Number	Target	sgRNA #	Genotyping
01	CTSD	1	1 bp insertion
02	CTSD	1	1 bp insertion
03	CTSD	1	10 bp deletion
04	CTSD	1	1 bp insertion
05	CTSD	1	1 bp insertion
06	CTSD	1	157 bp deletion
07	CTSD	1	1 bp insertion
08	CTSD	1	44 bp deletion
09	CTSD	1	185 bp insertion
10	CTSD	1	1 bp insertion
11	CTSD	1	7 bp insertion
12	CTSD	1	23 bp deletion
13	CTSD	1	38 bp deletion
14	CTSD	1	1 bp insertion
15	CTSD	1	1 bp insertion
16	CTSD	1	2 bp deletion
17	CTSD	1	5 bp deletion
18	CTSD	2	47 bp deletion
19	CTSD	2	8 bp deletion
20	CTSD	2	8 bp deletion
21	CTSD	2	2 bp deletion
22	CTSD	2	11 bp deletion
23	CTSD	2	8 bp deletion
24	CTSD	2	8 bp deletion
25	CTSD	2	8 bp deletion

Number	Target	sgRNA #	Genotyping
26	CTSD	2	8 bp deletion
27	CTSD	2	8 bp deletion
28	CTSD	2	8 bp deletion
29	CTSD	2	118 bp deletion
30	CTSD	2	8 bp deletion
31	CTSD	2	8 bp deletion
32	CTSD	2	8 bp deletion*
33	CTSD	2	2 bp deletion
34	CTSD	2	17 bp deletion
35	CTSD	2	8 bp deletion*
36	CTSD	2	8 bp deletion**
37	CTSD	2	1 bp deletion**
38	CTSD	2	1 bp deletion**
39	CTSD	2	88 bp deletion
40	CTSD	2	1 bp deletion
41	CTSD	2	8 bp deletion
42	CTSD	2	1 bp deletion
43	CTSD	2	1 bp deletion
44	CTSD	2	1 bp deletion
45	CTSD	2	1 bp deletion
46	CTSD	2	1 bp deletion
47	CTSD	2	1 bp deletion
48	CTSD	2	4 bp deletion
49	CTSD	2	1 bp deletion
50	CTSD	2	1 bp deletion

