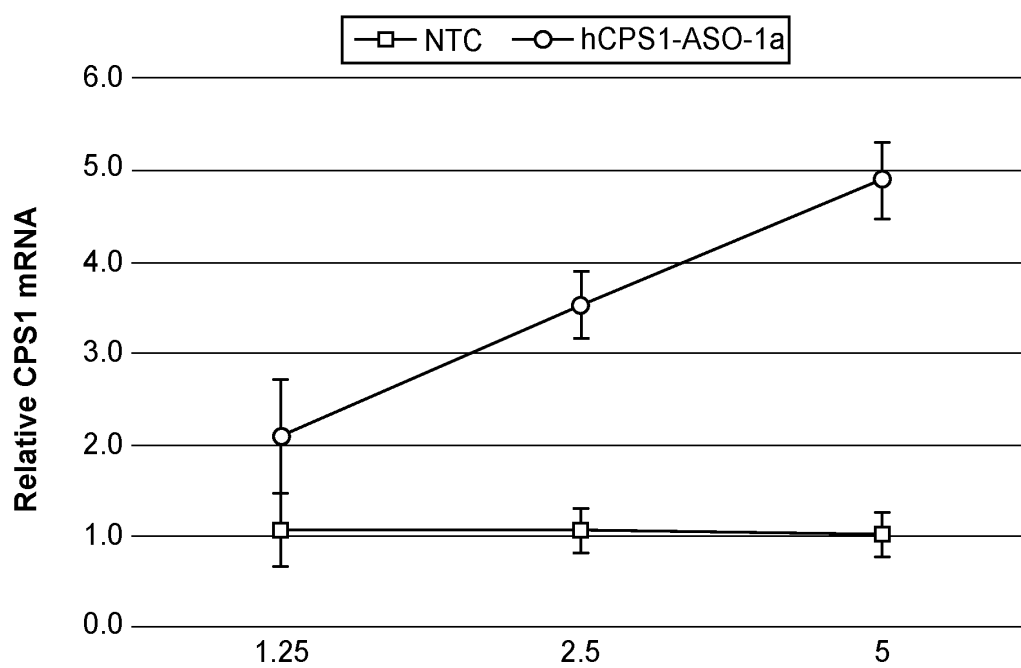


FIG. 3

Oligo	Sequence																									SEQ ID NO		
hCPS1-ASO-1a								T	G	C*	A	G	G	C	A	C	A	C	A	T	C*	A	G	G	C*		16	
hCPS1-ASO-1g								T	G	C*	A	G	G	C	A	C	A	C	A	T	C*	A	G	G	C*		22	
hCPS1-ASO-2							A	T	G	C*	A	G	G	C	A	C	A	C	A	T	C*	A	G	G	C*	T	23	
hCPS1-ASO-3							A	A	T	G	C*	A	G	G	C	A	C	A	C	A	T	C*	A	G	G	C*	T	24
hCPS1-ASO-5a							A	A	T	G	C*	A	G	G	C	A	C	A	C	A	T	C*	A	G			26	
hCPS1-ASO-6a	T	G	A	A	T	G	C	A	G	G	C	A	G	G	C	A	C	A	C	A*	A	T	C*				27	

FIG. 4A

CPS1 mRNA levels in hepatocyte donor 511A

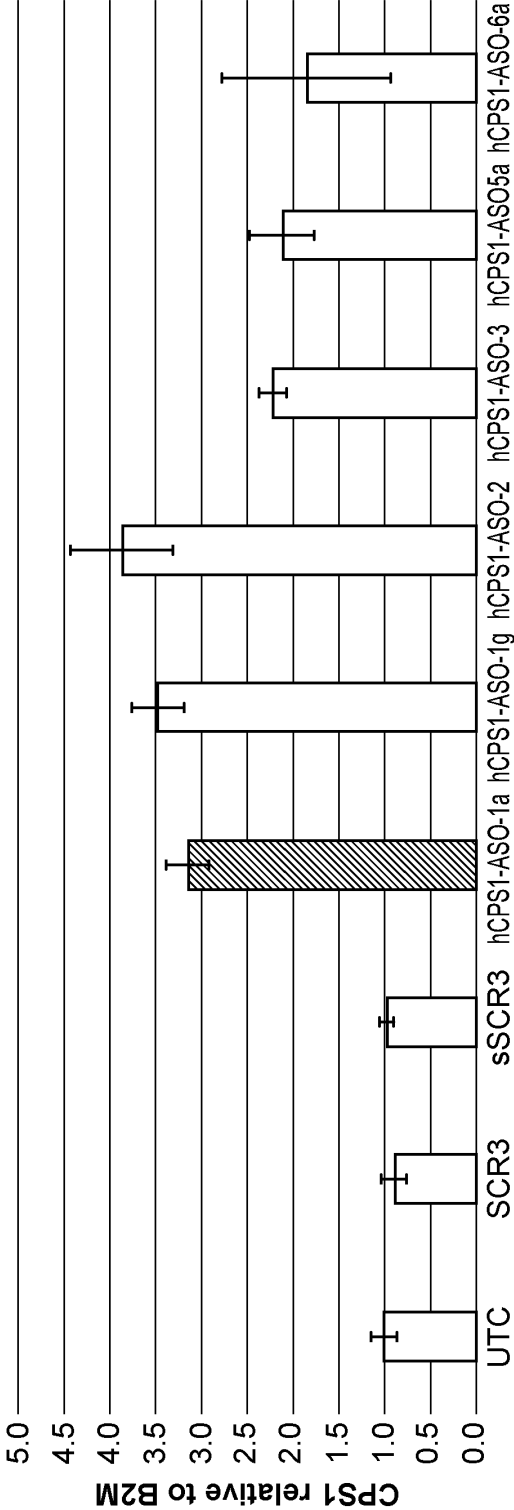


FIG. 4B

MOE

PO

LNA

*C: 5-Methyl C

Oligo	Sequence																												SEQ ID NO		
hCPS1-ASO-1a																															16
hCPS1-ASO-1b																															17
hCPS1-ASO-1c																															18
hCPS1-ASO-1d																															19
hCPS1-ASO-1e																															20
hCPS1-ASO-1f																															21
hCPS1-ASO-1g																															22
hCPS1-ASO-2																															23
hCPS1-ASO-3																															24
hCPS1-ASO-4a																															25
hCPS1-ASO-5a																															26
hCPS1-ASO-6a																															27
hCPS1-ASO-4b																															28
hCPS1-ASO-5b																															29
hCPS1-ASO-6b																															30
hCPS1-ASO-7a																															31
hCPS1-ASO-8a																															32
hCPS1-ASO-9a																															33
hCPS1-ASO-10a																															34
hCPS1-ASO-11a																															35
hCPS1-ASO-12a																															36
hCPS1-ASO-13a																															37
hCPS1-ASO-14a																															38
hCPS1-ASO-15a																															39
hCPS1-ASO-9b																															40

FIG. 5A

[illegible]

FIG. 5A (Cont.)

