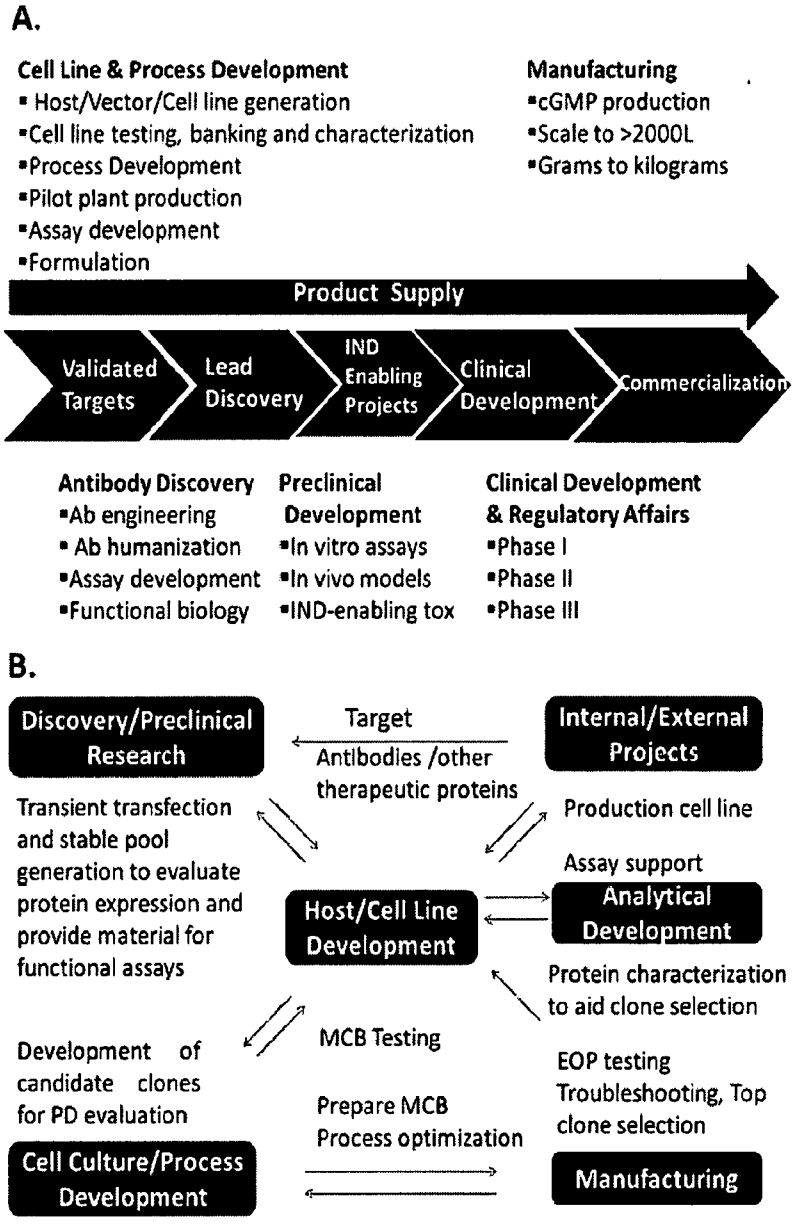

A.
Cell Line & Process Development
▪ Host/Vector/Cell line generation
▪Cell line testing, banking and characterization
▪Process Development
▪Pilot plant production
▪Assay development
▪Formulation
Manufacturing
▪cGMP production
▪Scale to >2000L
▪Grams to kilograms
Product Supply
Validated Targets
Lead Discovery
IND Enabling Projects
Clinical Development
Commercialization
Antibody Discovery
▪Ab engineering
▪ Ab humanization
▪Assay development
▪Functional biology
Preclinical Development
▪In vitro assays
▪In vivo models
▪IND-enabling tox
Clinical Development & Regulatory Affairs
▪Phase I
▪Phase II
▪Phase III
B.
Discovery/Preclinical Research
Target
Antibodies /other therapeutic proteins
Internal/External Projects
Transient transfection and stable pool generation to evaluate protein expression and provide material for functional assays
Production cell line
Assay support
Host/Cell Line Development
Analytical Development
Protein characterization to aid clone selection
Development of candidate clones for PD evaluation
MCB Testing
EOP testing
Troubleshooting, Top clone selection
Prepare MCB
Process optimization
Cell Culture/Process Development
Manufacturing

FIG. 1

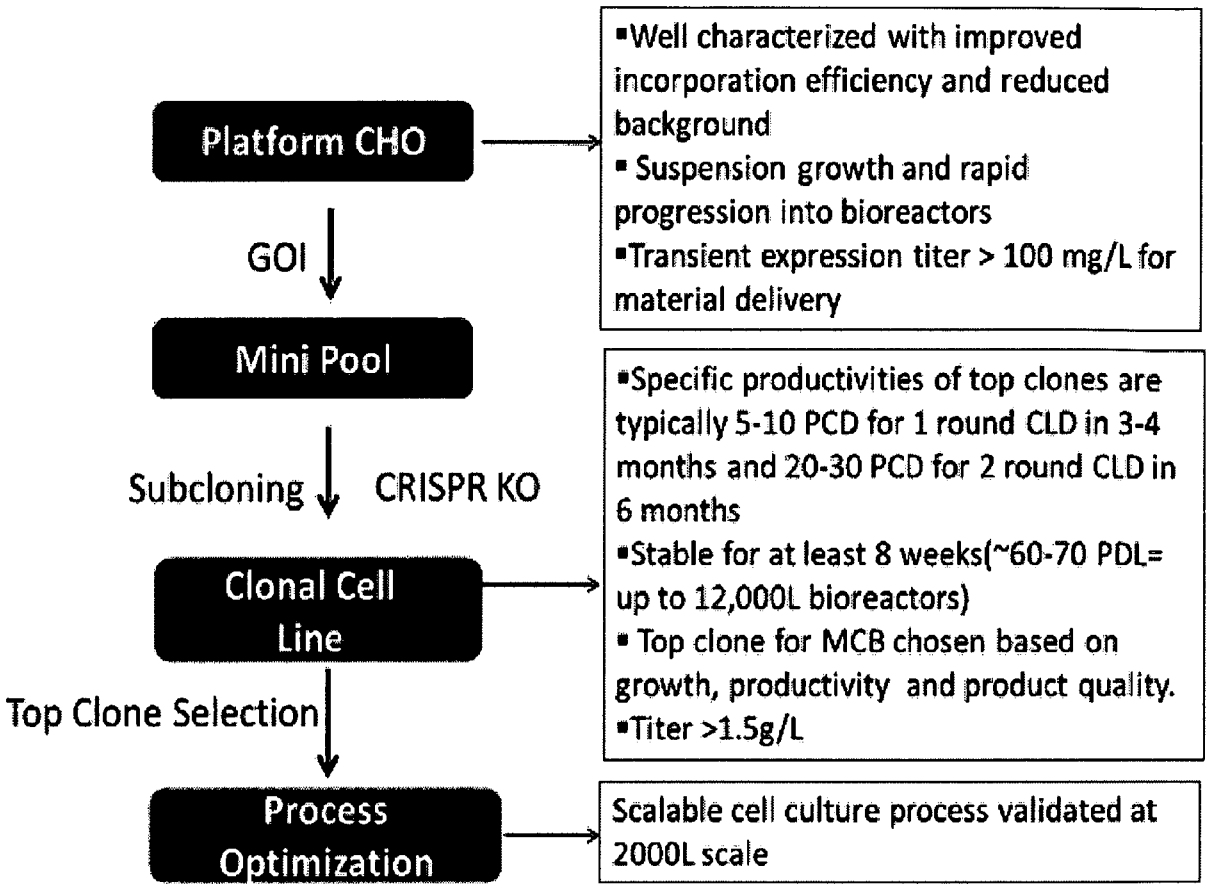

Platform CHO
GOI
Mini Pool
Subcloning
CRISPR KO
Clonal Cell Line
Top Clone Selection
Process Optimization
▪Well characterized with improved incorporation efficiency and reduced background
▪ Suspension growth and rapid progression into bioreactors
▪Transient expression titer > 100 mg/L for material delivery
▪Specific productivities of top clones are typically 5-10 PCD for 1 round CLD in 3-4 months and 20-30 PCD for 2 round CLD in 6 months
▪Stable for at least 8 weeks(~60-70 PDL= up to 12,000L bioreactors)
▪ Top clone for MCB chosen based on growth, productivity and product quality.
▪Titer >1.5g/L
Scalable cell culture process validated at 2000L scale

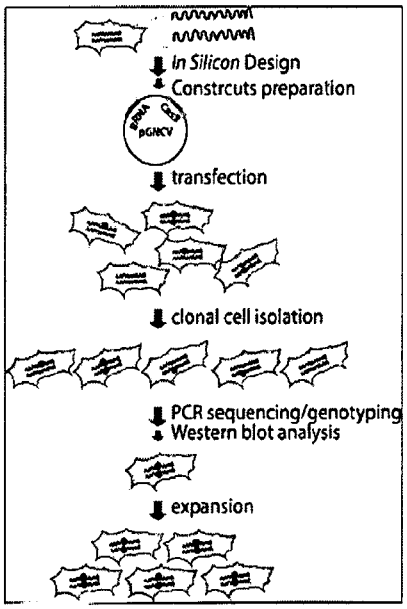
FIG. 2

A.