Figure 1

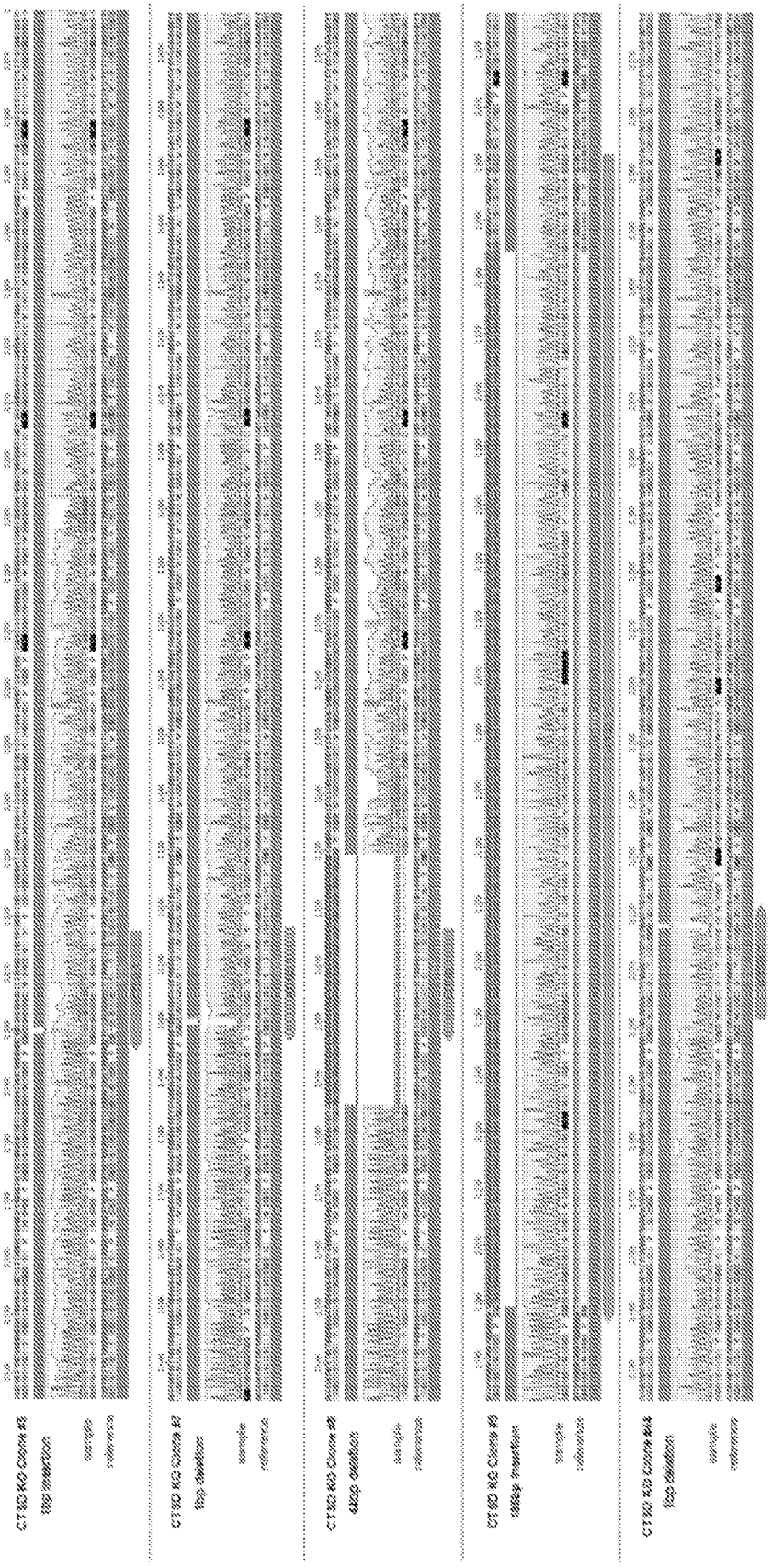


Figure 2

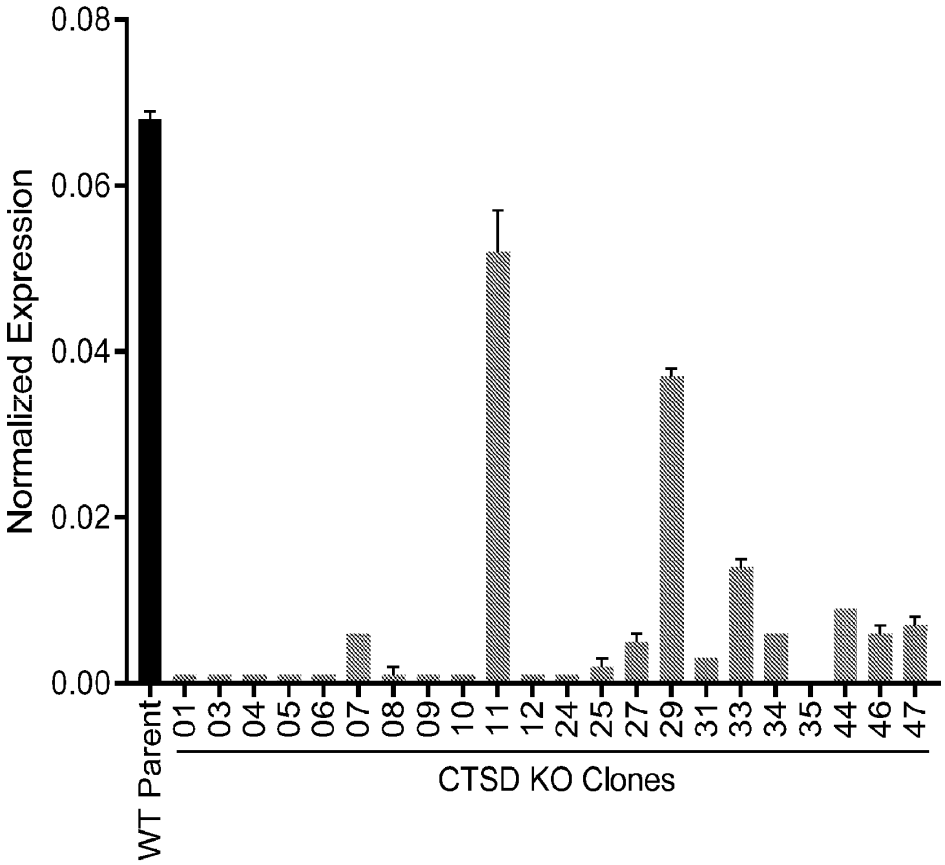

0.08
0.06
0.04
0.02
0.00
Normalized Expression
WT Parent
01
03
04
05
06
07
08
09
10
11
12
24
25
27
29
31
33
34
35
44
46
47
CTSD KO Clones

