

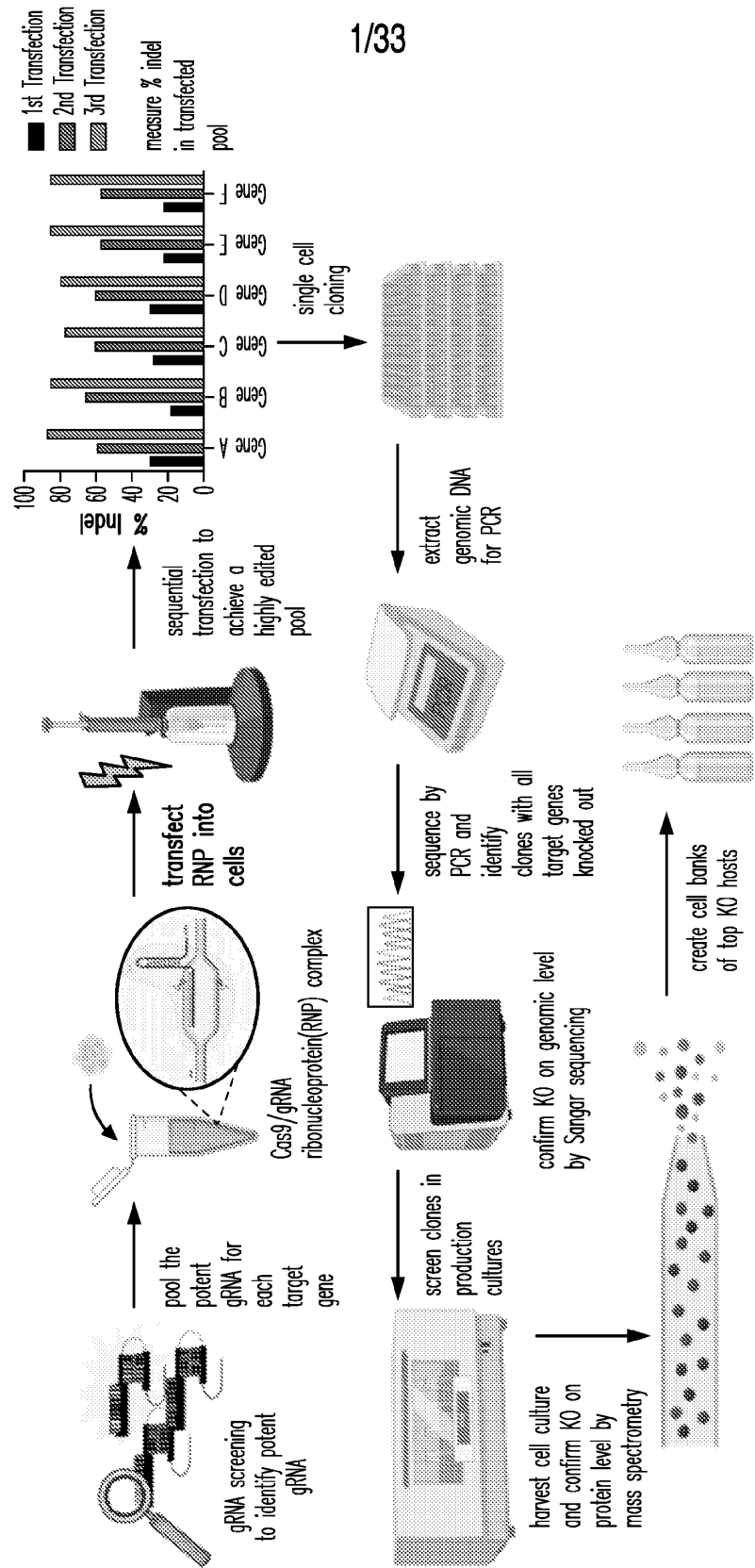
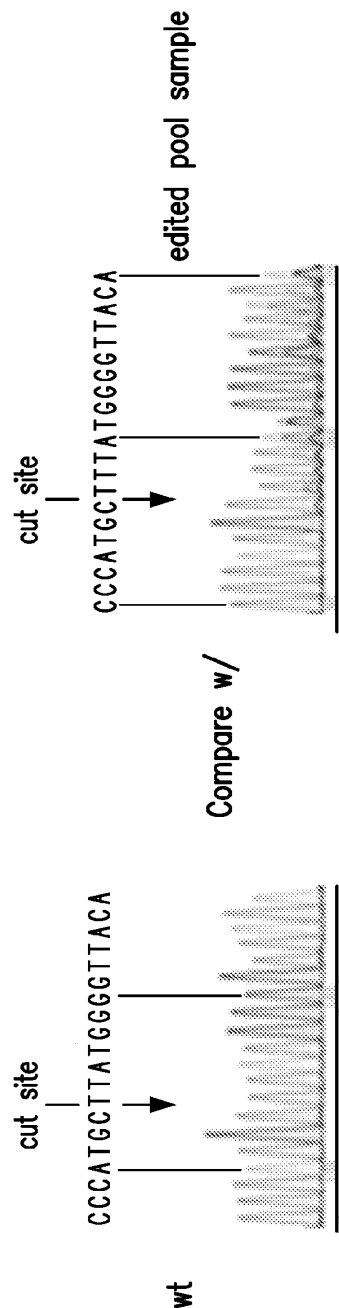


FIG. 1



Generate a matrix of possible modifications, for ex:

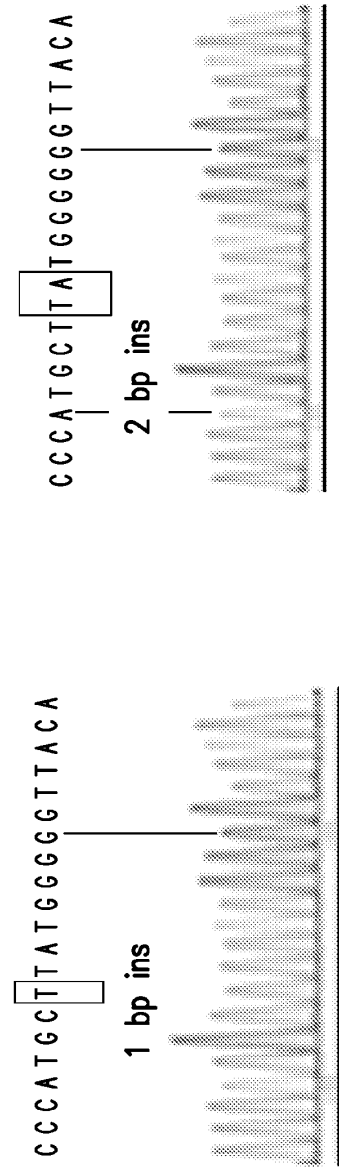


FIG. 2

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ICE (?) =Indel		r ² (?)		K0-Score (?)																																
73		0.98		68																																
INDEL	CONTRIBUTION ▼	SEQUENCE																																		
+1	50.3%	A	C	C	A	T	C	T	T	T	T	A	A	T	G	G	C	A	C	C	C	A	T	G	C	N	T	T	A	T	G	G	G	T	T	A
0	25.3%	A	C	C	A	T	C	T	T	T	T	A	A	T	G	G	C	A	C	C	C	A	T	G	C	T	T	A	T	G	G	G	T	T	A	
+2	6.8%	A	C	C	A	T	C	T	T	T	T	A	A	T	G	G	C	A	C	C	C	A	T	G	C	N	N	T	T	A	T	G	G	G	T	T
-1	5.3%	A	C	C	A	T	C	T	T	T	T	A	A	T	G	G	C	A	C	C	C	A	T	G	C	-	T	A	T	G	G	G	T	T	A	
-2	2.1%	A	C	C	A	T	C	T	T	T	T	A	A	T	G	G	C	A	C	C	C	A	T	G	C	-	-	A	T	G	G	G	T	T	A	
-6	2%	A	C	C	A	T	C	T	T	T	T	A	A	T	G	G	C	A	C	C	C	A	T	G	C	-	-	-	-	-	-	-	-	-	-	
-6	1.4%	A	C	C	A	T	C	T	T	T	T	A	A	T	G	G	C	A	C	C	C	A	-	-	-	-	-	-	-	-	-	-	-	-	-	

In a bidallelic cell, for example:

Indel (%)	KO (%)	Genotype
99	99	Homozygote frameshift -->KO
50	50	Heterozygote (WT/frameshift)
99	50	Heterozygote (frameshift/back-in-frame indel)
0	0	WT

FIG. 2 continued

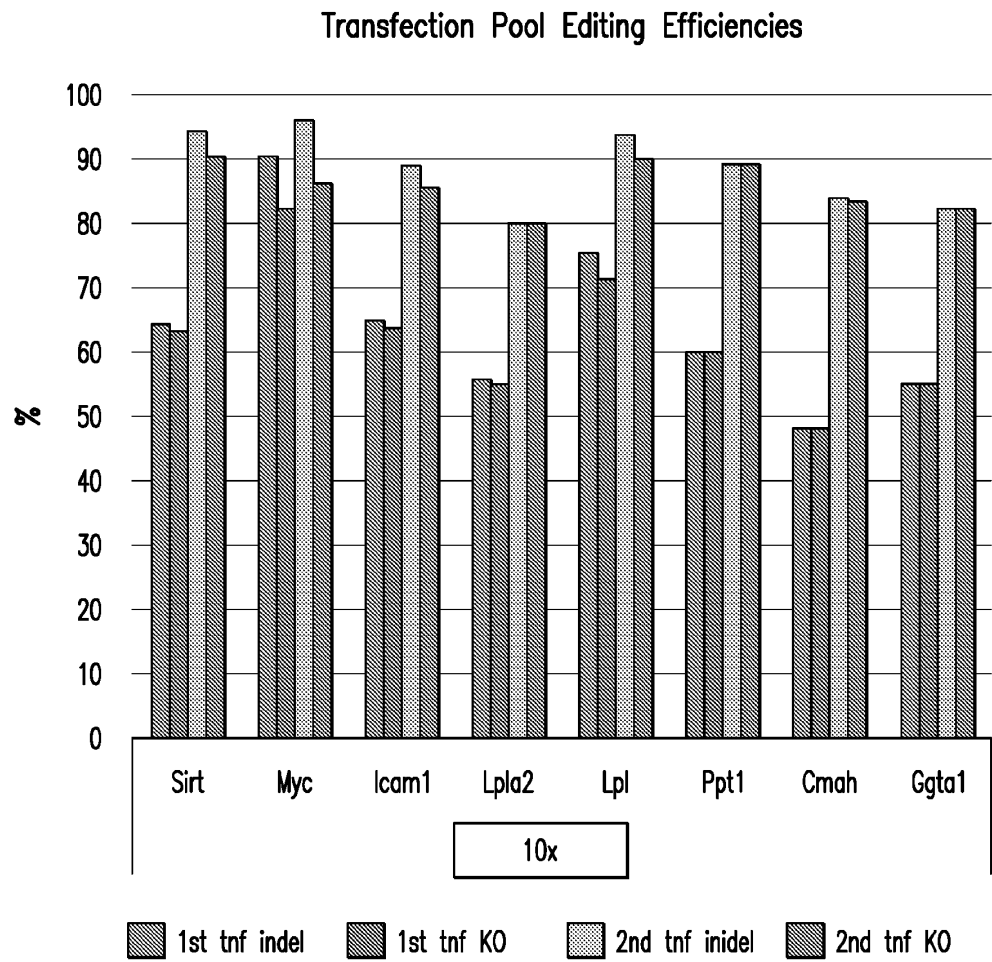


FIG. 3

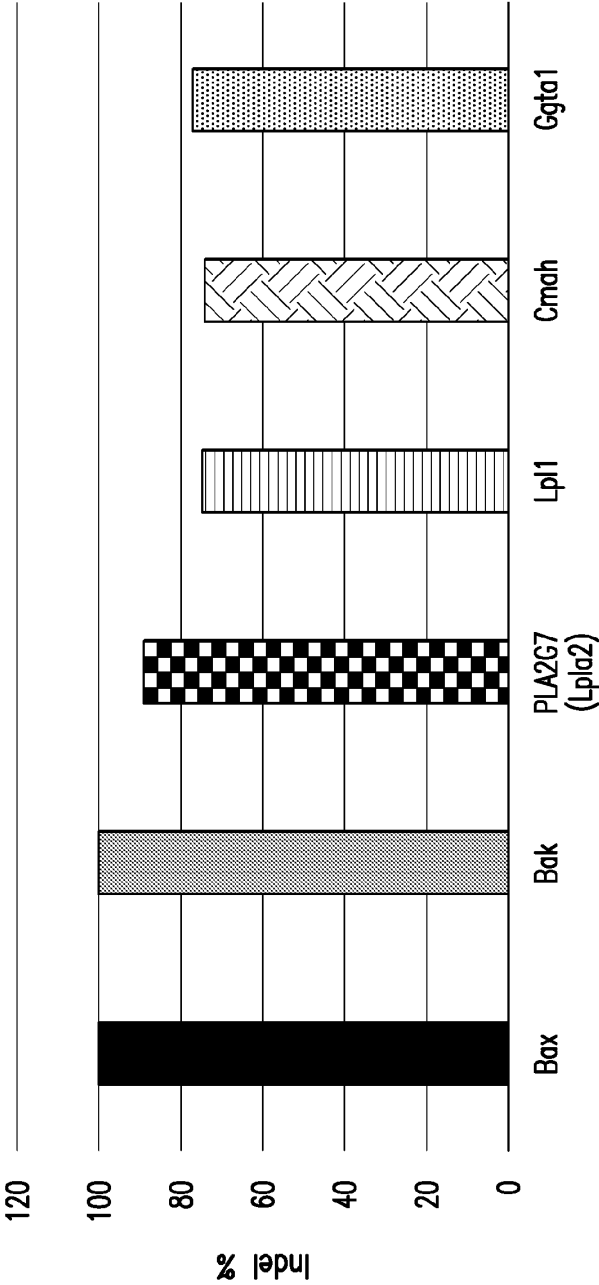


FIG. 4

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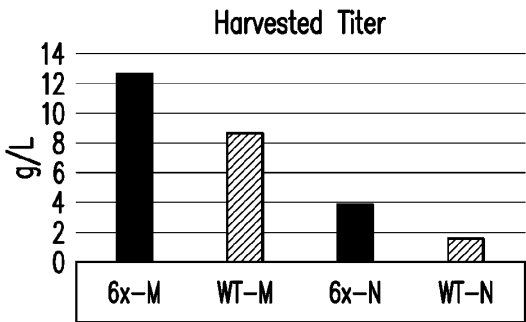