FACS SCD yields 3 fold of monoclonal outgrowths than traditional LDC

	Seeding Density	Deposition Rate	Outgrowth Rate	Monoclonal Outgrowth Rate
FACS SCD	1 cell/well	63%	53%	49%
LDC	0.5 cell/well	72%	65%	32%

B.

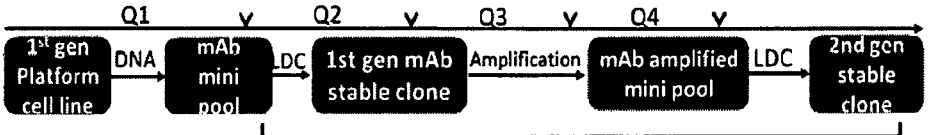


CRISPy program (CHO specific)
- *Zero off-target gRNA sequences*
- *Early exons*

Pooled cells Surveyor assay
- *30-90% KO efficiency*

Screening and Characterization
1. HT targeted DNA sequencing: *50-80% KO efficiency*
2. Western blot analysis *50-90% KO efficiency*
3. Functional assay

C.



1st gen Platform-GS

Antibody	CLD	Titer g/L	Scale
mAbF-1st	MP-Amp-LDC	1.0	5 L bioreactor
mAbH-1st	MP-LDC-Clonepix	0.5	2000 L bioreactor

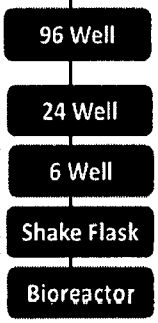
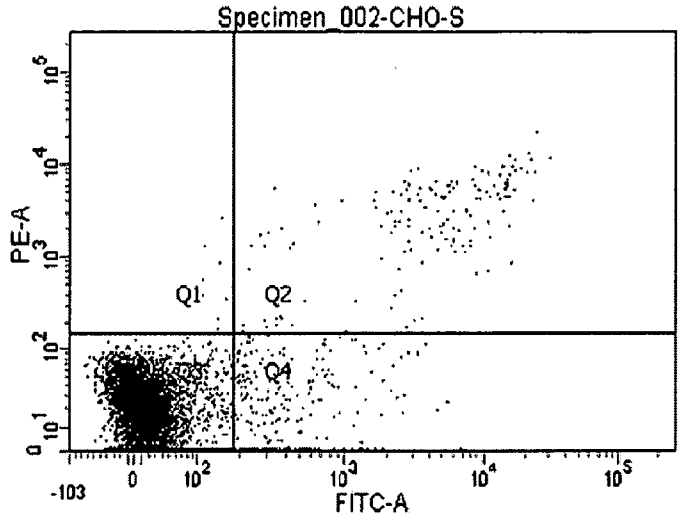
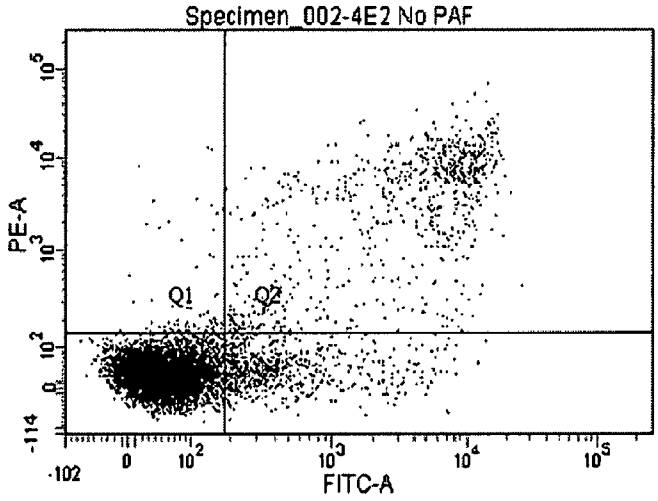


FIG. 3

A.



B.



Cell Line	Viable Cell (Q3)	Early Apoptotic Cell (Q4)	Late Apoptotic Cells (Q2)	Dead Cells (Q1)
CHO-S	96 %	2.4 %	1.5 %	0.1 %
4E2	85 %	6.7 %	7.4 %	0.7 %

FIG. 4

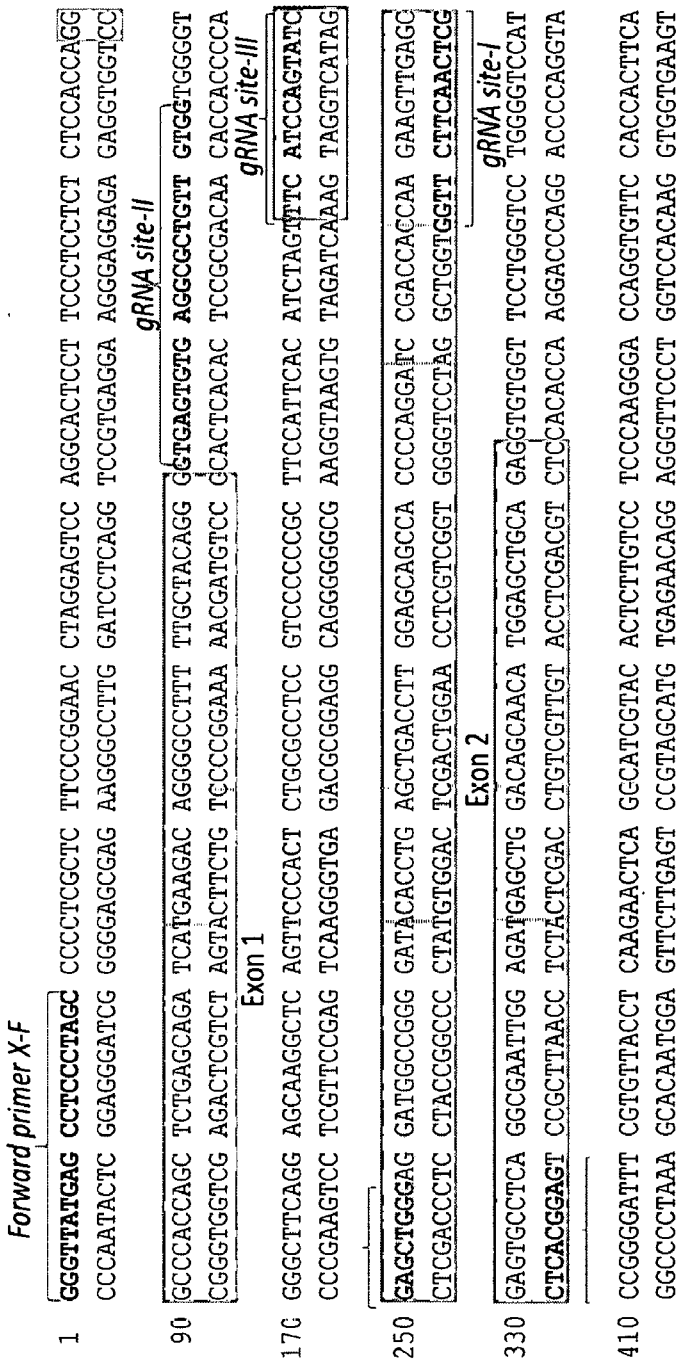

Forward primer X-F
gRNA site-II
gRNA site-III
Exon 1
Exon 2
gRNA site-I
Reverse primer X-R

