FIG. 1/55

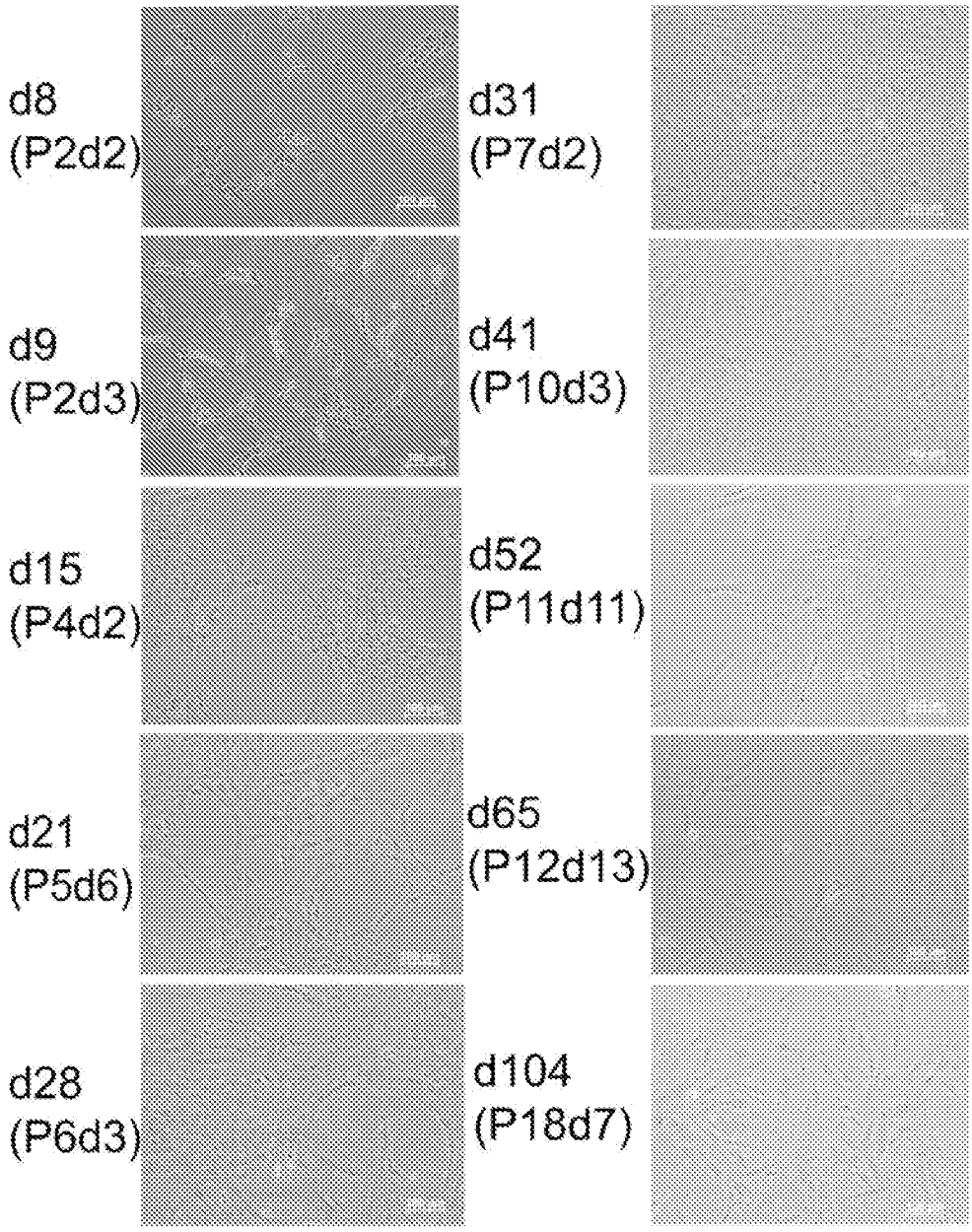


FIGURE 1

FIG. 2/55

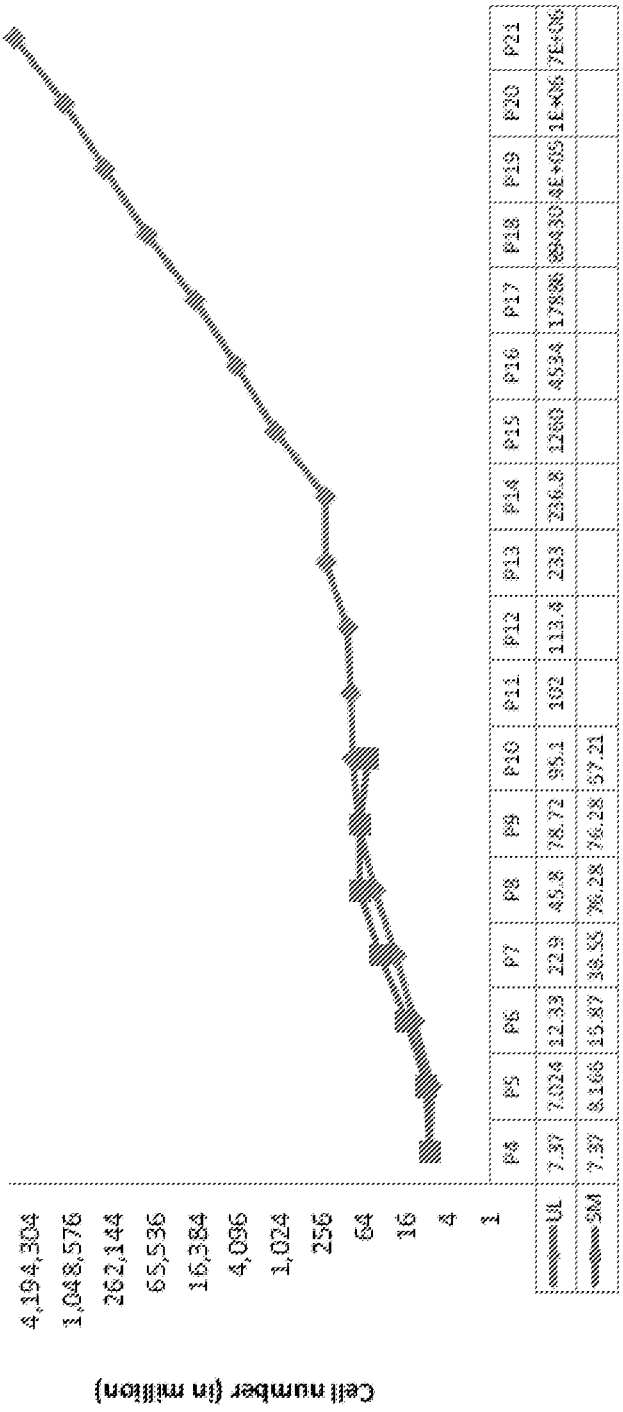


FIGURE 2

FIG. 3/55

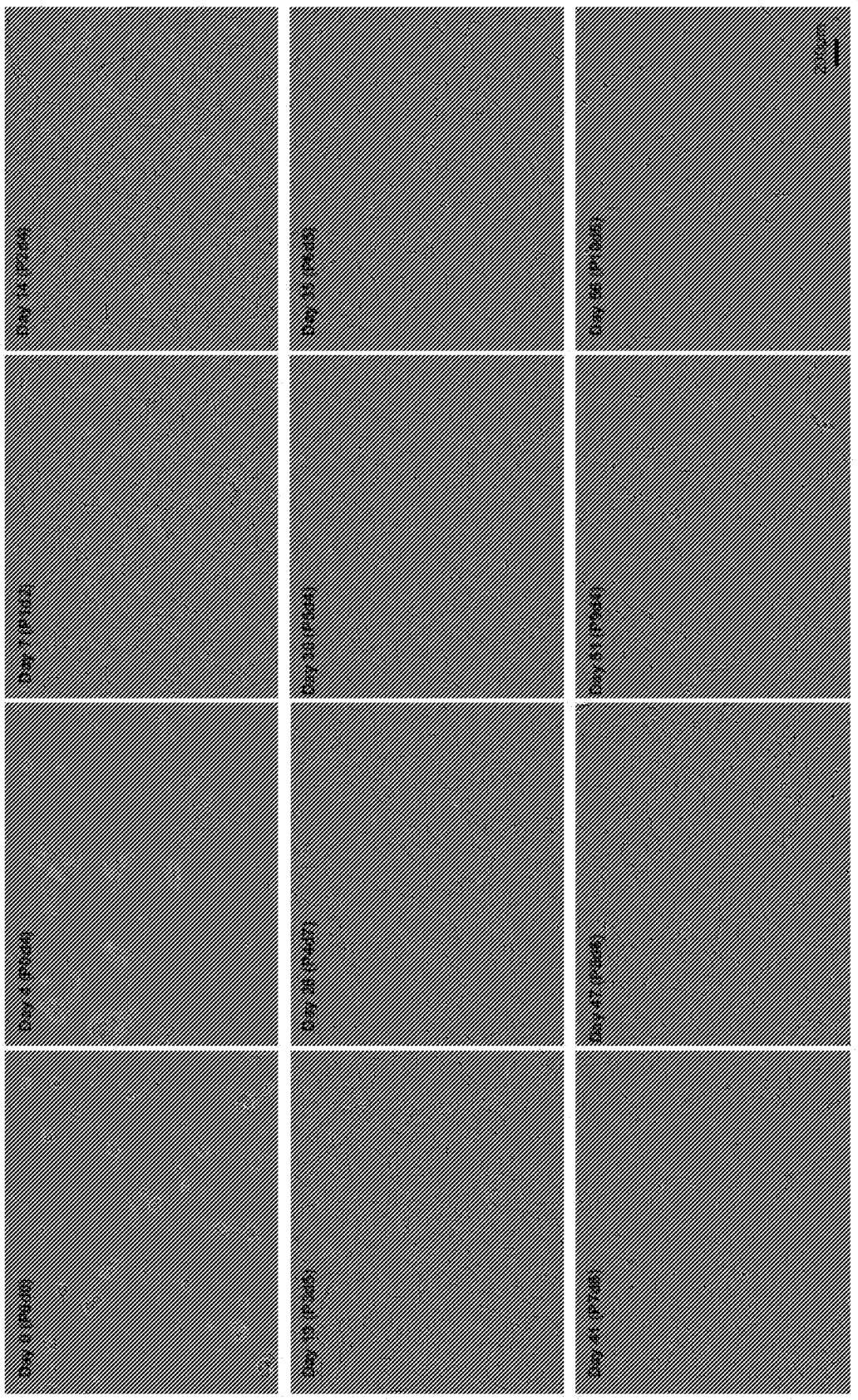
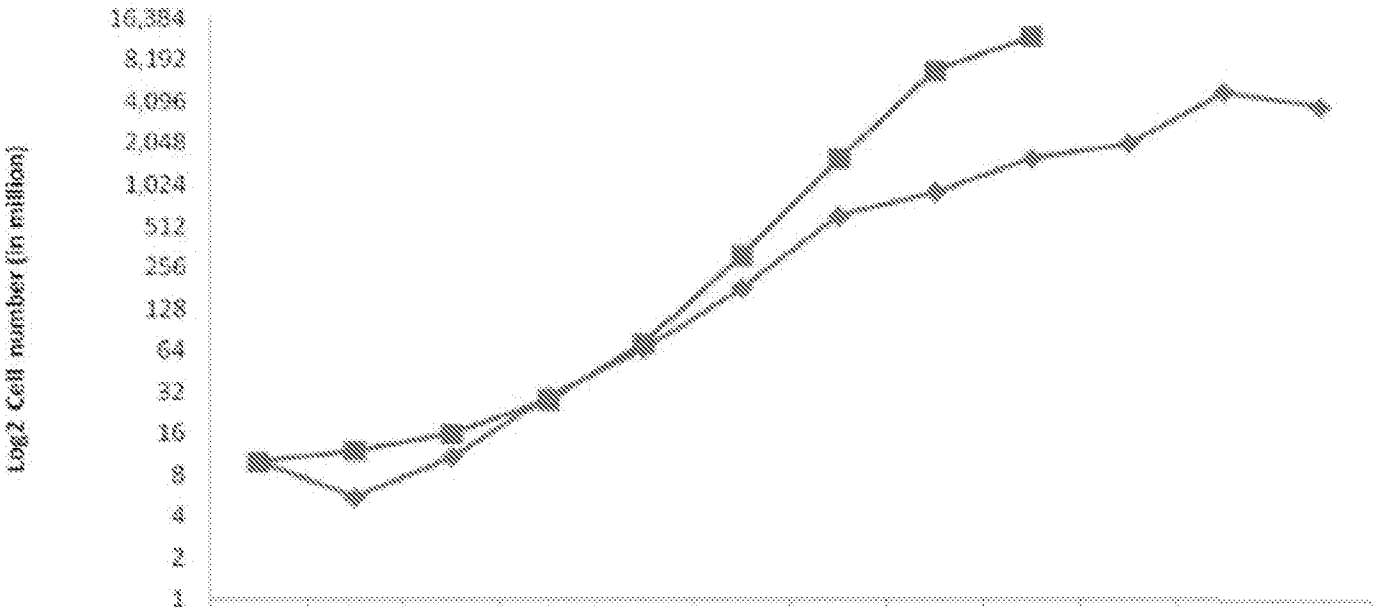


FIGURE 3



	P0 (d0)	P1 (d5)	P2 (d10)	P3 (d15)	P4 (d19)	P5 (d26)	P6 (d30)	P7 (d35)	P8 (d41)	P9 (d47)	P10 (d51)	P11 (d56)
cell number (in million)	10	12	16	28	72	315	1,575	6,931	12,120			
cell number (in million)	10	6	11	30	66	184	606	905	1,592	2,038	4,770	3,720

The blue donation was used in patients at ~P5, resulting in visual improvements

FIGURE 4

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FIG. 5/55

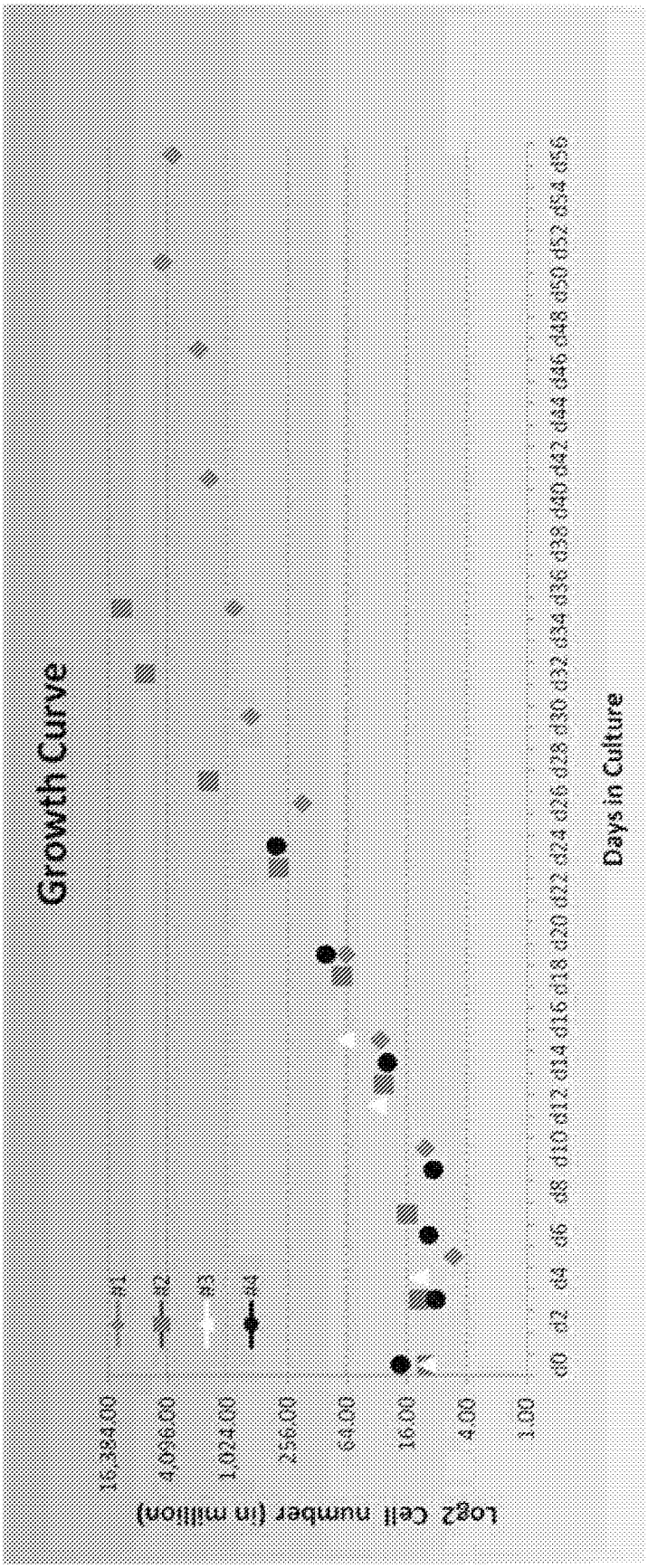
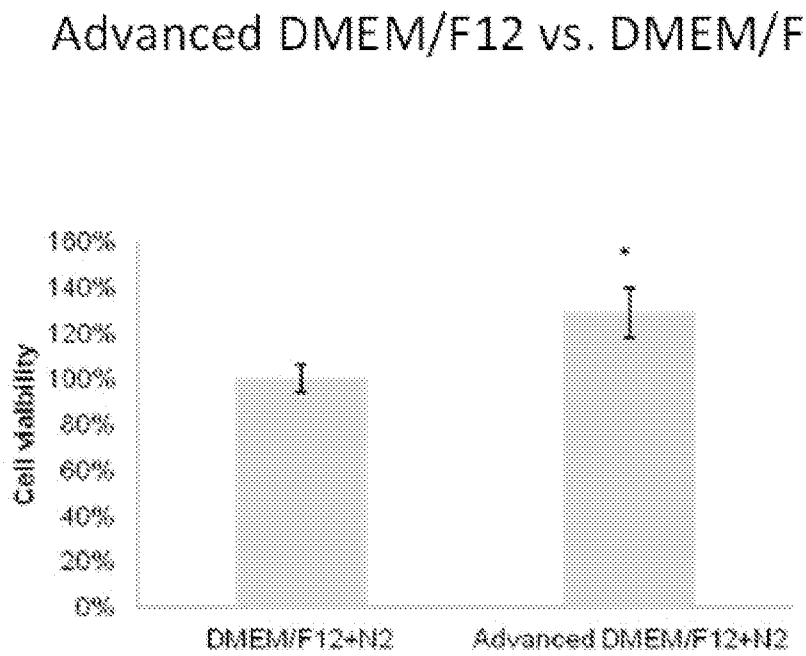


FIGURE 5

FIG. 6/55

A



B

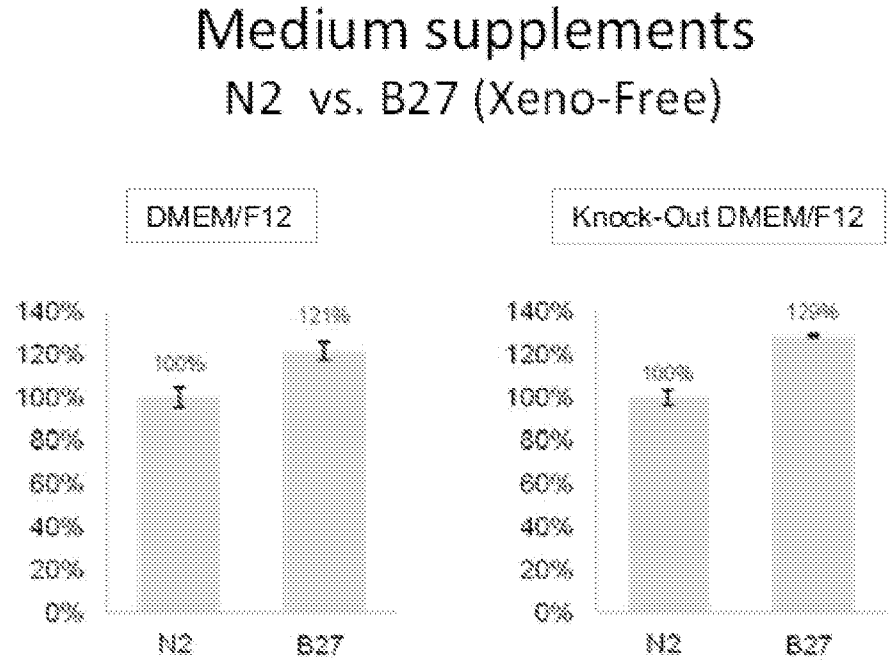
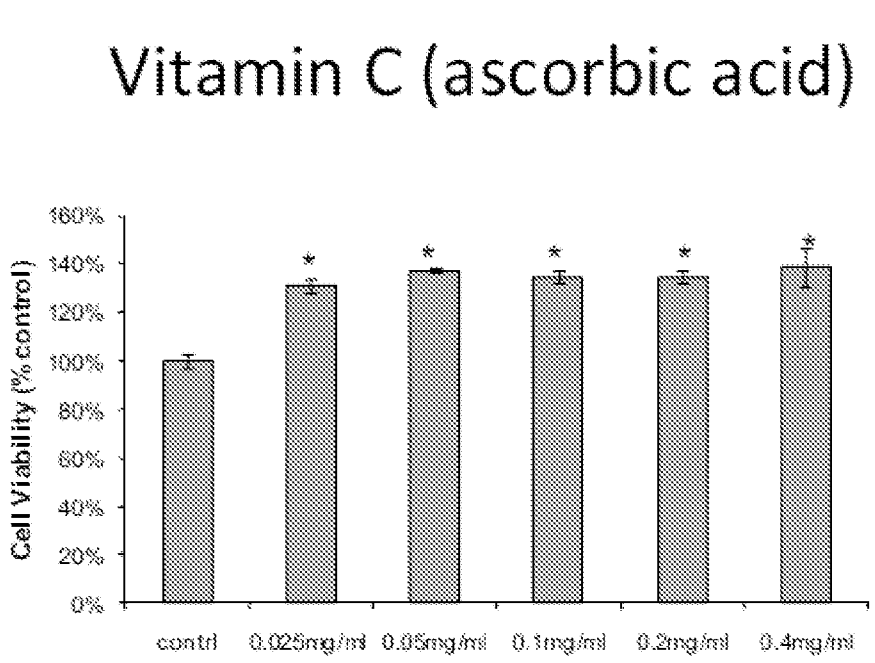