FIG. 5A

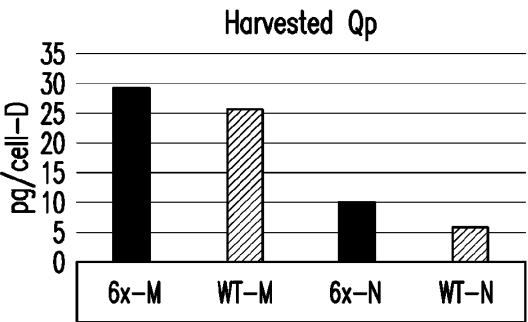


FIG. 5B

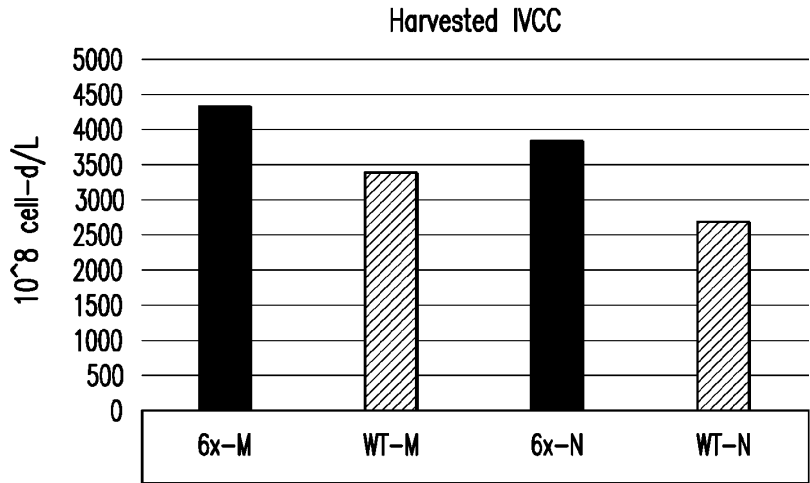


FIG. 5C

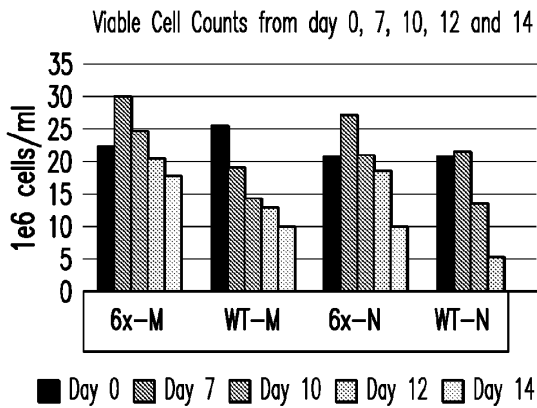


FIG. 5D

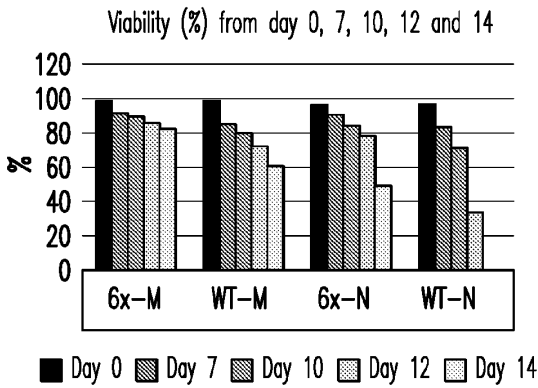


FIG. 5E

CHO bioreactor cultures	Size	Charge Distribution			Glycoform	NGNA (position)		
	Aggregate%	Acidic%	Main%	Basic%	Alpha-Gal (%)	2111*	2121	2122
6x mAb-M	3.1	61.6	19.6	18.8	1.4	N/A	N/A	N/A
WT mAb-M	2.1	60.3	22.9	16.8	4.3	N/A	N/A	N/A
6x mAb-N	43.2	N/A	N/A	N/A	1.1	+	-	-
WT mAb-N	32.7	N/A	N/A	N/A	4.4	+	+	+

*NGNA 2111 has the same mass as 2021 (NANA)

NGNA glycan isoforms key: the figure below represents an example of 2121 glycan isoform. The first number represents GlcNAc modification, the second number Fucose modification, the third number Hex sugar (in this case Galactose), and the fourth number represents Sialic Acid on the core N-glycan moiety (2 GlcNAc-3 Mannose) shown in the red box.

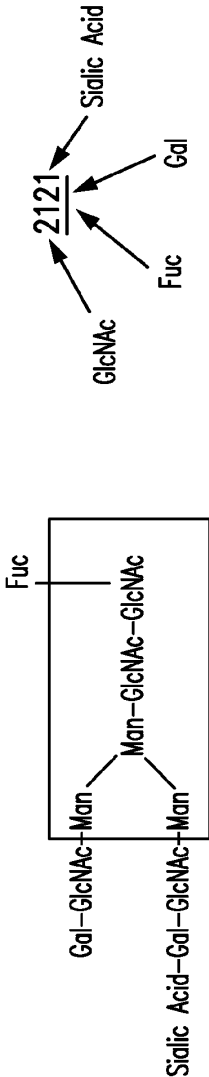


FIG. 5F

KO indel for hosts (assessed by genomic DNA screening except
Bax and Bak1)

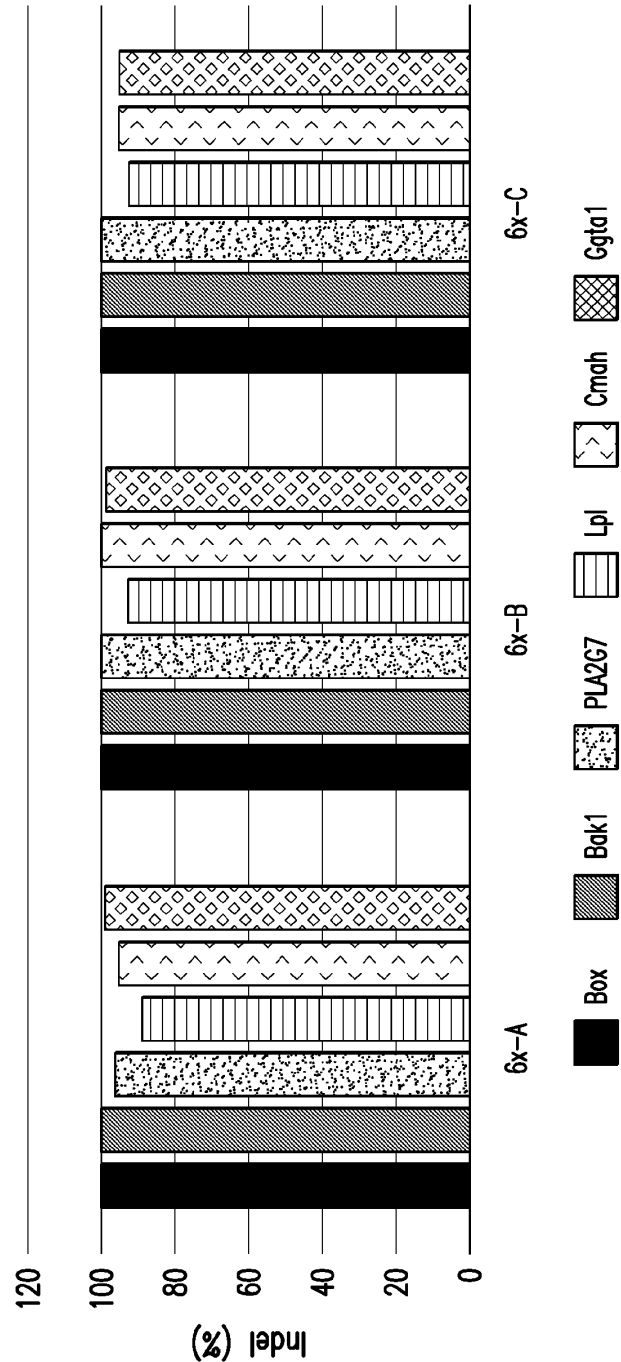


FIG. 6

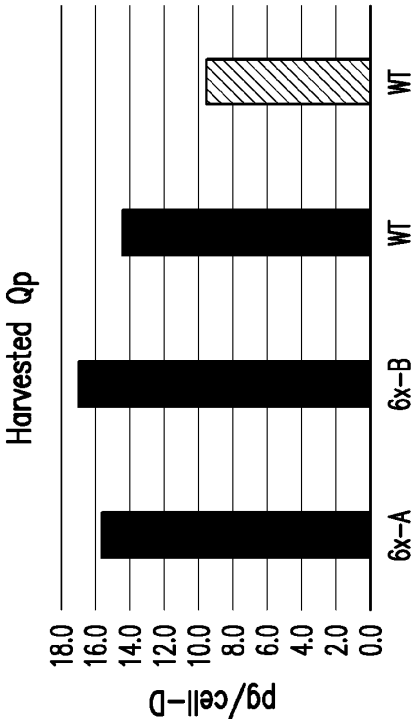


FIG. 7B

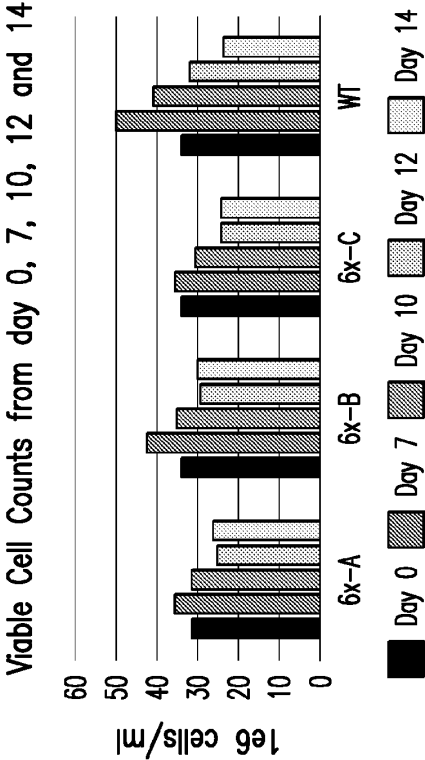


FIG. 7D

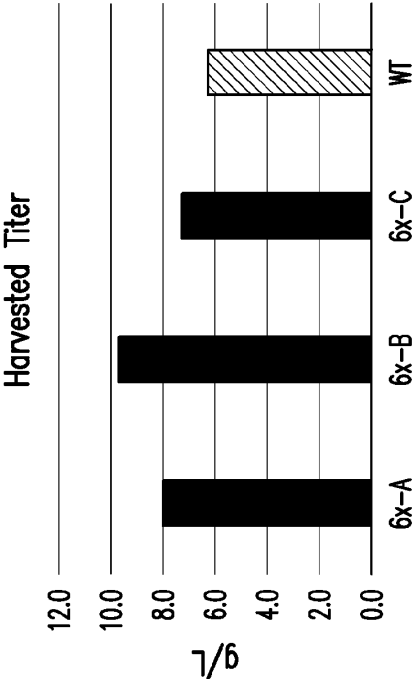


FIG. 7A

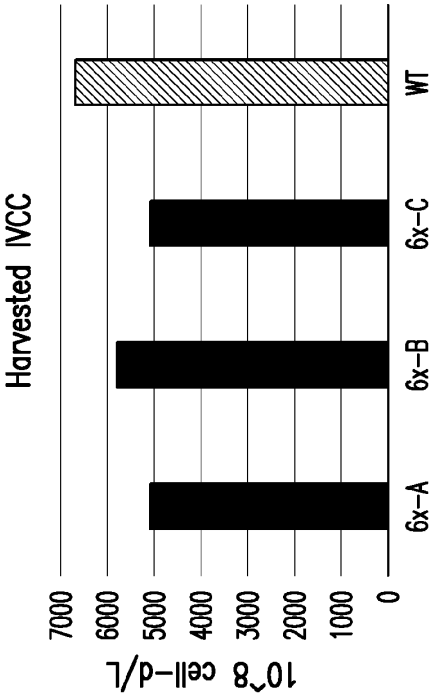


FIG. 7C

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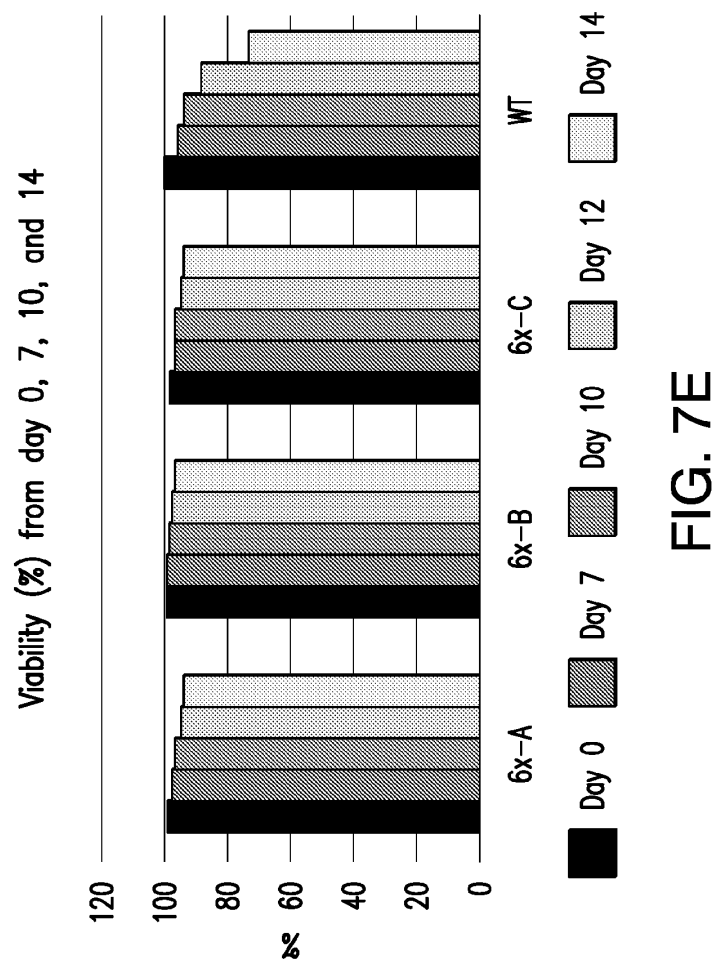