FIG. 5

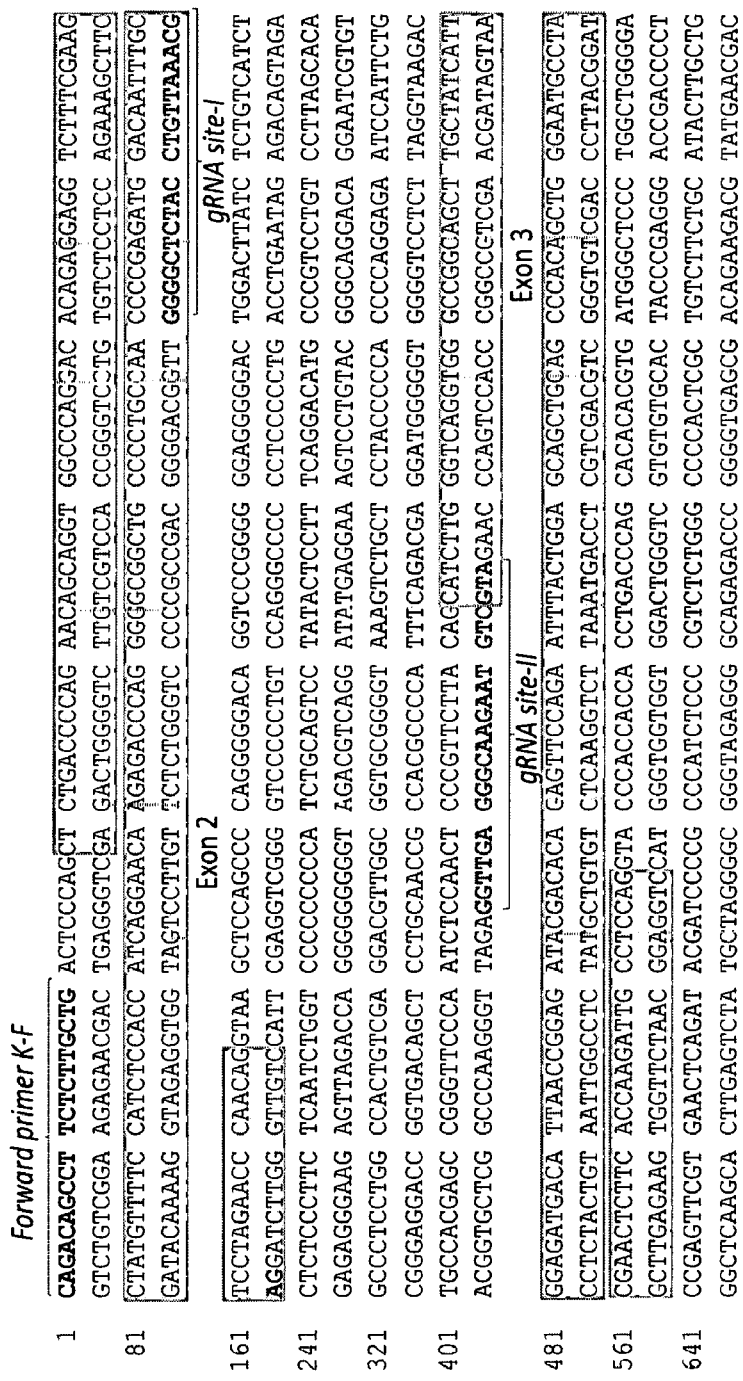
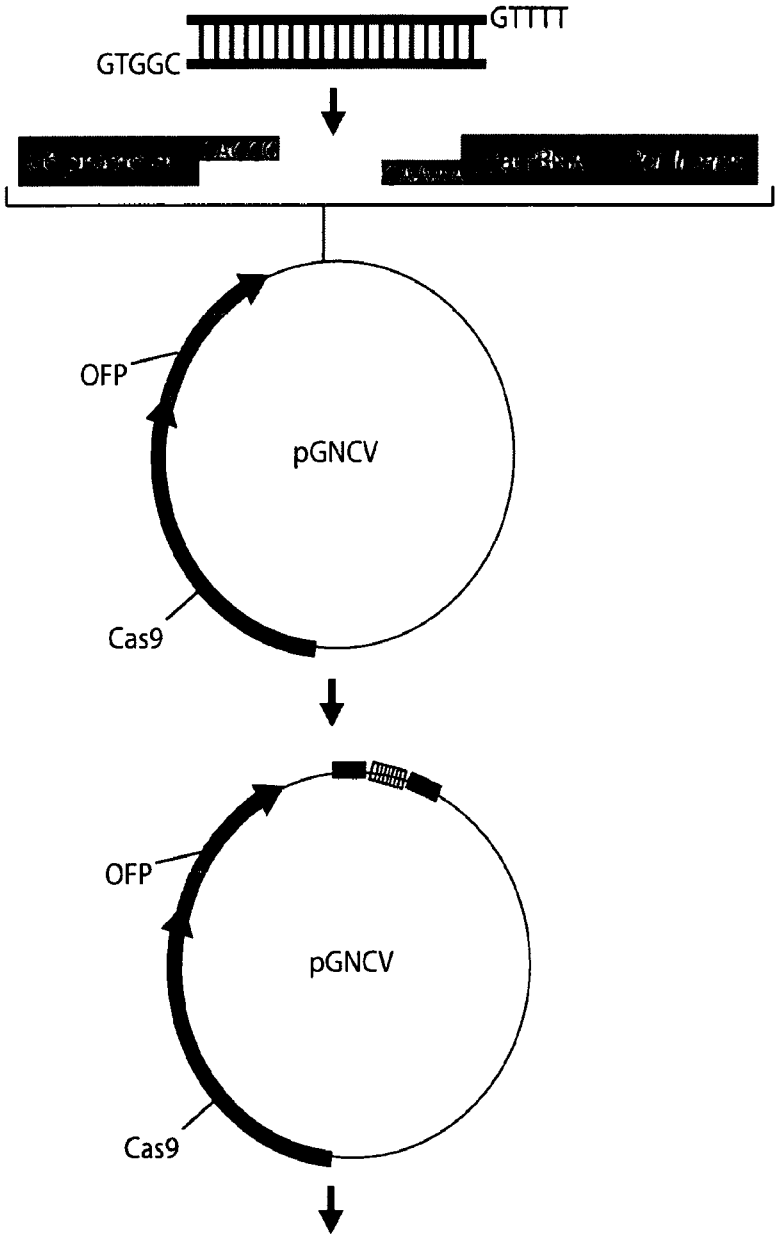

Forward primer K-F
Exon 2
gRNA site-I
gRNA site-II
Exon 3
Reverse primer K-R

FIG. 6



transfection, single cell deposition, screening by DNA sequencing

FIG. 7

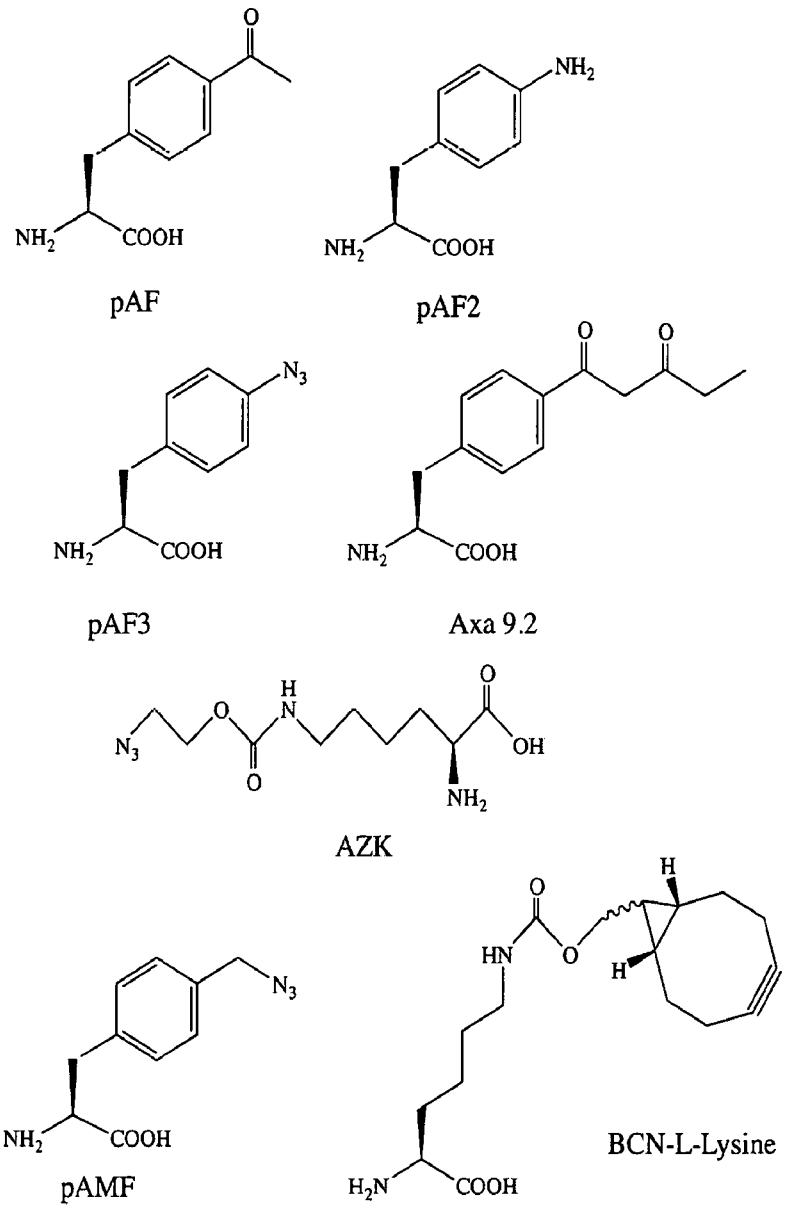


FIG. 8

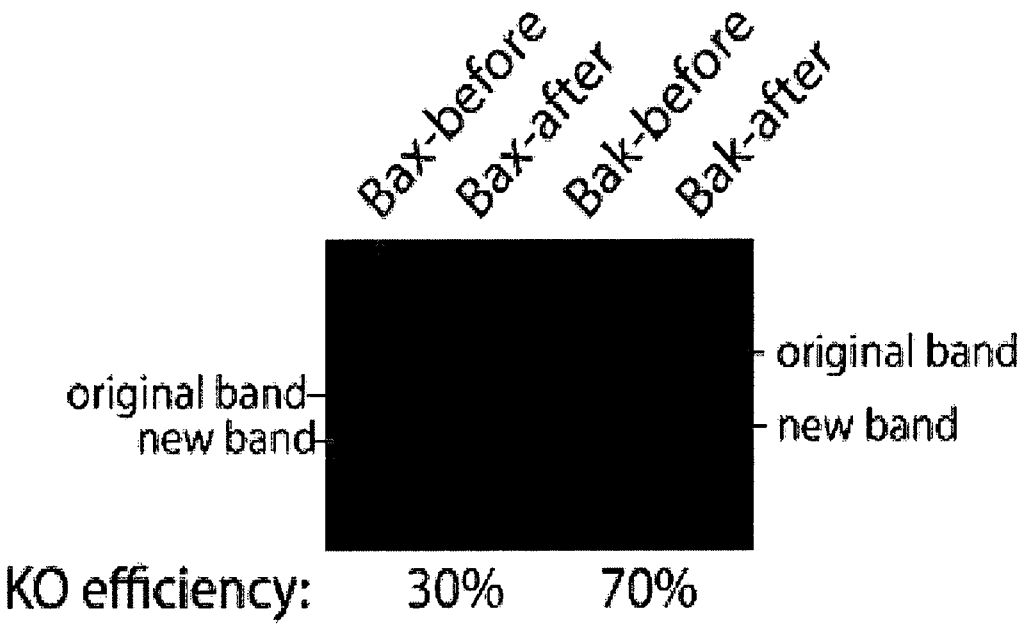

Bax-before
Bax-after
Bak-before
Bak-after
original band
new band
original band
new band
KO efficiency:
30%
70%