Oligo	Sequence																	SEQ ID NO
mCPS1-ASO-1	T	G	G	A	C	A	G	C	T	T	G	G	G	A	G	G	A	51
mCPS1-ASO-2	C	A	T	A	A	T	T	G	A	C	A	G	T	T	G	G	G	52
mCPS1-ASO-3	G	T	A	T	G	A	T	G	T	C	A	T	T	G	G	A	A	53
mCPS1-ASO-4	G	G	G	T	T	A	C	A	T	A	G	C	T	T	A	A	A	54
mCPS1-ASO-5	G	C	C	C	A	T	G	A	A	A	G	C	T	T	C	C	T	55
mCPS1-ASO-6	T	A	T	G	T	C	A	A	T	T	G	T	A	T	G	A	C	56
mCPS1-ASO-7	G	G	G	T	C	T	T	A	T	T	C	A	G	C	T	A	C	57
mCPS1-ASO-8	T	C	T	G	A	T	G	A	A	T	G	A	G	C	A	C	C	58
mCPS1-ASO-9	A	C	C	C	C	T	G	A	C	T	G	C	C	C	A	A	G	59
mCPS1-ASO-10	G	G	T	G	C	T	T	G	T	T	A	T	G	T	T	G	C	60
mCPS1-ASO-11	G	T	A	C	A	T	A	G	G	C	T	G	T	T	T	A	C	61
mCPS1-ASO-12	C	C	T	A	C	A	T	C	A	T	G	T	C	C	T	A	A	62
mCPS1-ASO-13	T	C	C	A	G	A	G	A	A	A	G	T	G	C	C	A	C	63
mCPS1-ASO-14	A	C	C	T	T	C	A	T	A	A	T	T	G	G	G	C	T	64
mCPS1-ASO-15	C	A	G	T	A	T	C	C	T	T	T	G	T	T	C	C	C	65
mCPS1-ASO-16	T	T	T	G	A	C	C	C	A	C	T	C	T	T	A	C	C	66
mCPS1-ASO-17	G	T	T	G	A	C	C	C	A	G	T	G	A	A	T	G	T	67
mCPS1-ASO-18	G	G	T	T	G	T	A	G	T	C	T	A	G	T	C	T	A	68

FIG. 5B

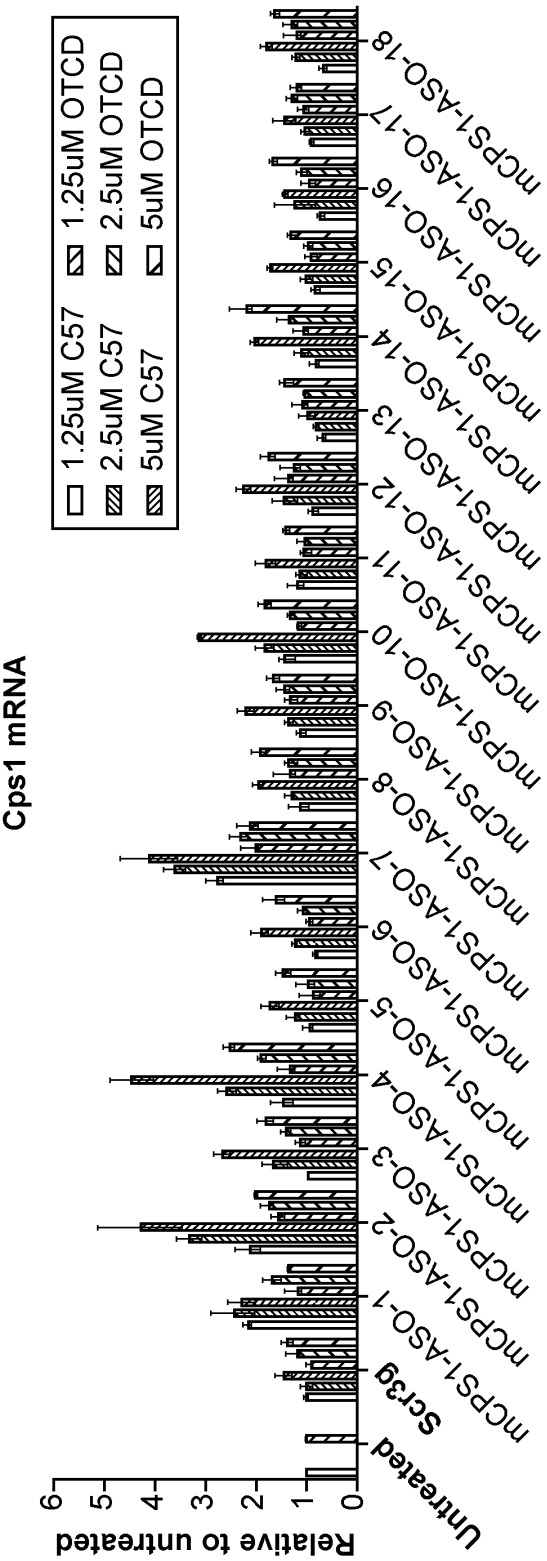


FIG. 6A

First tier	CS7BL6			OTCD		
	1.25uM	2.5uM	5uM	1.25uM	2.5uM	5uM
	FC	FC	FC	FC	FC	FC
mCPS1-ASO-2	2.12	3.33	4.30	1.58	1.77	2.03
mCPS1-ASO-3	0.99	1.66	2.68	1.12	1.44	1.80
mCPS1-ASO-4	1.49	2.60	4.47	1.32	1.91	2.54
mCPS1-ASO-7	2.77	3.62	4.13	2.02	2.33	2.14
mCPS1-ASO-12	0.91	1.45	2.26	1.37	1.26	1.76
mCPS1-ASO-9	1.13	1.37	2.21	1.32	1.45	1.67
mCPS1-ASO-10	1.45	1.83	3.14	1.17	1.32	1.84

FIG. 6B

Second tier	CS7BL6			OTCD		
	1.25uM	2.5uM	5uM	1.25uM	2.5uM	5uM
	FC	FC	FC	FC	FC	FC
mCPS1-ASO-1	2.16	2.46	2.29	1.16	1.70	1.37
mCPS1-ASO-5	0.95	1.24	1.73	0.89	1.00	1.48
mCPS1-ASO-6	0.82	1.26	1.94	0.97	1.08	1.62
mCPS1-ASO-11	1.19	1.15	1.82	1.07	1.03	1.44
mCPS1-ASO-8	1.18	1.31	1.98	1.32	1.40	1.94
mCPS1-ASO-14	0.82	1.11	2.04	1.07	1.37	2.20
mCPS1-ASO-18	0.69	1.22	1.81	1.20	1.30	1.65
mCPS1-ASO-15	0.85	1.03	1.73	0.91	0.97	1.32