FIG. 7E

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CHO cultures expressing mAb-M	Size	Charge Distribution		
	Aggregate%	Acidic%	Main%	Basic%
6x-A	1.9	67.6	31.3	1.1
6x-B	1.9	68.4	30.3	1.3
6x-C	2.2	67.2	30.6	2.2
WT	2.1	67.5	31.2	1.3

FIG. 7F

CHO bioreactor cultures	Harvest Titer (g/L)	Harvest Qp pg/cell-d	Harvest Viability %	Harvest VCC 10 ⁶ cell/mL	Harvest IVCC 10 ⁸ cell/d/L	alpha-Gal %	NGNA %
mAb-N							
6x-A	4.6	19.1	94	32.3	2410	0.5	<0.1
6x-B	4.6	15.5	96	36.4	2970	0.4	<0.1
6x-C	4.7	17.6	91	33.4	2671	0.4	<0.1
WT	3.7	10.9	96	46.6	3403	5.8	2.0

FIG. 8

Indel % for 9x and 10x KO hosts
(assessed by genomic DNA screening except Bax and Bak1)

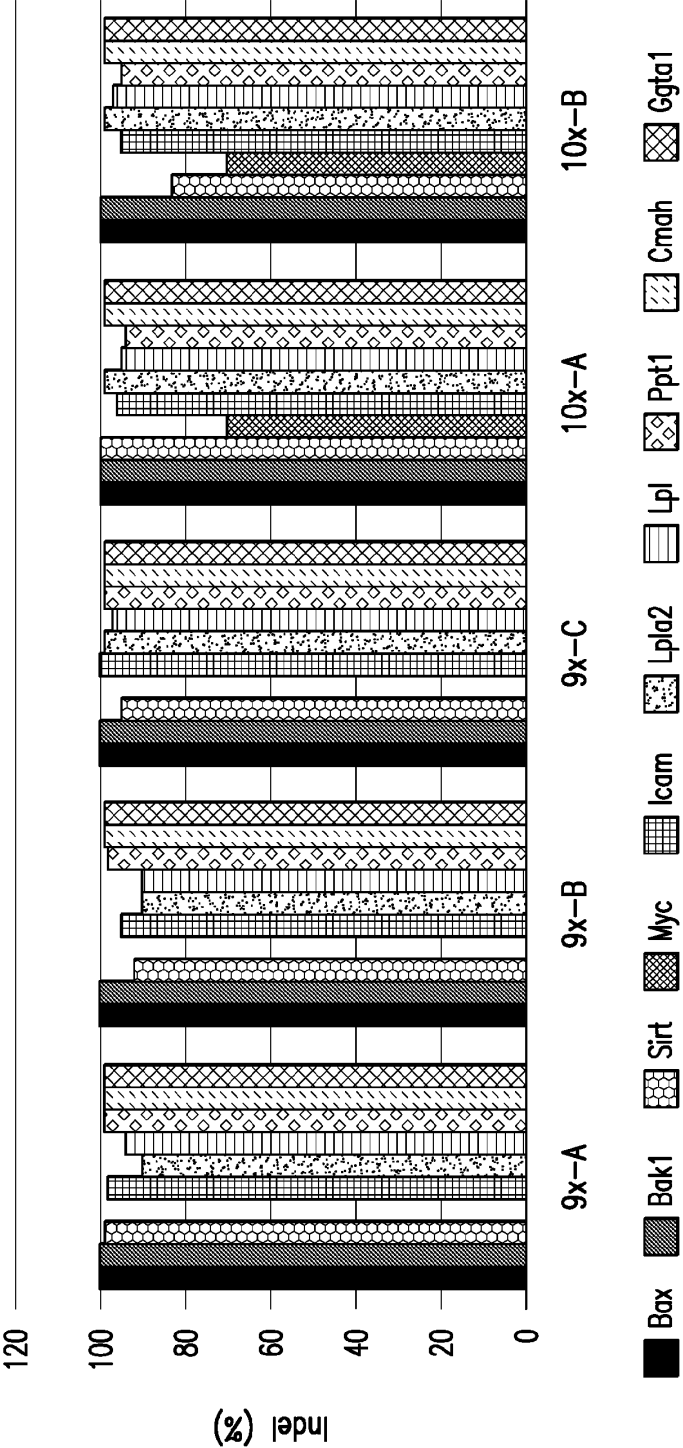


FIG. 9

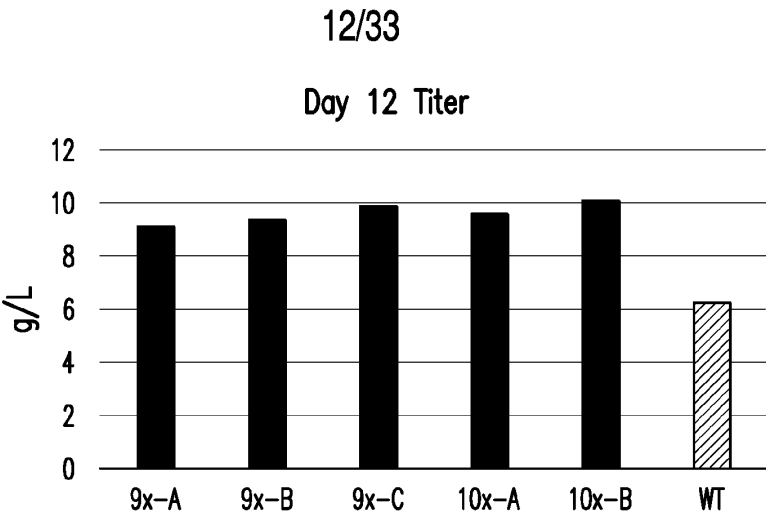


FIG. 10A

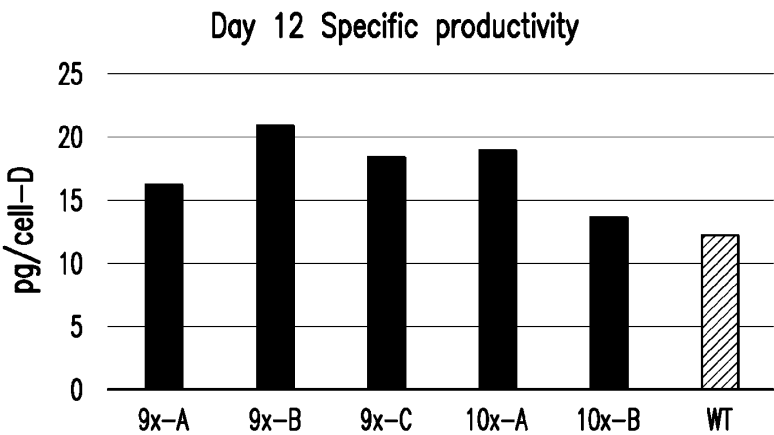


FIG. 10B

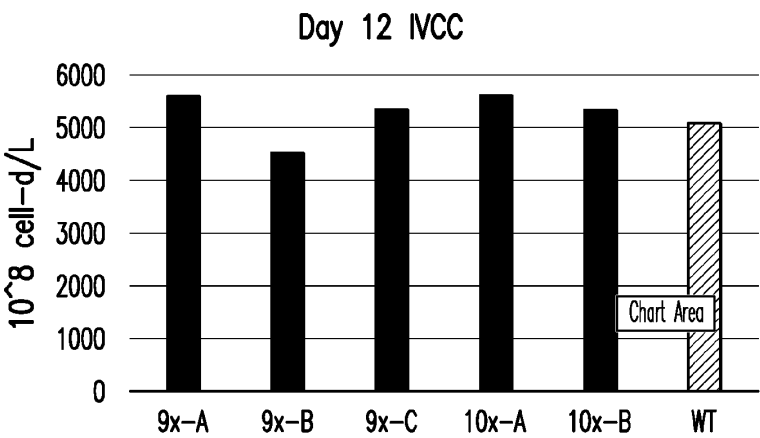


FIG. 10C

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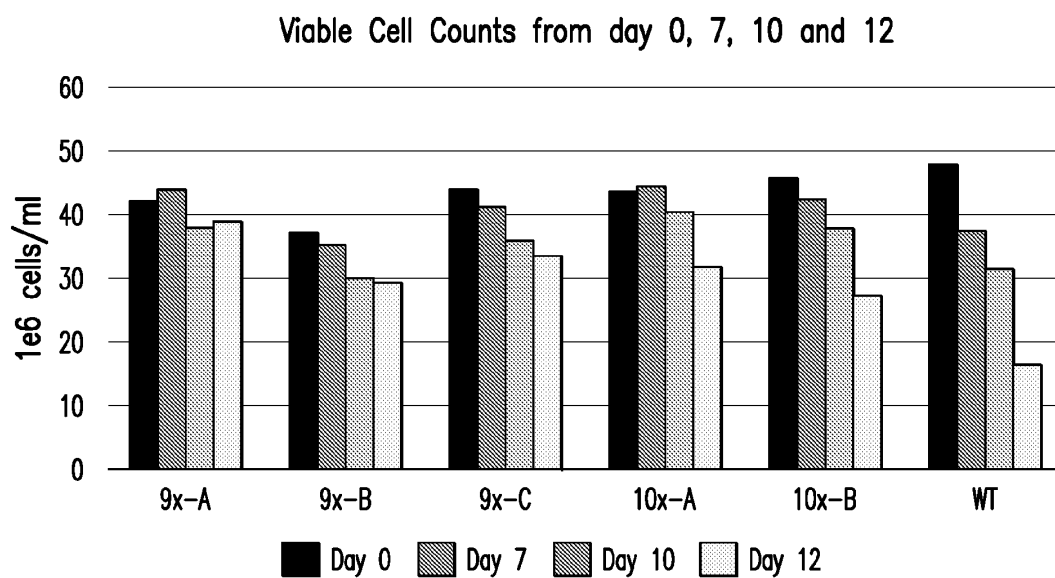


FIG. 10D

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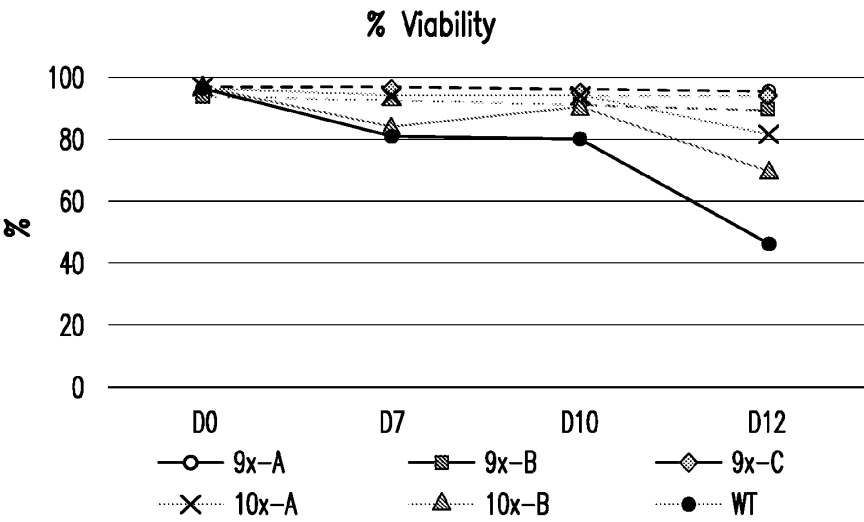


FIG. 10E

CHO cultures expressing mAb-H	% Aggregate	Charge Distributions		
		% Acidic	% Main	% Basic
9x-A	3.8	40.0	56.5	3.8
9x-B	4.5	42.0	54.5	3.6
9x-C	3.7	39.6	57.1	3.4
10x-A	4.9	40.7	55.3	4.0
10x-B	4.7	39.8	55.3	4.9
WT	2.7	40.2	55.6	4.1

FIG. 10F

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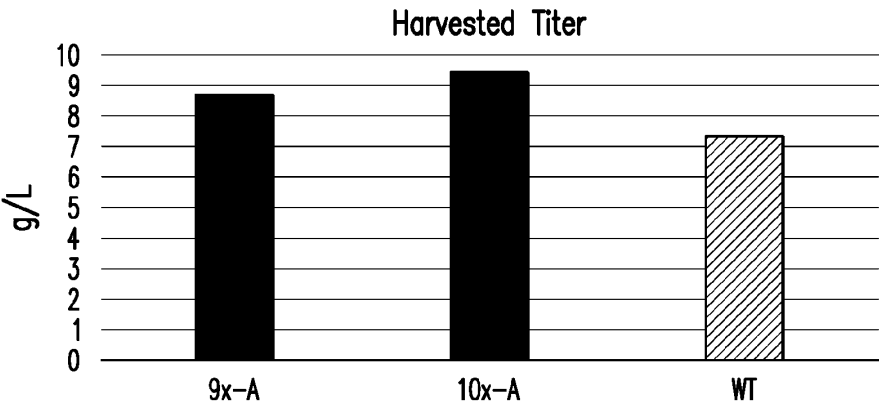