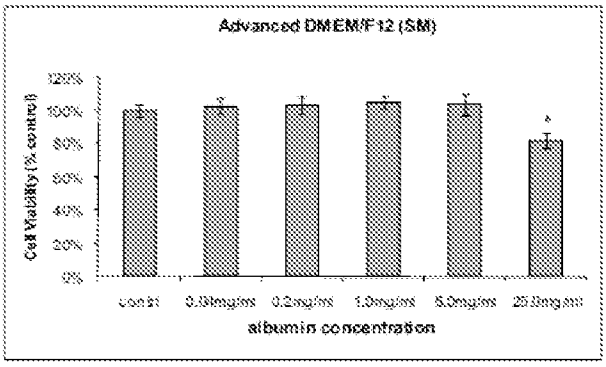
FIGURE 6

FIG. 7/55

A



B



C

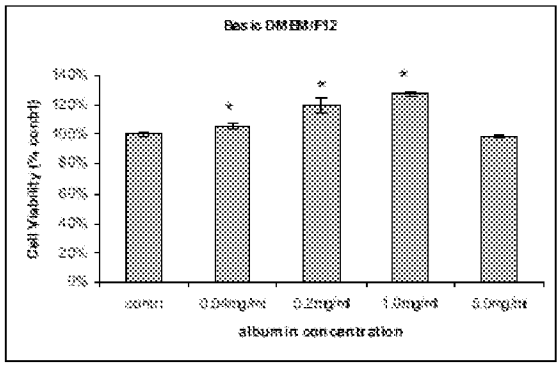


FIGURE 7

FIG. 8/55

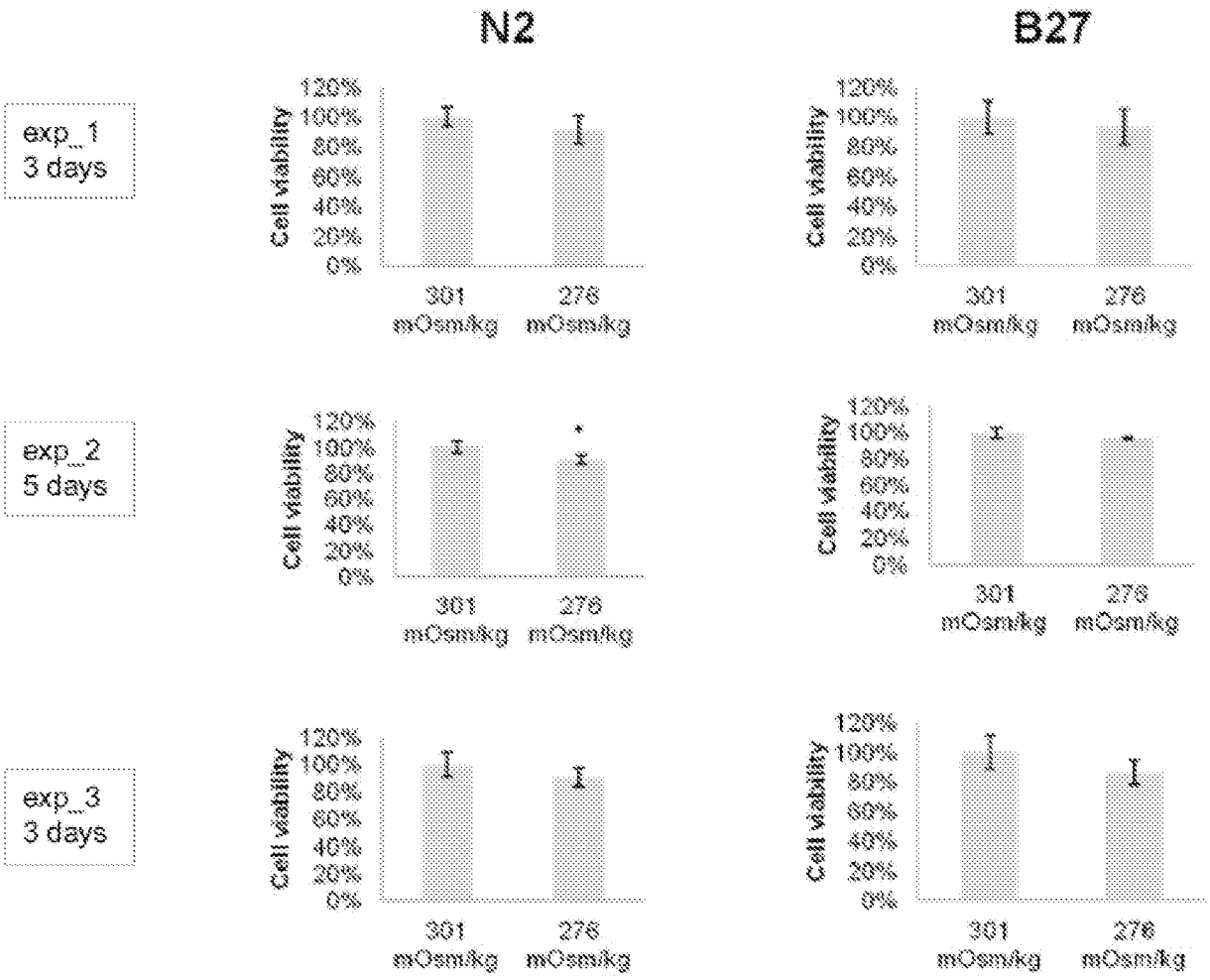


FIGURE 8

FIG. 9/55

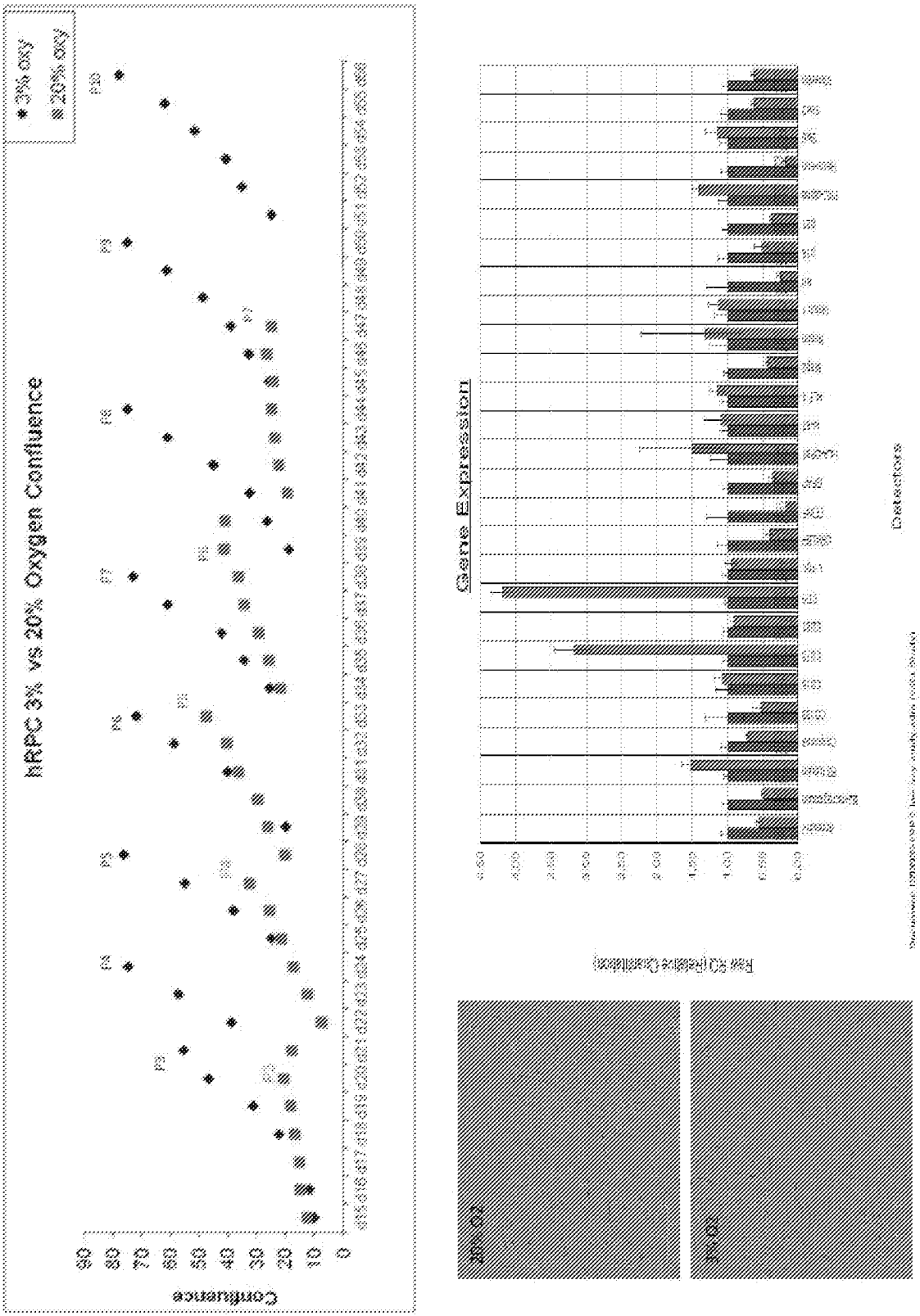


FIGURE 9

FIG. 10/55

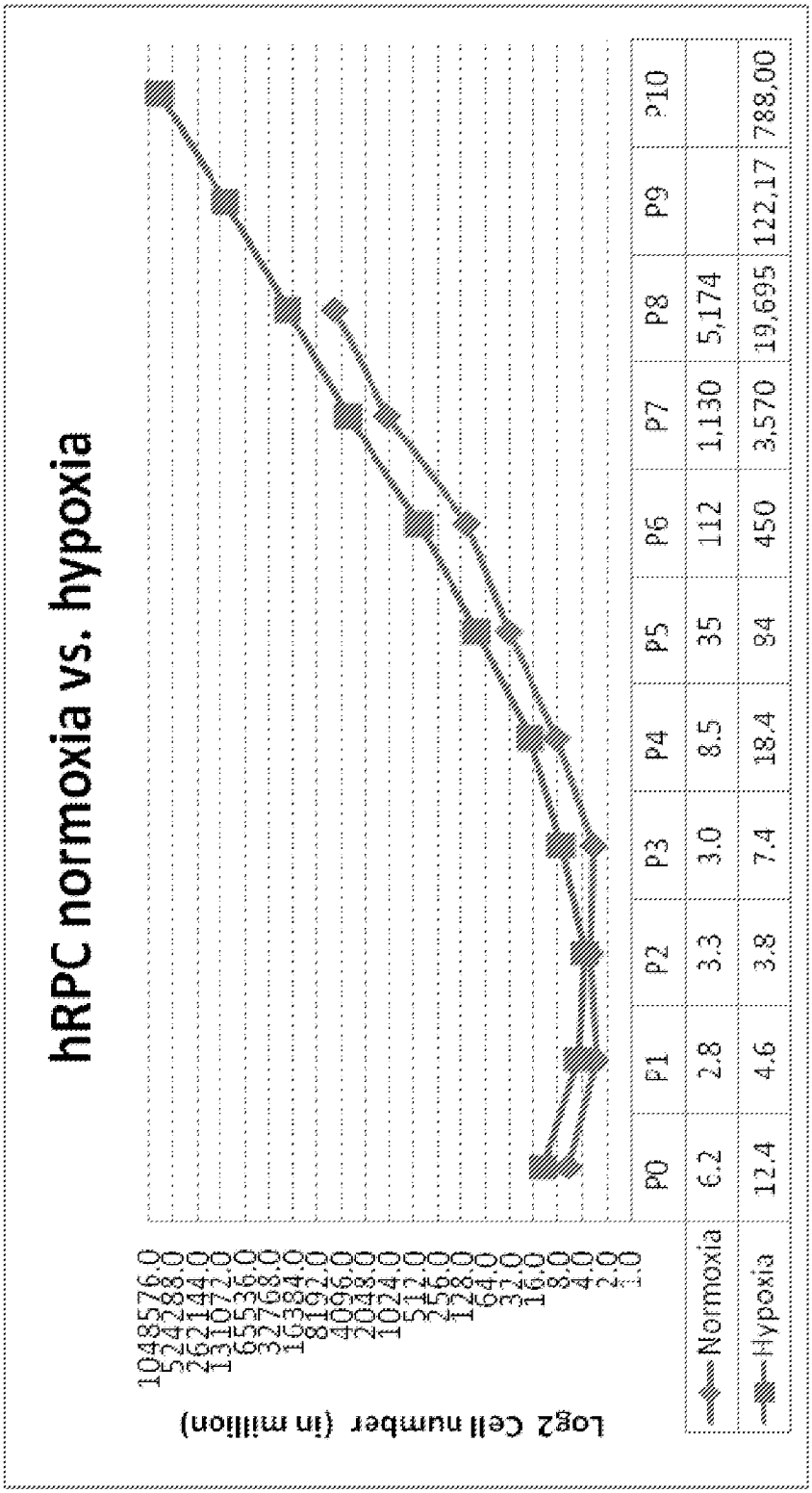


FIGURE 10

FIG. 11/55

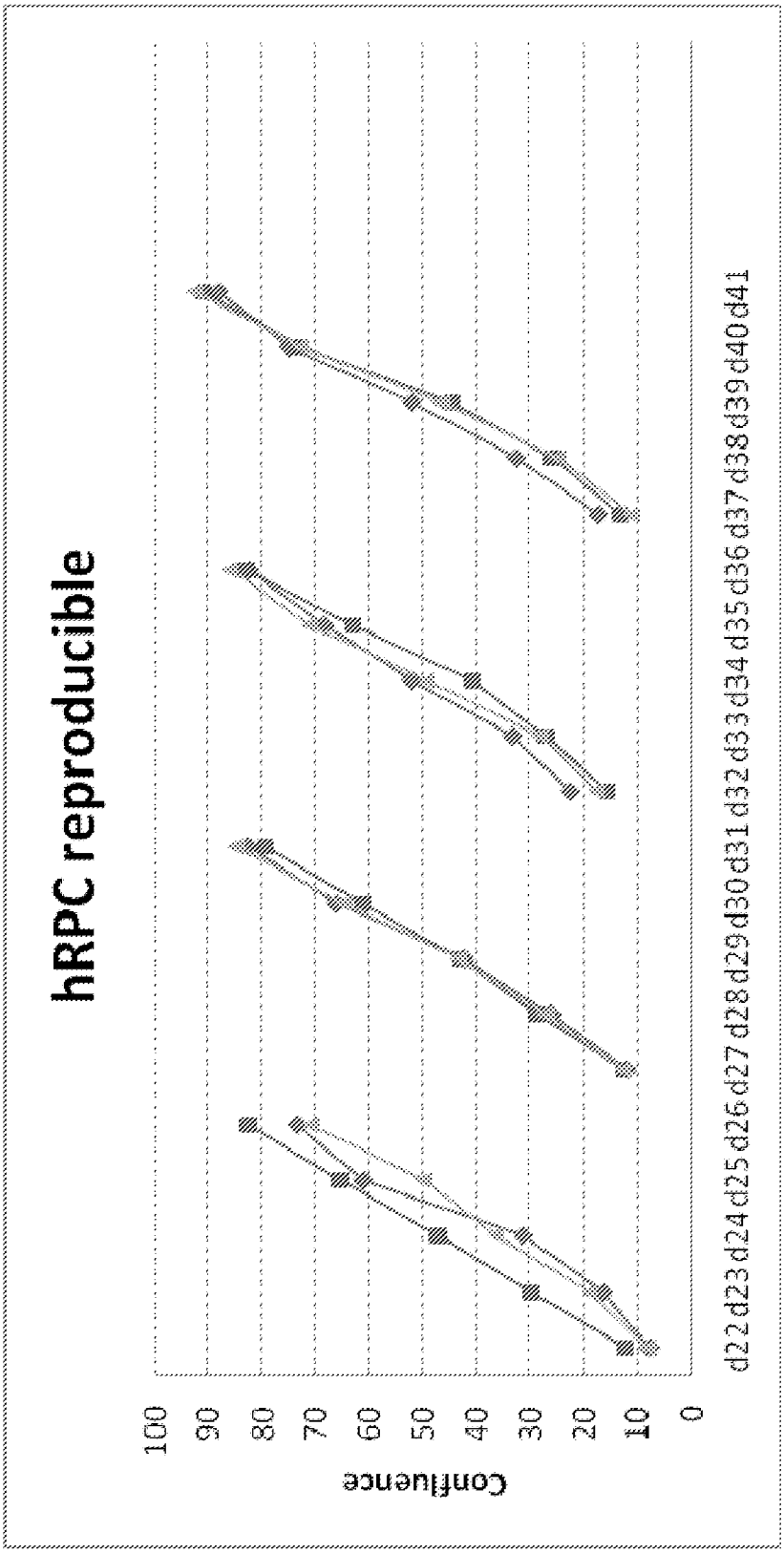


FIGURE 11

FIG. 12/55

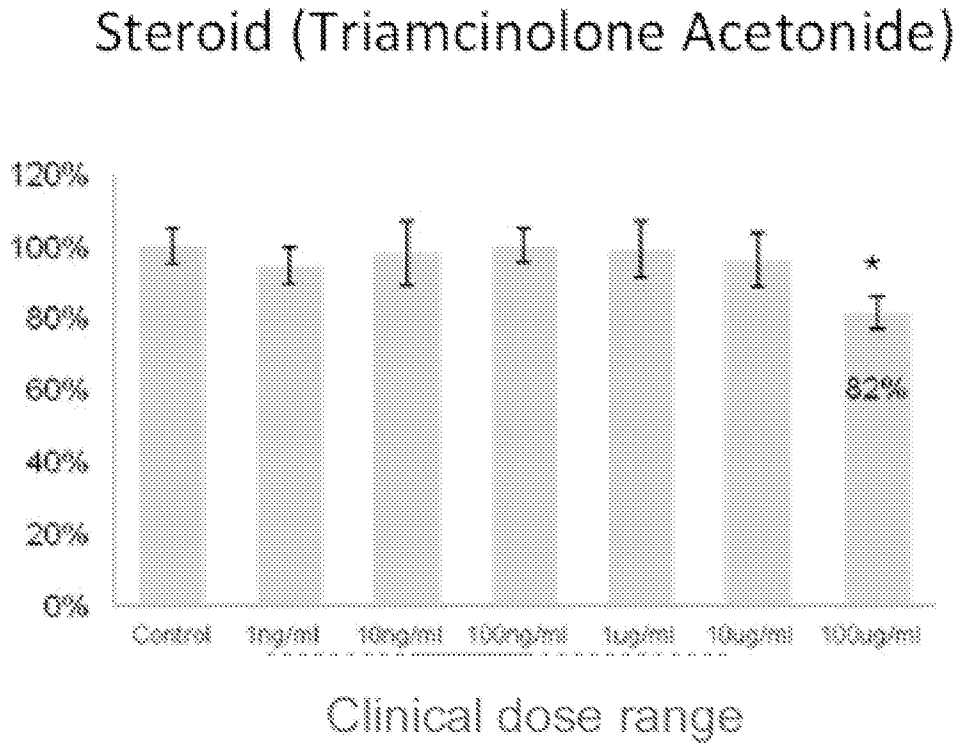
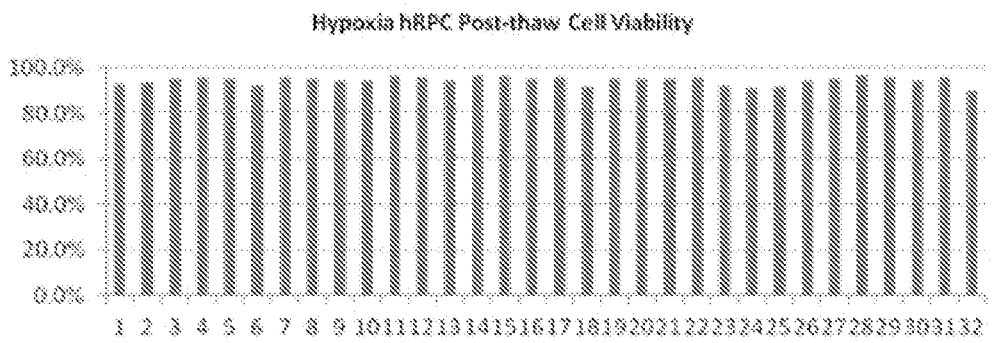
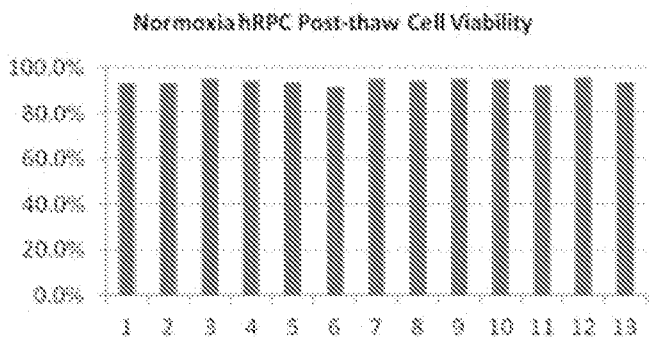