FIG. 6C

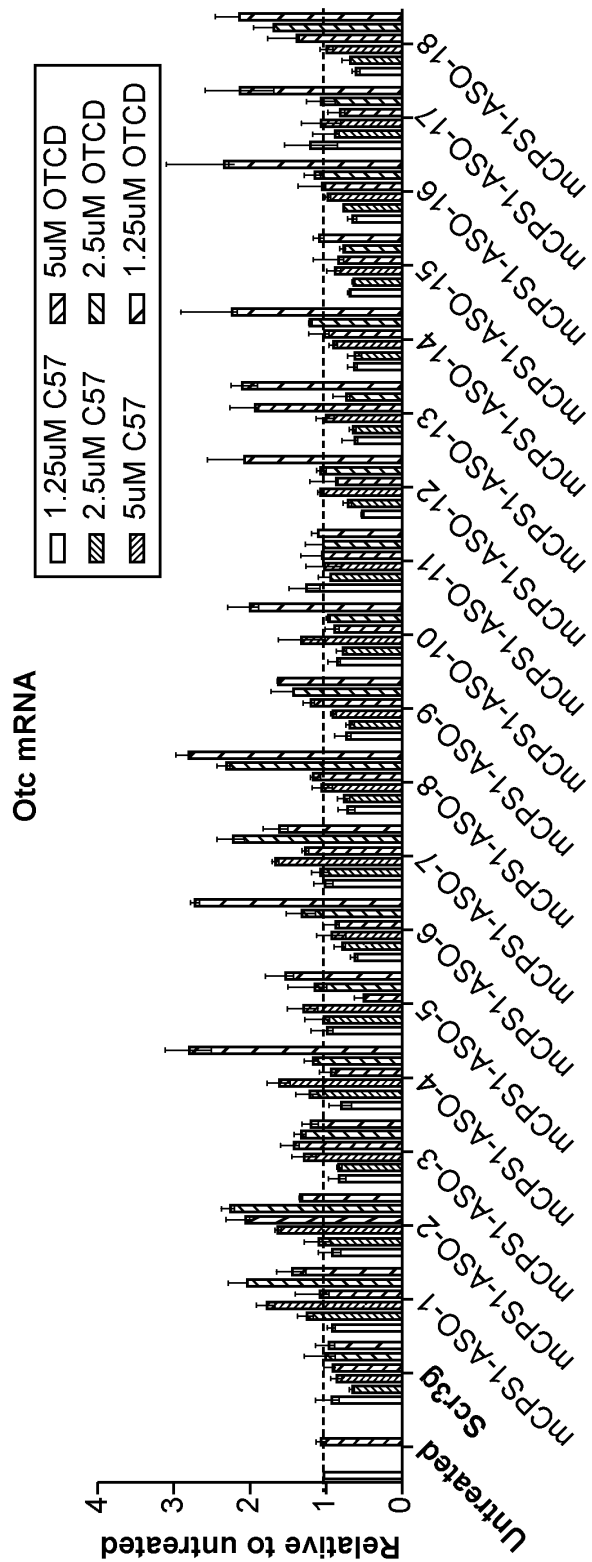


FIG. 7A

First tier	CS7BL6			OTCD		
	1.25uM	2.5uM	5uM	1.25uM	2.5uM	5uM
	FC	FC	FC	FC	FC	FC
mCPS1-ASO-2	0.92	1.09	1.64	2.06	2.27	2.00
mCPS1-ASO-3	0.83	0.83	1.29	1.42	1.33	2.17
mCPS1-ASO-4	0.79	1.21	1.62	0.93	1.17	2.80
mCPS1-ASO-7	1.04	1.07	1.67	1.27	2.23	1.62
mCPS1-ASO-12	0.52	0.72	1.07	0.86	1.08	2.08
mCPS1-ASO-9	0.73	0.69	0.90	1.20	1.43	1.63
mCPS1-ASO-10	0.85	0.77	1.32	0.88	0.98	2.00

FIG. 7B

Second tier	CS7BL6			OTCD		
	1.25uM	2.5uM	5uM	1.25uM	2.5uM	5uM
	FC	FC	FC	FC	FC	FC
mCPS1-ASO-1	0.92	1.27	1.79	1.09	2.04	1.44
mCPS1-ASO-5	0.98	1.04	1.30	0.50	1.15	1.54
mCPS1-ASO-6	0.62	0.78	0.93	0.87	1.31	2.73
mCPS1-ASO-11	1.26	0.95	1.03	1.05	1.04	1.10
mCPS1-ASO-8	0.72	0.76	1.05	1.18	2.31	2.81
mCPS1-ASO-14	0.63	0.63	0.91	1.03	1.22	2.24
mCPS1-ASO-18	0.60	0.69	0.99	1.39	1.69	2.14
mCPS1-ASO-15	0.69	0.64	0.89	0.84	0.77	1.09