FIG. 11A

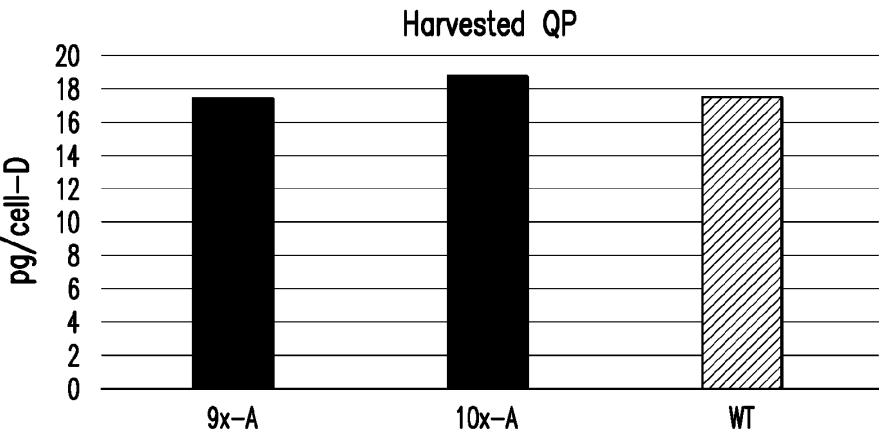


FIG. 11B

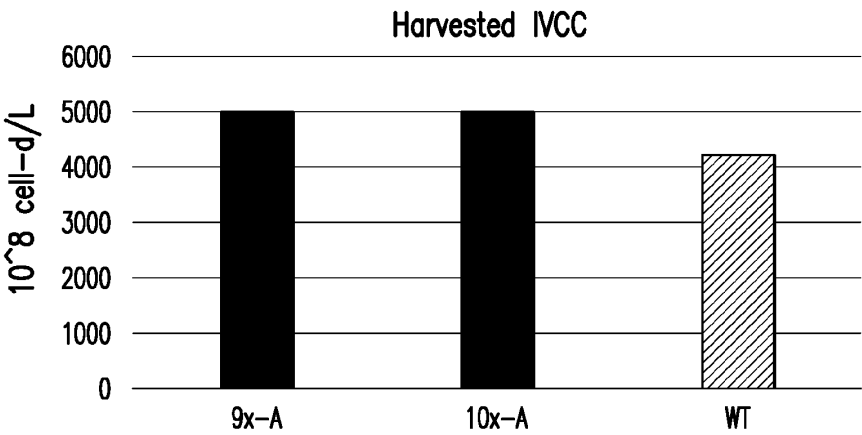


FIG. 11C

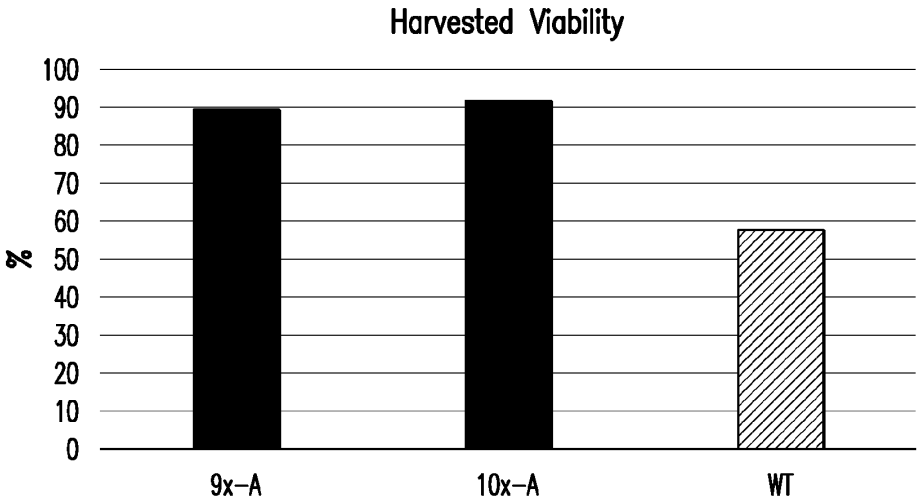


FIG. 11D

CHO cultures expressing mAb-I	Size	Charge Distribution			Glycoform
	% Aggregate	% Acidic	% Main	% Basic	Alpha-Gal (%)
9x-A	2.6	52.49	21.39	26.12	0.2
10x-A	3.2	69.08	19.83	11.08	0.2
WT	2.2	47.3	25.42	27.28	1.6

FIG. 11E

CHO Cultures	Day 14 Cell Culture Performance					Charge Distribution			Size
	Titer (g/L)	Qp	NCC	Viability (%)	Acidics (%)	Main (%)	Basics (%)	Aggregates (%)	
Clone ID (mAb-H)									
10xclone D	9.1	24.2	3769	92.5	34.8	61.3	3.9	4.5	
10xclone E	8.9	21.1	4227	92.9	33.6	62.6	3.8	4.4	
10xclone F	10.3	29.0	3534	97.5	36.2	60.5	3.3	3.8	
WT	8.1	18.4	4428	85.3	41.6	55.3	3.2	3.2	

FIG. 12

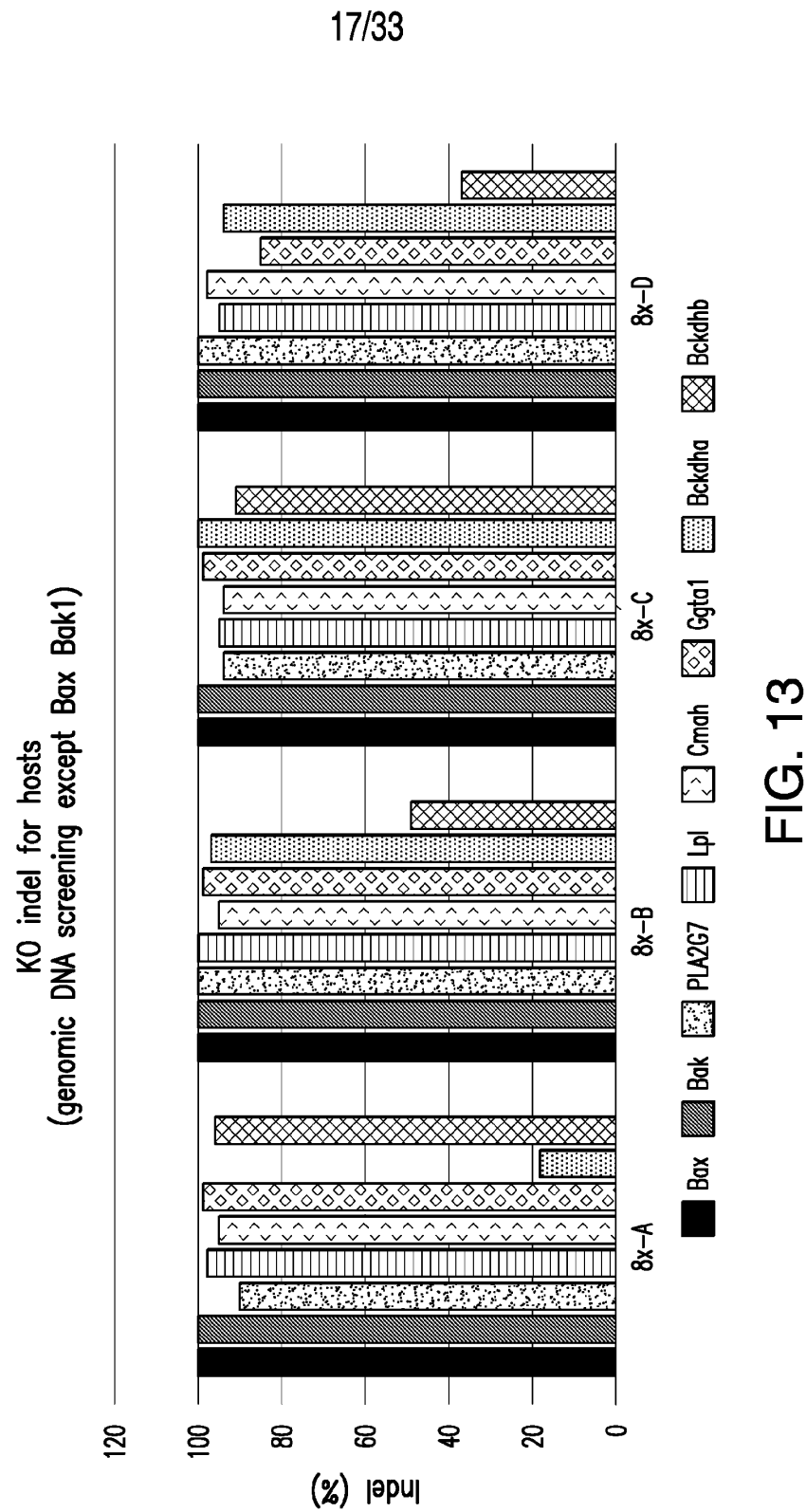


FIG. 13

CHO bioreactor cultures	Harvest Titer	Harvest Qp	Harvest Viability	Harvest VCC	Harvest NCC
mAb-N	(g/L)	pg/cell-d	%	10 ⁶ cell/mL	10 ⁸ cell-d/L
8x-A	4.6	6	90	42	7423
8x-B	4.7	6	89	43	7773
8x-C	4.5	6	91	46	8022
8x-D	5.3	8	90	37	6850
WT	4	10	85	17	4036

FIG. 14

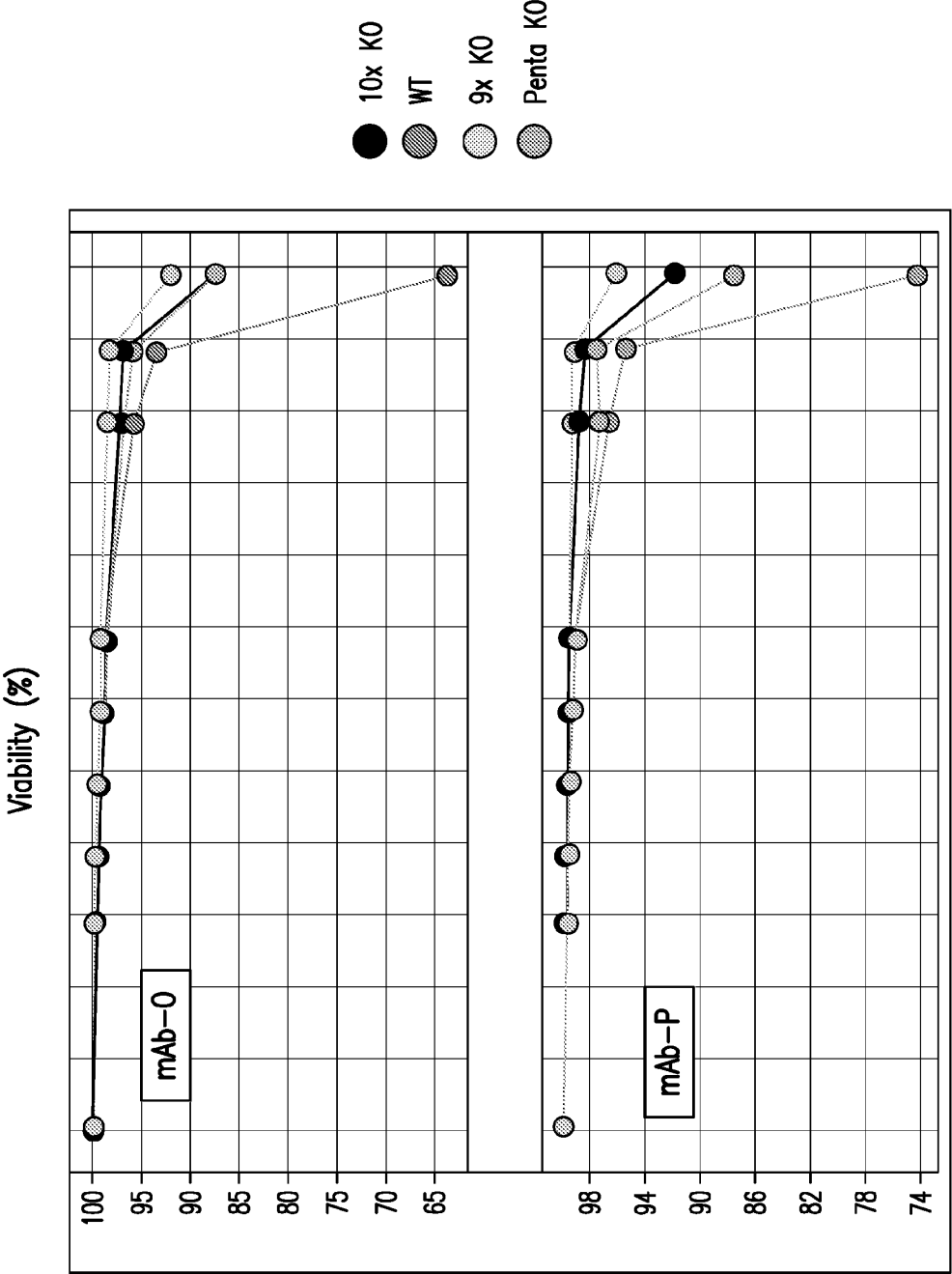


FIG. 15A

Cell line		HCPs, ELISA (ng/mg)	Specific FAR Rate (ng/mg/d)	Relative Change in Specific FAR Rate (%)
mAb-0	9x KO	16	2.89	43.89
	10x KO	11	1.87	28.48
	WT	17	6.57	100
	Penta KO	22	1.81	27.48
mAb-P	9x KO	430	7.15	22.60
	10x KO	693	10.25	32.38
	WT	644	31.65	100
	Penta KO	448	27.30	86.25