FIG. 9

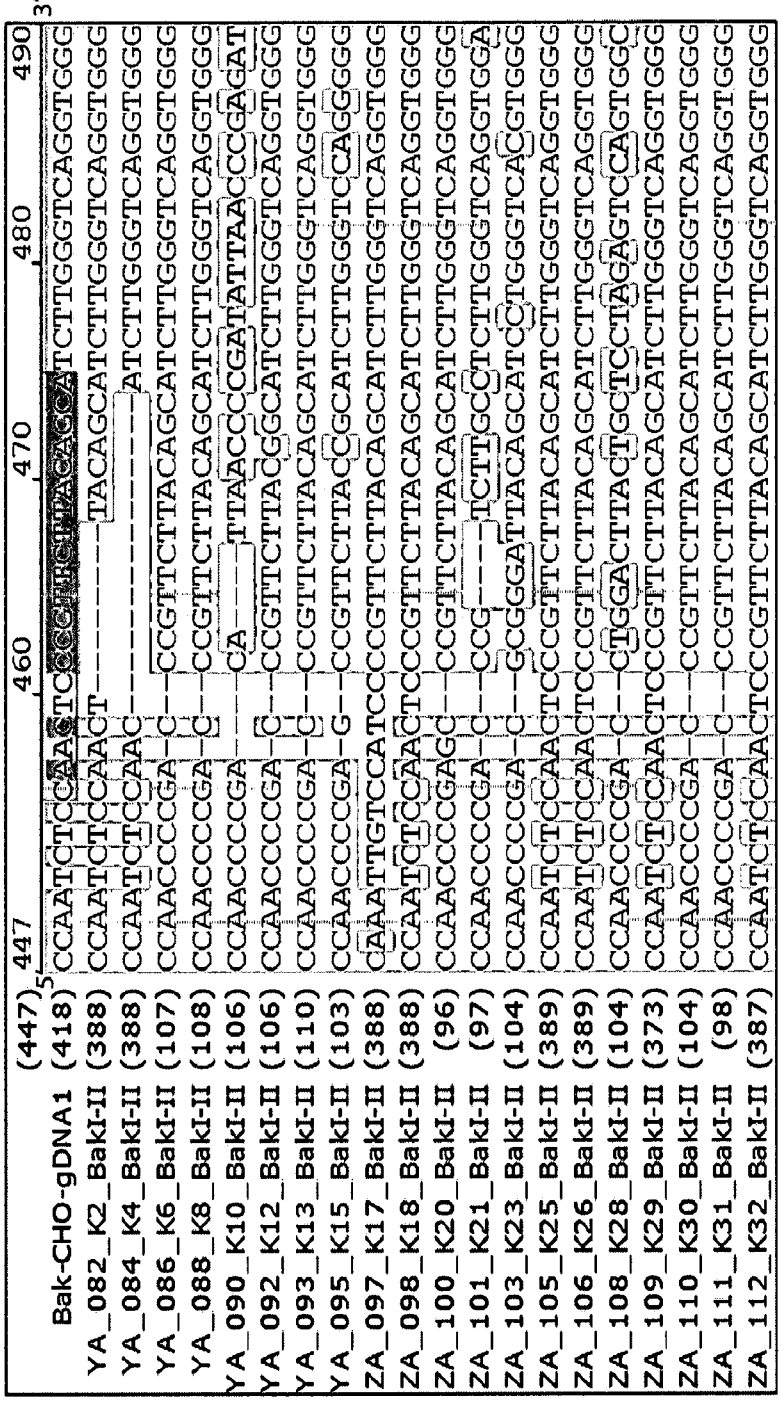

5'
3'
(447)
447
460
470
480
490
Bak-CHO-gDNA1 (418)
YA_082_K2_Bak-II (388)
YA_084_K4_Bak-II (388)
YA_086_K6_Bak-II (107)
YA_088_K8_Bak-II (108)
YA_090_K10_Bak-II (106)
YA_092_K12_Bak-II (106)
YA_093_K13_Bak-II (110)
YA_095_K15_Bak-II (103)
ZA_097_K17_Bak-II (388)
ZA_098_K18_Bak-II (388)
ZA_100_K20_Bak-II (96)
ZA_101_K21_Bak-II (97)
ZA_103_K23_Bak-II (104)
ZA_105_K25_Bak-II (389)
ZA_106_K26_Bak-II (389)
ZA_108_K28_Bak-II (104)
ZA_109_K29_Bak-II (373)
ZA_110_K30_Bak-II (104)
ZA_111_K31_Bak-II (98)
ZA_112_K32_Bak-II (387)

FIG. 10

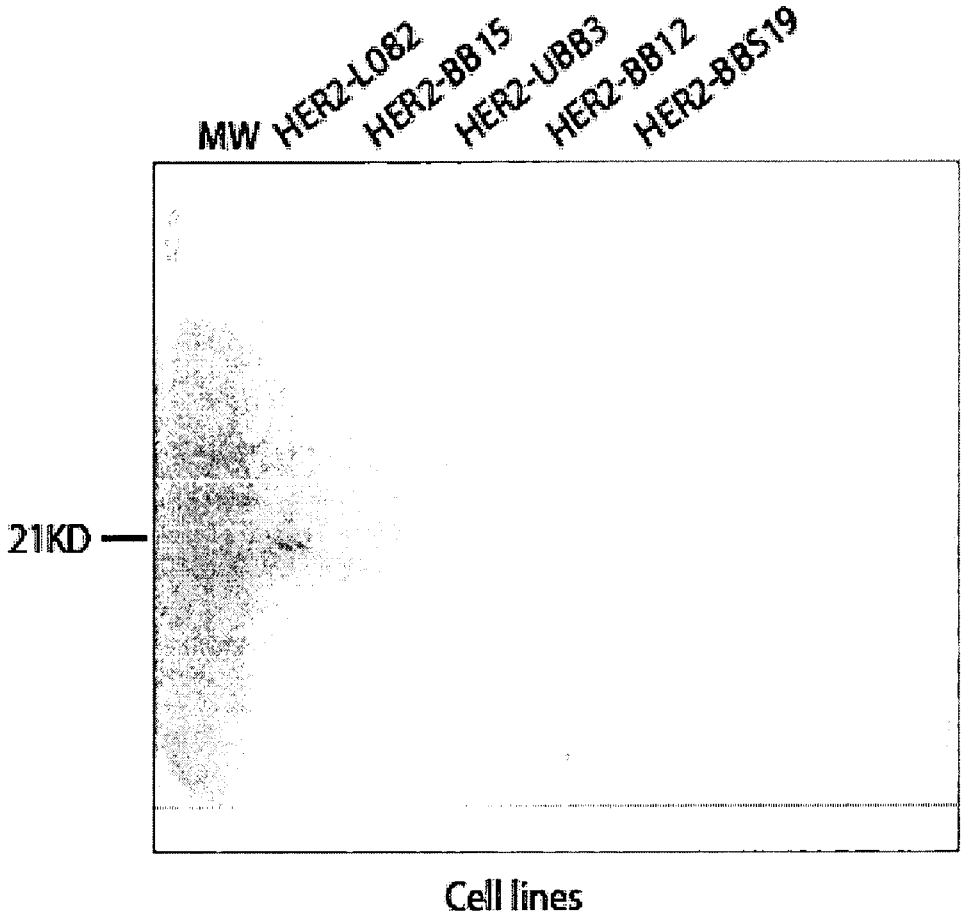
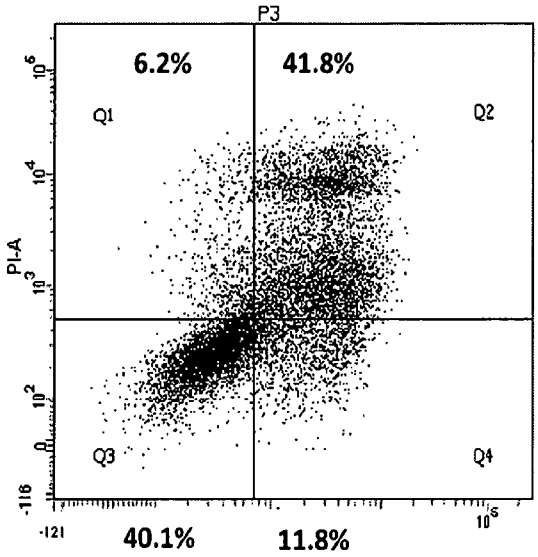
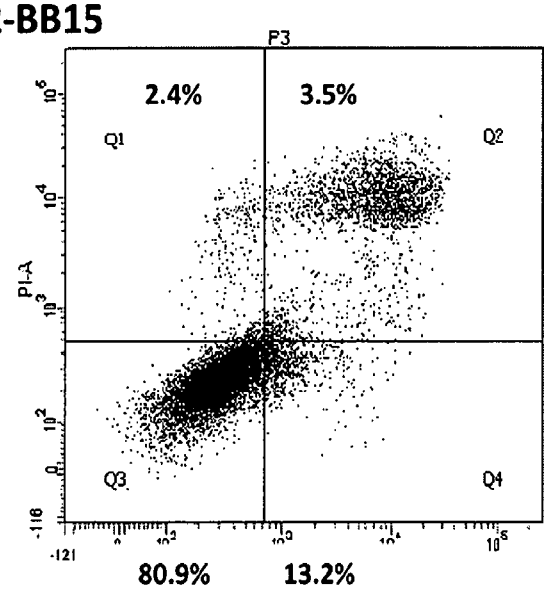