FIGURE 12

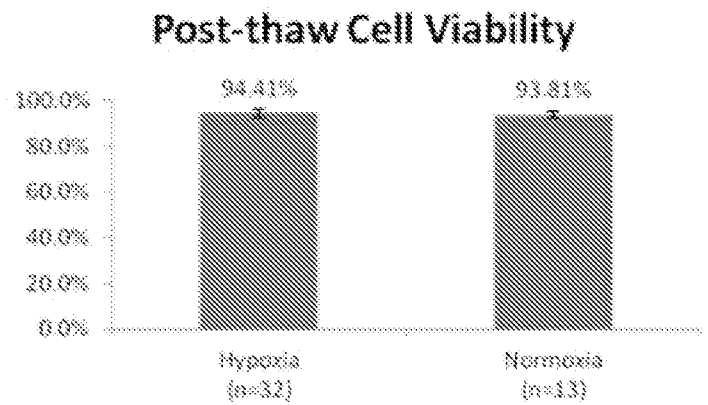
A



B



C



D

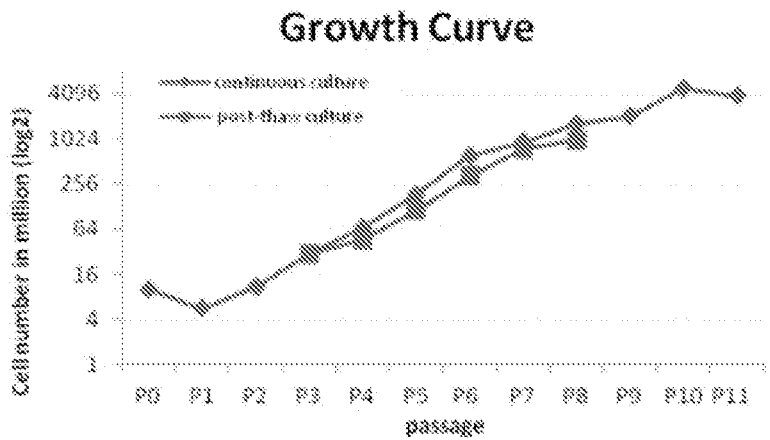


FIGURE 13

FIG. 14/55

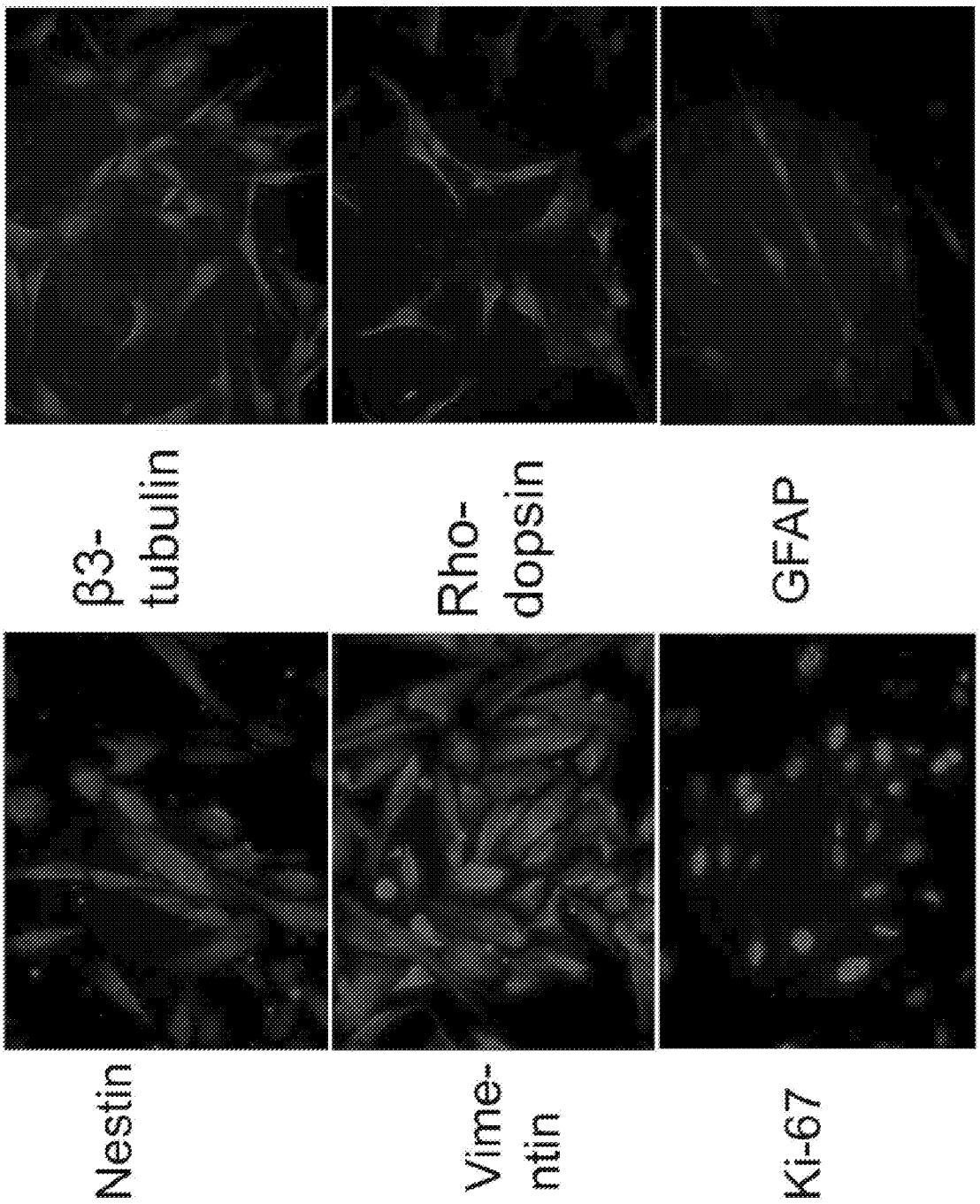


FIGURE 14

In UL

Gene profile by time point

D10=1 (as control)

Endogenous control: β-actin

Time point:

- D13 (0.5 month)
- D31 (1 month)
- D52 (2 months)
- D97 (3 months)
- D114 (4 months)

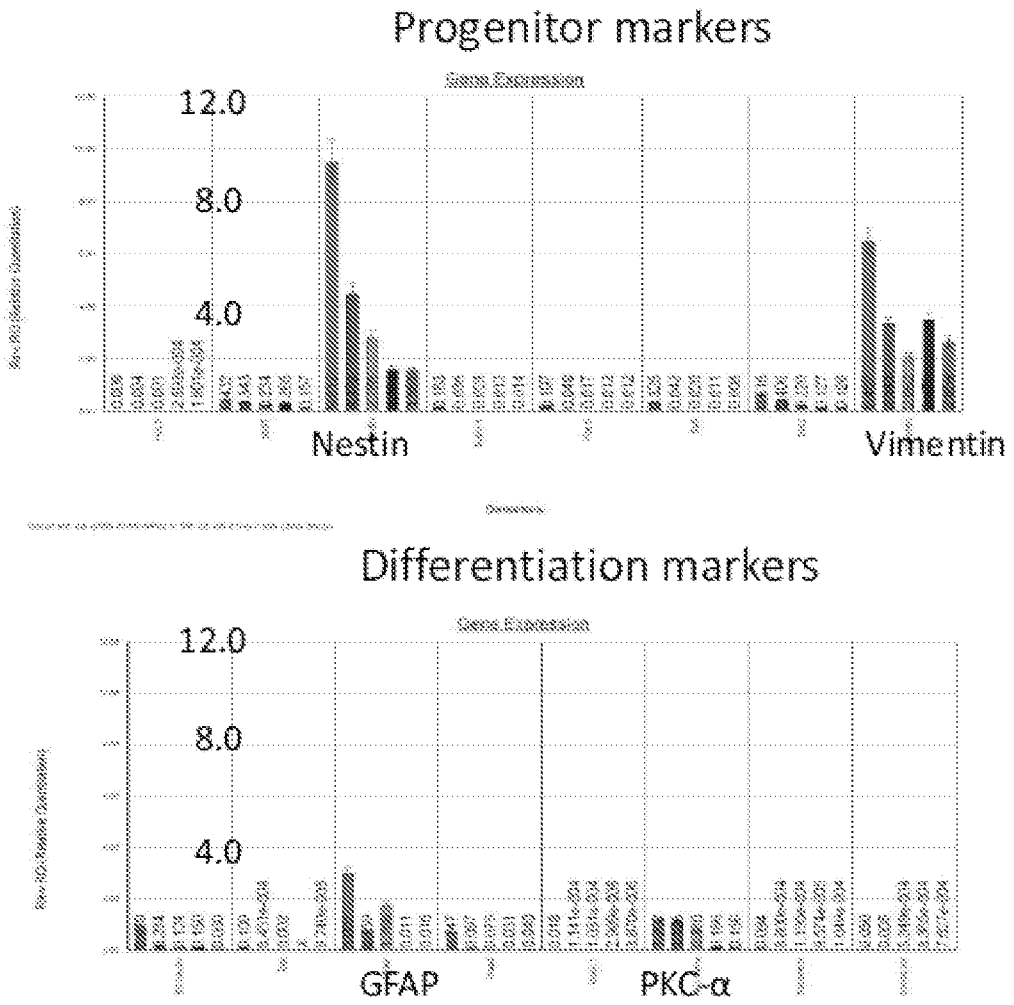
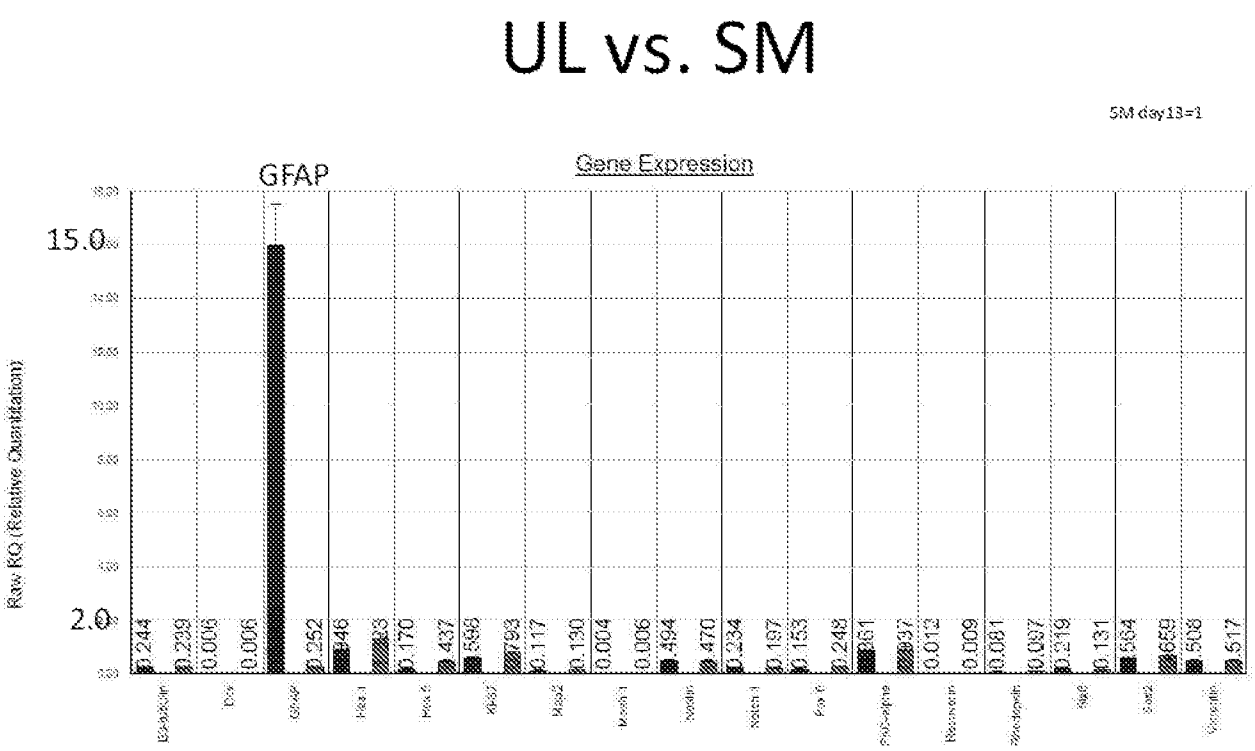


FIGURE 15

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FIG. 16/55

A



B

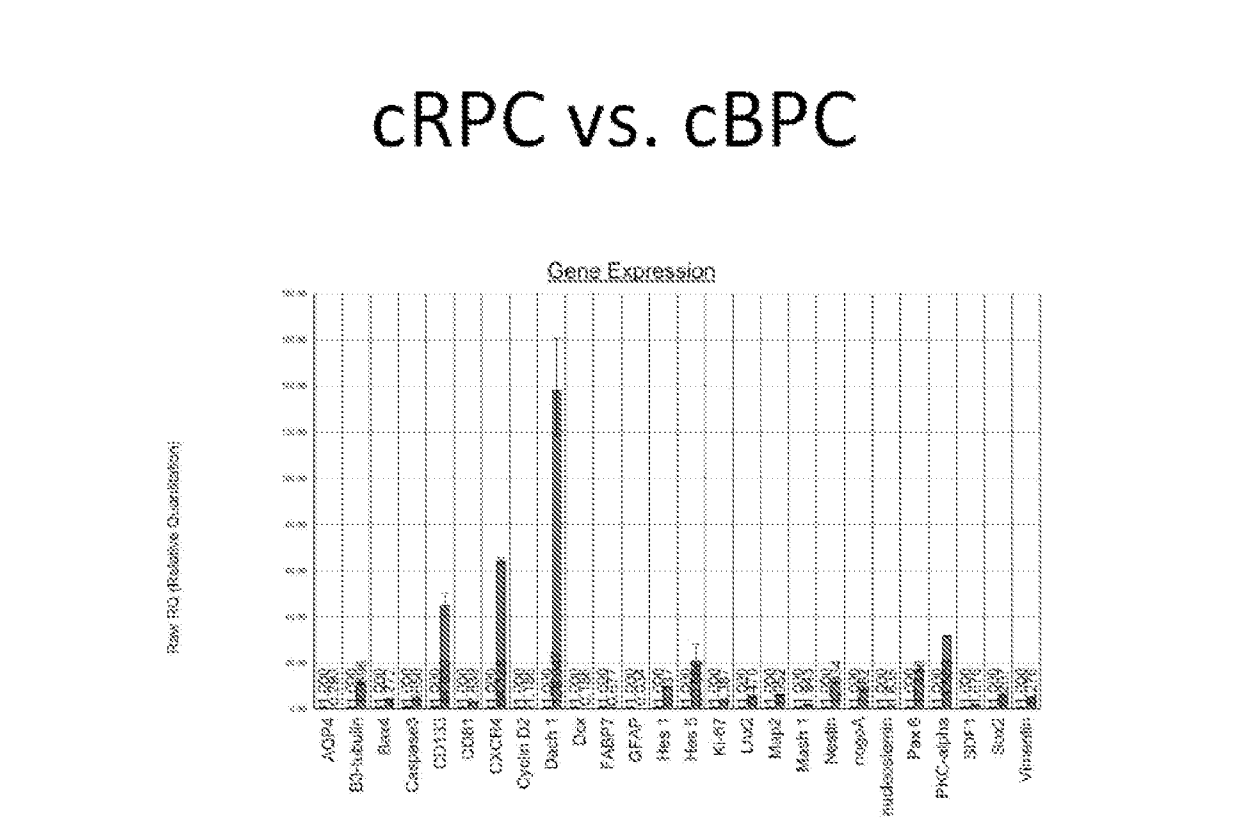


FIGURE 16

WO 2012/158910

PCT/US2012/038342

ANTIBODIES USED Labeling

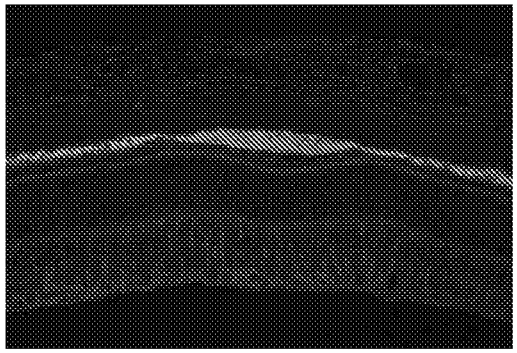
Anti-RFP	injected cells
Anti-vimentin	Müller cells
Anti-rod opsin	rod outer segments and some rod cell bodies as the protein redistributes due to the degeneration

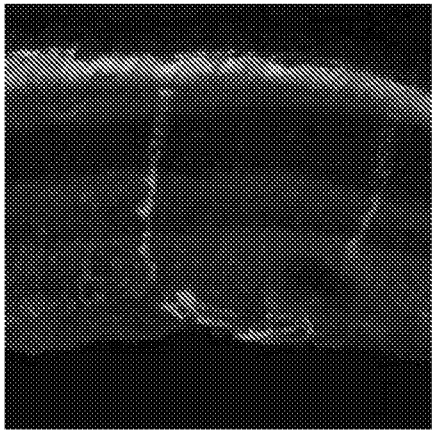
OR

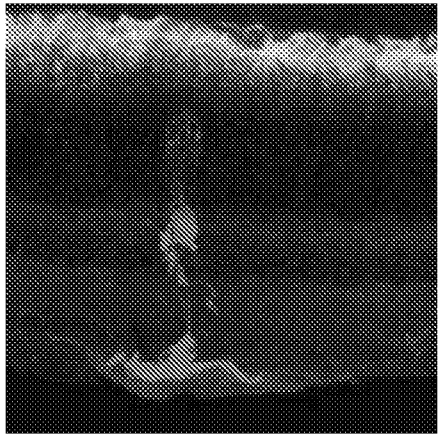
Anti-Ezrin	RPE microvilli and Müller cell microvilli at the OLM