FIG. 15B

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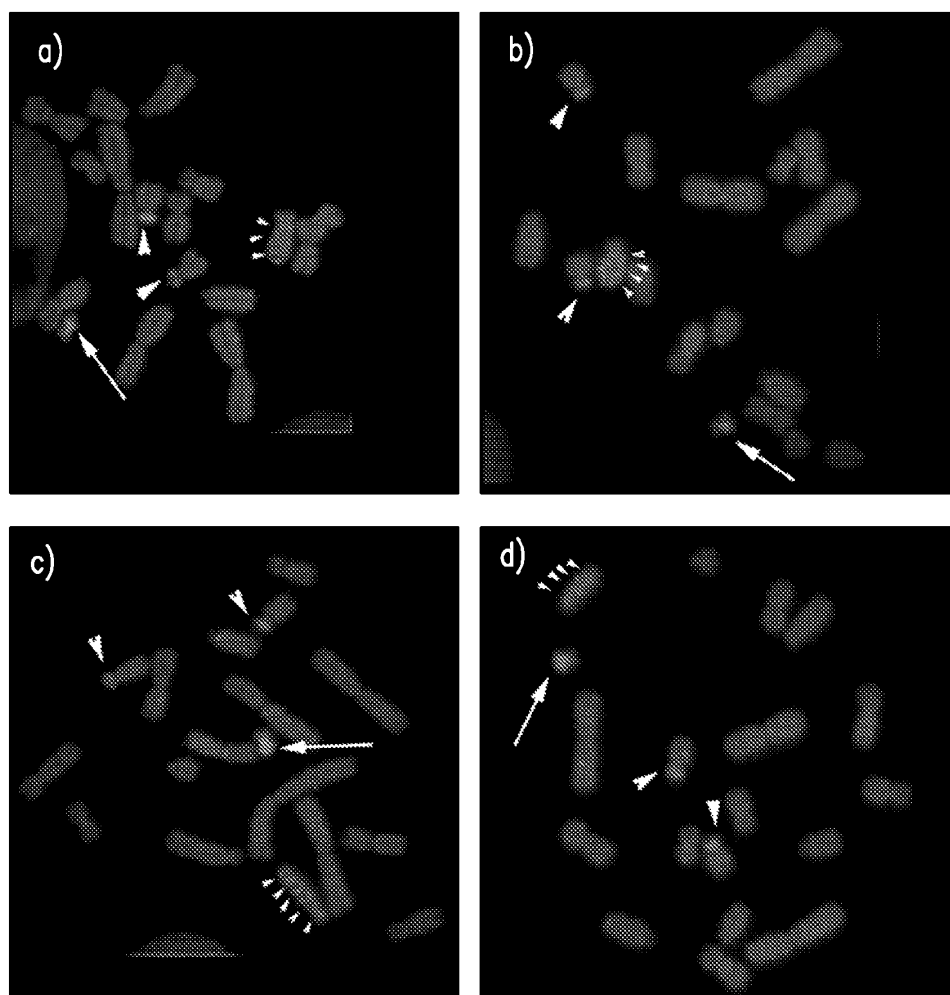


FIG. 16

RVLP DNA Copy Number Analysis		
CHO-Host	CHO-K1 Based Host (CHO-K1-M)	Targeted Integration Host (TI 11-9)
RVLP copies per cell	~70	~60

FIG. 17

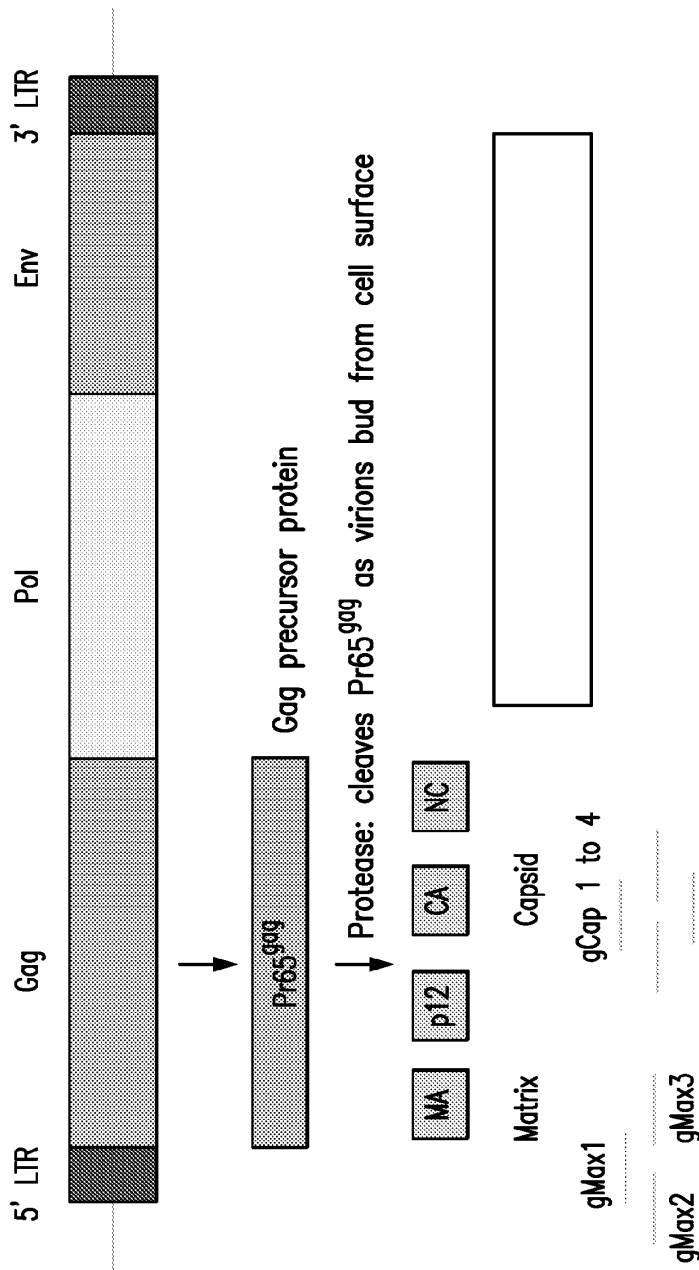


FIG. 18

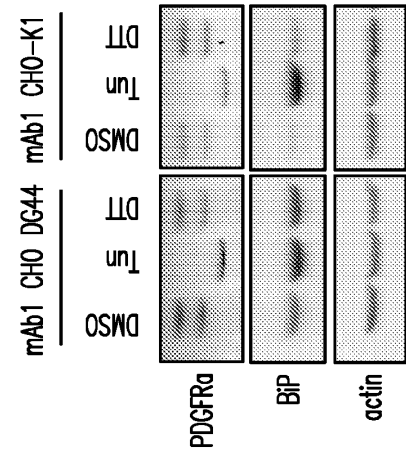


FIG. 19C

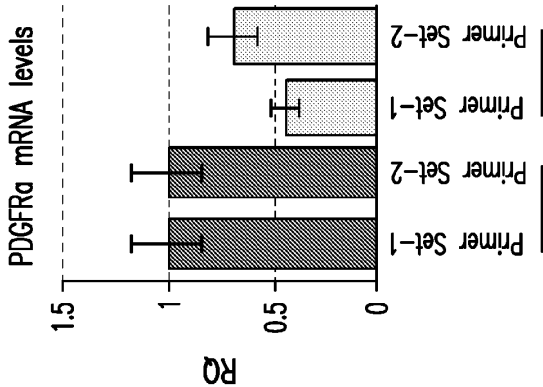


FIG. 19B

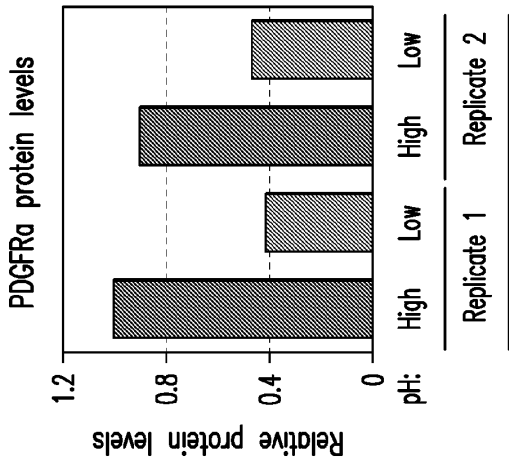


FIG. 19A

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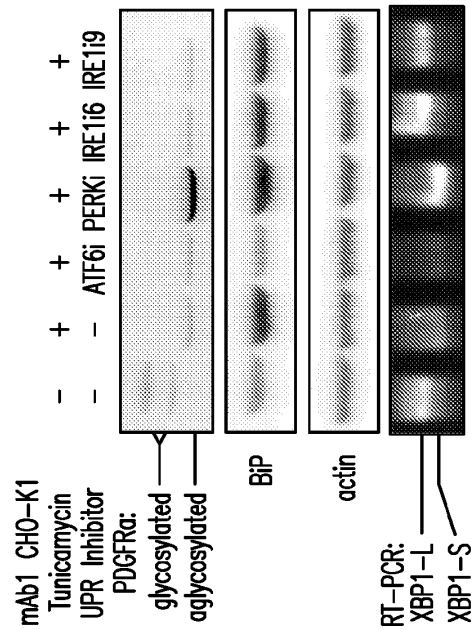


FIG. 19E

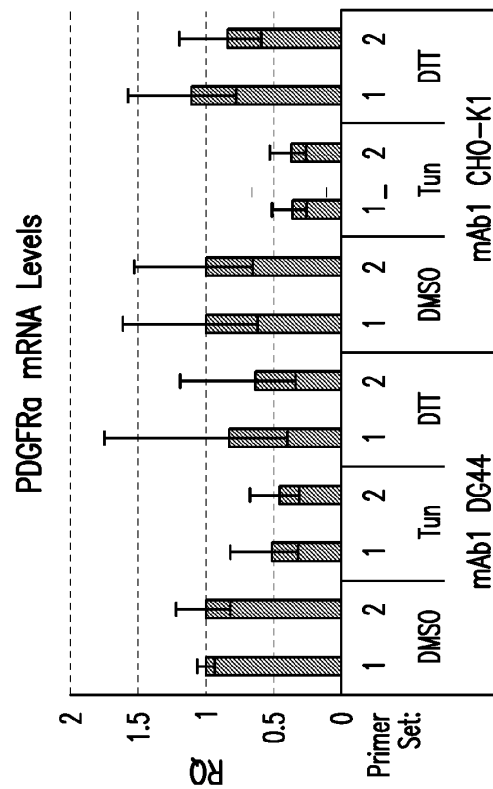


FIG. 19D

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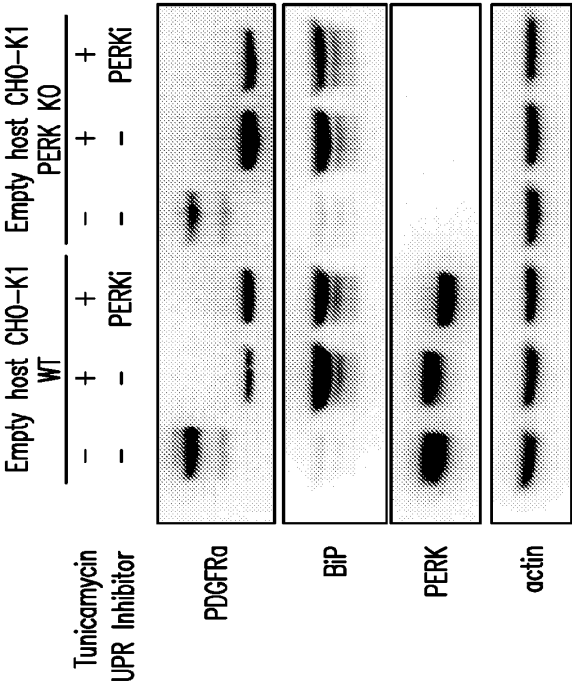


FIG. 19G

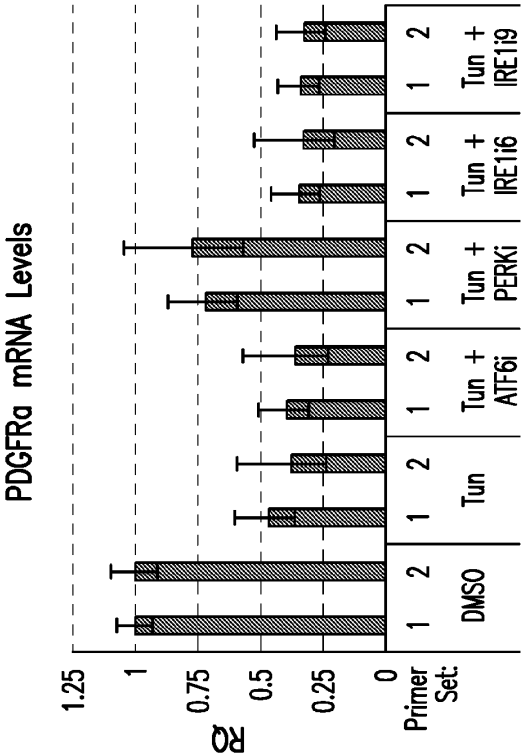
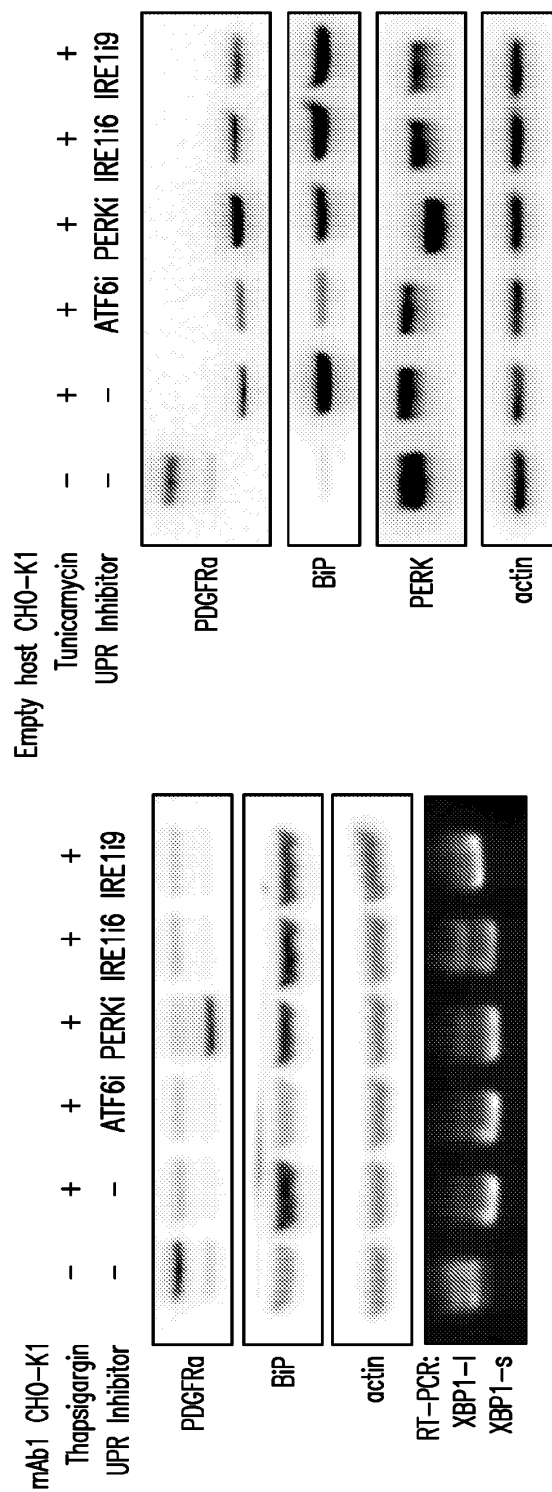