MW
HER2-L082
HER2-BB15
HER2-UBB3
HER2-BB12
HER2-BBS19
21KD
Cell lines

FIG. 11

A. HER2-L082



B. HER2-BB15



Cell Line	Viable Cell (Q3)	Early Apoptotic Cell (Q4)	Late Apoptotic Cell (Q2)	Dead Cell (Q1)
HER2-L082	40.1%	11.8%	41.8%	6.2%
HER2-BB15	80.9%	13.2%	3.5%	2.4%

FIG. 12

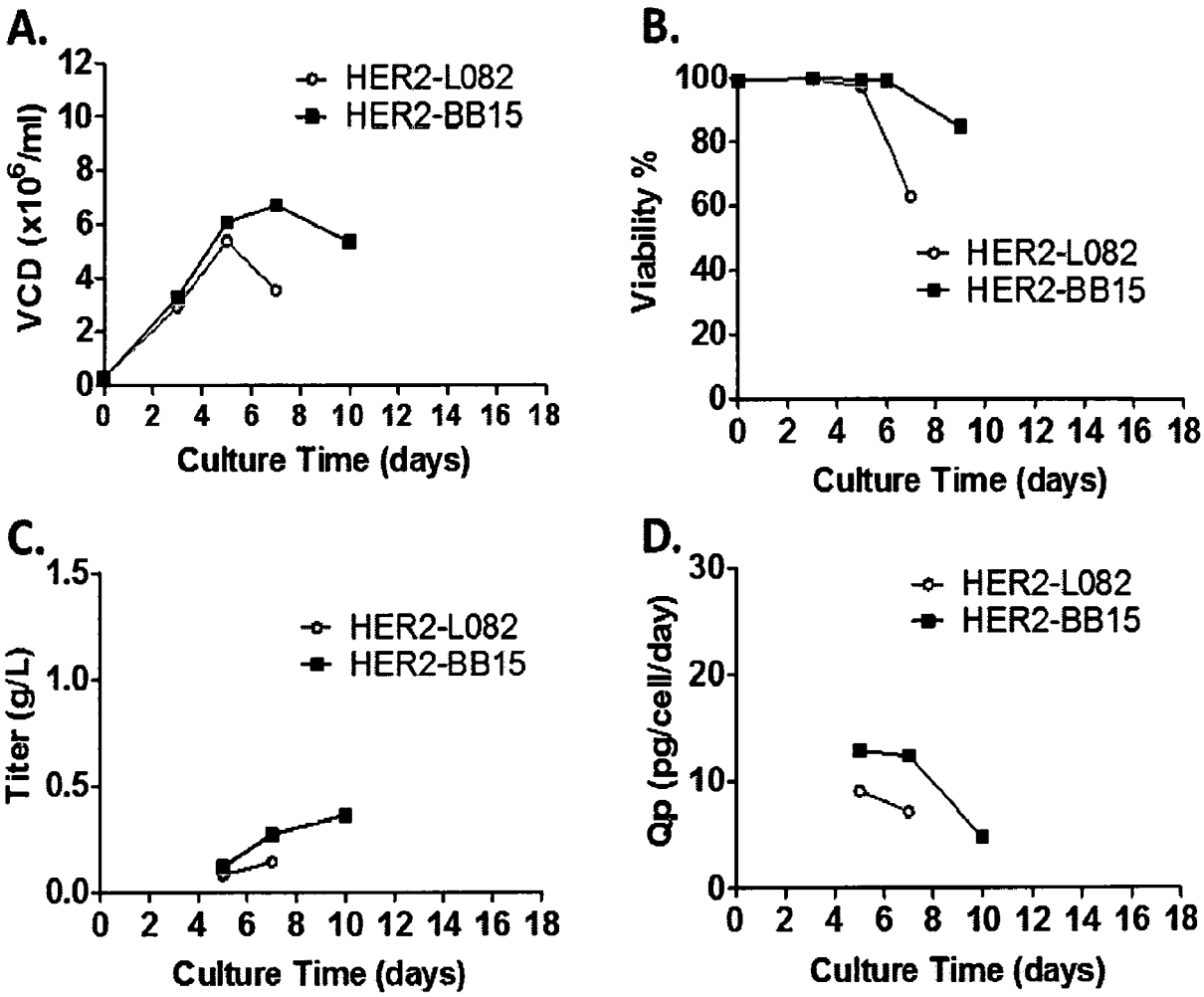

A.
VCD (x10^6/ml)
HER2-L082
HER2-BB15
Culture Time (days)
B.
Viability %
HER2-L082
HER2-BB15
Culture Time (days)
C.
Titer (g/L)
HER2-L082
HER2-BB15
Culture Time (days)
D.
Qp (pg/cell/day)
HER2-L082
HER2-BB15
Culture Time (days)

FIG. 13

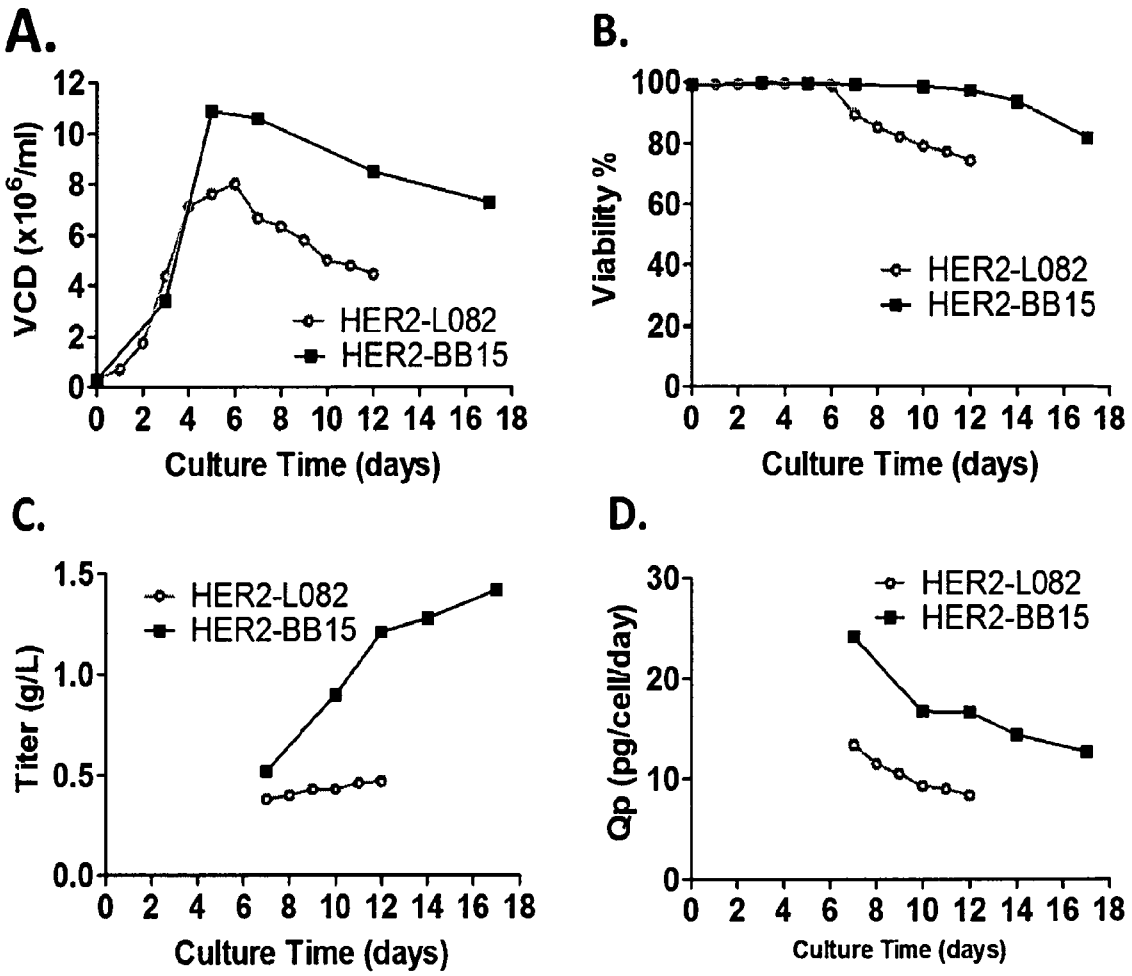

A.
VCD (x10^6/ml)
Culture Time (days)
HER2-L082
HER2-BB15
B.
Viability %
Culture Time (days)
HER2-L082
HER2-BB15
C.
Titer (g/L)
Culture Time (days)
HER2-L082
HER2-BB15
D.
Qp (pg/cell/day)
Culture Time (days)
HER2-L082
HER2-BB15