OR

Protein kinase C	rod bipolar cells







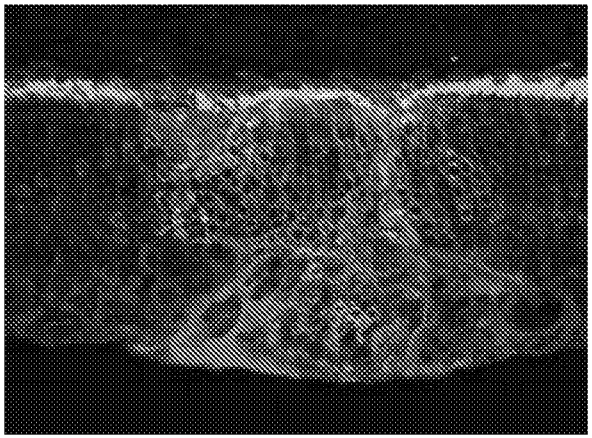


FIGURE 17

FIG. 18/55

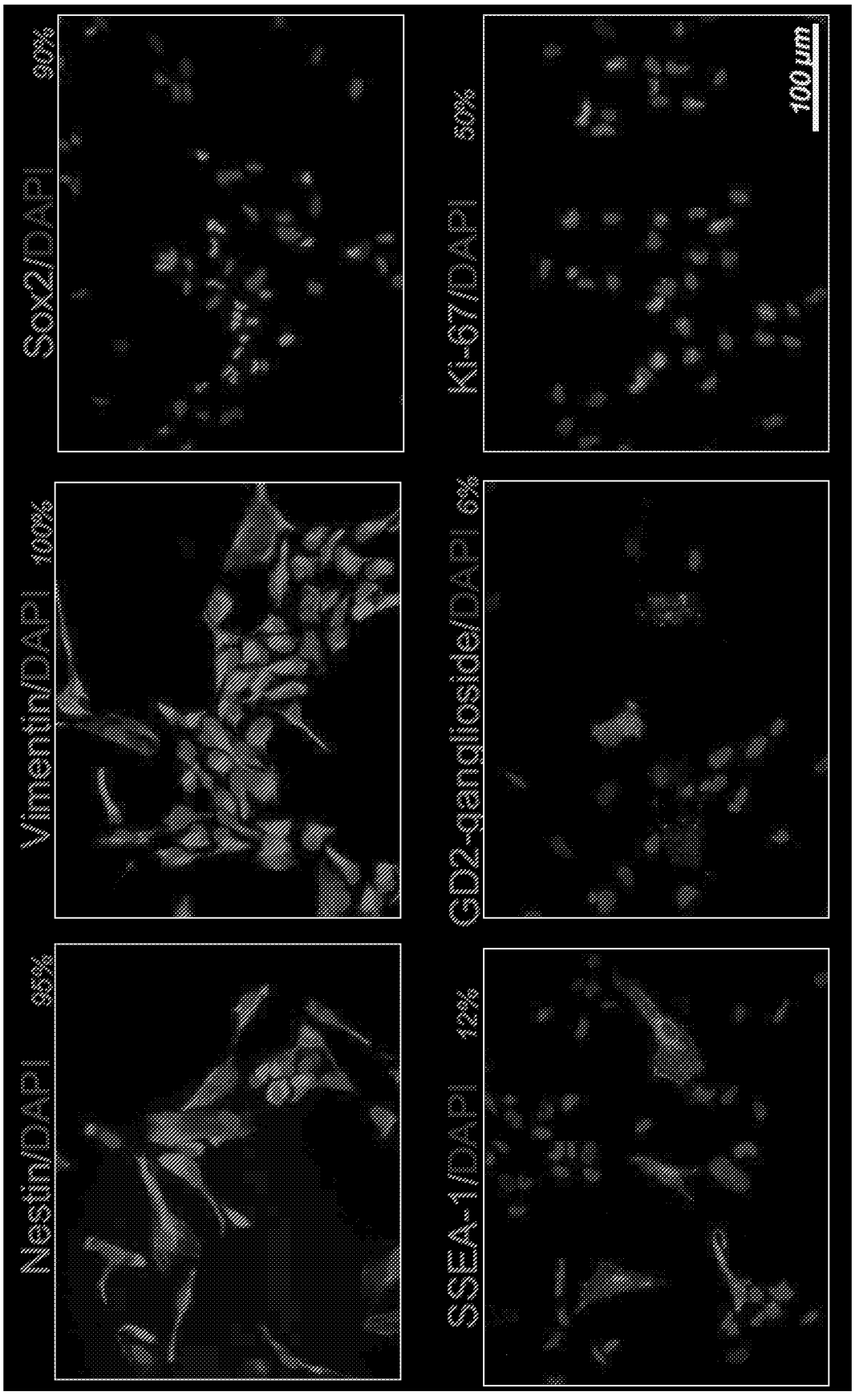


FIGURE 18

FIG. 19/55

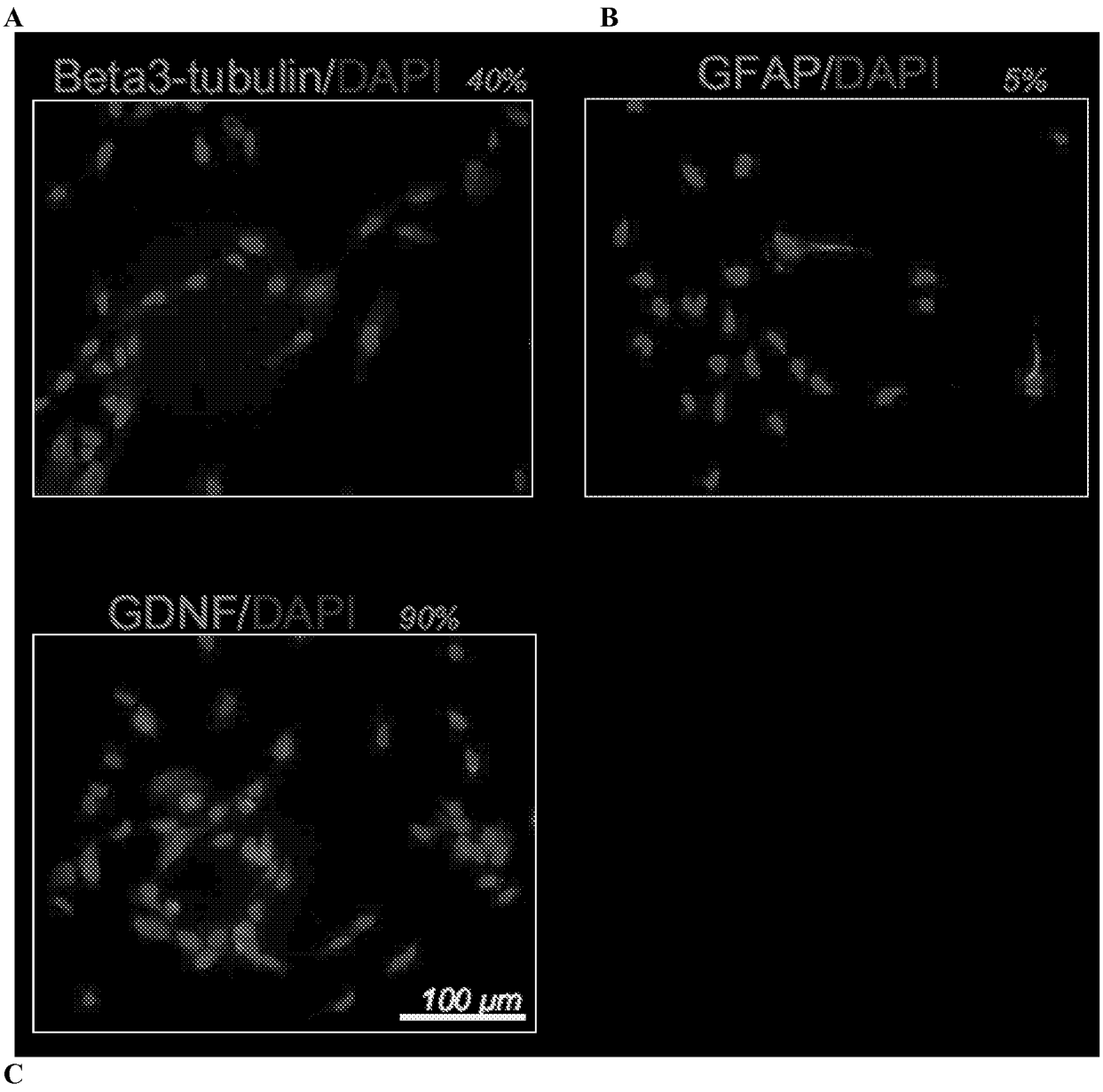


FIGURE 19

FIG. 20/55

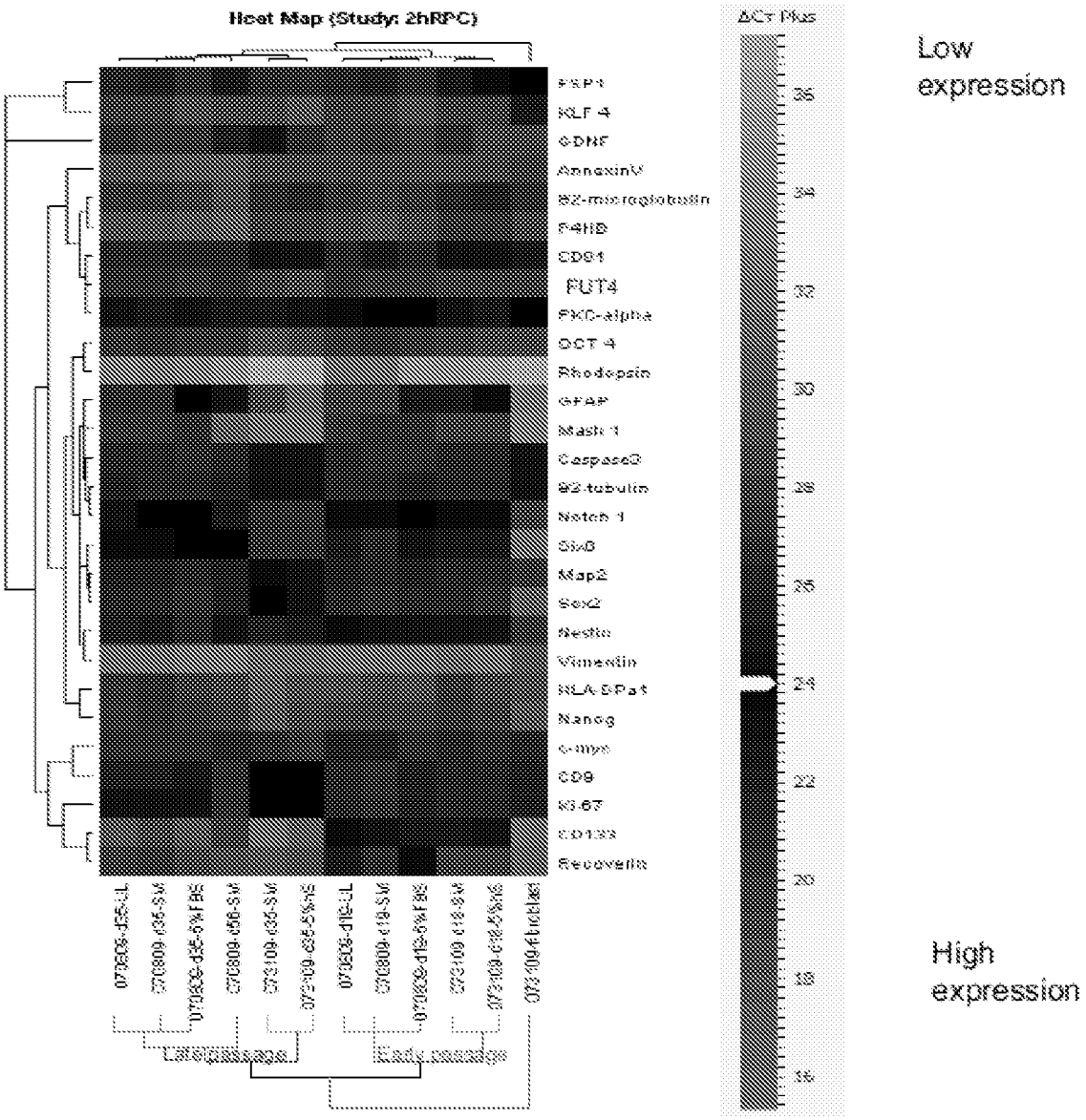
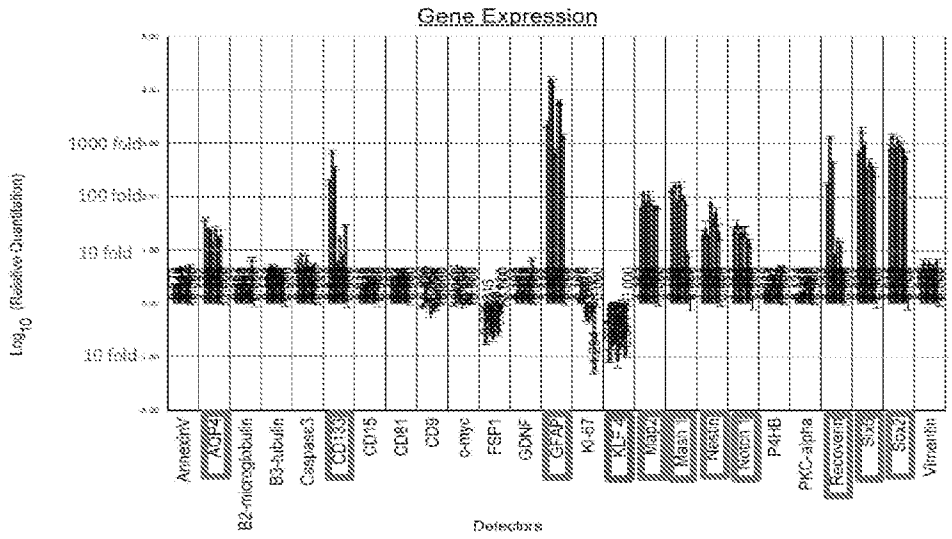


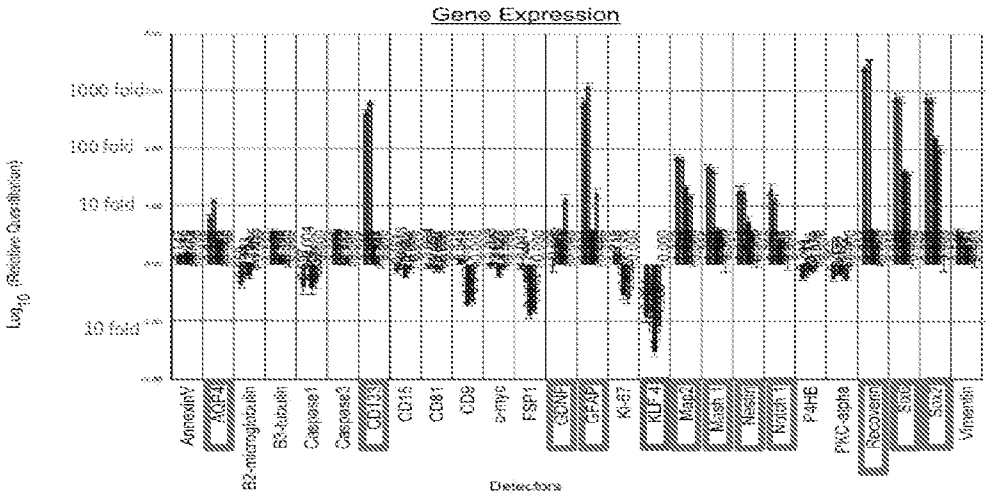
FIGURE 20

FIG. 21/55

A



B



C

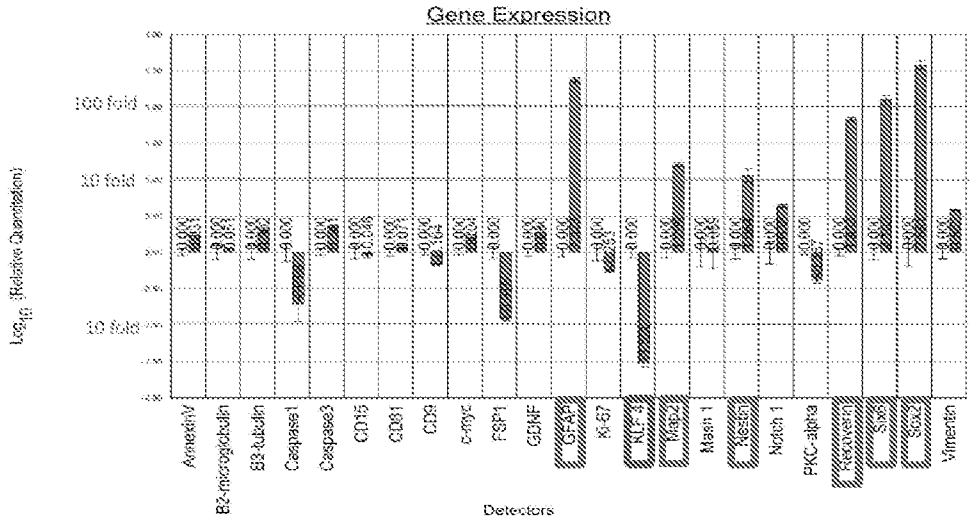


FIGURE 21

Top 10 genes up-regulated >10 fold (hRPC vs h-fibroblast=1)

	070809hRPC	073109hRPC	011310hRPC
1	AQP4	AQP4	
2	CD133	CD133	
3	**GFAP**	**GFAP**	**GFAP**
4 ** (down)	Klf4	Klf4	Klf4
5	Map2	Map2	Map2
6	Mash1	Mash1	
7	Nestin	Nestin	Nestin
8	Notch1	Notch1	
9	**Recoverin**	**Recoverin**	**Recoverin**
10	**six6**	**six6**	**six6**
11	sox2	sox2	sox2

FIGURE 22

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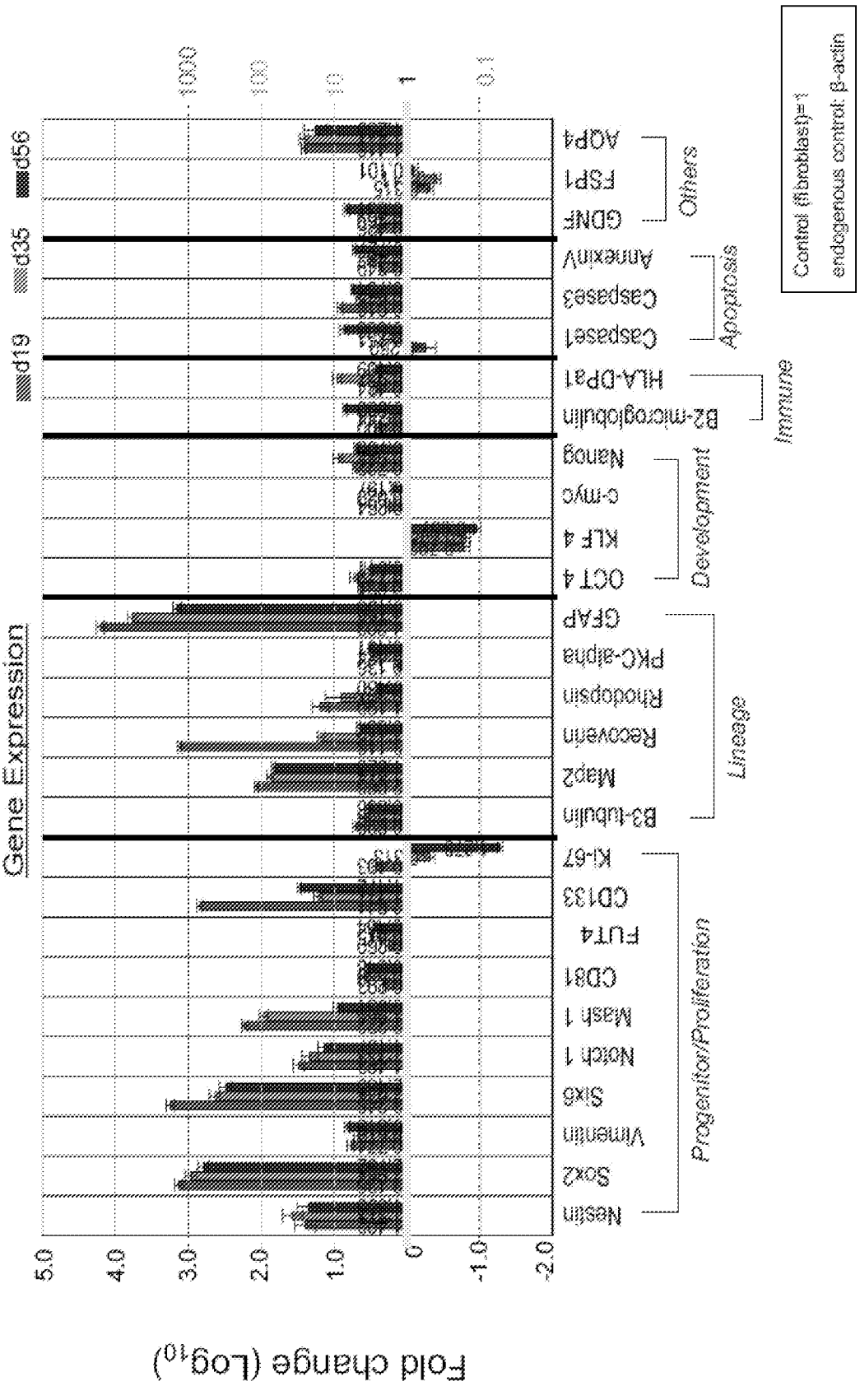