Figure 3

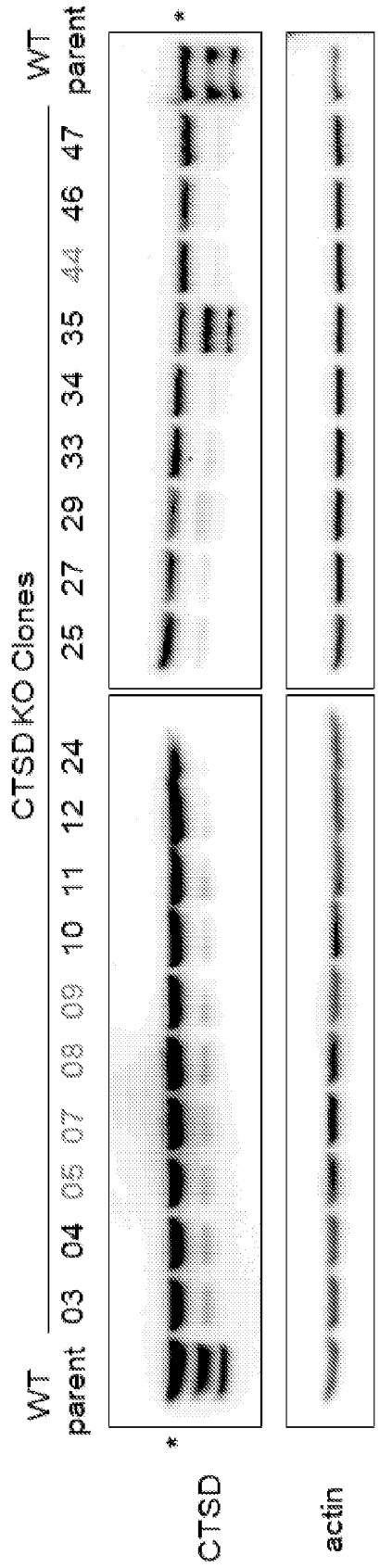

WT parent
03
04
05
07
08
09
10
11
12
24
CTSD KO Clones
25
27
29
33
34
35
44
46
47
WT parent
*
*
CTSD
actin