FIG. 19F



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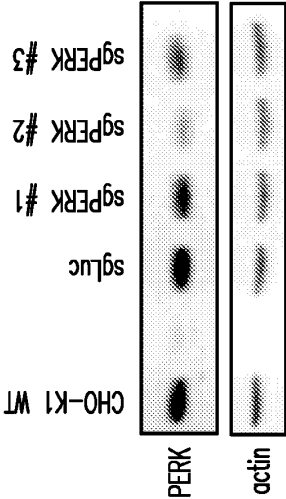


FIG. 20D

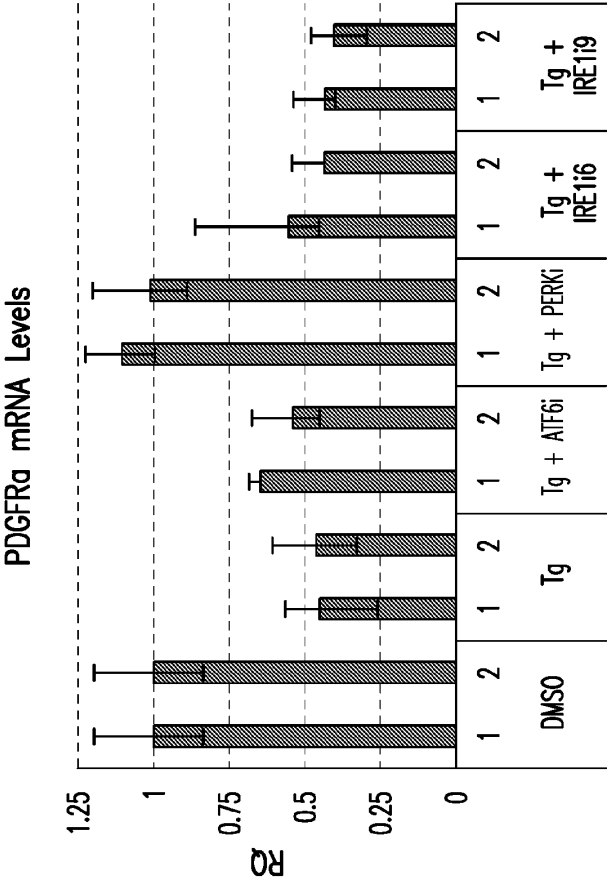


FIG. 20C

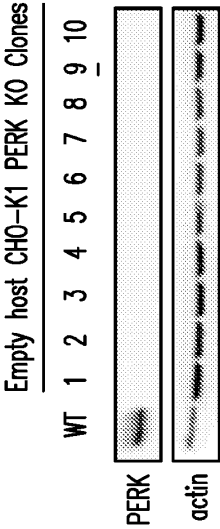


FIG. 20E

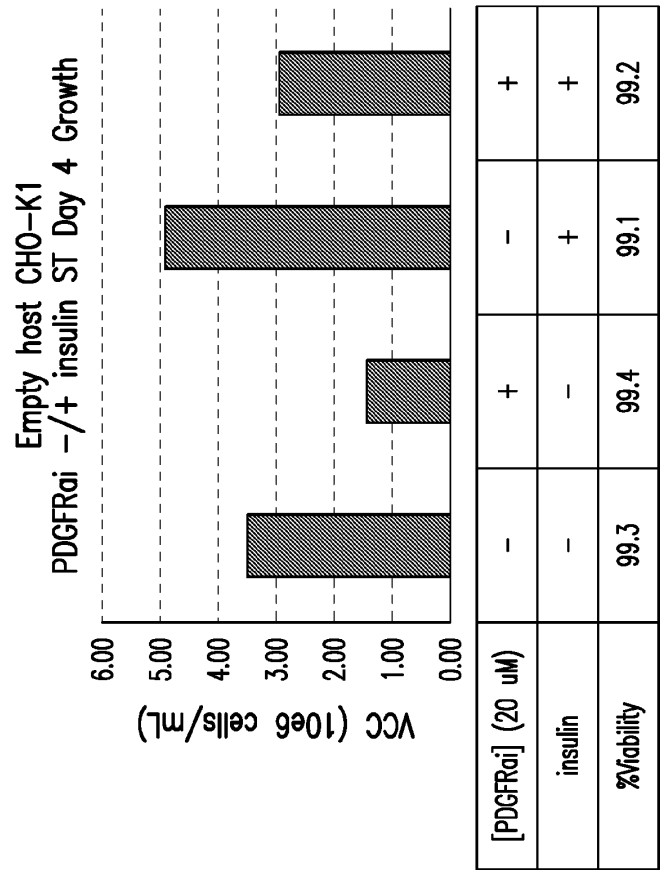


FIG. 21B

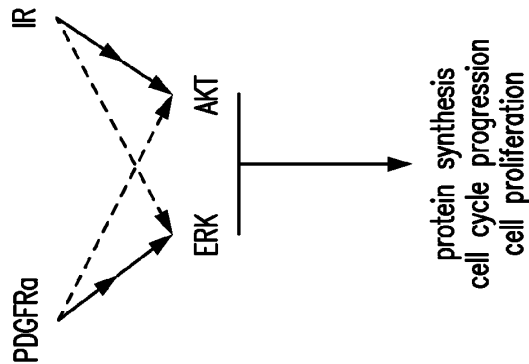


FIG. 21A

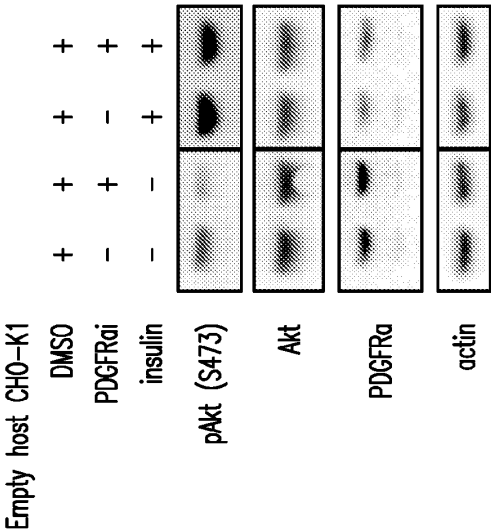
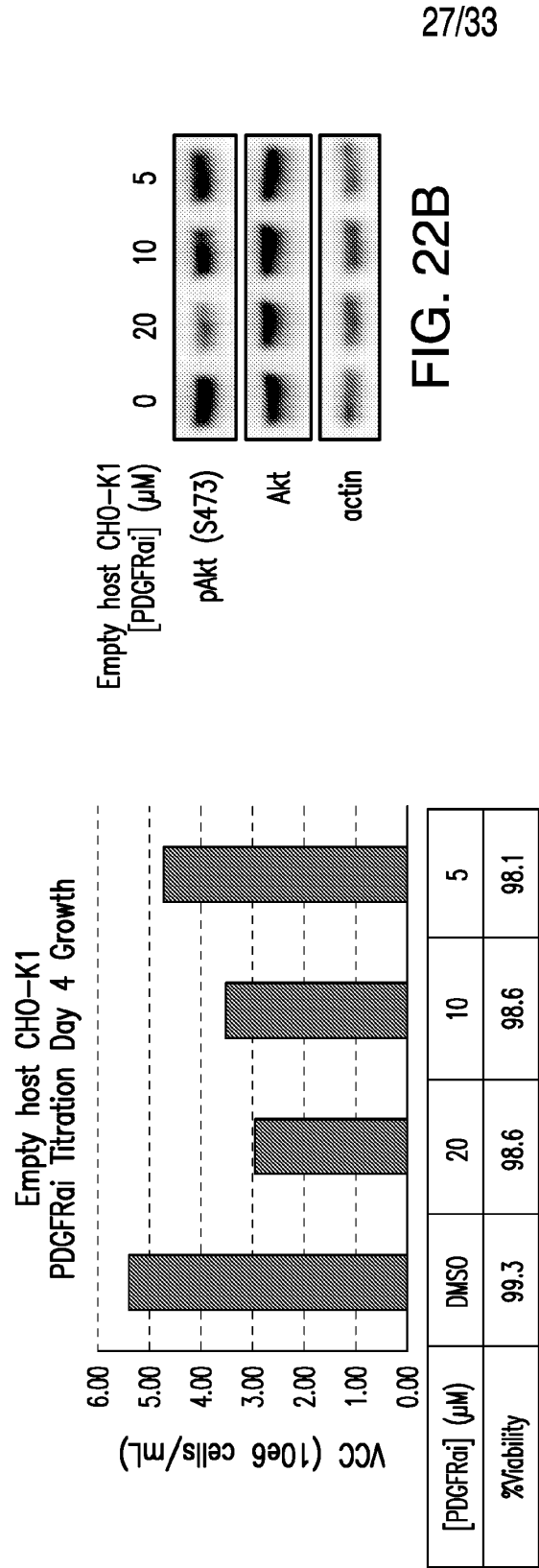


FIG. 21C

PDGFRa inhibition on mAb2 CHO-K1 Production					
Day 12 Parameter	Relative IVCC	%viability	Relative Titer	Relative Qp	
Control	1.00	96.40	1.00	1.00	
+PDGFRai	0.62	94.13	0.75	1.20	
+PDGFRai +insulin	0.77	93.50	0.81	1.05	

FIG. 21D



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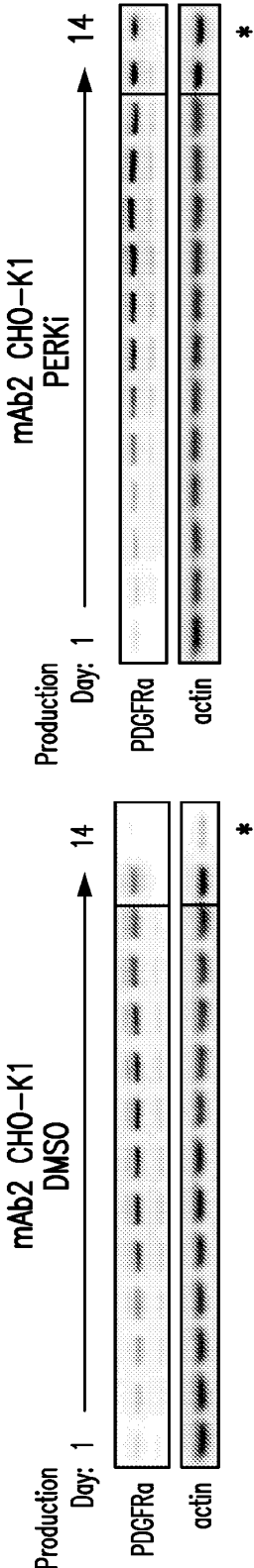


FIG. 22C

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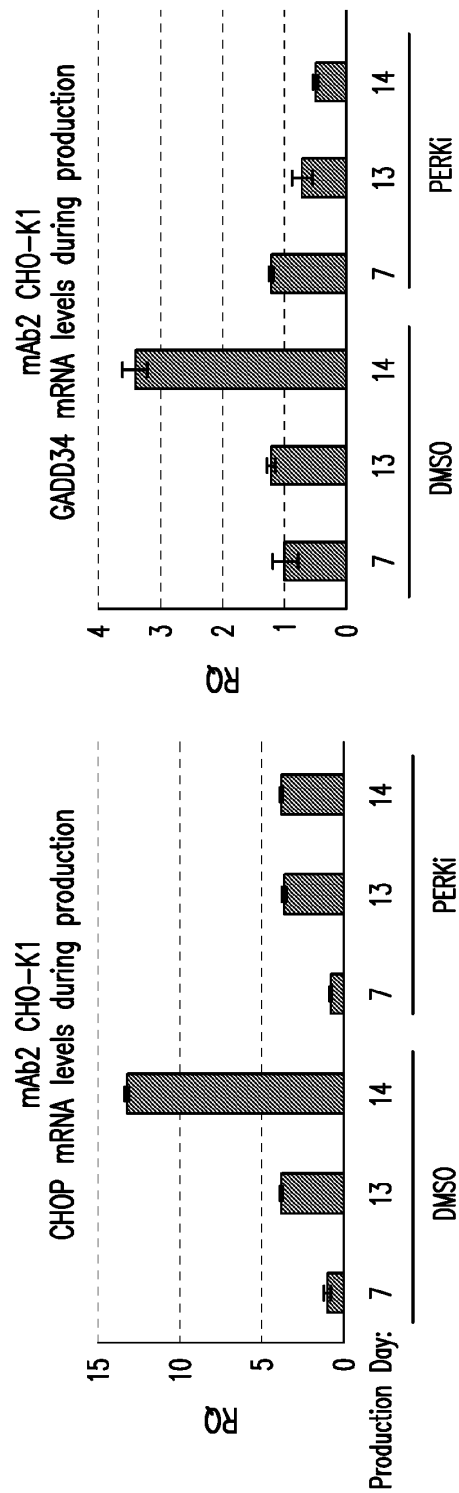