FIG. 23/55

FIGURE 23

FIG. 24/55

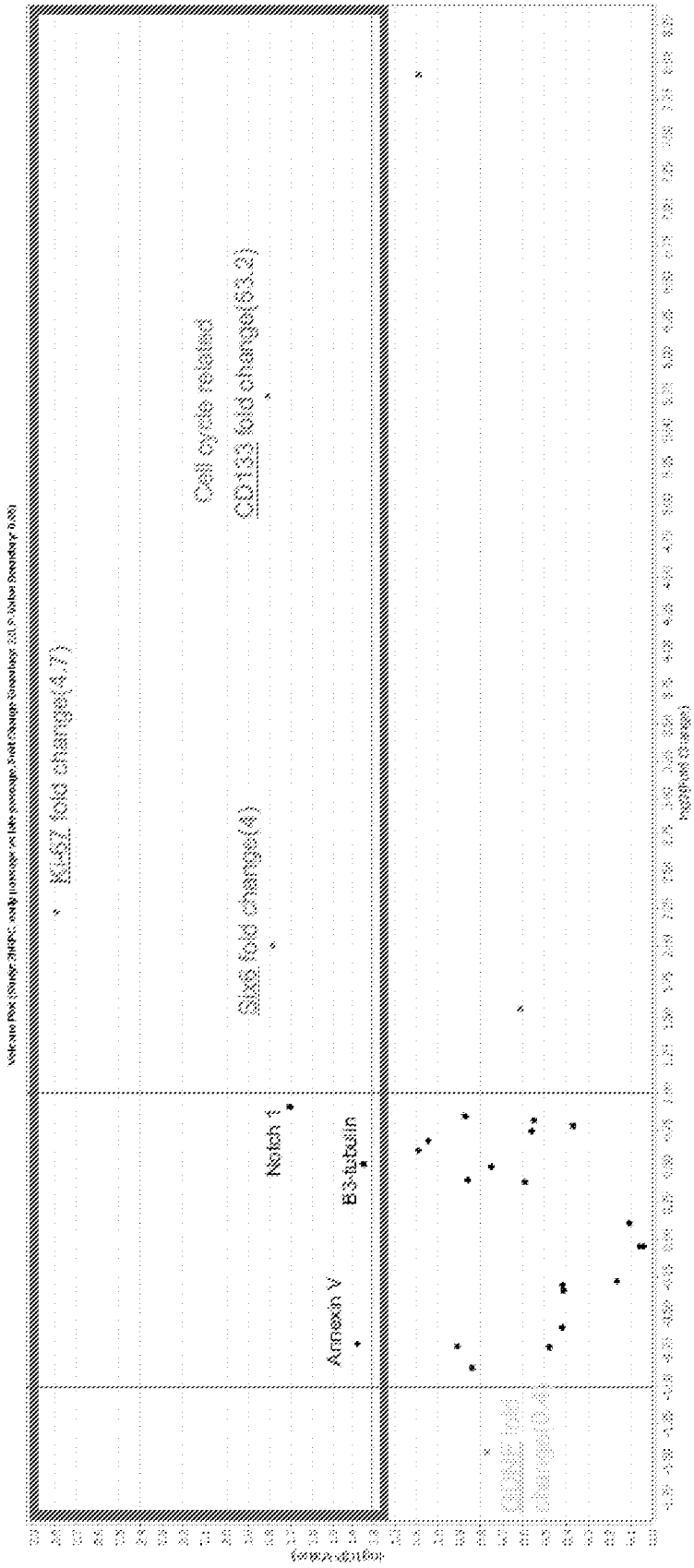


FIGURE 24

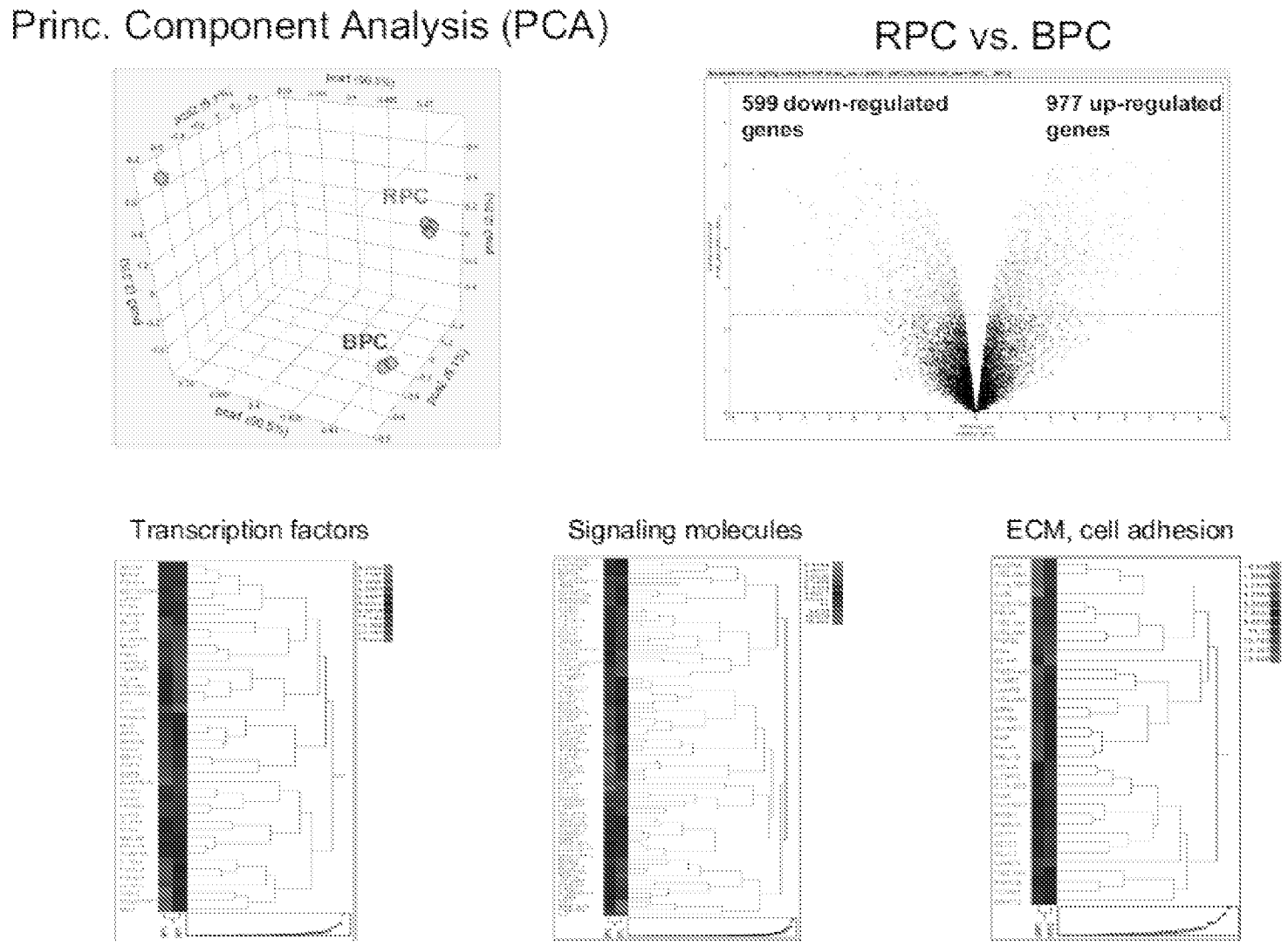


FIGURE 25

WO 2012/158910 PCT/US2012/038342

FIG. 26/55

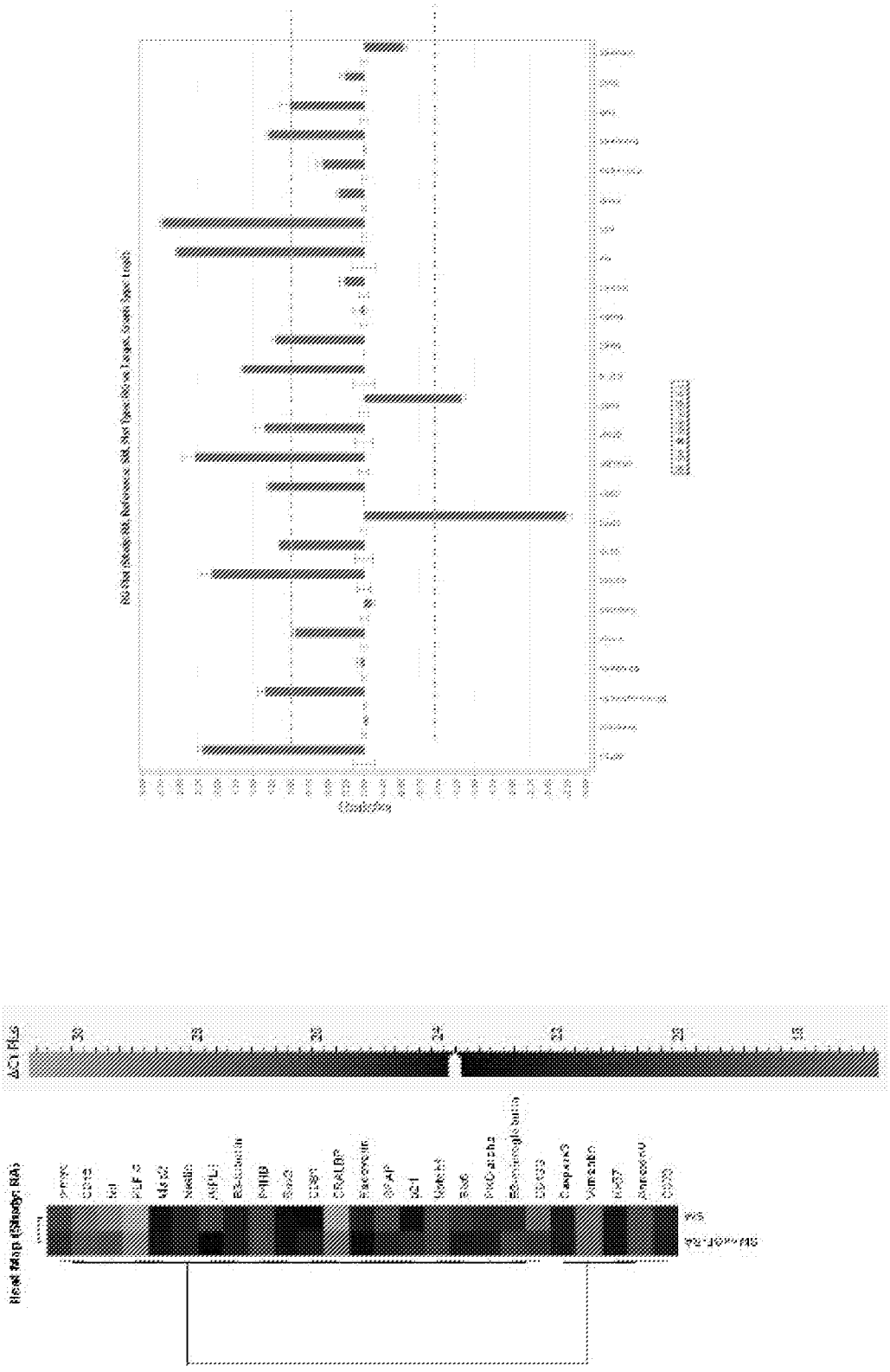


FIGURE 26

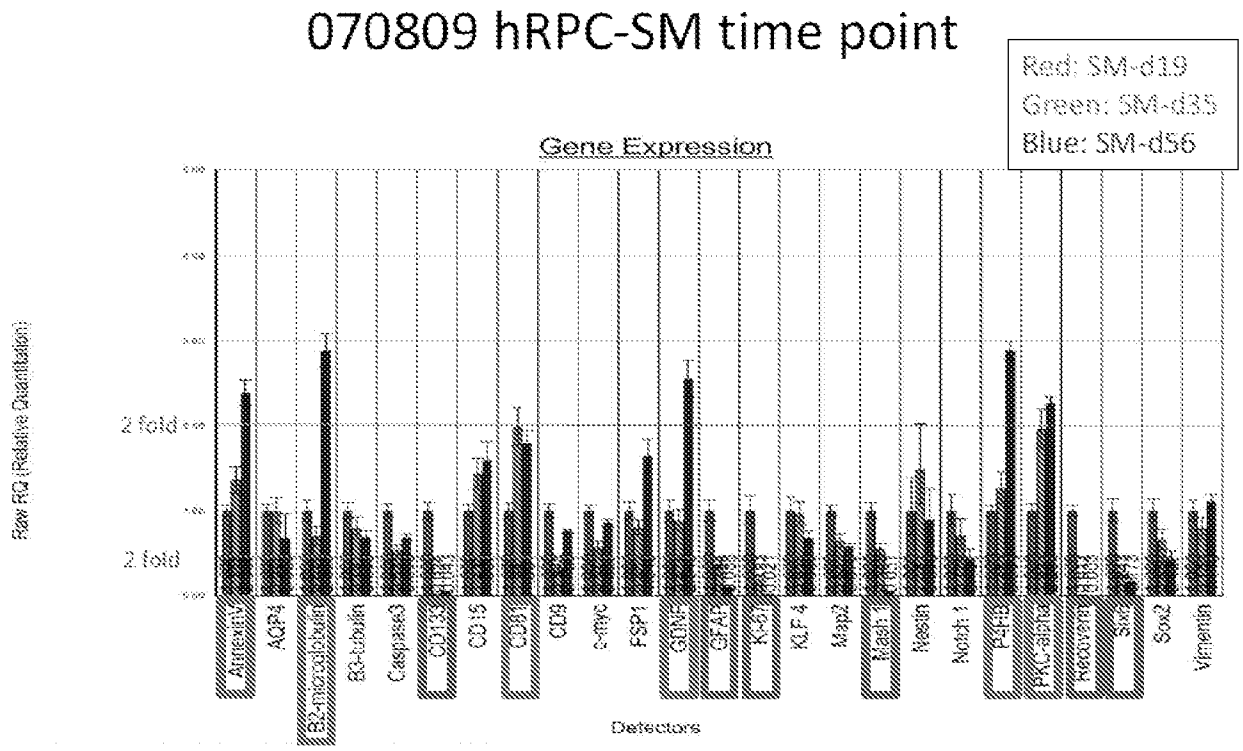
hRPC time point design

012208hRPC		070809hRPC			073109hRPC		011310hRPC
SM-d17 ~1		SM-d19~1	SM-UL-d19~1	SM-5%FBS-d19~1	SM-d18~1	SM-5%hS-d18~1	SM-d22
SM-d22	UL-d22	SM-d35	SM-UL-d35	SM-5%FBS-d35	SM-d35	SM-5%hS-d35	
SM-d27	UL-d27	SM-d56					
SM-d38	UL-d38						
SM-d48	UL-d48						
SM-d72	UL-d72						
SM-d99	UL-d99						

FIGURE 27

FIG. 28/55

A



B

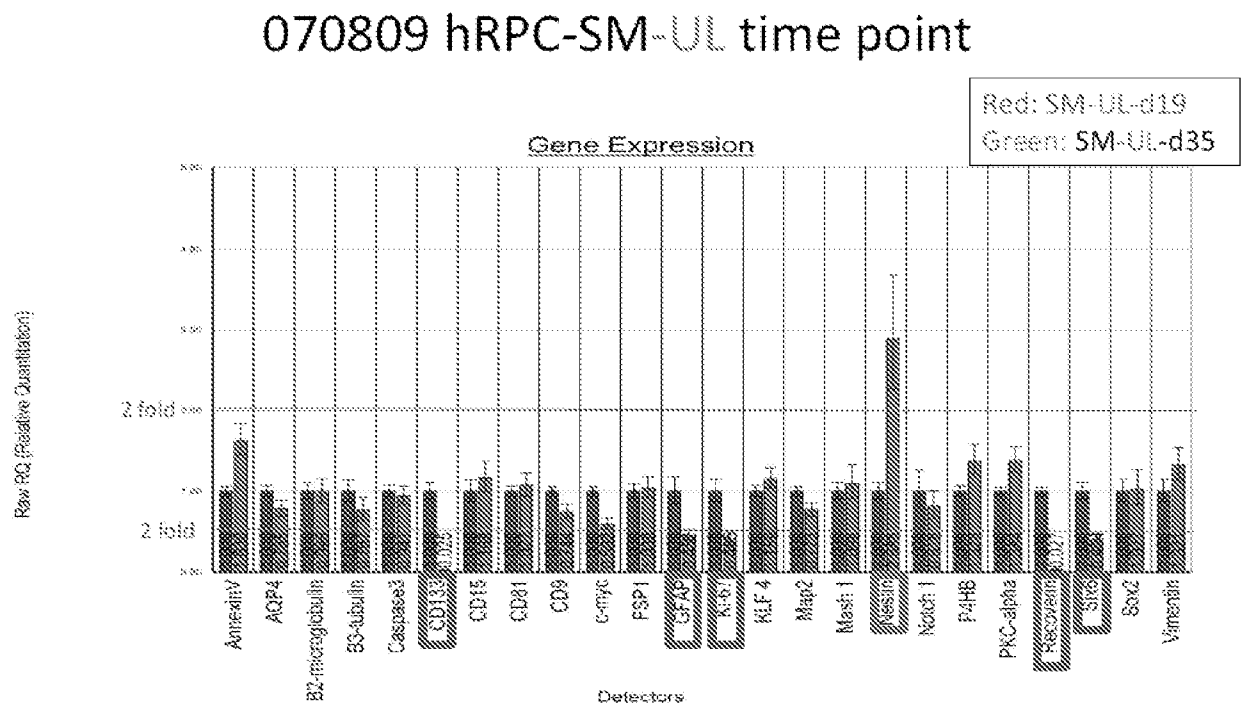
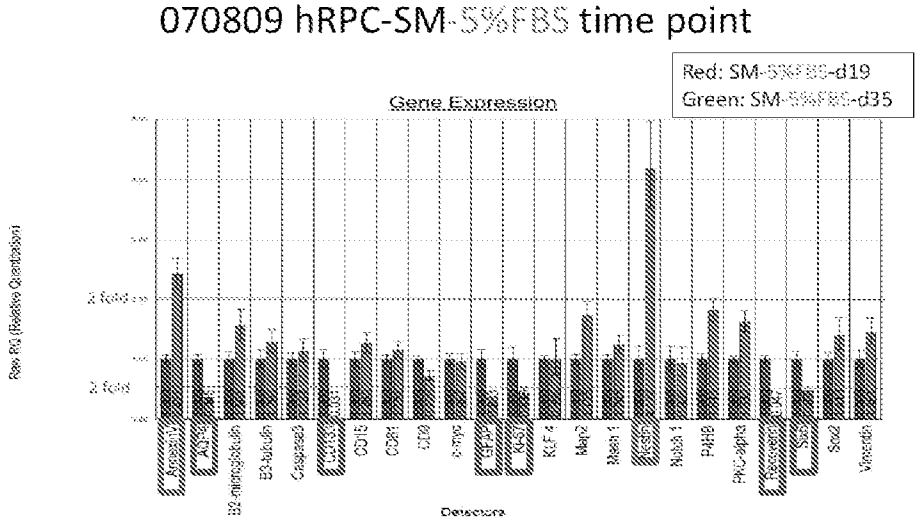


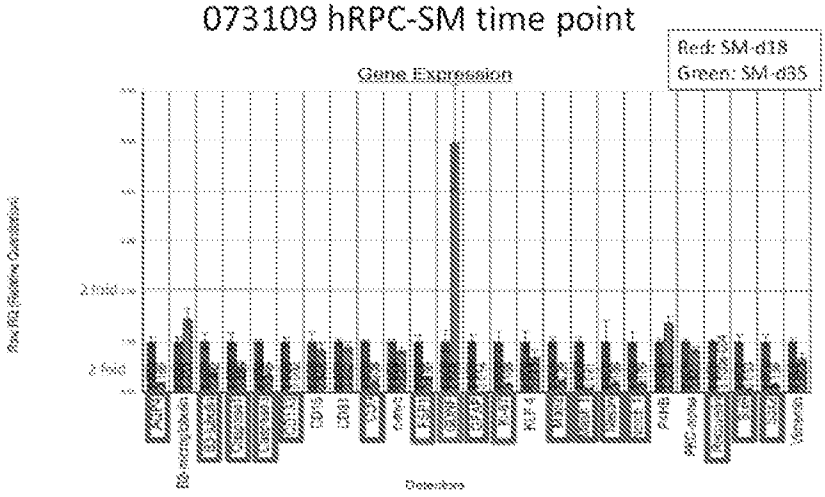
FIGURE 28

FIG. 29/55

A



B



C

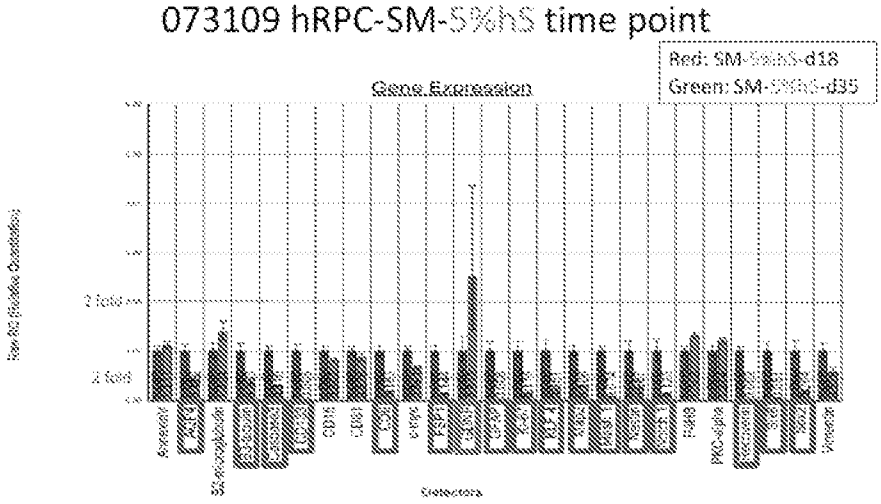


FIGURE 29

hRPC time point comparison

Red ↓ green ↑

01220thRPC		07009hRPC			07310thRPC	
SM	UL	SM	SM-UL	SM-5%FBS	SM	SM-5%hS
AQP4	AQP4			AQP4	AQP4	AQP4
b3-tubulin?	b3-tubulin?				b3-tubulin	b3-tubulin
caspase-1	caspase-1				caspase-1	x
caspase-3	caspase-3				caspase-3	caspase-3
CD9	CD9				CD9	CD9
FSP1	FSP1				FSP1	FSP1
		CD133	CD133	CD133	CD133	CD133
CD81	CD81	CD81				
GDNF	GDNF	GDNF	GDNF?	GDNF?	GDNF	GDNF
GFAP	GFAP	GFAP	GFAP	GFAP	GFAP	GFAP
KI67	KI67	KI67	KI67	KI67	KI67	KI67
Klf4	Klf4					Klf4
Map2	Map2				Map2	Map2
Nestin	Nestin		Nestin	Nestin	Nestin	Nestin
		Mash1			Mash1	Mash1
Notch1	Notch1				Notch1	Notch1
		P4HB				
PKCa?		PKCa				
Recoverin	Recoverin	Recoverin	Recoverin	Recoverin	Recoverin	Recoverin
six6	six6	Six6	Six6	Six6	Six6	Six6
Sox2	Sox2				Sox2	Sox2
vimentin	vimentin					
	CD15?					
b2-microglobulin	b2-microglobulin	b2-microglobulin				
c-myc	c-myc					
AnexinV	AnexinV	AnexinV		AnexinV		

FIGURE 30

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FIG. 31/55

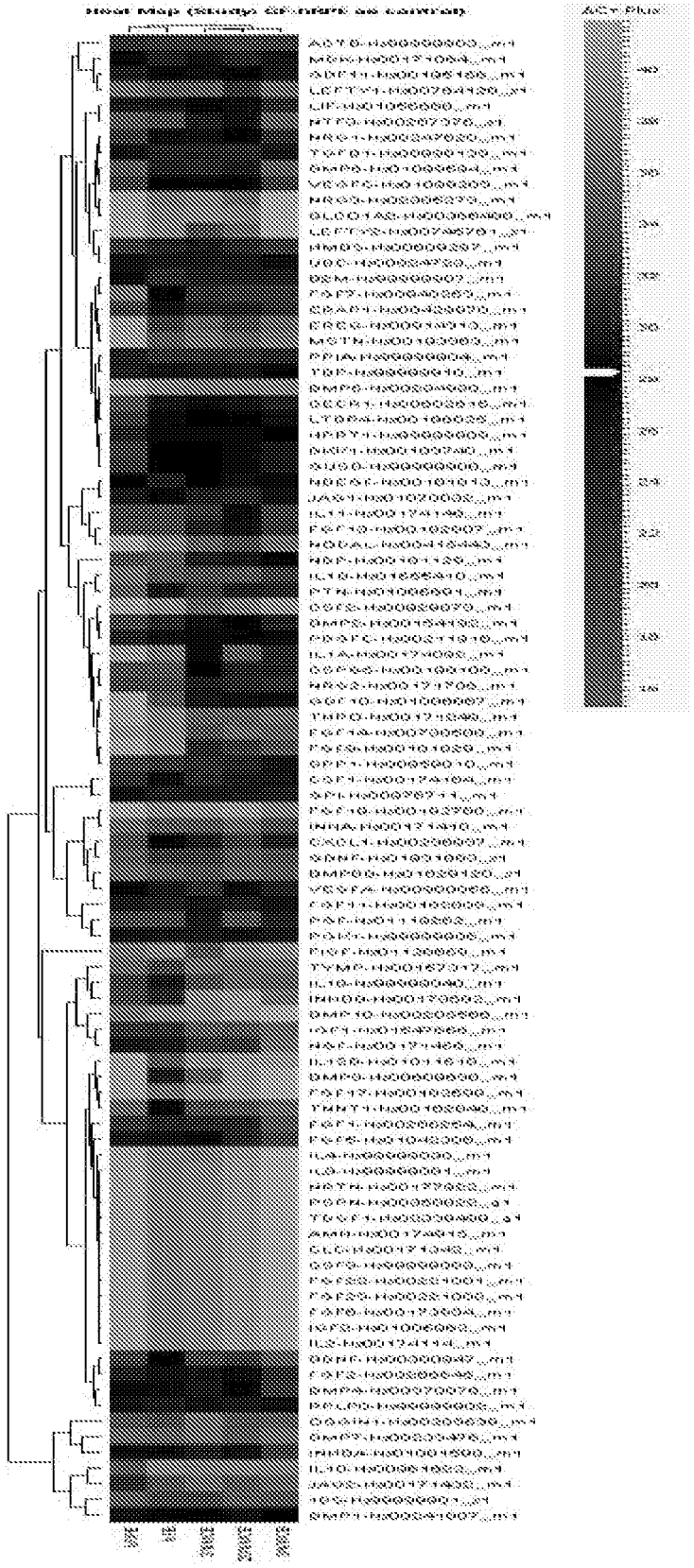


FIGURE 31

FIG. 32/55

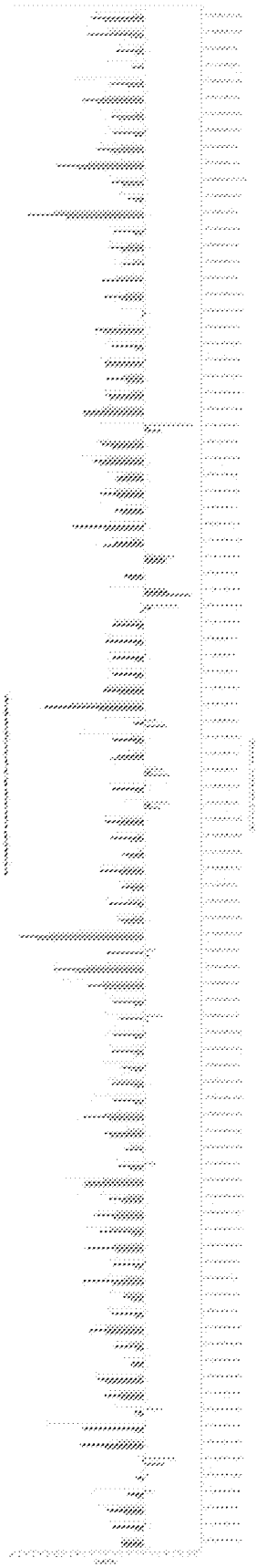
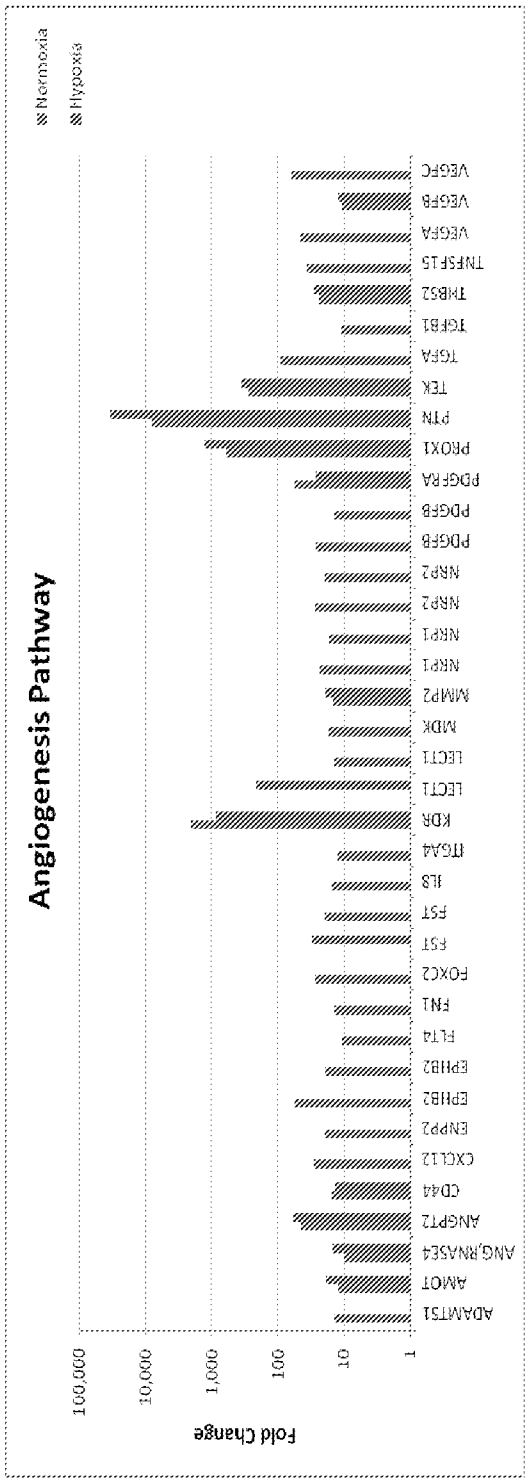
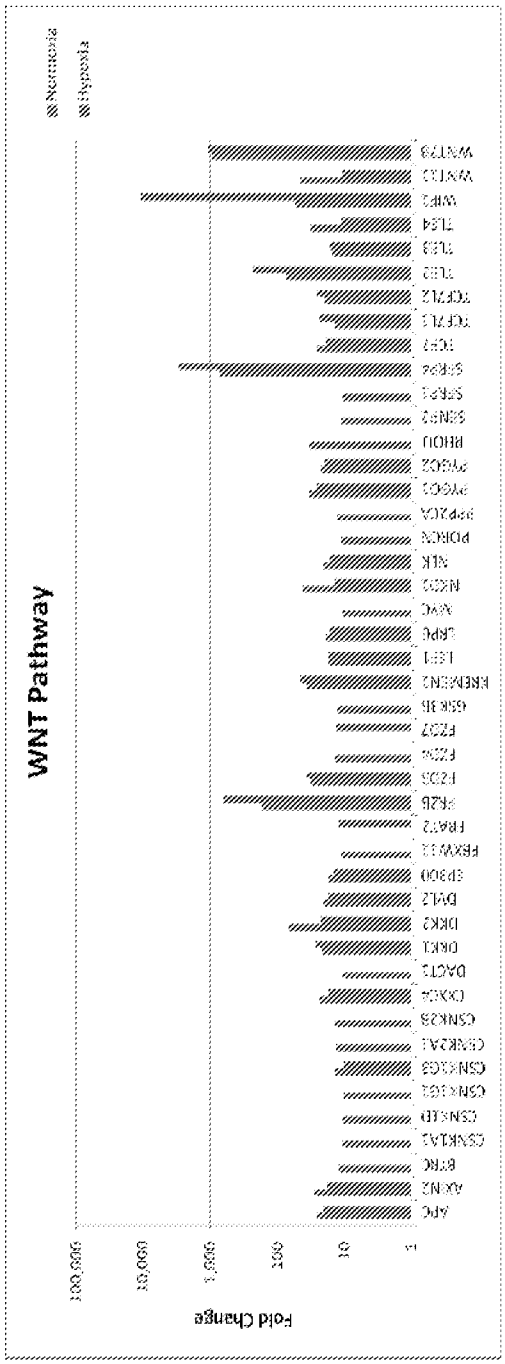