FIG. 14

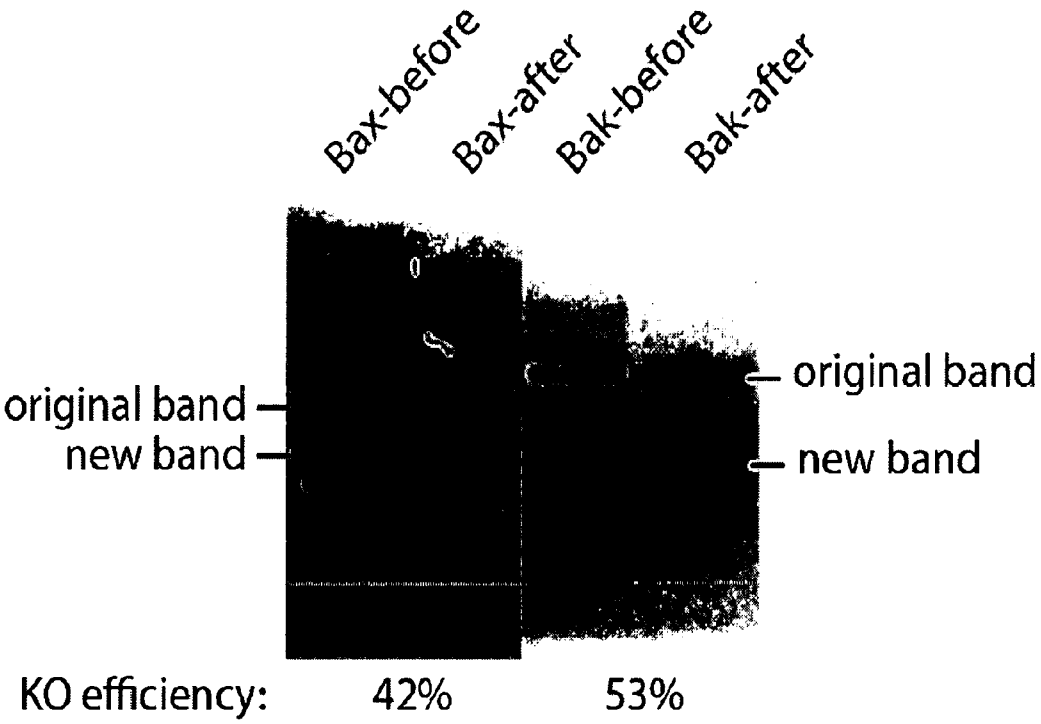

Bax-before
Bax-after
Bak-before
Bak-after
original band
new band
original band
new band
KO efficiency:
42%
53%

FIG. 15

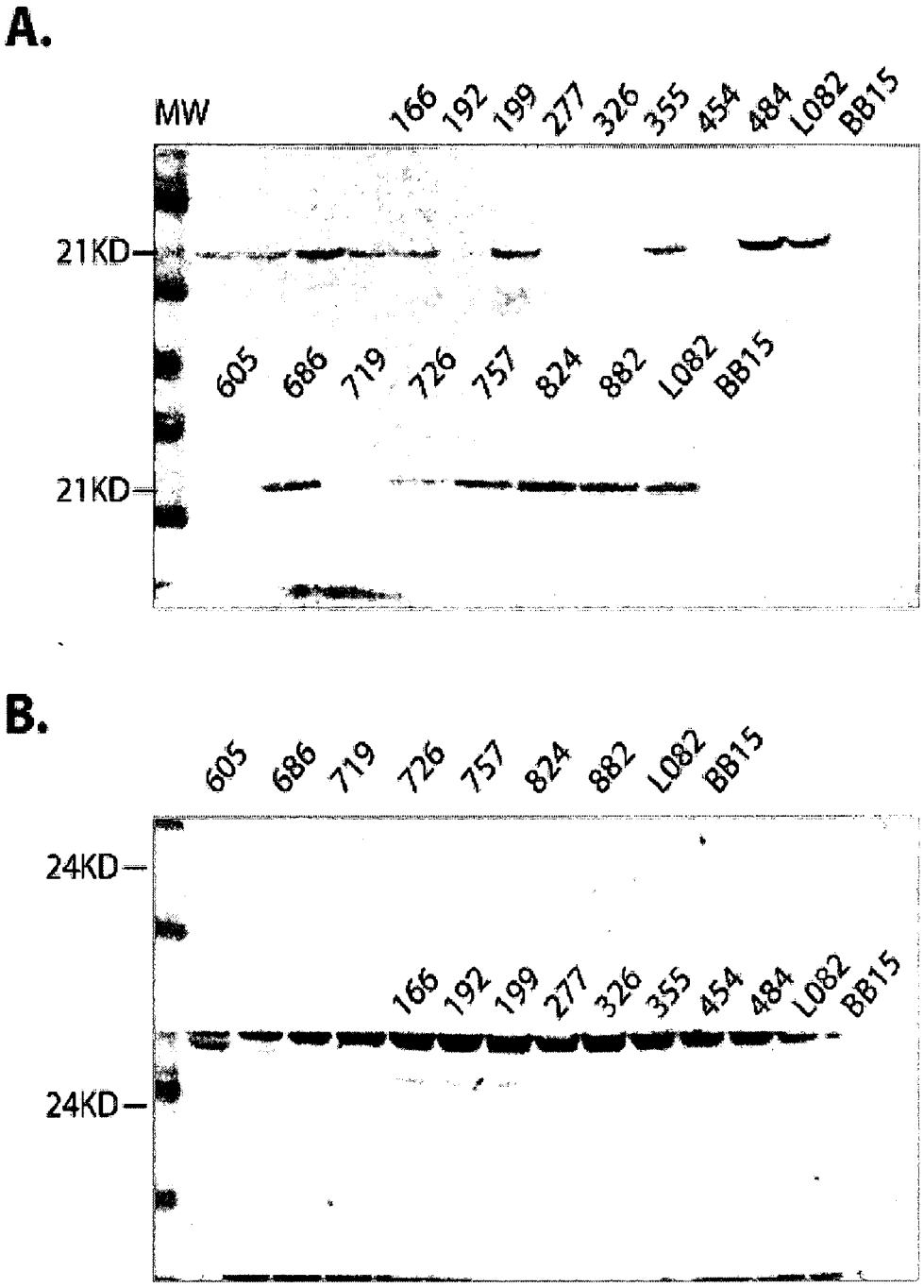
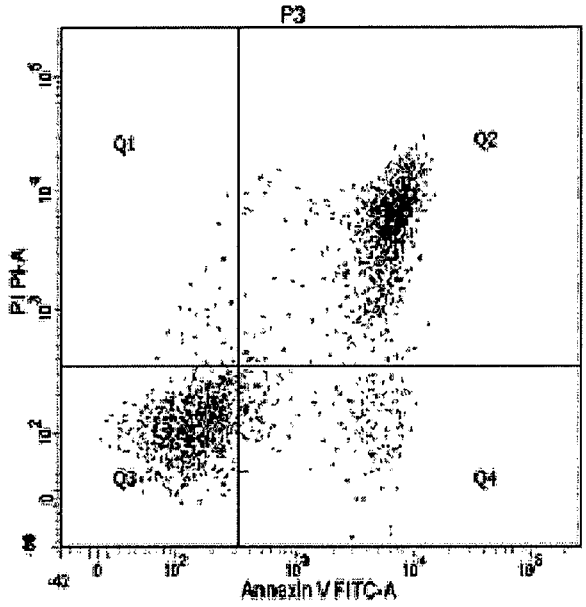
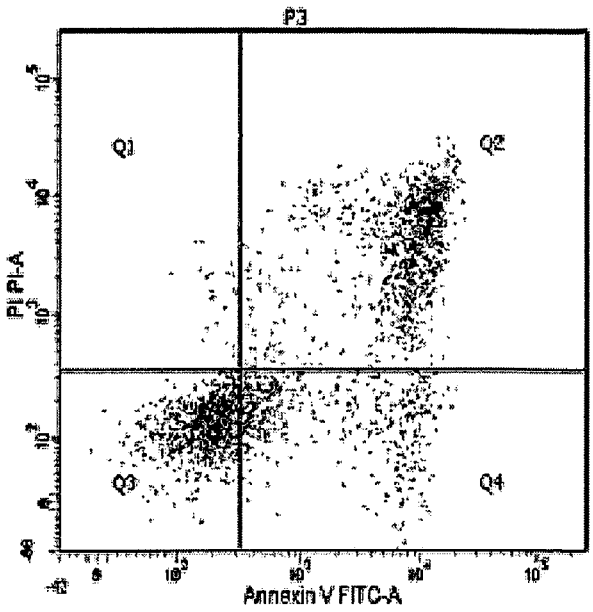

A.
MW
166
192
199
277
326
355
454
484
L082
BB15
21KD
605
686
719
726
757
824
882
L082
BB15
21KD
B.
605
686
719
726
757
824
882
L082
BB15
24KD
166
192
199
277
326
355
454
484
L082
BB15
24KD