FIG. 22D

PERK KO on mAb2 CHO-K1 Production					
Day 14 Parameter	Relative MCC	%Viability	Relative Titer	Relative Qp	
WT	1.00	95.9	1.00	1.00	
PERK KO 2	0.55	51.5	0.97	1.78	
PERK KO 3	0.83	64.9	1.07	1.29	
PERK KO 4	0.88	77.9	1.15	1.30	
PERK KO 6	0.85	60.3	1.18	1.40	
PERK KO 7	0.80	71.4	0.96	1.20	

FIG. 23B

mAb2 CHO-K1

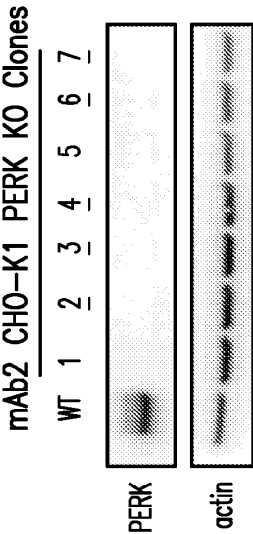


FIG. 23A

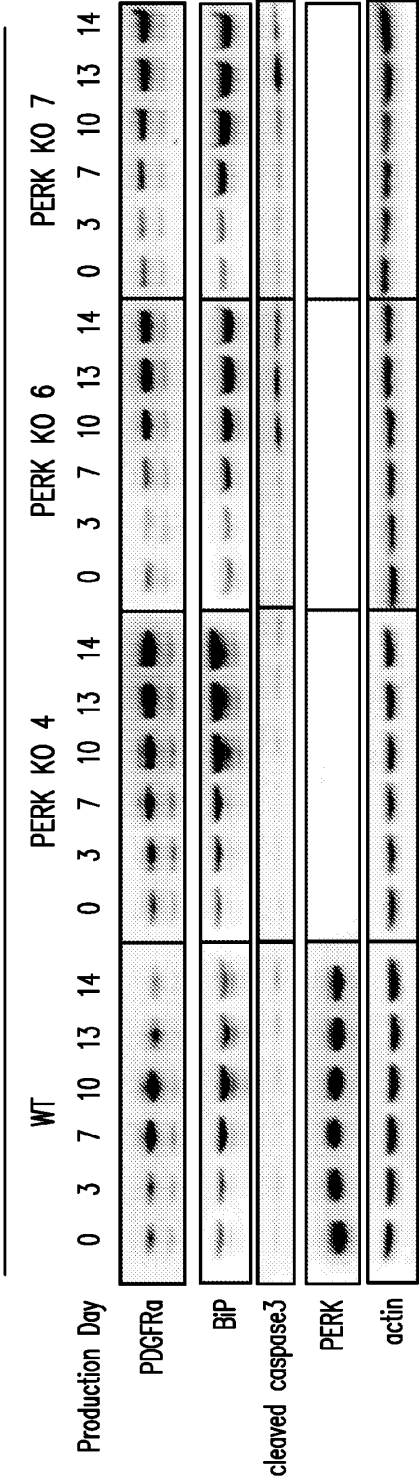


FIG. 23C

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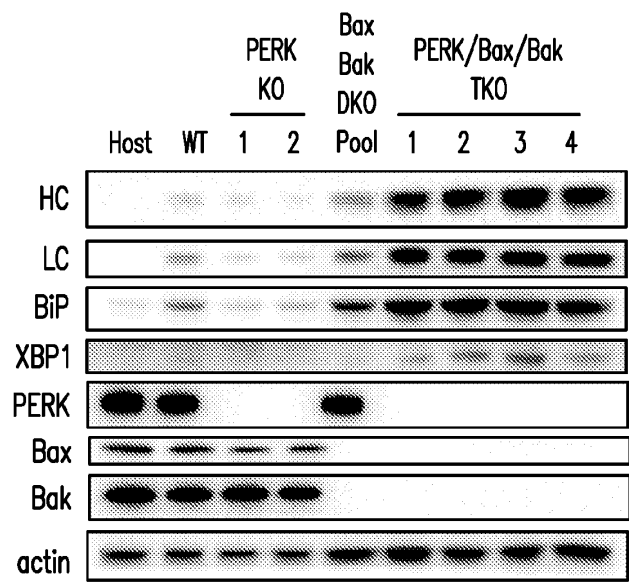


FIG. 24A

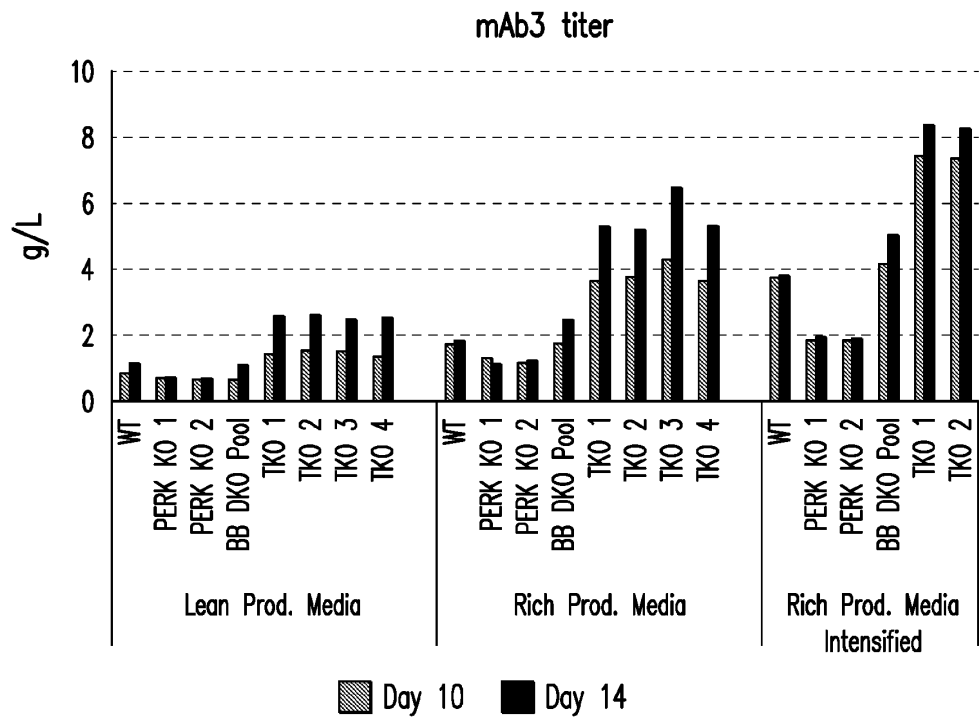


FIG. 24B

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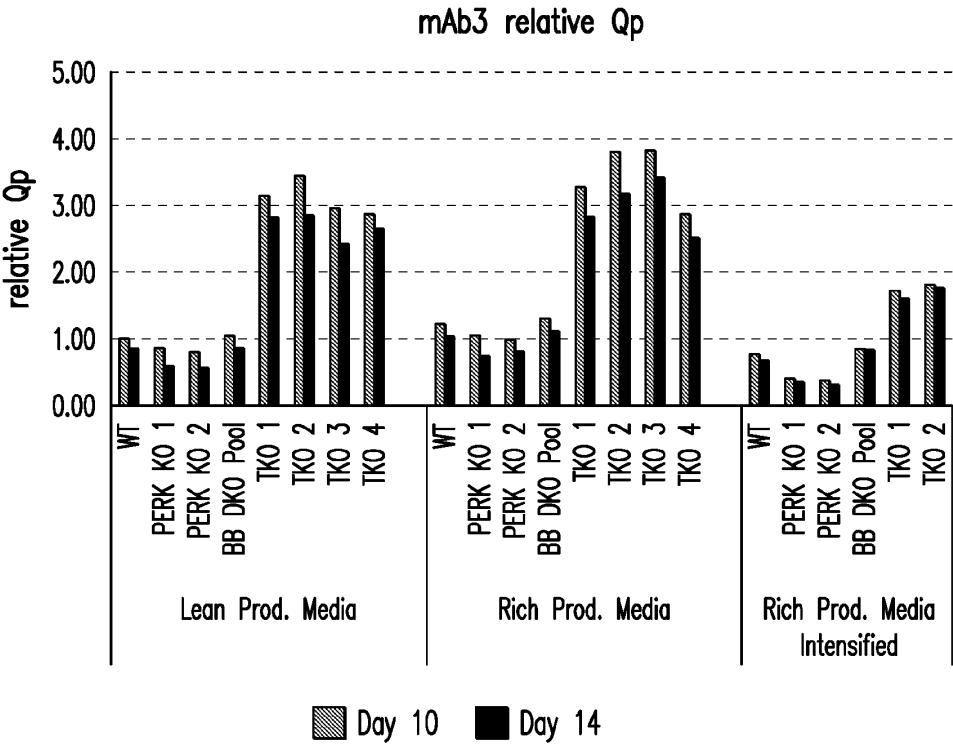


FIG. 24C

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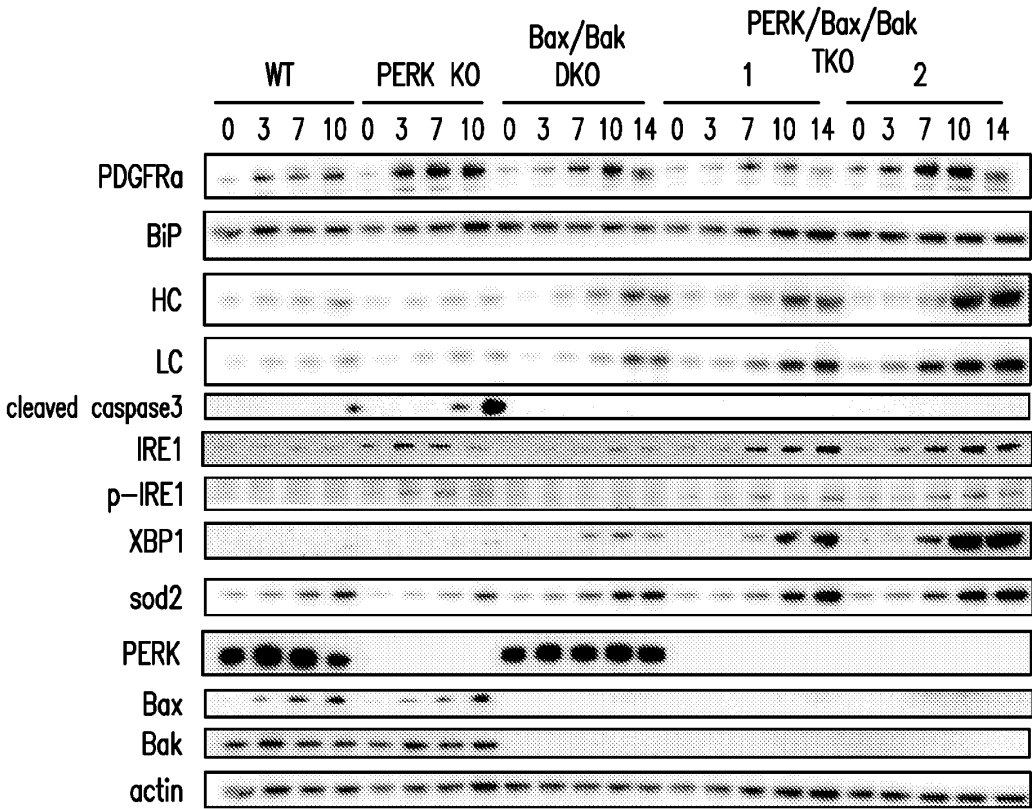


FIG. 24D

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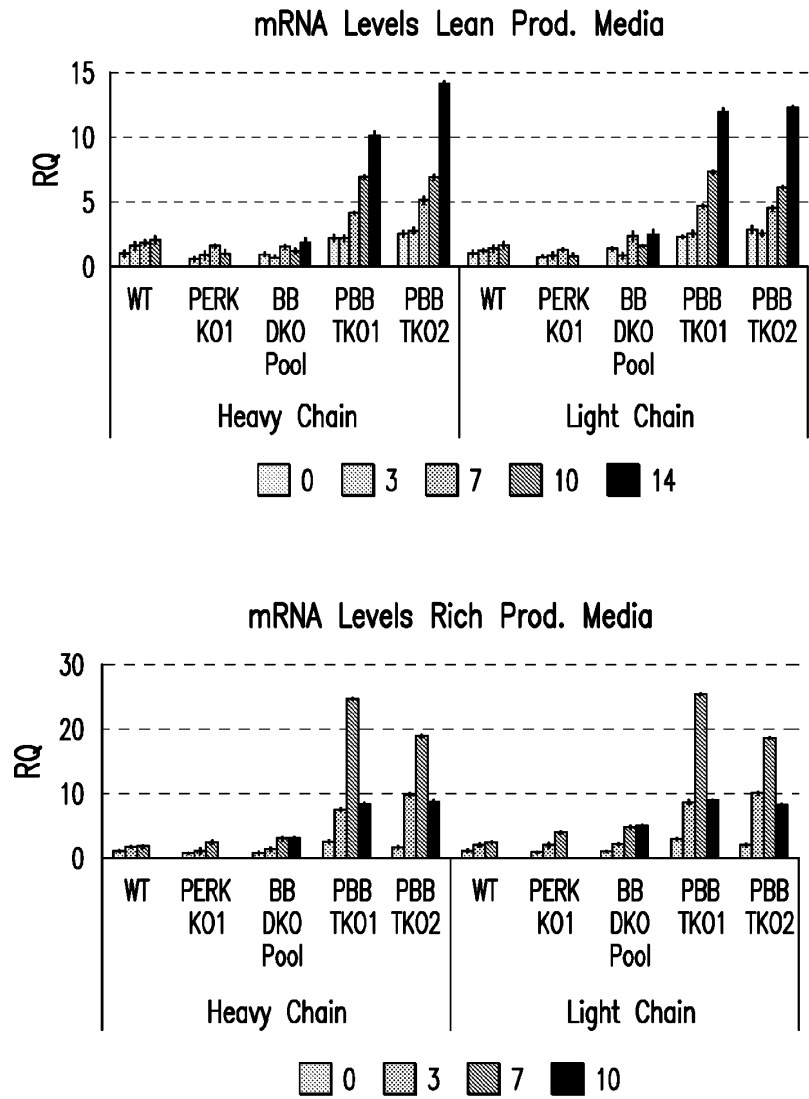