FIGURE 32

FIG. 33/55



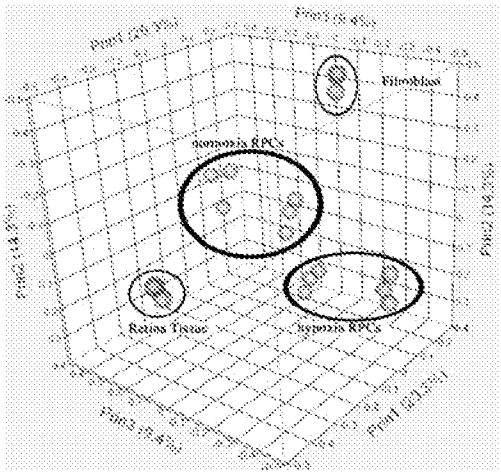


A B

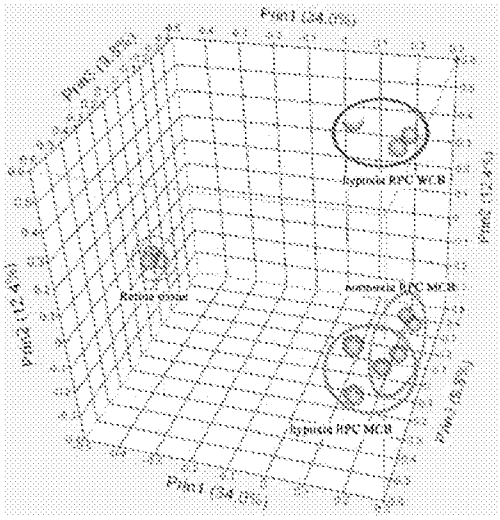
FIGURE 33

FIG. 34/55

A



B



C

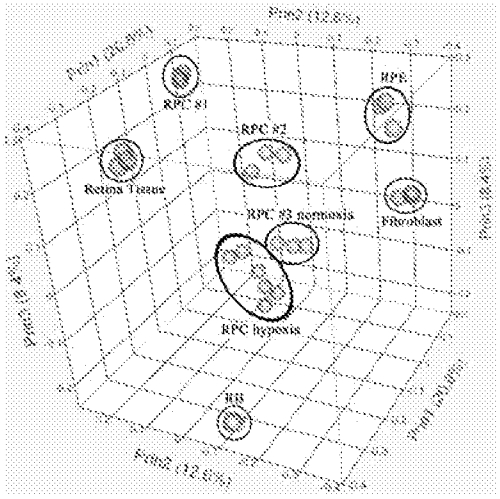


FIGURE 34

FIG. 35/55

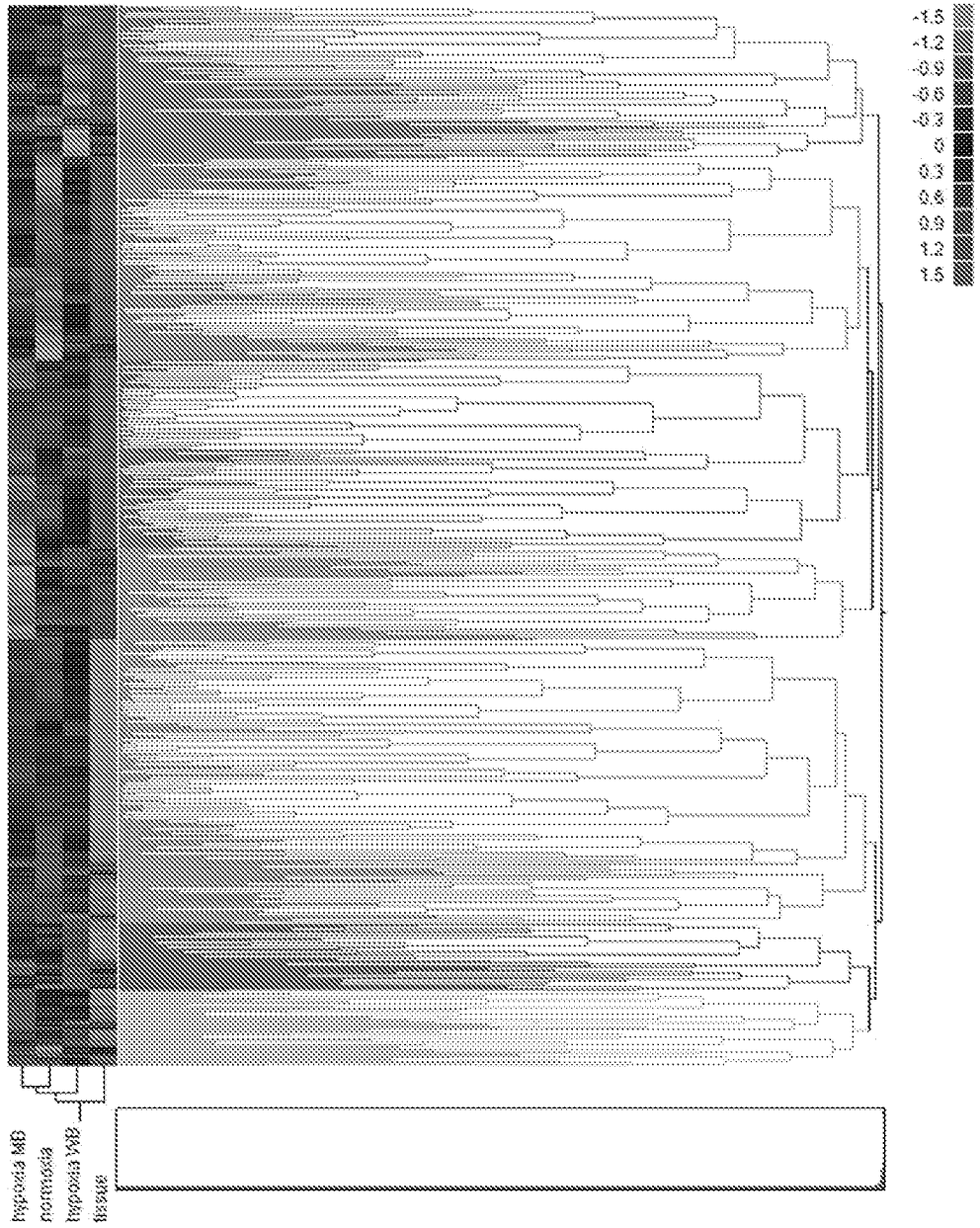


FIGURE 35

FIG. 36/55

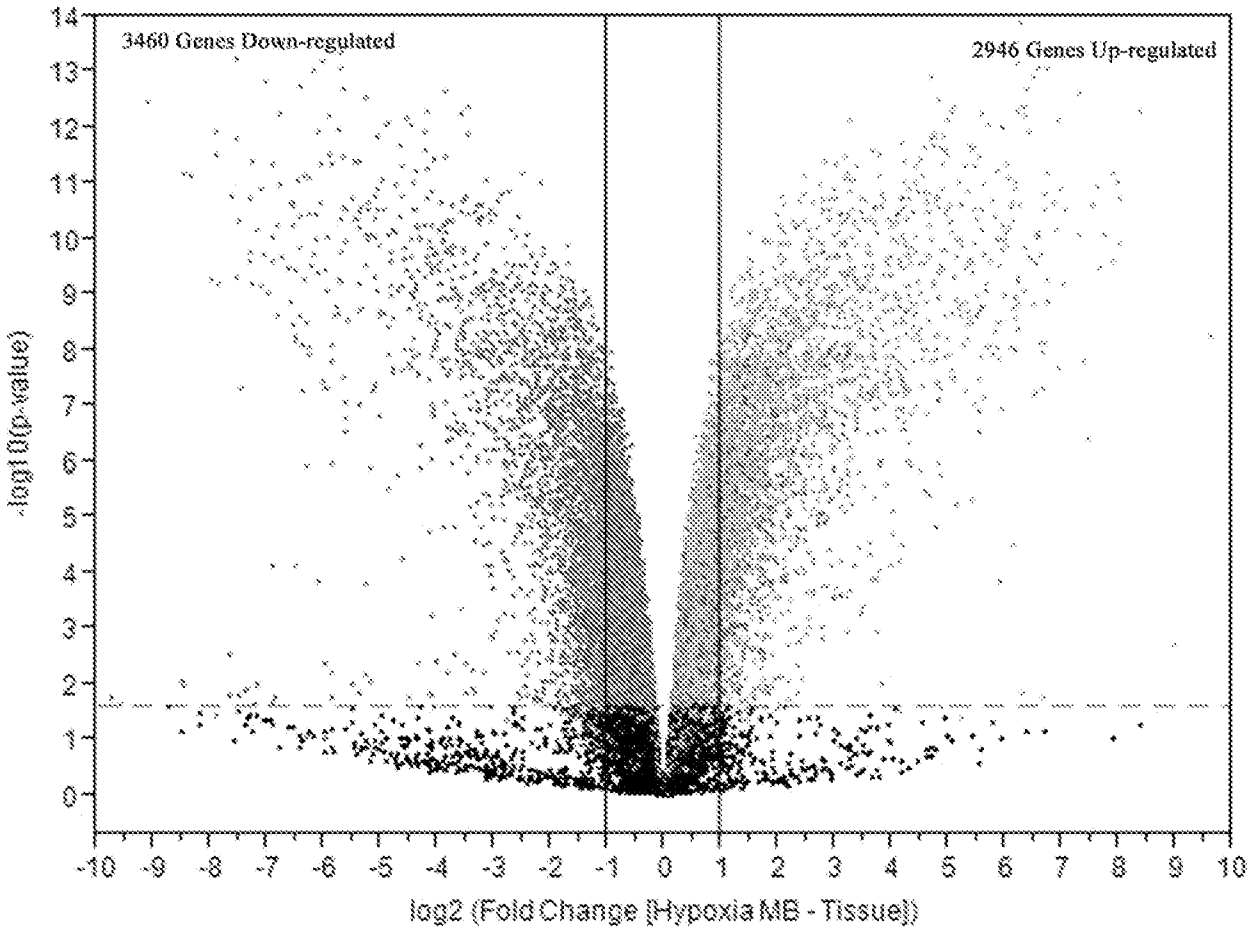
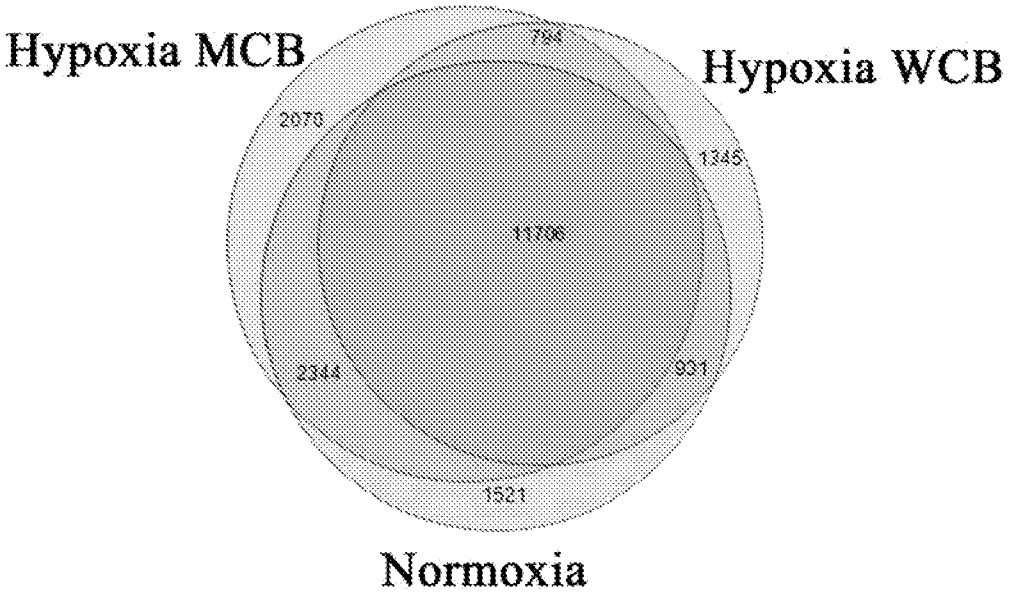


FIGURE 36

FIG. 37/55

A



B

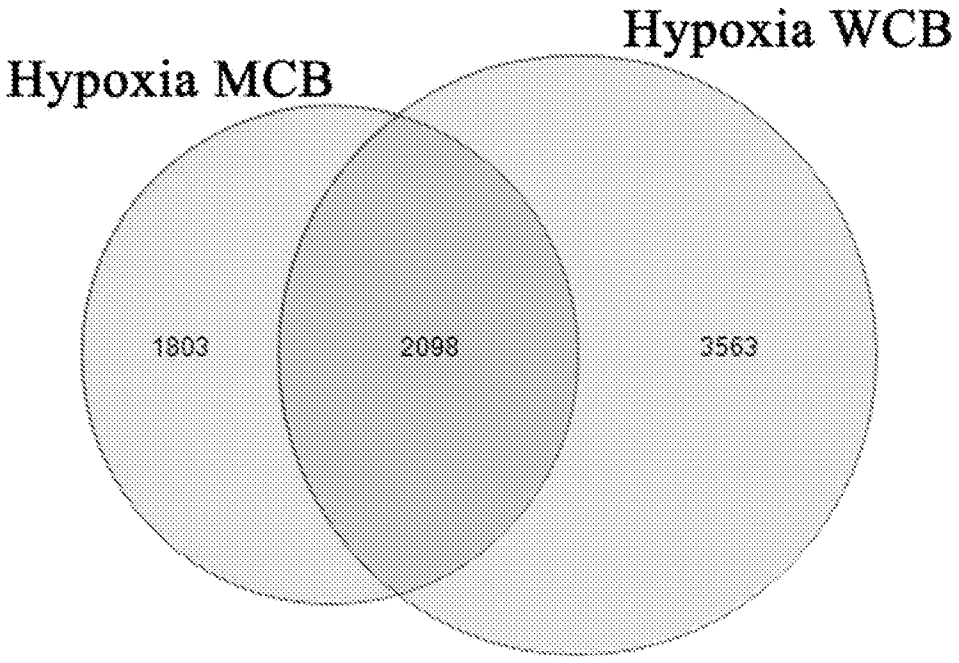
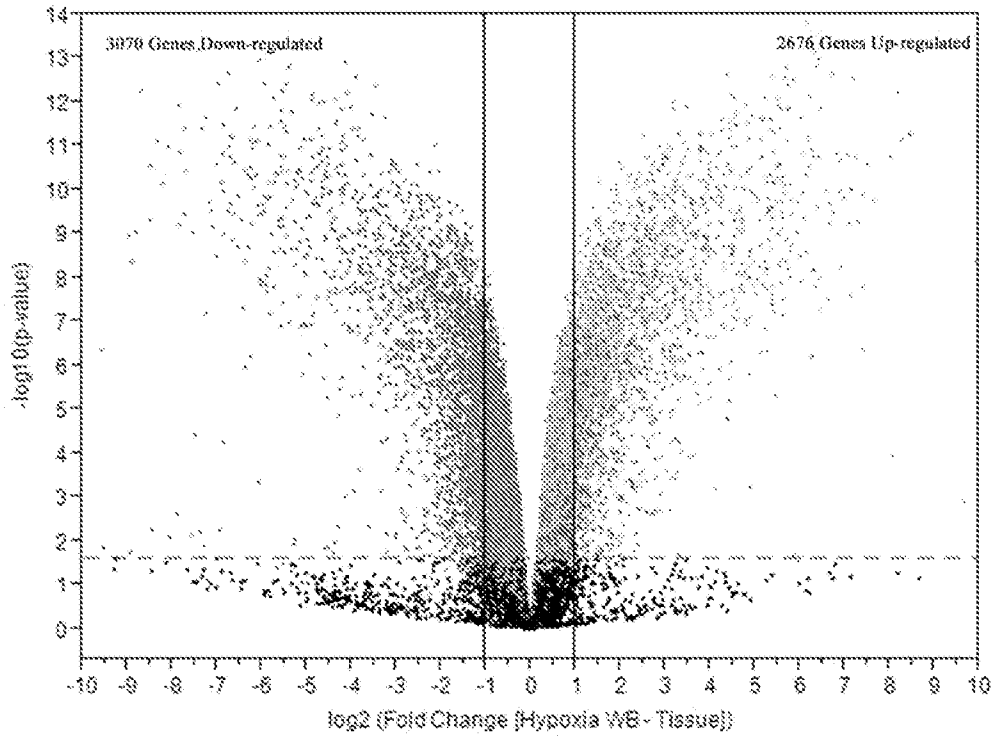


FIGURE 37

FIG. 38/55

A



B

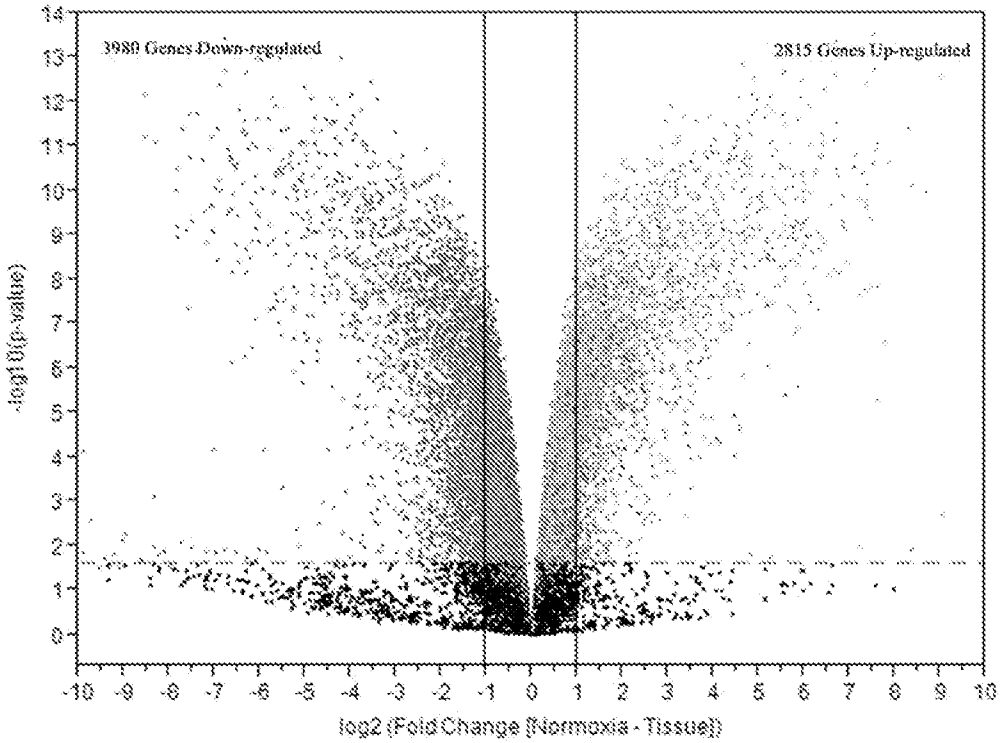
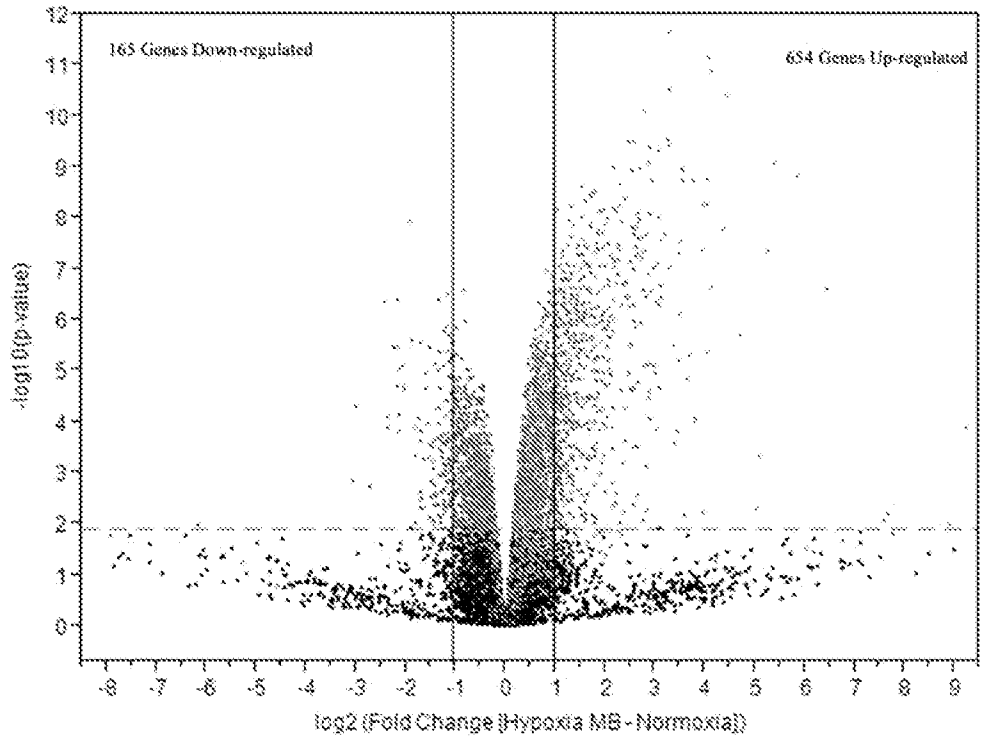