FIG. 16

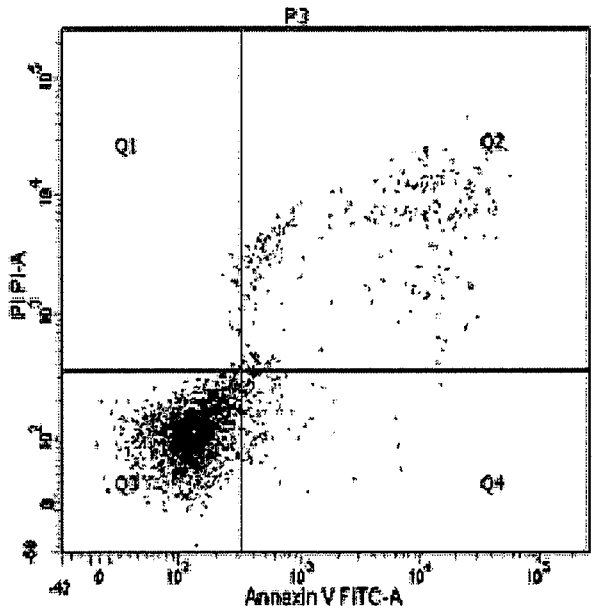
A. PSMA-484



B. PSMA-882



C. PSMA-192



D. PSMA-719

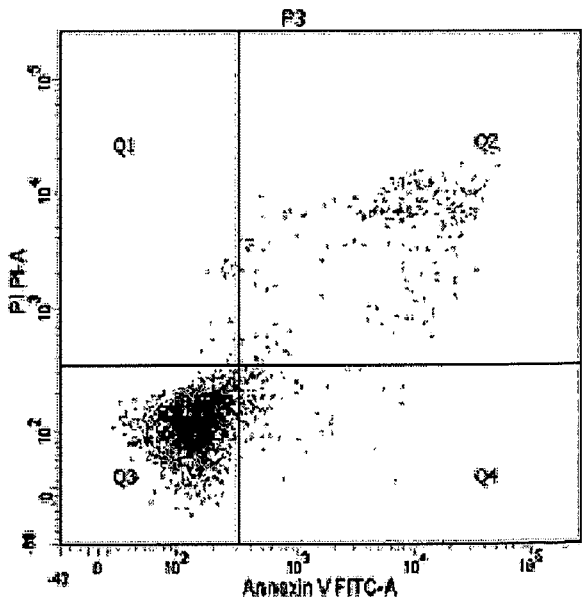


FIG. 17

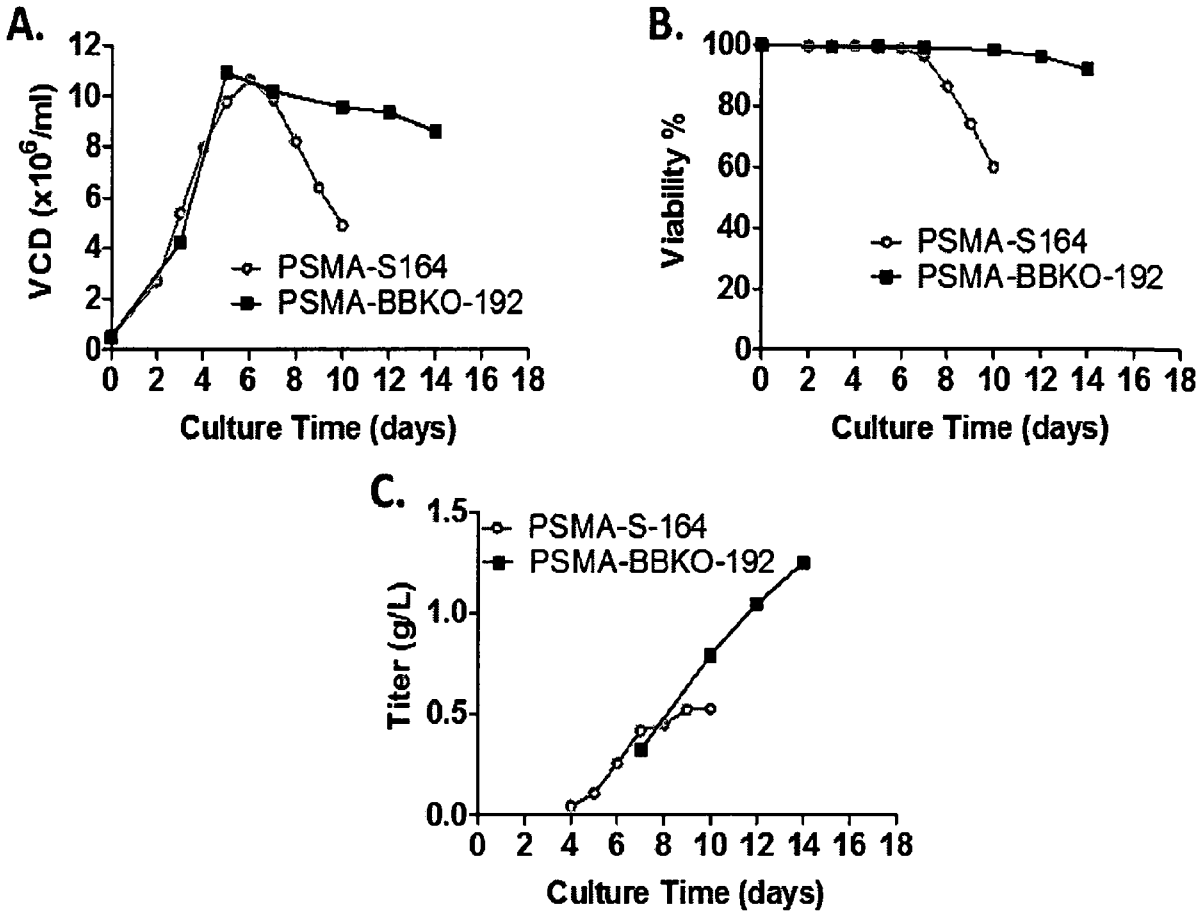

A.
VCD (x10^6/ml)
PSMA-S164
PSMA-BBKO-192
Culture Time (days)
B.
Viability %
PSMA-S164
PSMA-BBKO-192
Culture Time (days)
C.
Titer (g/L)
PSMA-S-164
PSMA-BBKO-192
Culture Time (days)

FIG. 18

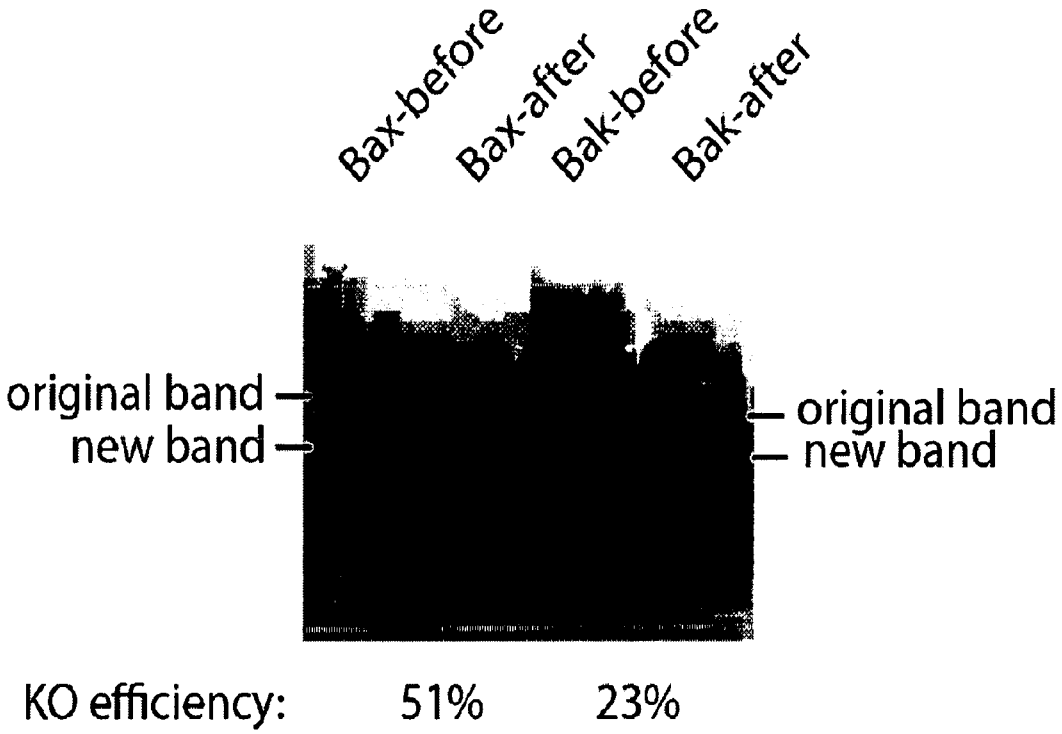

Bax-before
Bax-after
Bak-before
Bak-after
original band
new band
original band
new band
KO efficiency:
51%
23%