FIG. 7C

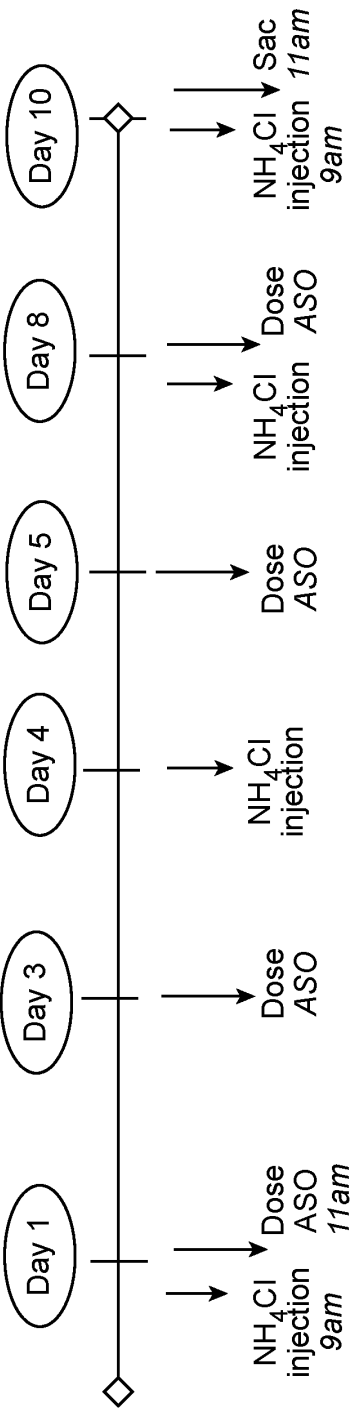


FIG. 8

FIG. 9A

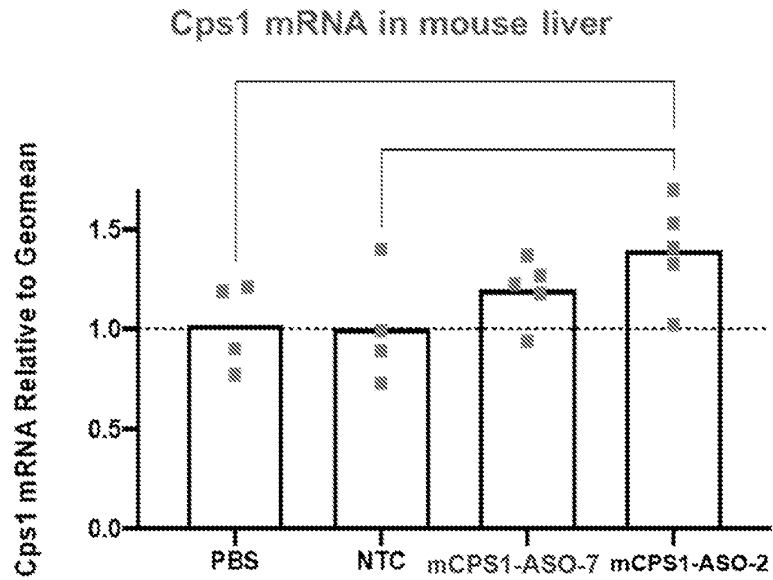


FIG. 9B

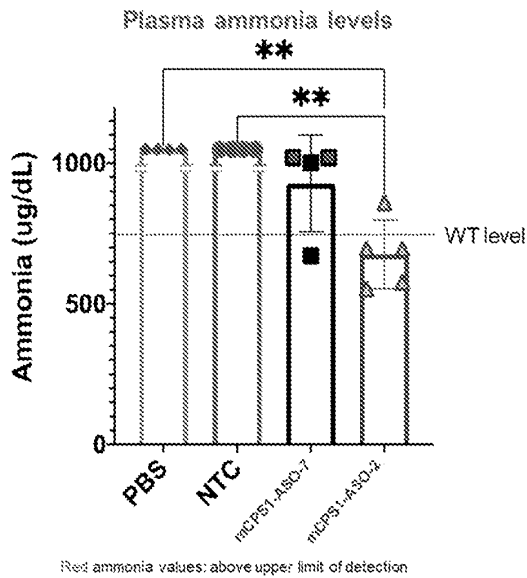


FIG. 9C

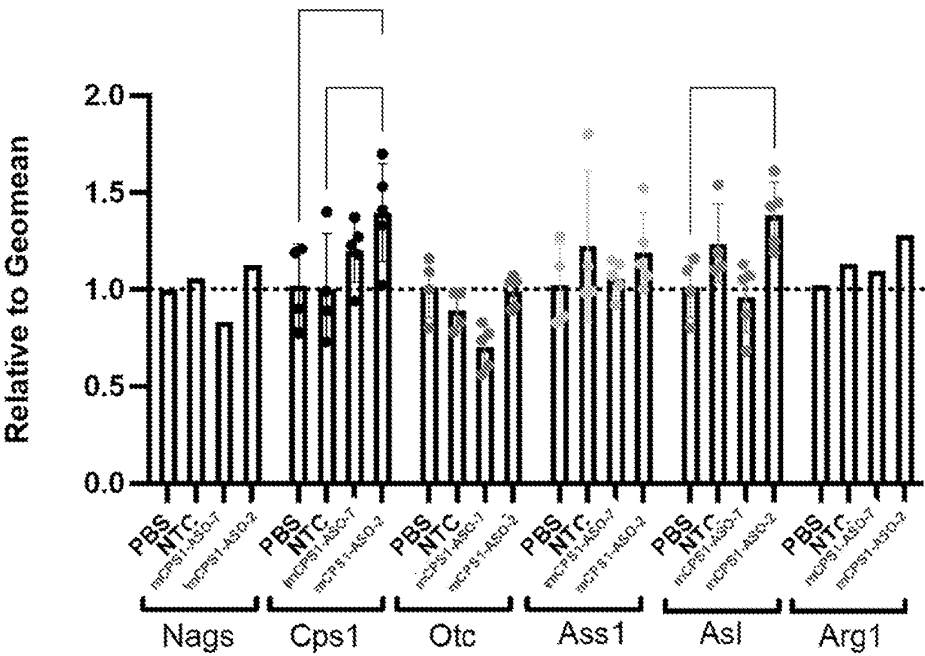


FIG. 9D

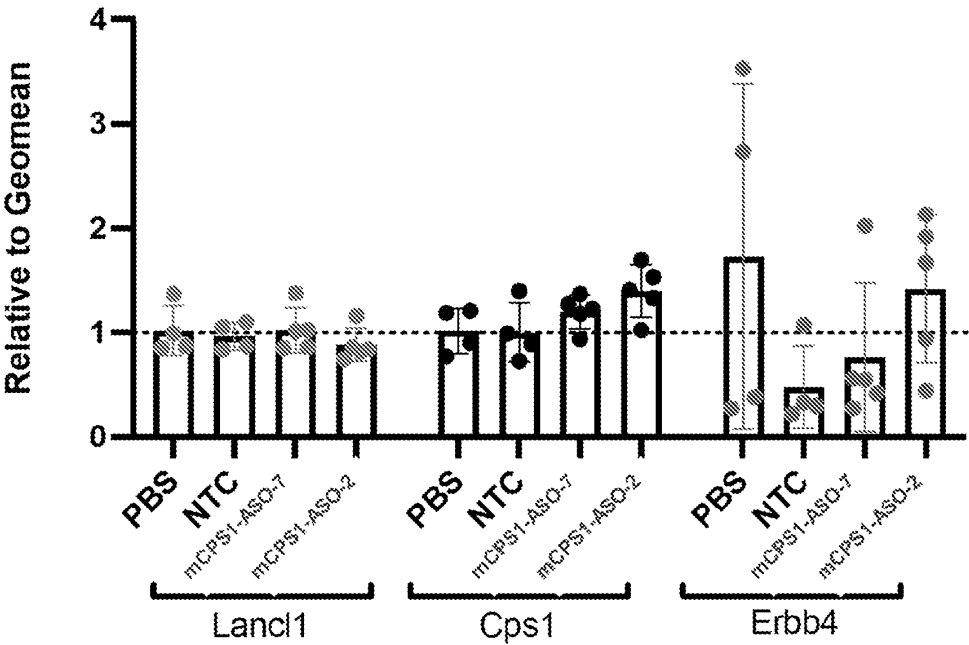


FIG. 10

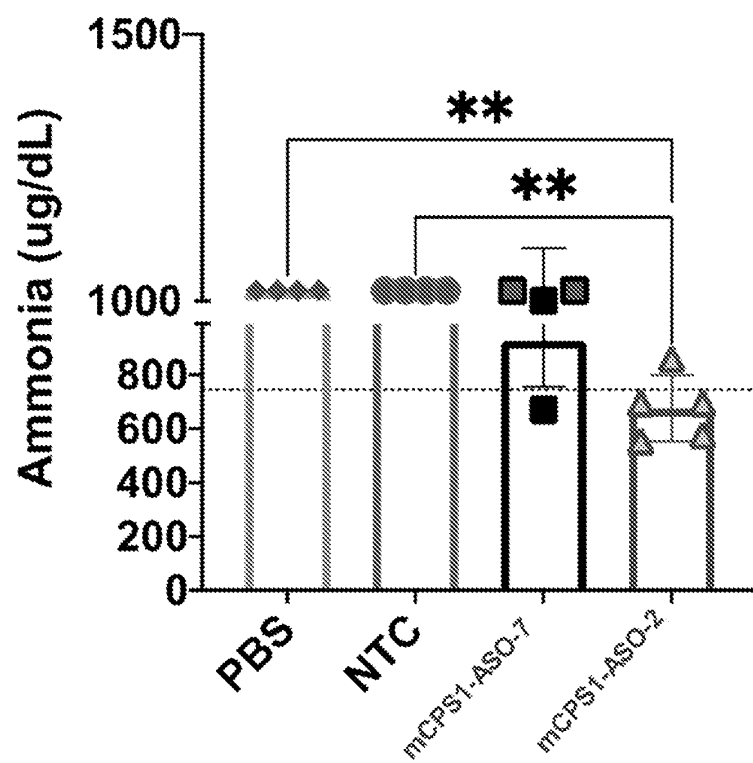