FIGURE 38

FIG. 39/55

A



B

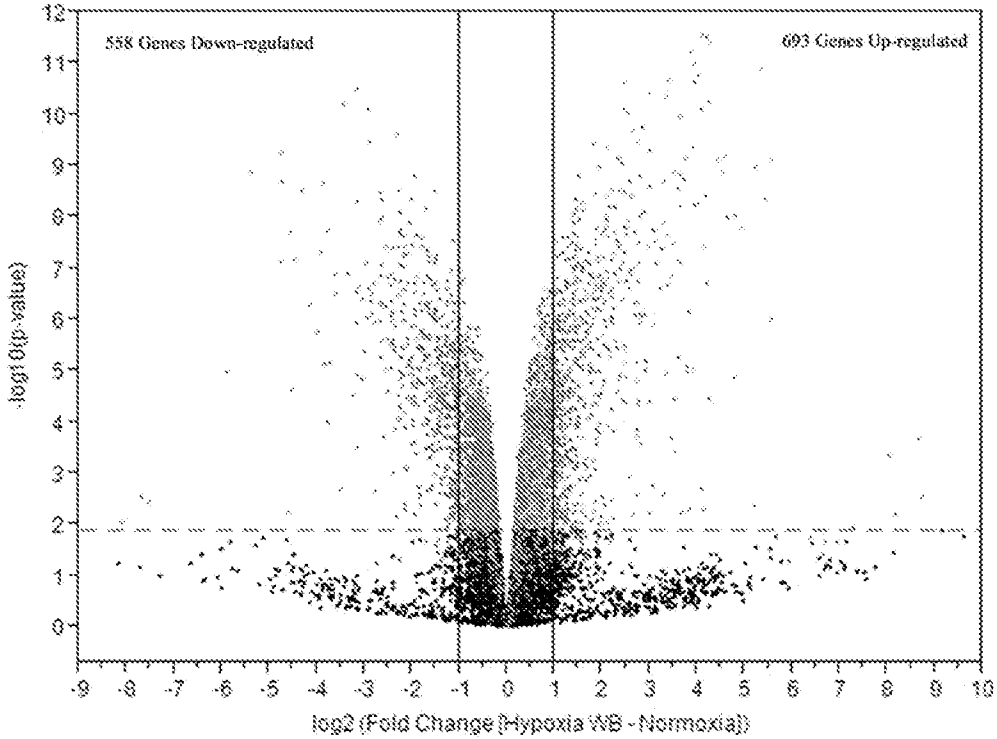


FIGURE 39

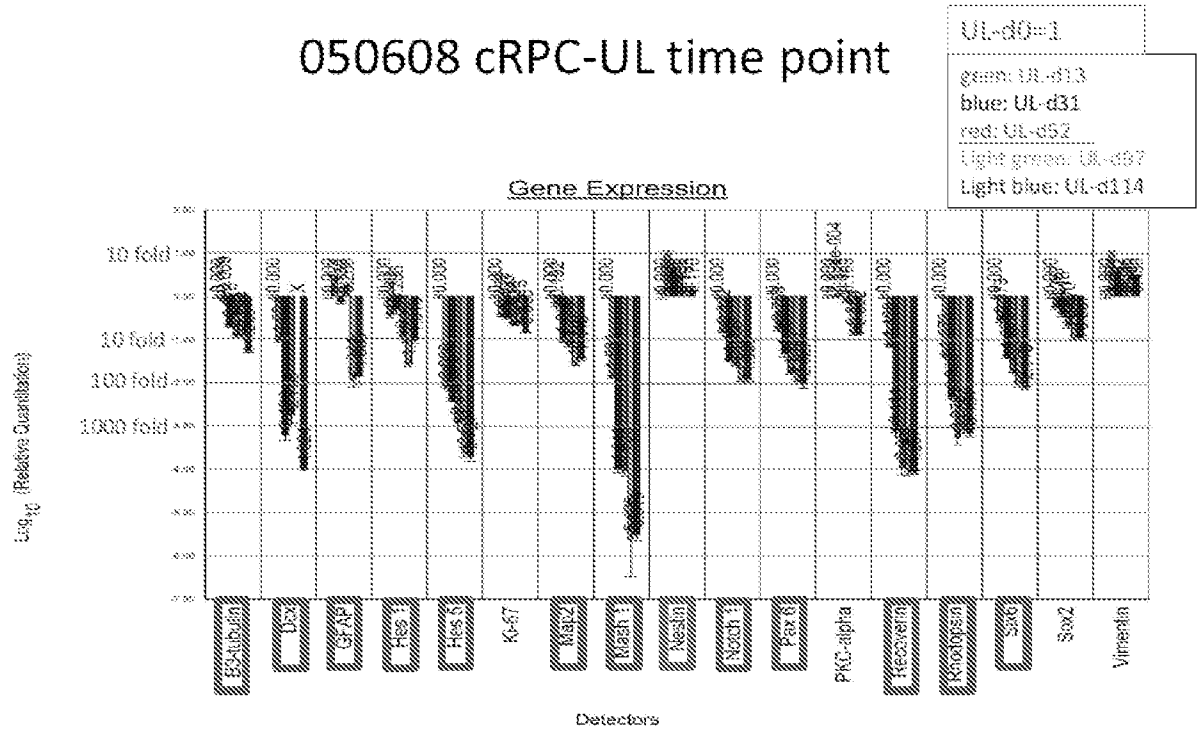
cRPC time point design

112707cRPC		050608cRPC		090808rcRPC	091208rcRPC
SM-d24	UL-d24	SM-d0=1	UL-d0=1	UL-d20	UL-d14=1
			UL-d13=1		UL-d135
		SM-d31	UL-d31		
			UL-d52		
			UL-d76		
			UL-d97		
			UL-d114		

FIGURE 40

FIG. 41/55

A



B

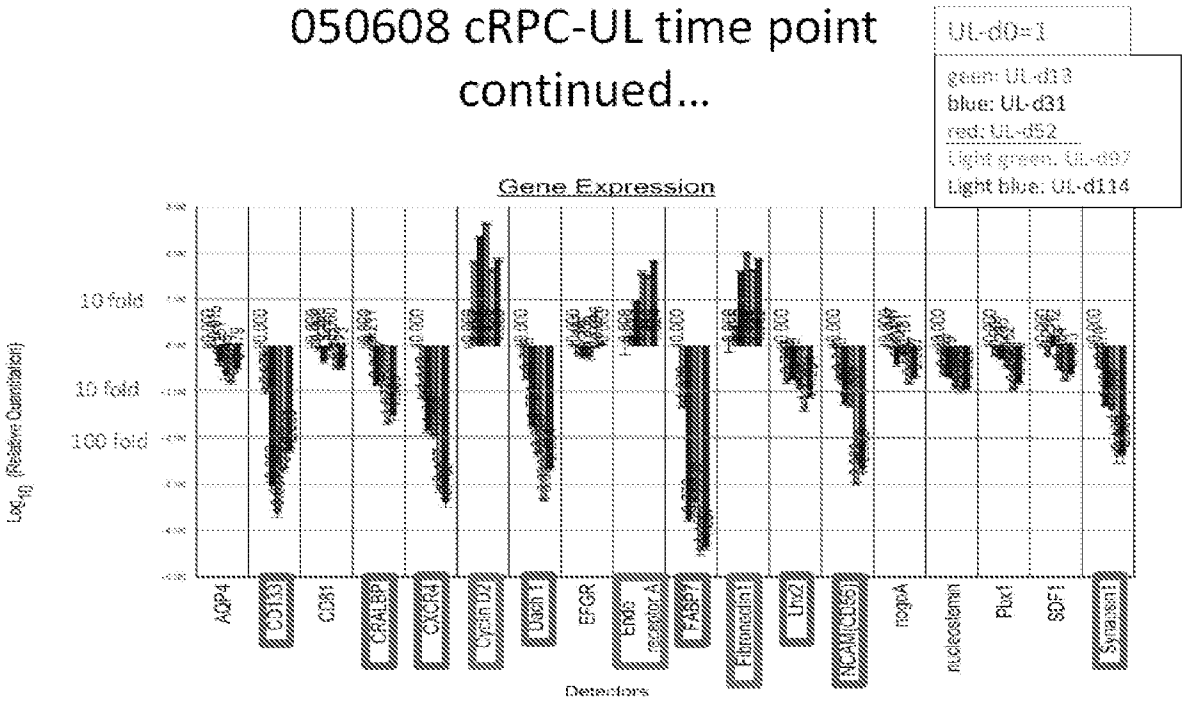
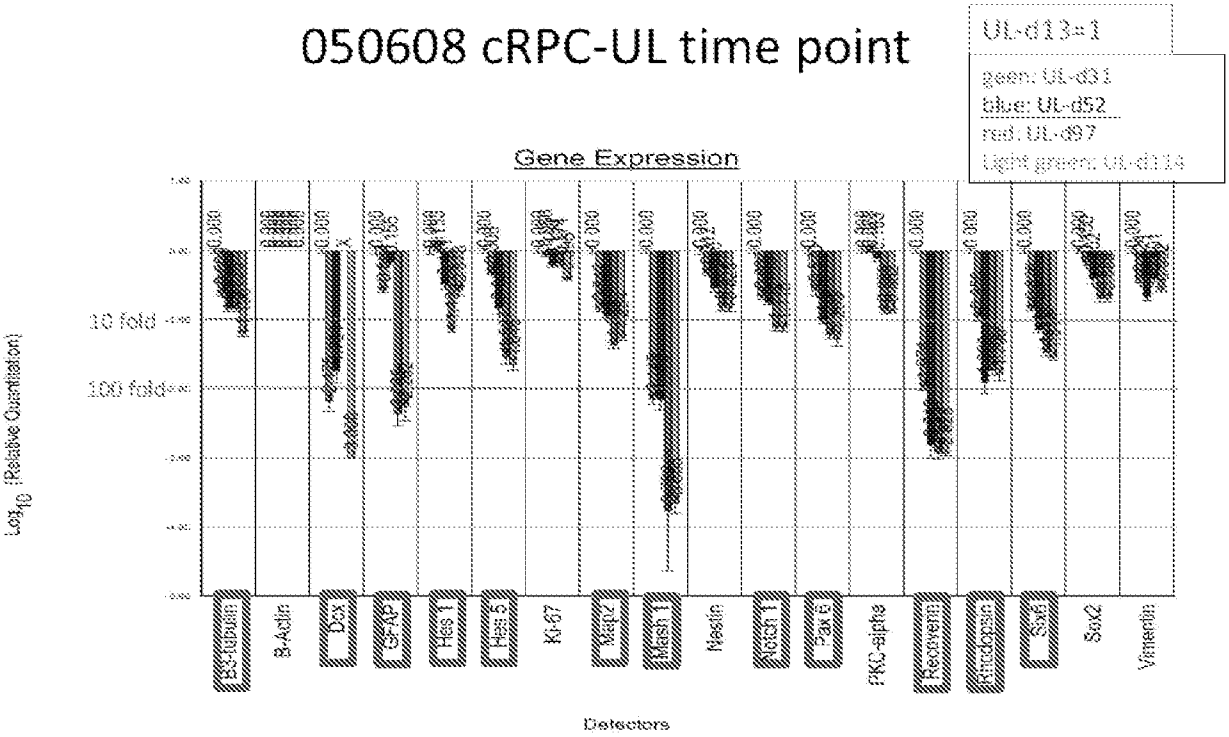


FIGURE 41

FIG. 42/55

A



B

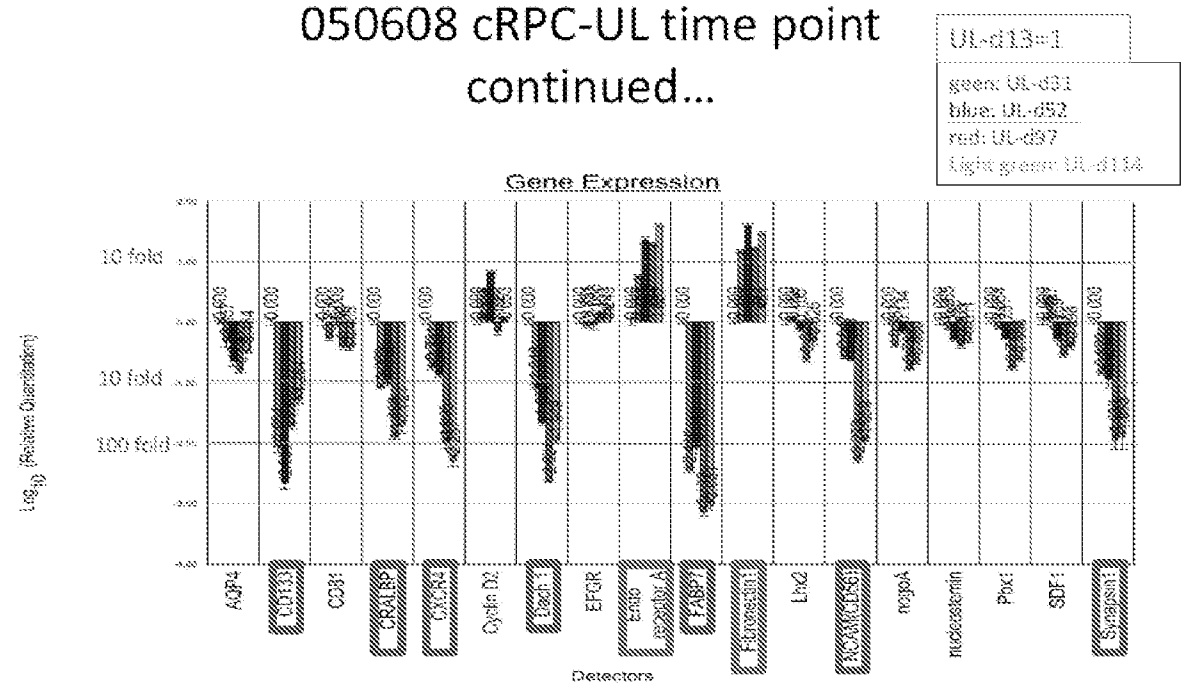
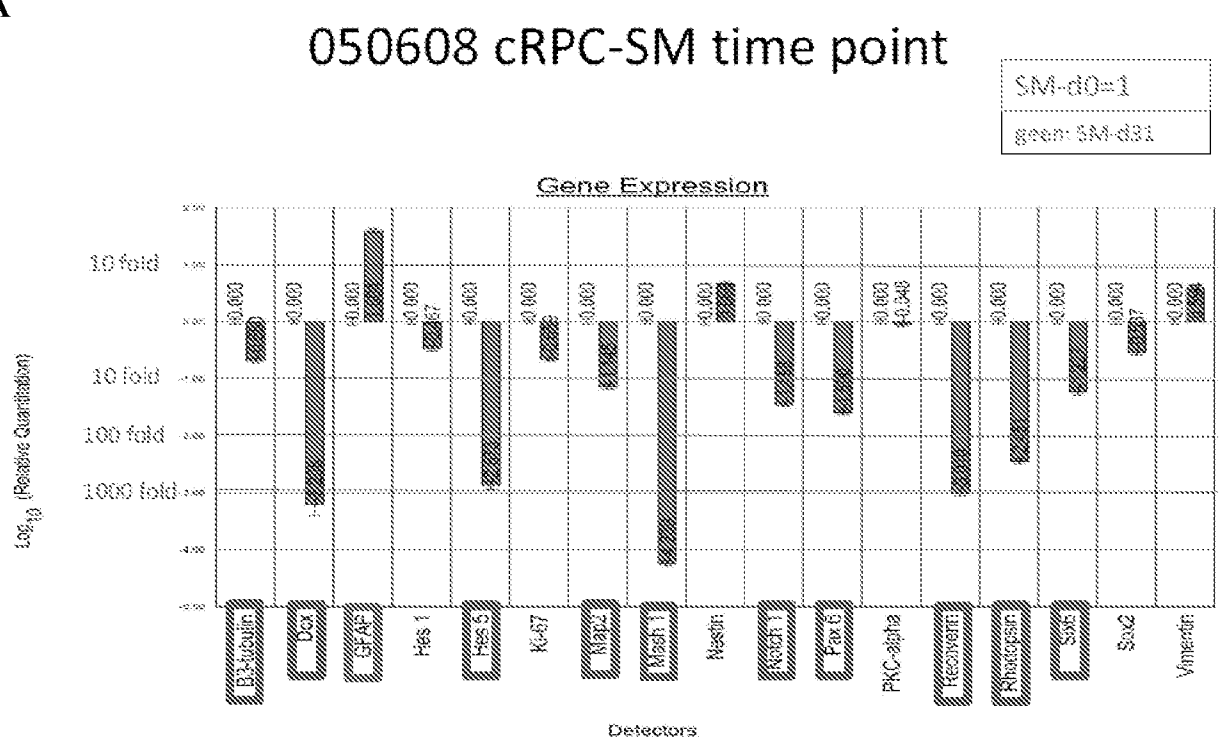


FIGURE 42

FIG. 43/55

A



B

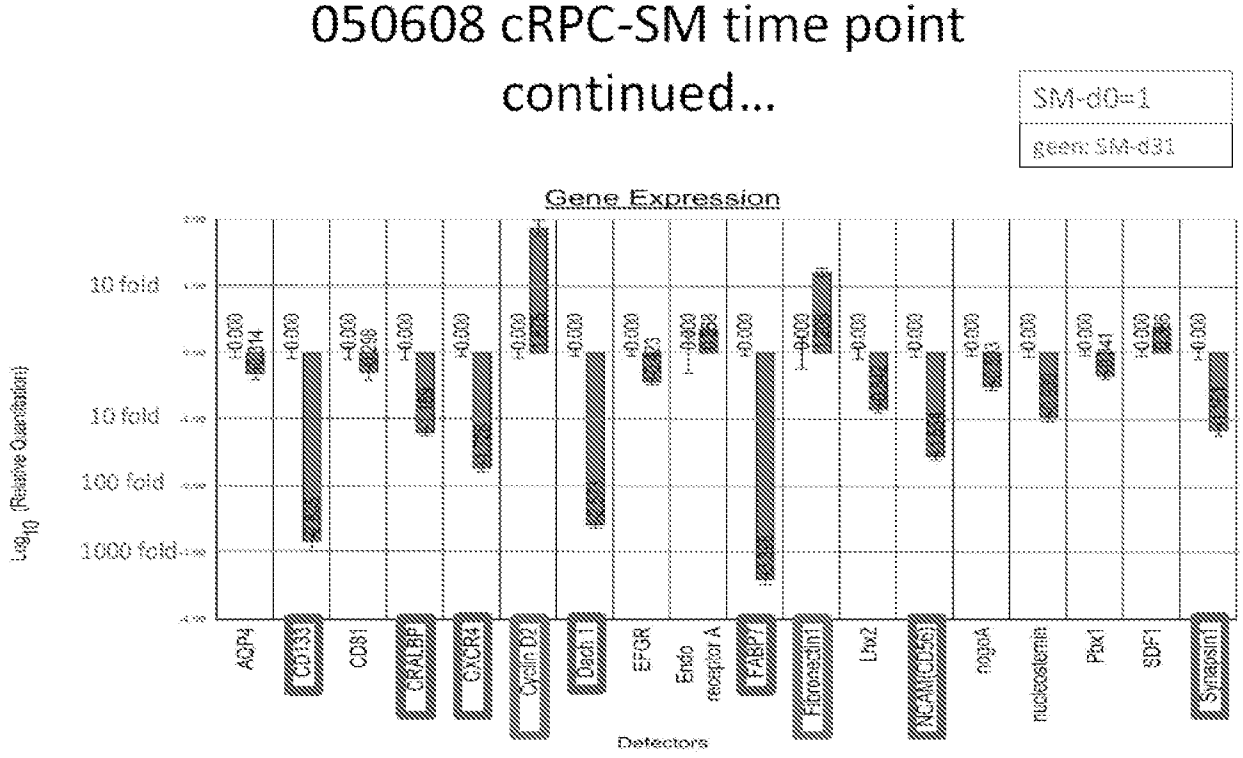


FIGURE 43

FIG. 44/55

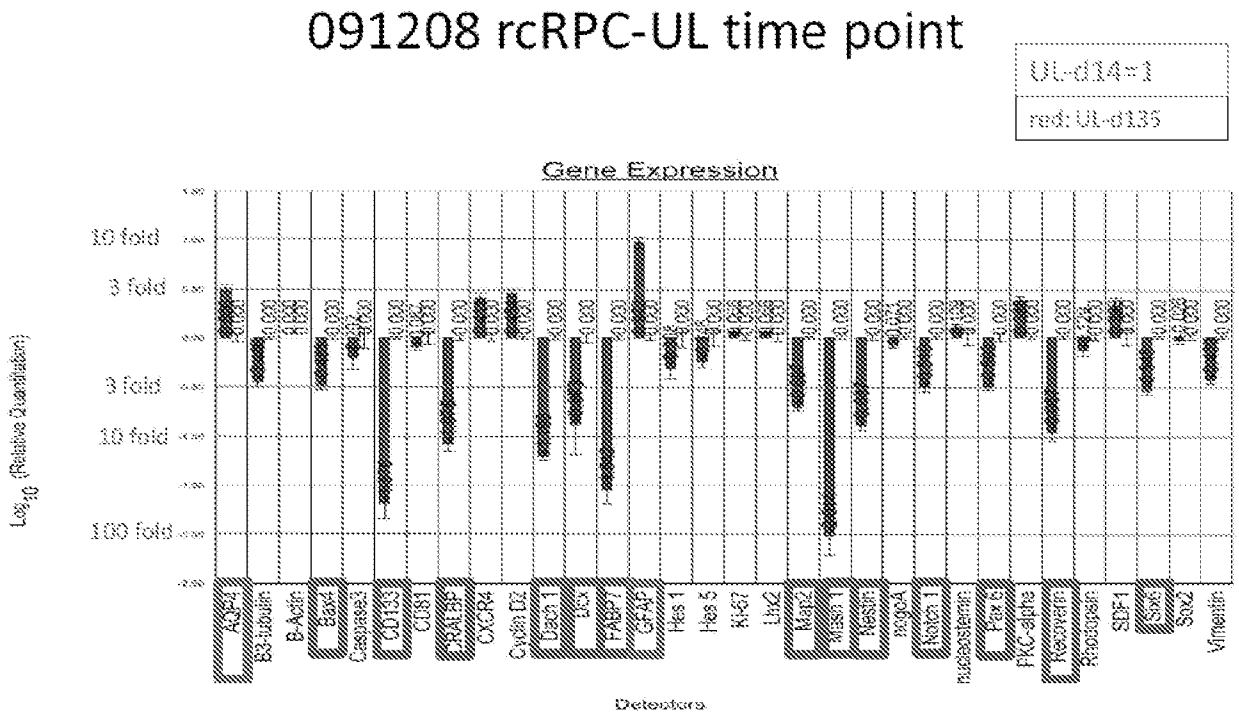
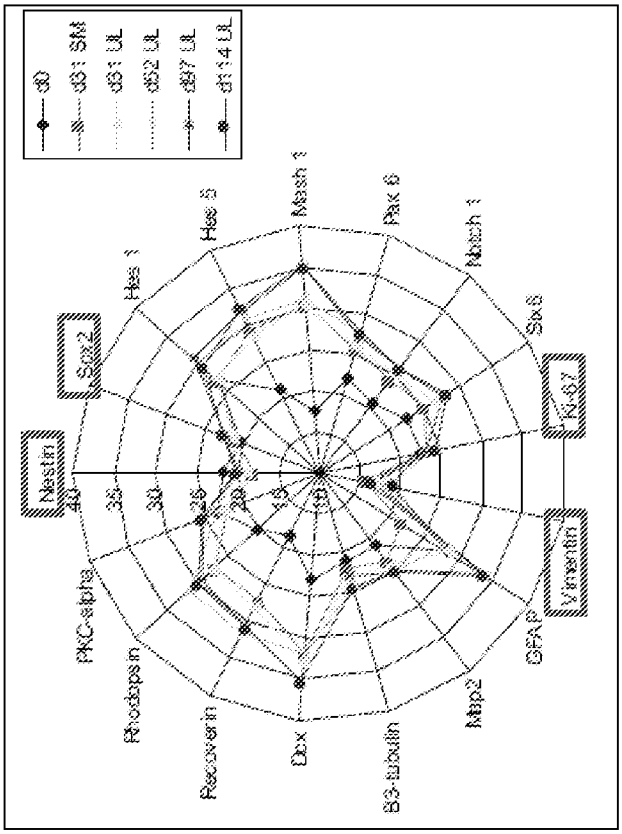