Figure 4

Figure 5A

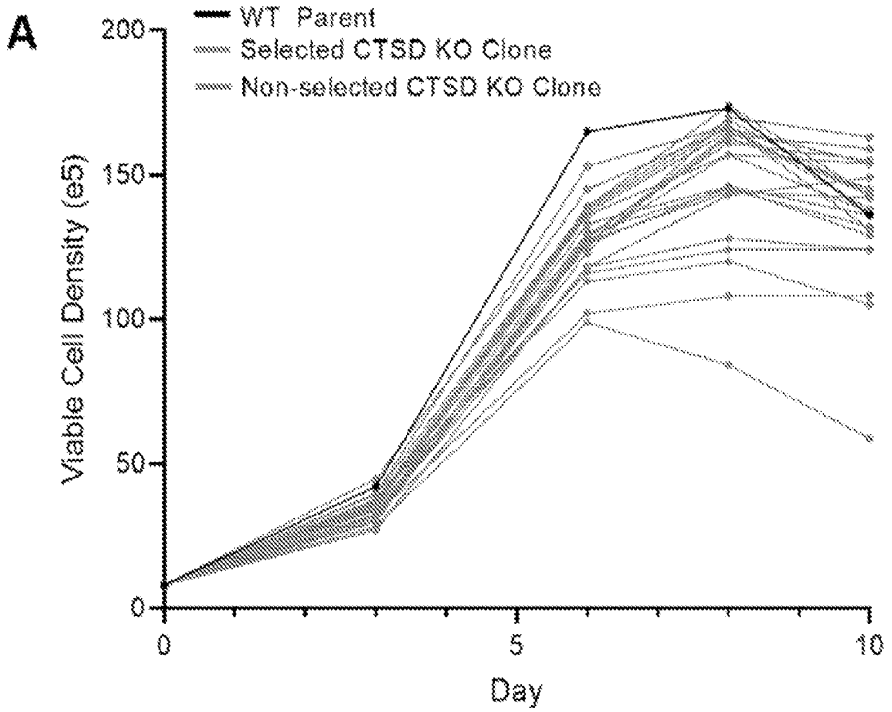


Figure 5B

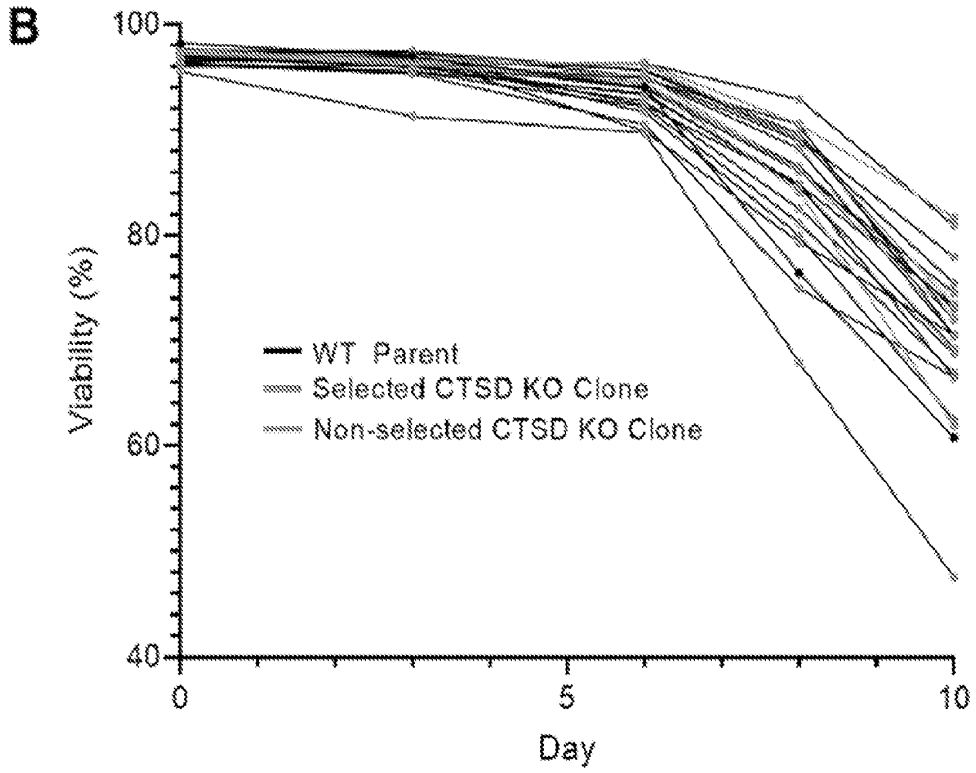
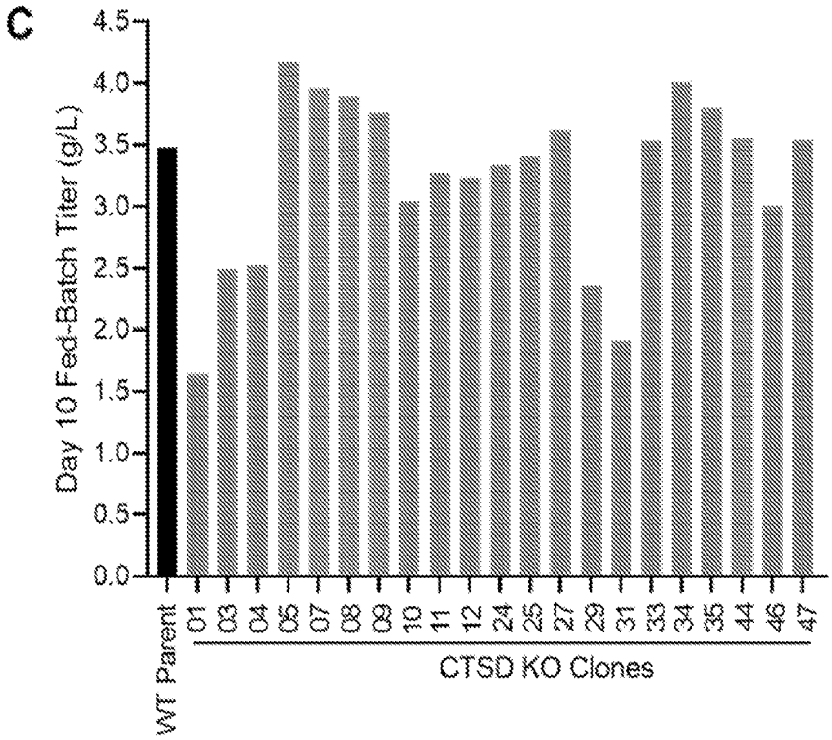