FIG. 19

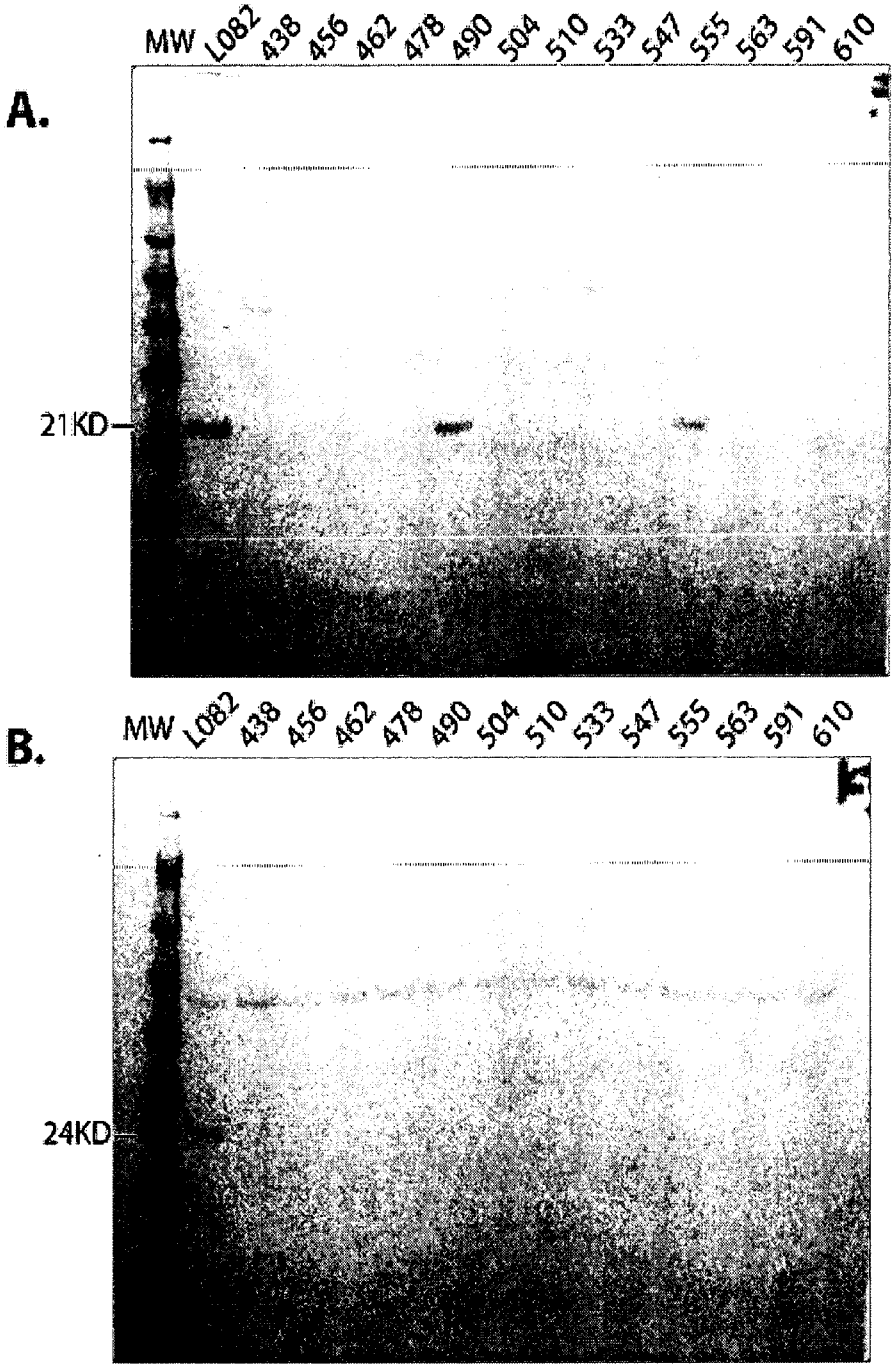
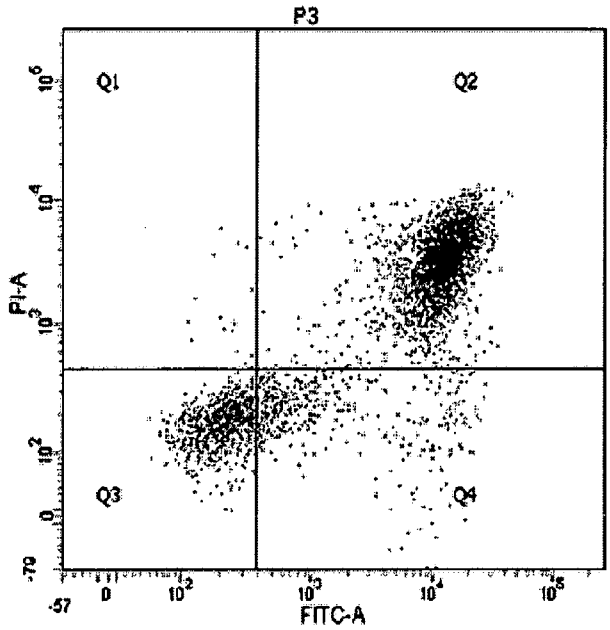
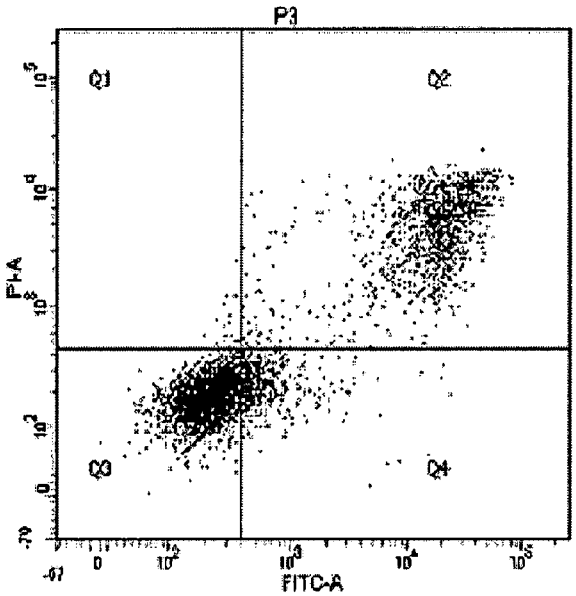

A.
MW
L082
438
456
462
478
490
504
510
533
547
555
563
591
610
21KD
B.
MW
L082
438
456
462
478
490
504
510
533
547
555
563
591
610
24KD

FIG. 20

A. CD70-MW-108



B. CD70-BBKO-563



Cell line	Viable cells (Q3)	Early Apoptotic Cells (Q4)	Late Apoptotic Cells (Q2)	Dead Cells (Q1)
CD70-MW-108	18.3 %	8.8 %	72.5 %	0.3 %
CD70-BBKO-563	60.3 %	11.4 %	27.9 %	0.5 %

FIG. 21

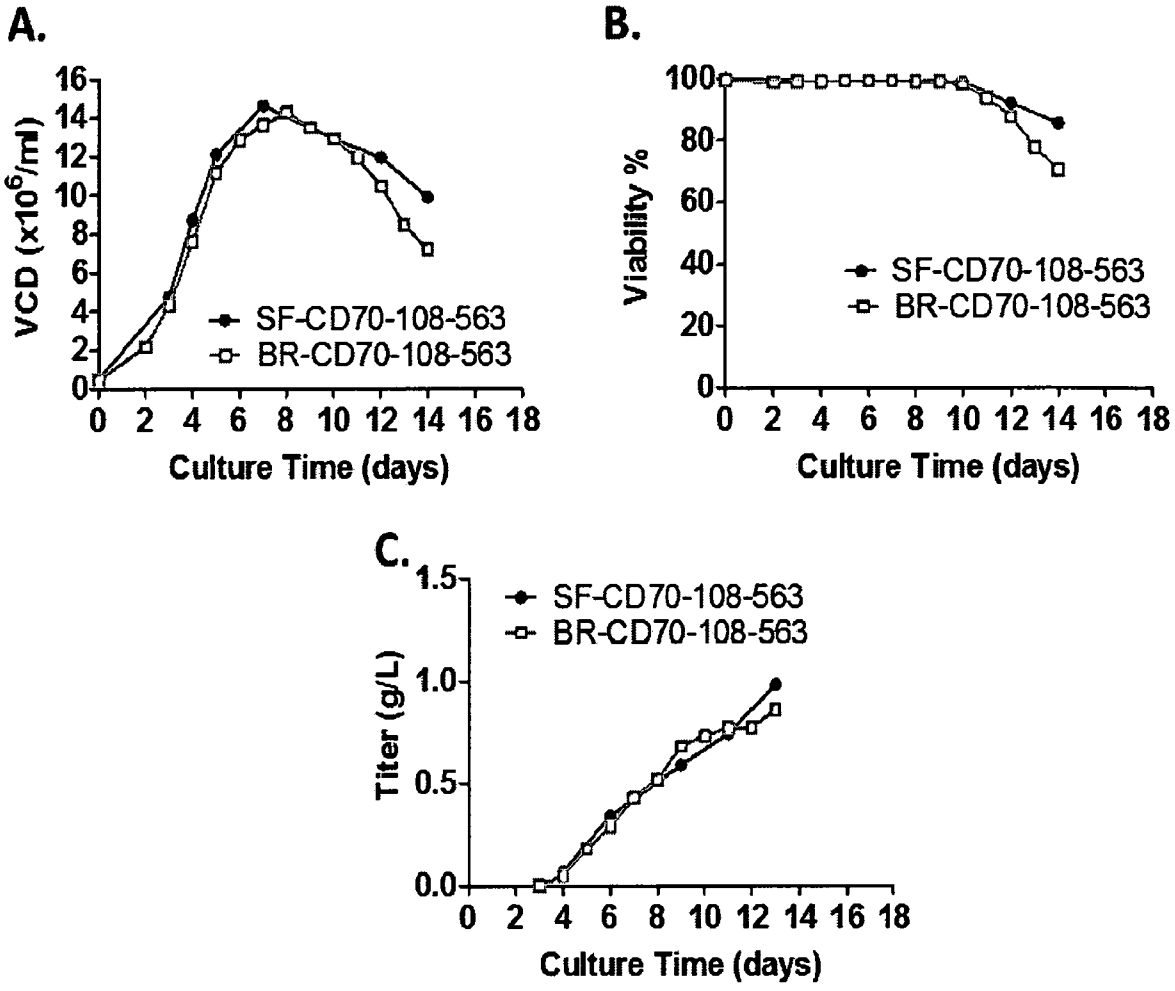

A.
VCD (x10^6/ml)
16
14
12
10
8
6
4
2
0
0 2 4 6 8 10 12 14 16 18
Culture Time (days)
SF-CD70-108-563
BR-CD70-108-563
B.
Viability %
100
80
60
40
20
0
0 2 4 6 8 10 12 14 16 18
Culture Time (days)
SF-CD70-108-563
BR-CD70-108-563
C.
Titer (g/L)
1.5
1.0
0.5
0.0
0 2 4 6 8 10 12 14 16 18
Culture Time (days)
SF-CD70-108-563
BR-CD70-108-563

FIG. 22