FIG. 11A

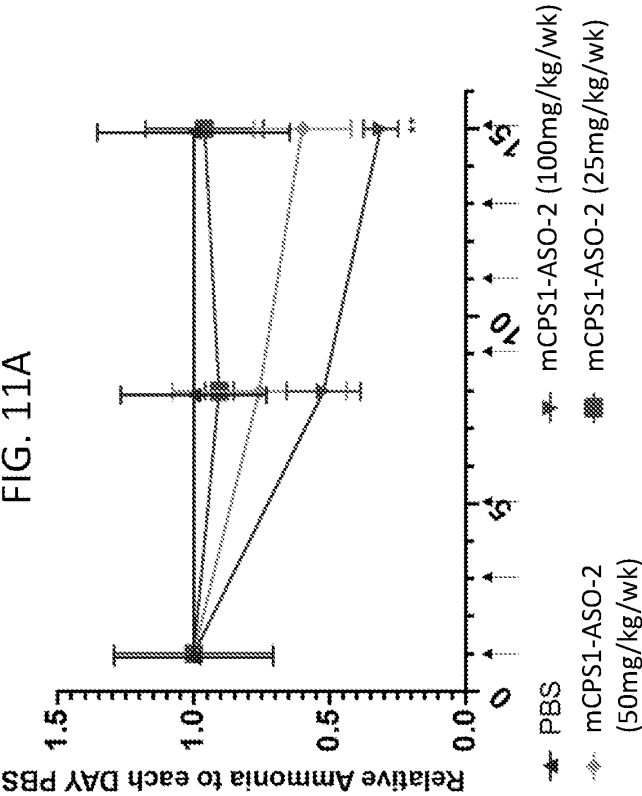


FIG. 11B

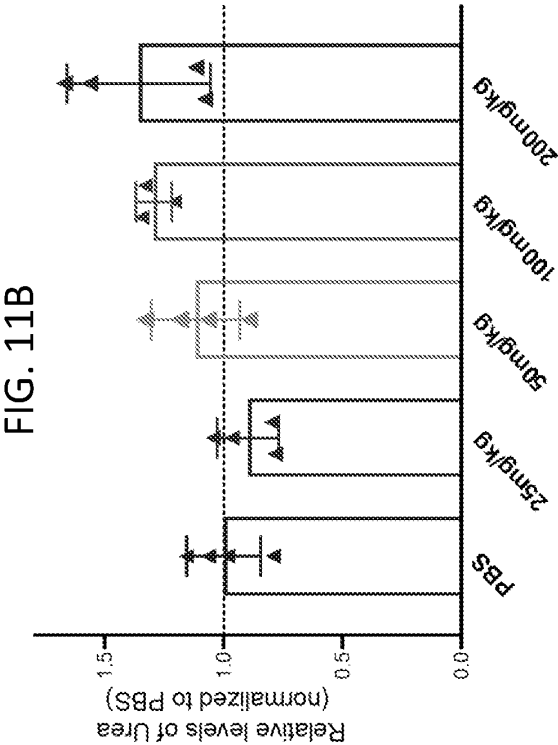


FIG. 11C

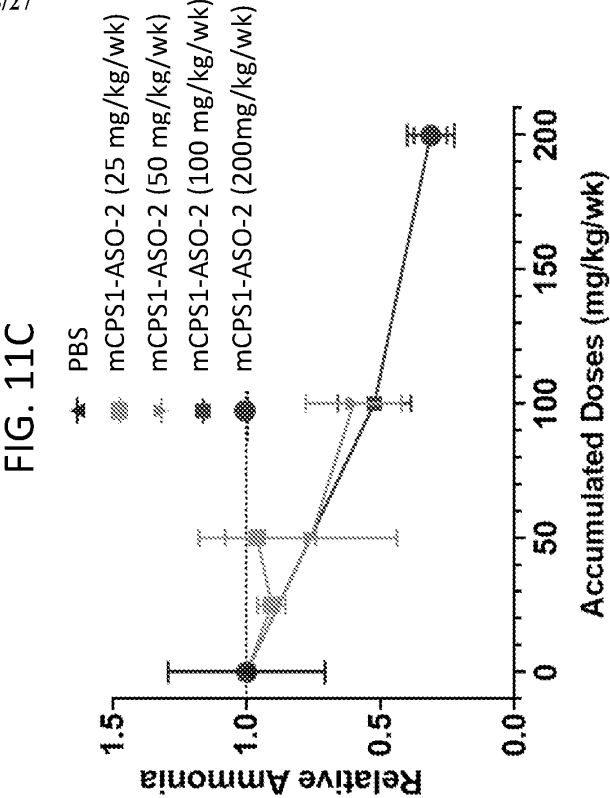


FIG. 12A

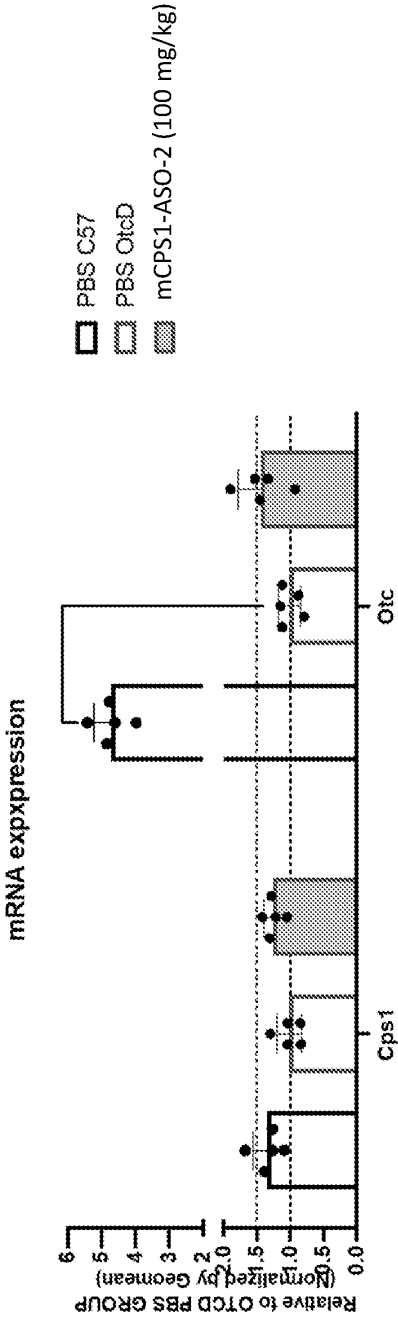


FIG. 12B

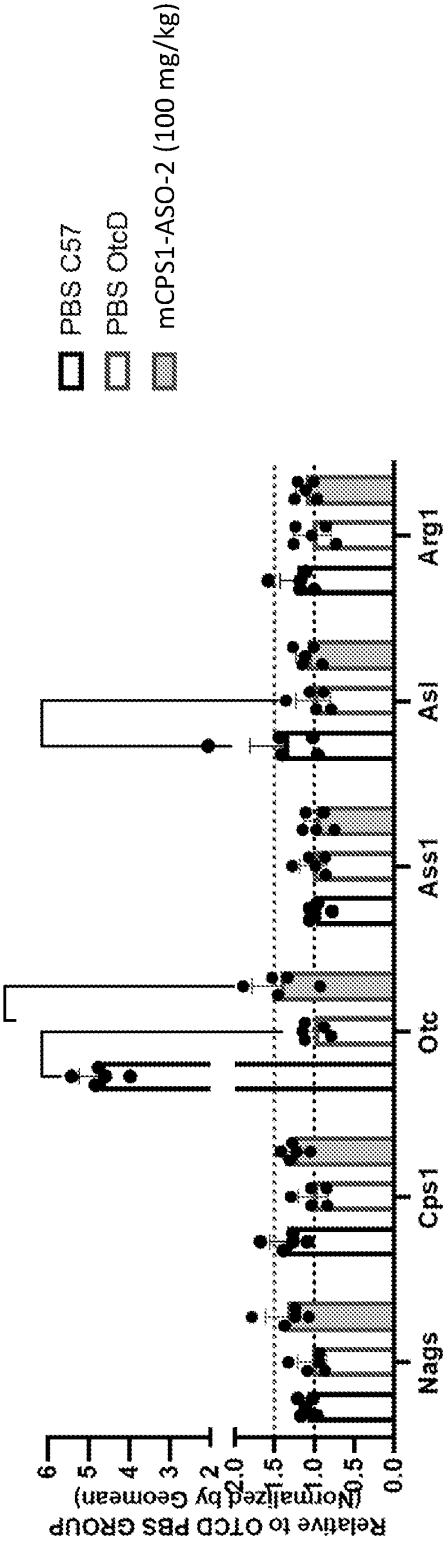
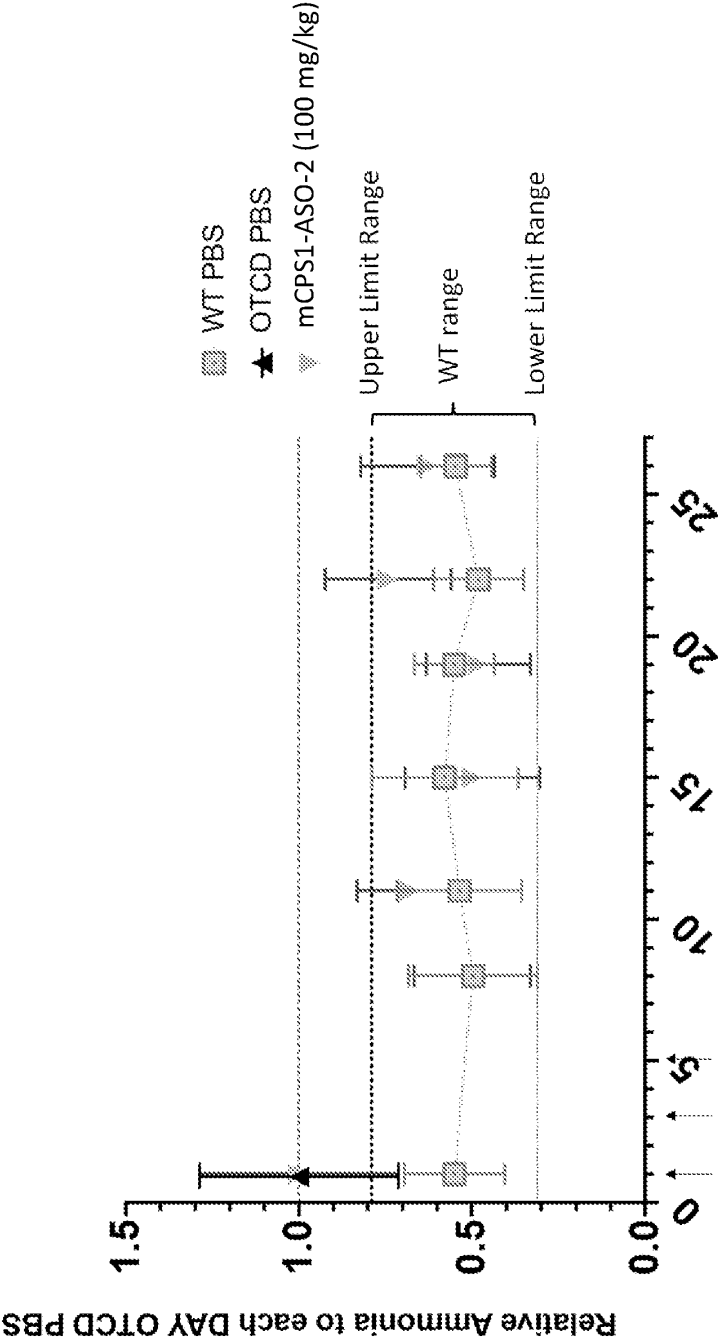