Figure 5C


C
Day 10 Fed-Batch Titer (g/L)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
WT Parent
01
03
04
05
07
08
09
10
11
12
24
25
27
29
31
33
34
35
44
46
47
CTSD KO Clones

Cell Type	Cathepsin D Activity (ppm)
WT Parent	50.6
CTSD KO clone 01	N/A*
CTSD KO clone 03	N/A*
CTSD KO clone 04	N/A*
CTSD KO clone 05	0
CTSD KO clone 07	0
CTSD KO clone 08	0
CTSD KO clone 09	0
CTSD KO clone 10	N/A*
CTSD KO clone 11	3.1
CTSD KO clone 12	N/A*
CTSD KO clone 24	0
CTSD KO clone 25	N/A*
CTSD KO clone 27	0
CTSD KO clone 29	N/A*
CTSD KO clone 31	N/A*
CTSD KO clone 33	0.1
CTSD KO clone 34	0
CTSD KO clone 35	29.5
CTSD KO clone 44	0
CTSD KO clone 46	N/A*
CTSD KO clone 47	N/A*

Figure 6

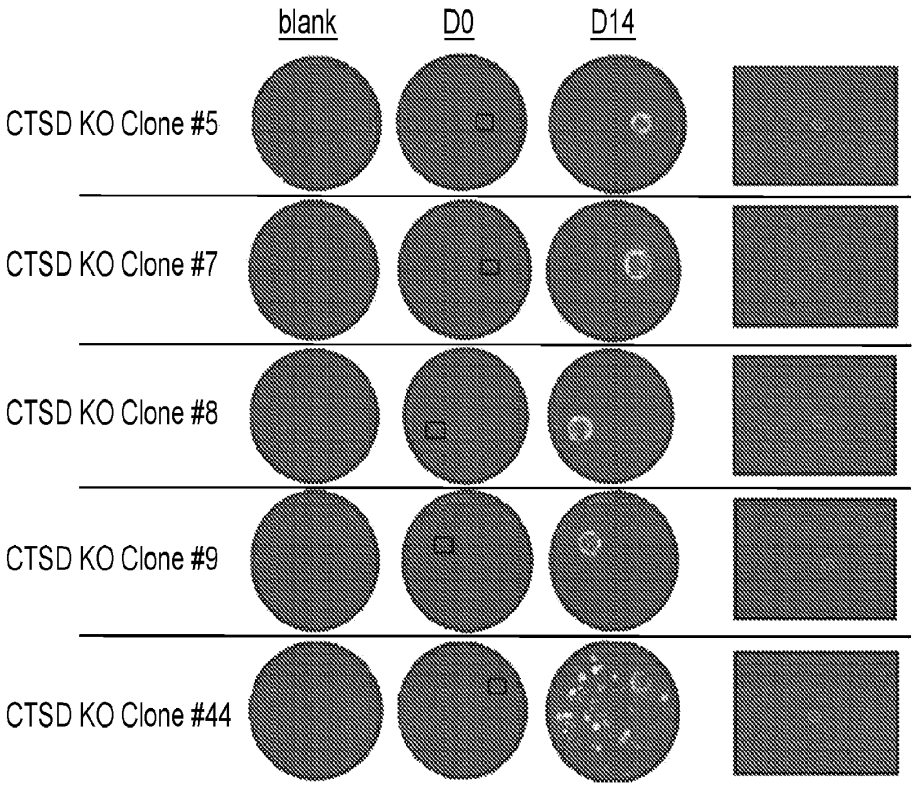

blank
D0
D14
CTSD KO Clone #5
CTSD KO Clone #7
CTSD KO Clone #8
CTSD KO Clone #9
CTSD KO Clone #44

Figure 7