FIG. 24E

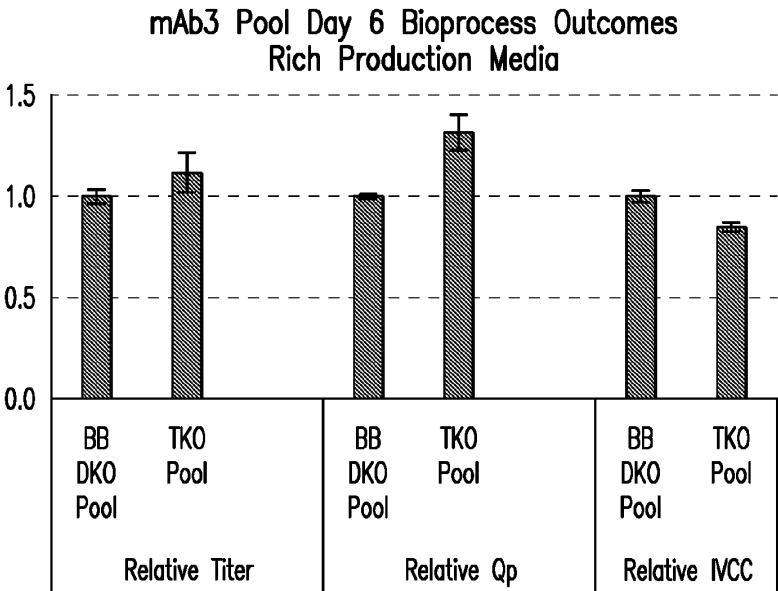


FIG. 25A

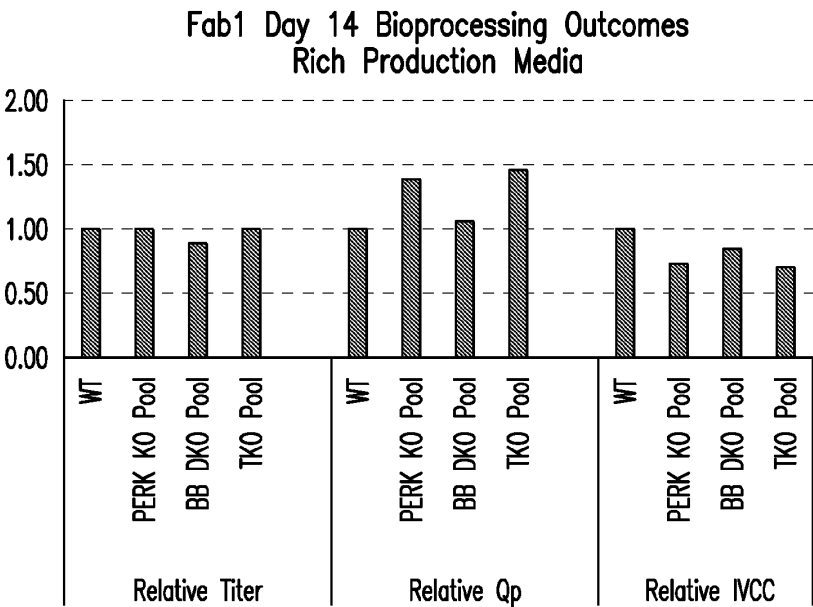


FIG. 25B

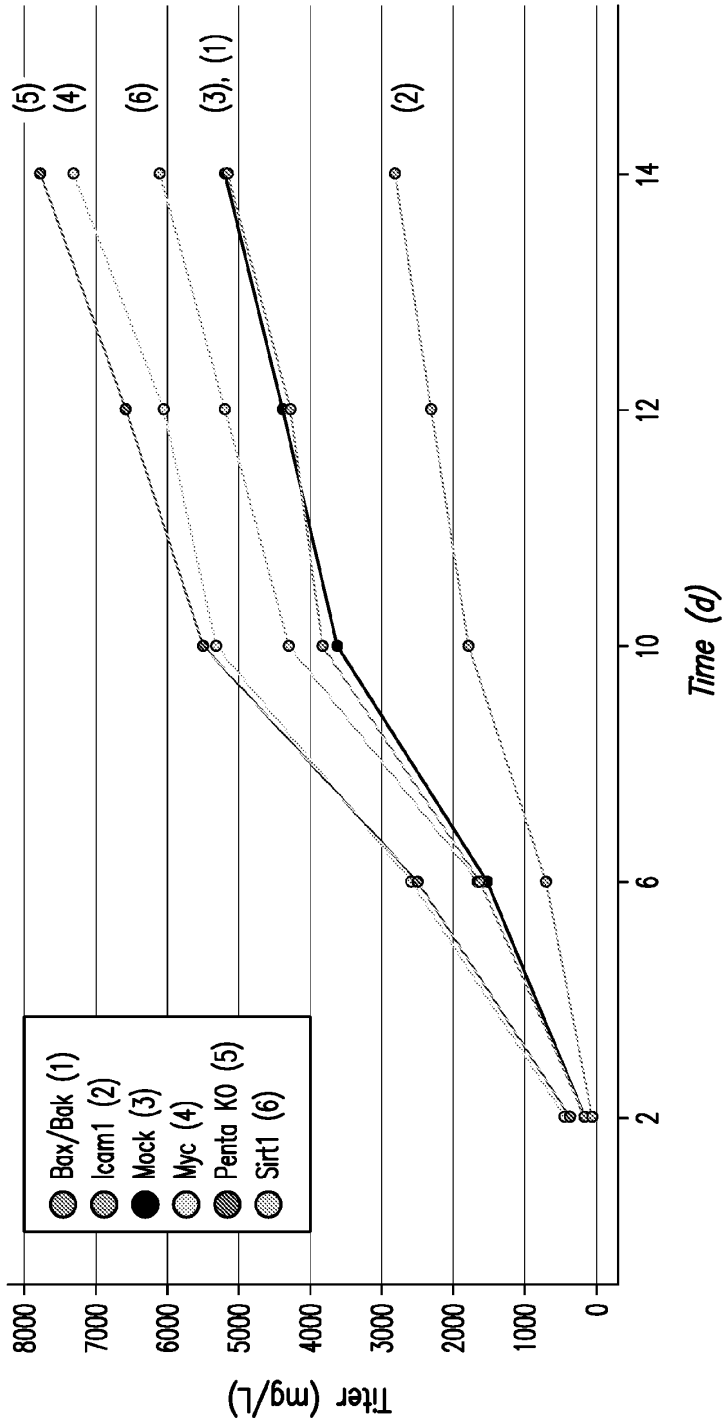


FIG. 26

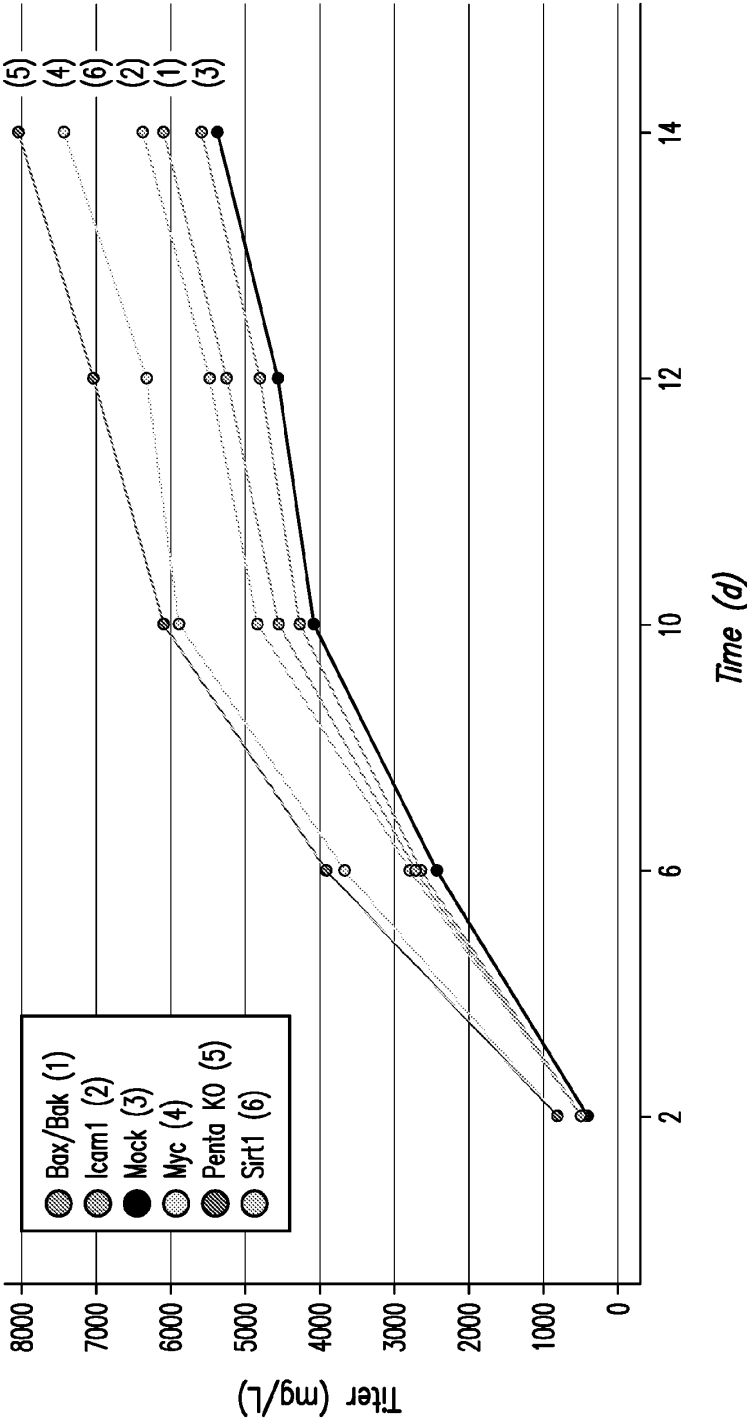


FIG. 27

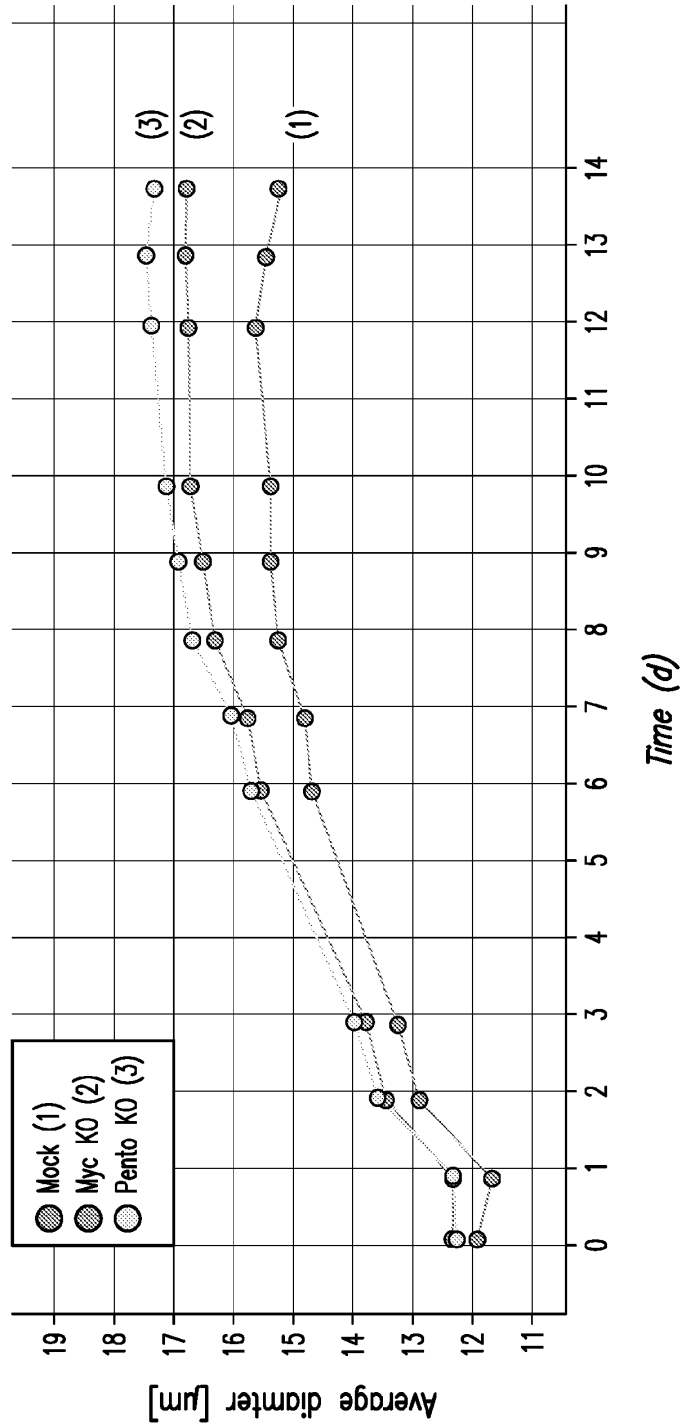


FIG. 28