FIG. 13



Two way ANOVA, *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$, ****: $P < 0.0001$

SEQIDNO	Name	Sequence	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
16	hCPS1-ASO-1a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
392	hCPS1-ASO-1h		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
393	hCPS1-ASO-1i		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
394	hCPS1-ASO-1j		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
395	hCPS1-ASO-1k		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
396	hCPS1-ASO-1l		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
397	hCPS1-ASO-1m		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
398	hCPS1-ASO-1n		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
399	hCPS1-ASO-1o		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
400	hCPS1-ASO-1p		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
401	hCPS1-ASO-1q		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
402	hCPS1-ASO-1r		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
403	hCPS1-ASO-1s		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
404	hCPS1-ASO-1t		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
405	hCPS1-ASO-1u		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
406	hCPS1-ASO-1v		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
407	hCPS1-ASO-82a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
408	hCPS1-ASO-1w		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
409	hCPS1-ASO-1x		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
410	hCPS1-ASO-87a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
411	hCPS1-ASO-88a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
412	hCPS1-ASO-89a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
414	hCPS1-ASO-1y		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
415	hCPS1-ASO-1z		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
416	hCPS1-ASO-1aa		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
417	hCPS1-ASO-1ab		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
418	hCPS1-ASO-1ac		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
419	hCPS1-ASO-1ad		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
420	hCPS1-ASO-1ae		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
421	hCPS1-ASO-1af		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
422	hCPS1-ASO-1ag		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
423	hCPS1-ASO-1ah		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
424	hCPS1-ASO-1ai		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
425	hCPS1-ASO-97a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
426	hCPS1-ASO-98a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
427	hCPS1-ASO-99a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										
428	hCPS1-ASO-100a		T	G	C	A	G	G	C	A	C	A	C	A	C	A	T	C	A	G	G	C	C										

FIG. 14

FIG. 14 (Cont. 1)

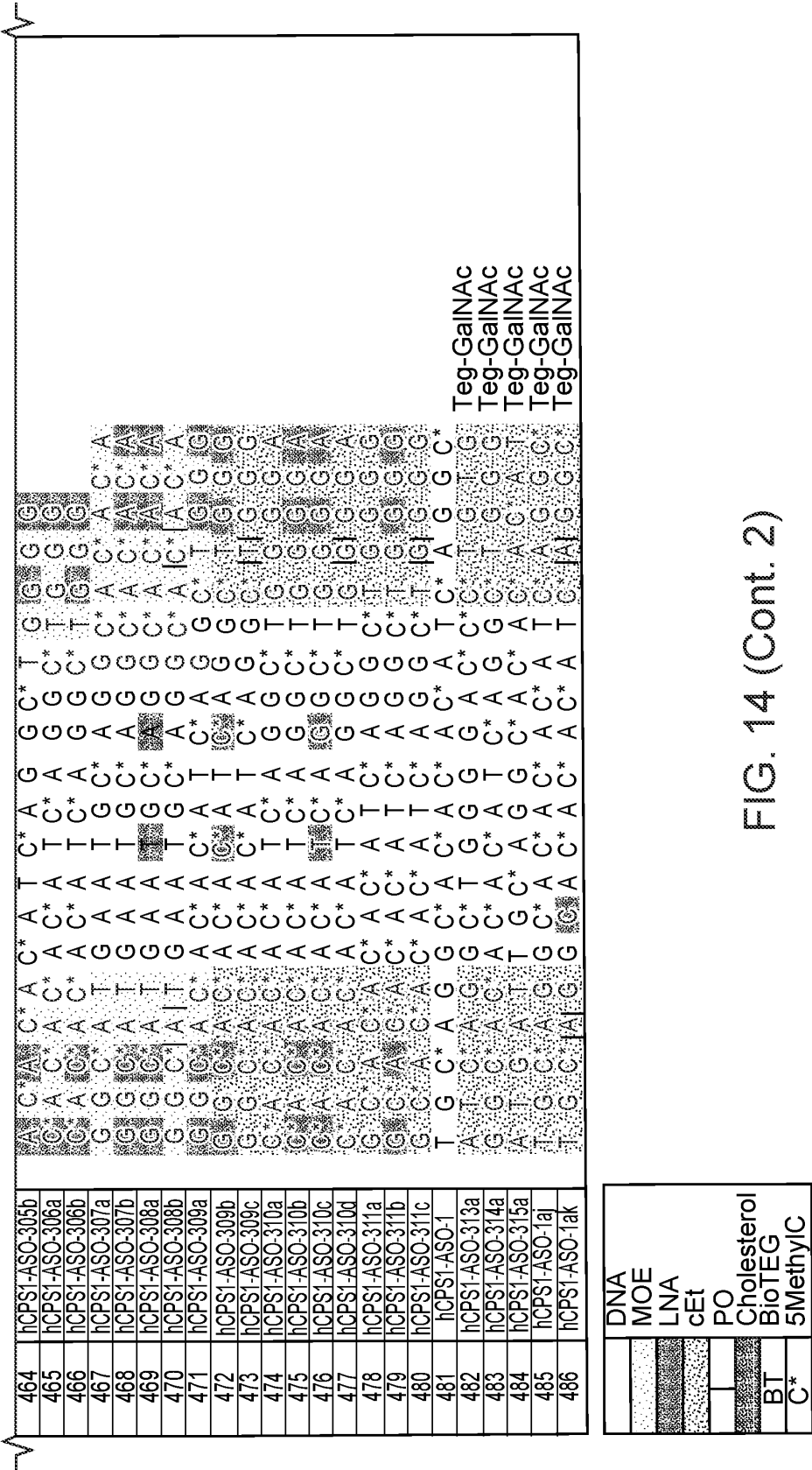


FIG. 14 (Cont. 2)

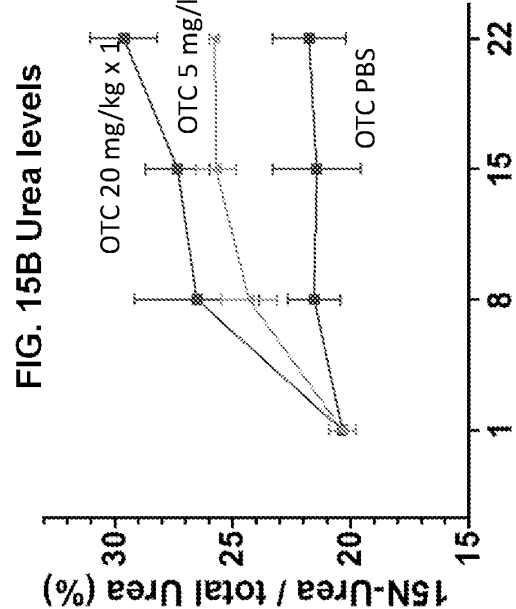


FIG. 15C
OTC Protein Levels

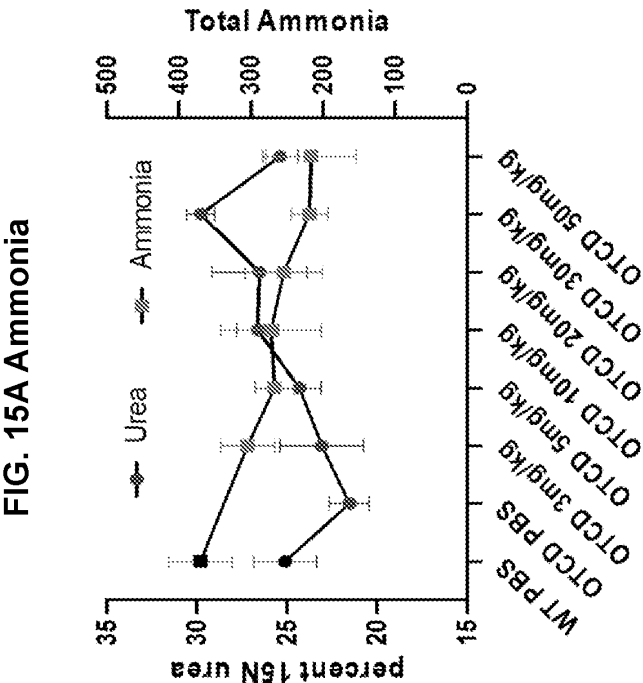
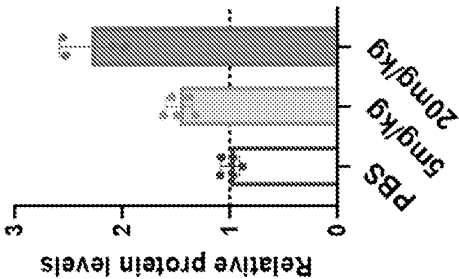


FIG. 16

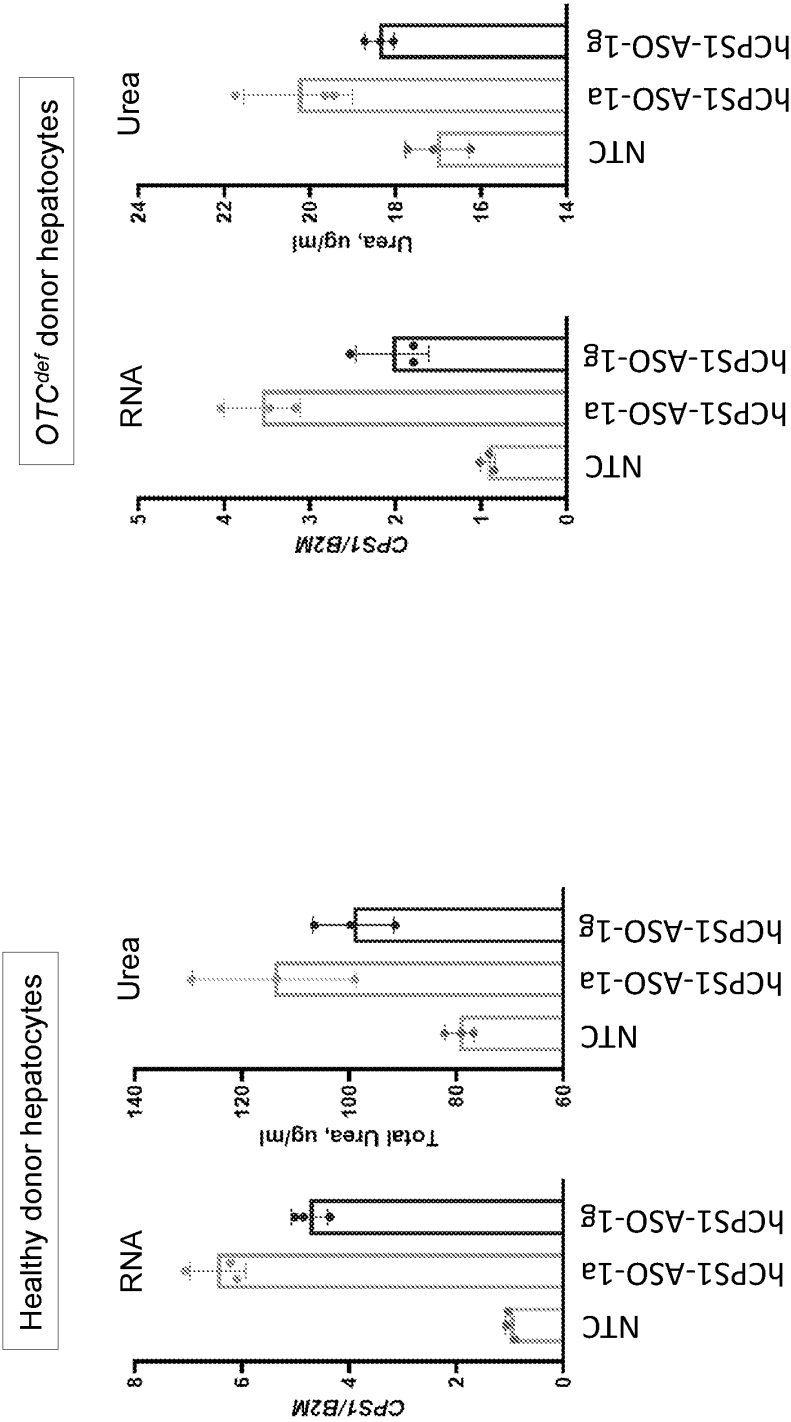


FIG. 17

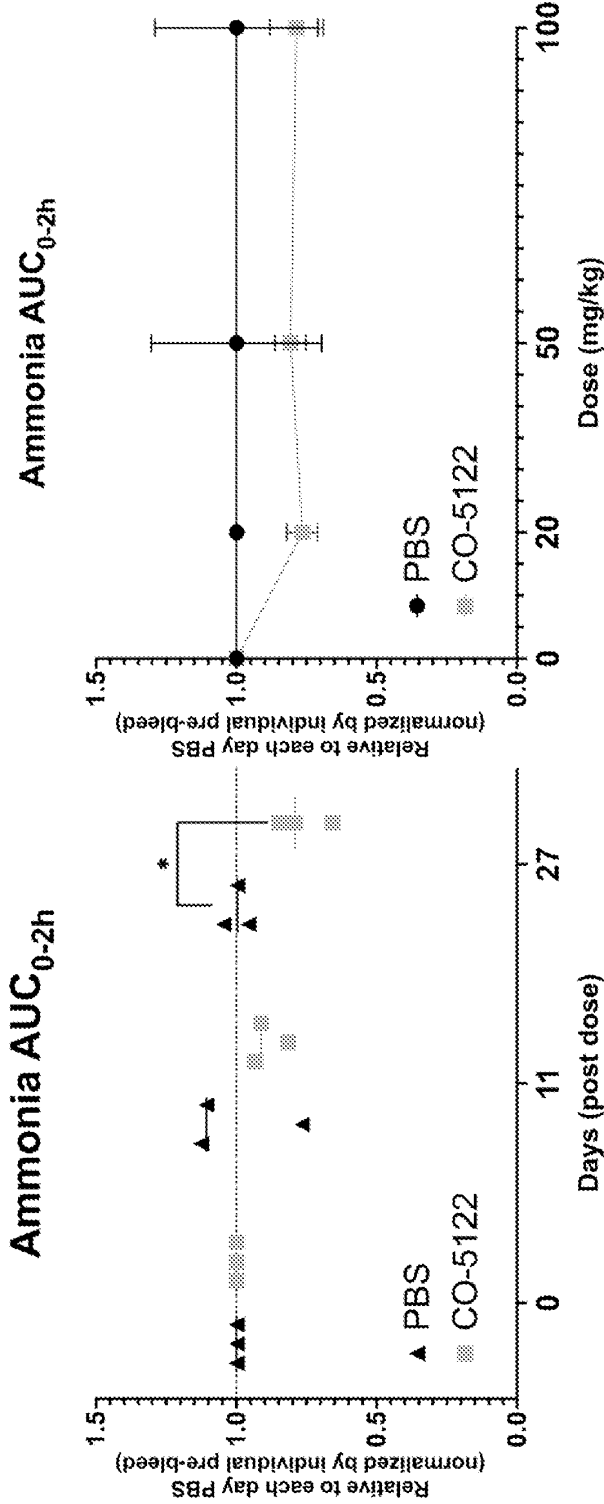
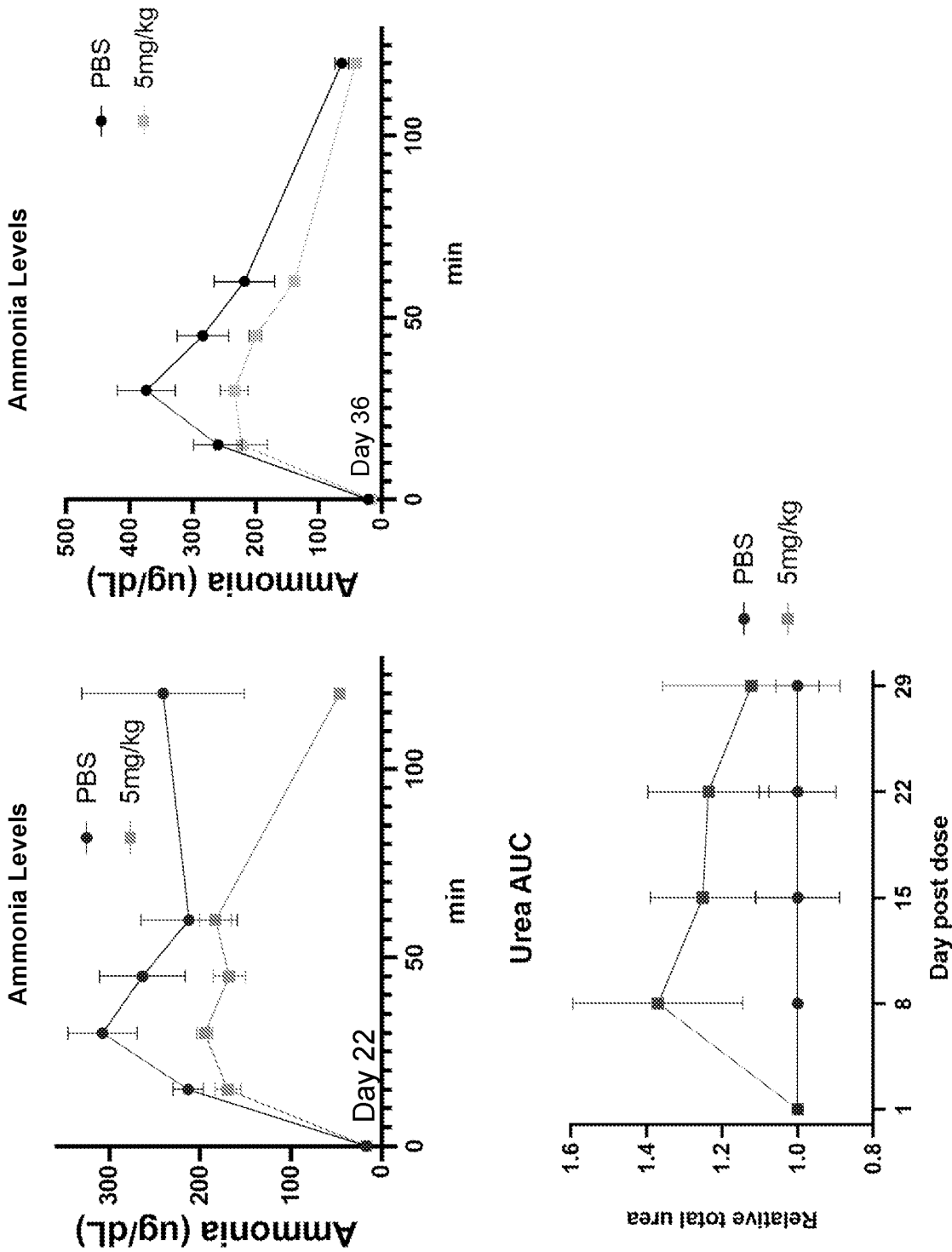


FIG. 18



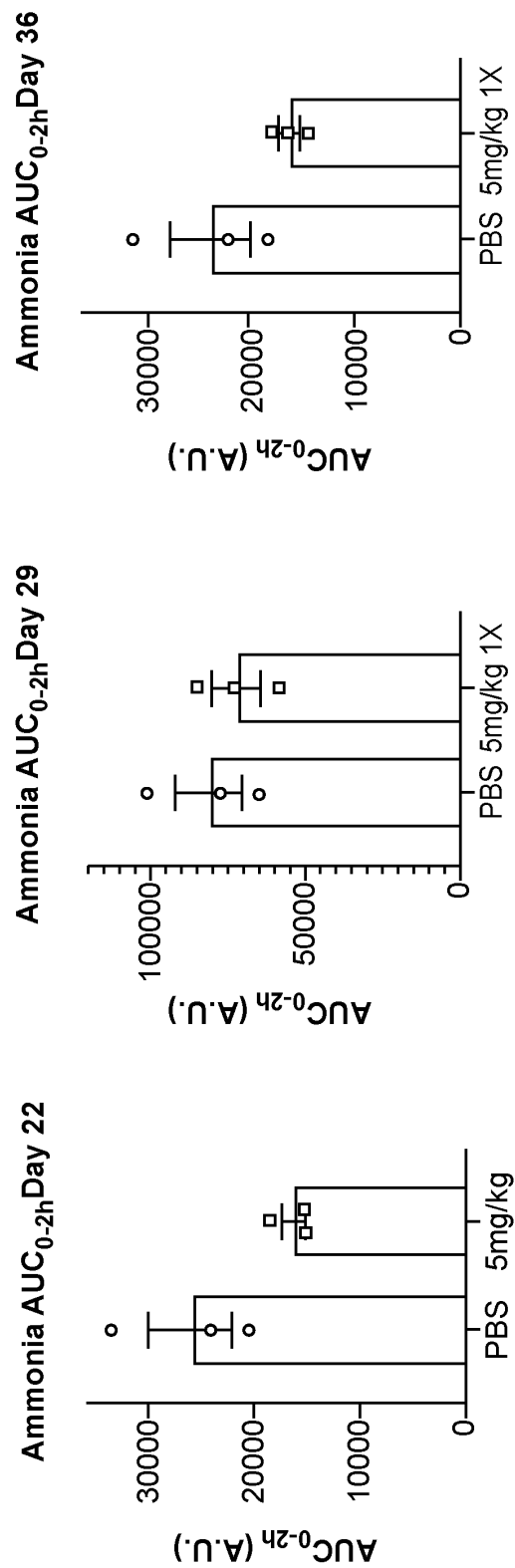


FIG. 19

FIG. 20