FIGURE 44

FIG. 45/55

cRPC time point



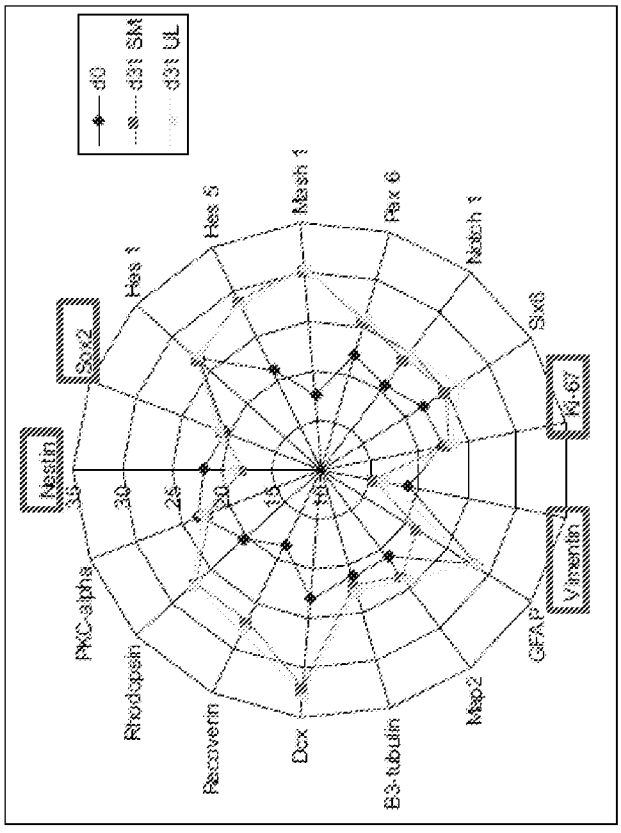


FIGURE 45

d0-d1	d13-d1	d0-d1	d14-d1	comments with RT-PCR
			AQP4	
b3-tubulin	b3-tubulin	b3-tubulin	b3-tubulin	
DCX	DCX	DCX	DCX	
Hes1	Hes1	Hes1	Hes1	
Hes5	Hes5	Hes5	Hes5	
Mash1	Mash1	Mash1	Mash1	
CD133	CD133	CD133	CD133	x
Pax6	Pax6	Pax6	Pax6	
GFAP	GFAP	GFAP	GFAP	
Ki67	Ki67	Ki67	Ki67	
Map2	Map2	Map2	Map2	
Nestin	Nestin	Nestin	Nestin	
Notch1	Notch1	Notch1	Notch1	
Rhodopsin	Rhodopsin	Rhodopsin	Rhodopsin	
PKC-a	PKC-a	PKC-a	PKC-a	
Recoverin	Recoverin	Recoverin	Recoverin	x
six6	six6	six6	six6	x
Sox2	Sox2	Sox2	Sox2	
AnexinV	AnexinV	AnexinV	AnexinV	
CRALBP	CRALBP	CRALBP	CRALBP	
CXCR4	CXCR4	CXCR4	CXCR4	
Cyclin D2	Cyclin D2	Cyclin D2	Cyclin D2	
Dach1	Dach1	Dach1	Dach1	
Endo receptorA	Endo receptorA	Endo receptorA	Endo receptorA	
FABP7	FABP7	FABP7	FABP7	related to Notch1
Fibronectin1	Fibronectin1	Fibronectin1	Fibronectin1	
Lhx2	Lhx2	Lhx2	Lhx2	
NCAM	NCAM	NCAM	NCAM	
Synapsin1	Synapsin1	Synapsin1	Synapsin1	
			Sox9	

FIGURE 46

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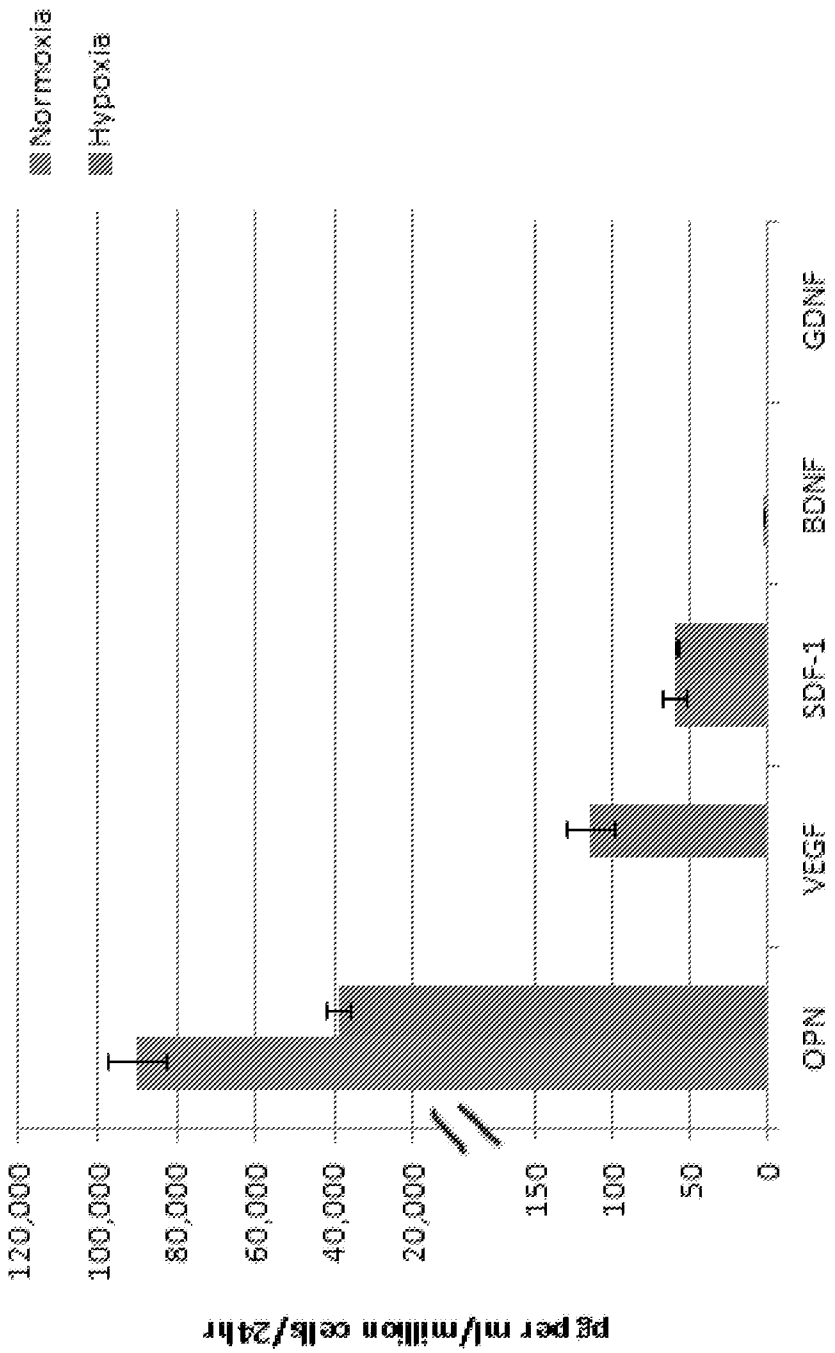


FIGURE 47

FIG. 48/55

	retina	cultured hRPC		
	retina tissue	**Normoxia hRPC**	**Hypoxia hRPC**	**ICC confirmed**
Nestin	86%	99%	99%	95%
Sox2	70%	90-99%	90-99%	90%
Ki67				40-50%
GFAP	0.5%	5-10%	5-10%	5%
MHC I	2%	90%	90%	
MHC II	0%	1-3%	0-1%	
FAS (CD95)	0%	40-60%	40-60%	
CXCR4	80%	5-30%	90%	
CD15	4-8%	4-8%	15-35%	12%
GD2	2%	2-4%	15%	6%

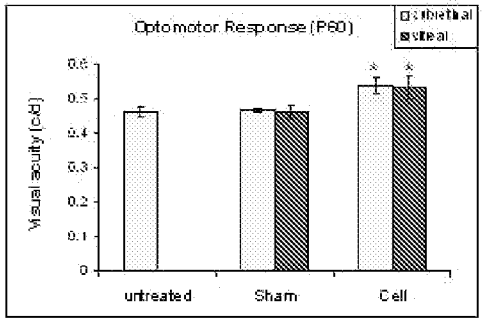
FIGURE 48

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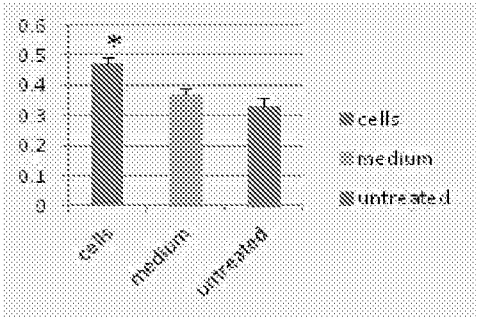
A

Optomotor response P60



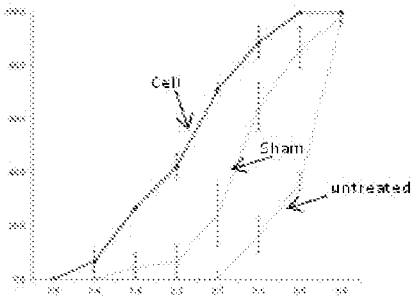
B

Optomotor response P90



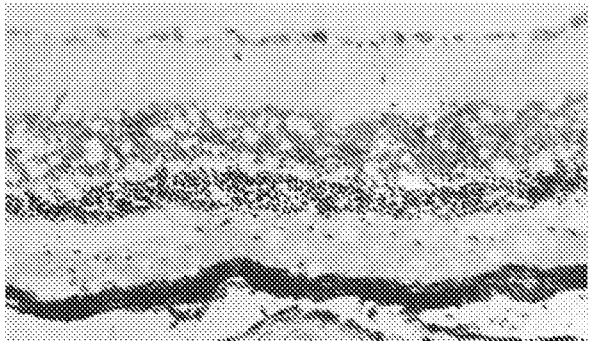
C

Luminance threshold response P90



D

Histology P60 (intravitreal injection)



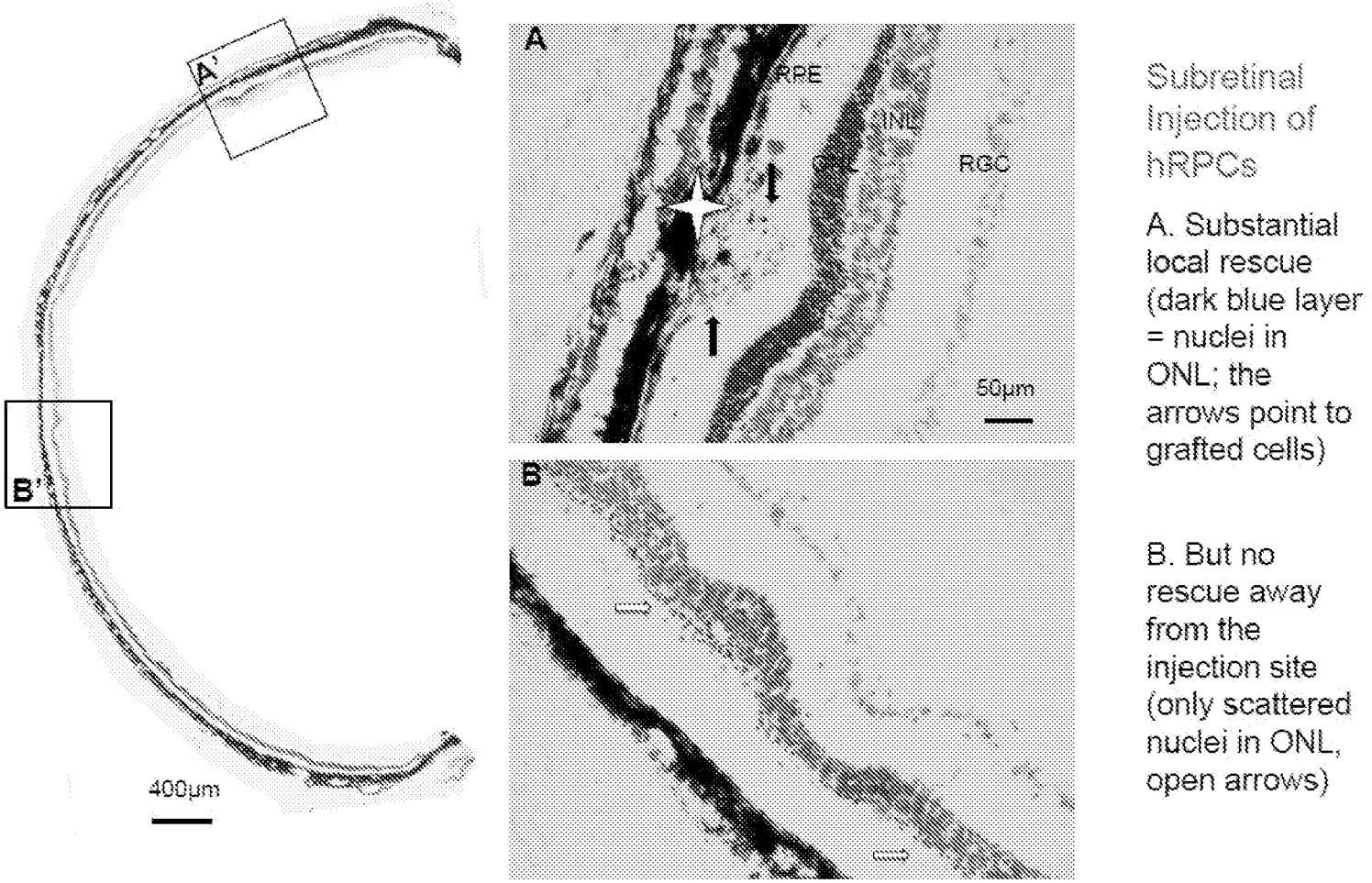
E

Histology P90 (intravitreal injection)



Widespread, persistent rescue of photoreceptor cells in dystrophic retina by hRPCs

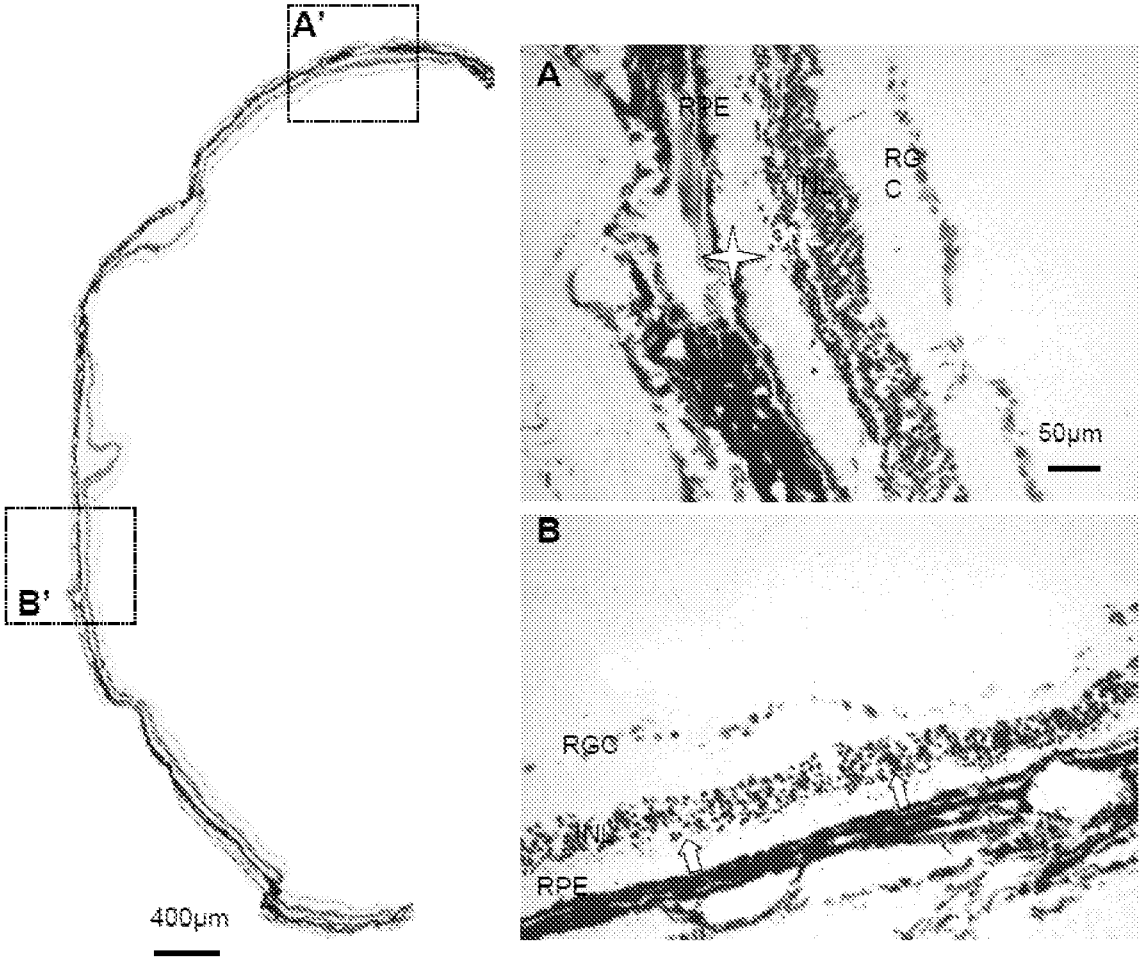
FIGURE 49



Subretinal injection of retinal progenitor cells (RPC) in RCS rat (performed at P21, viewed at P100). Left-montage image of cresyl violet stained retinal section.
A: high power image in outline A' showing injection site (star), donor cells (arrows) and ONL preservation. B: high power image in outline B' showing a single layer of ONL (arrows) in area away from the graft.

FIGURE 50

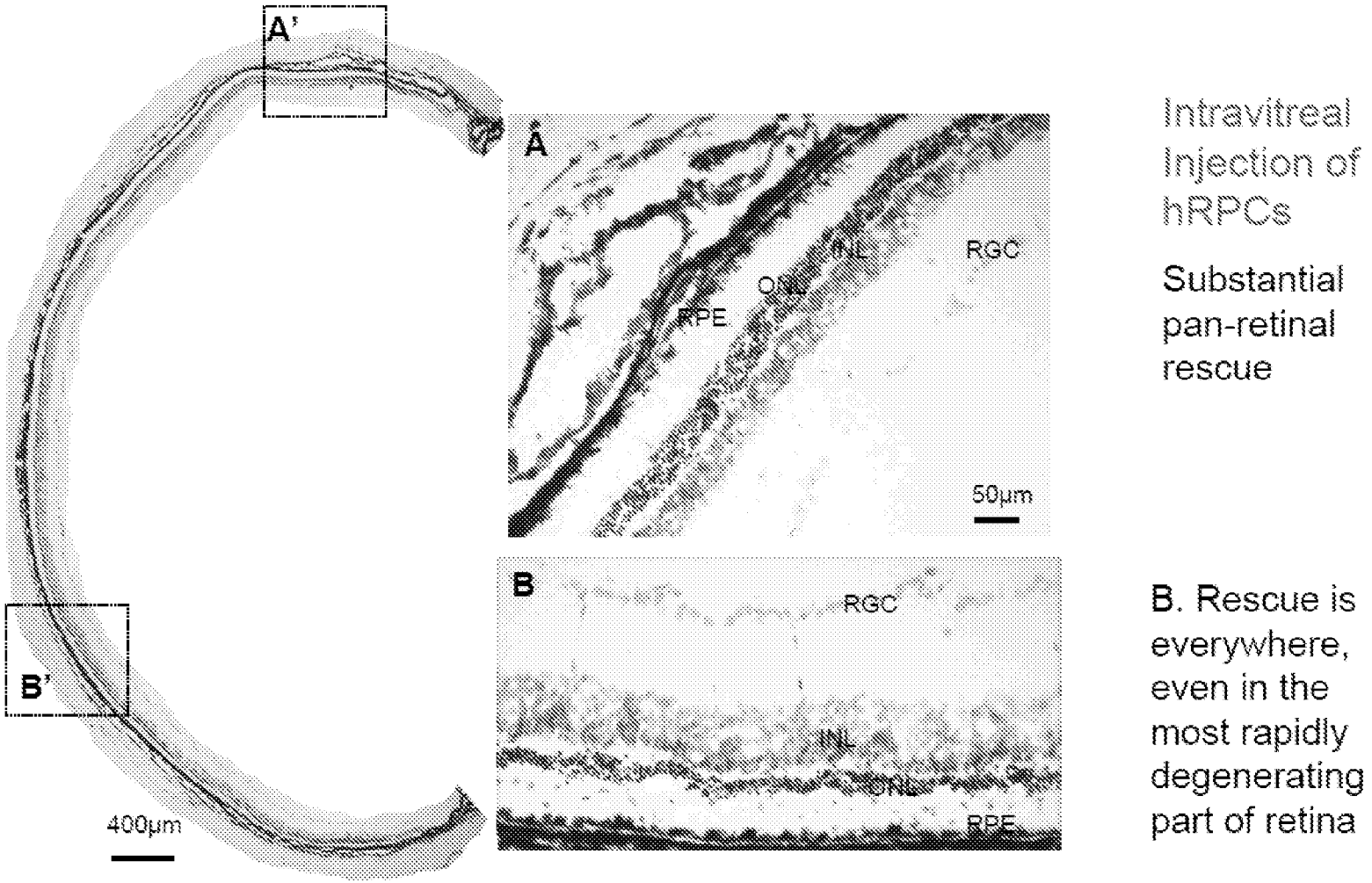
WO 2012/158910 PCT/US2012/038342



Subretinal injection of vehicle in RCS rat, viewed at P100: Left-montage image of cresyl violet stained section. A: high power image of outline A' showing injection site (star) and localized ONL rescue. B: high power image of outline B; showing a single layer of ONL (arrows) at area away from injection site.

FIGURE 51

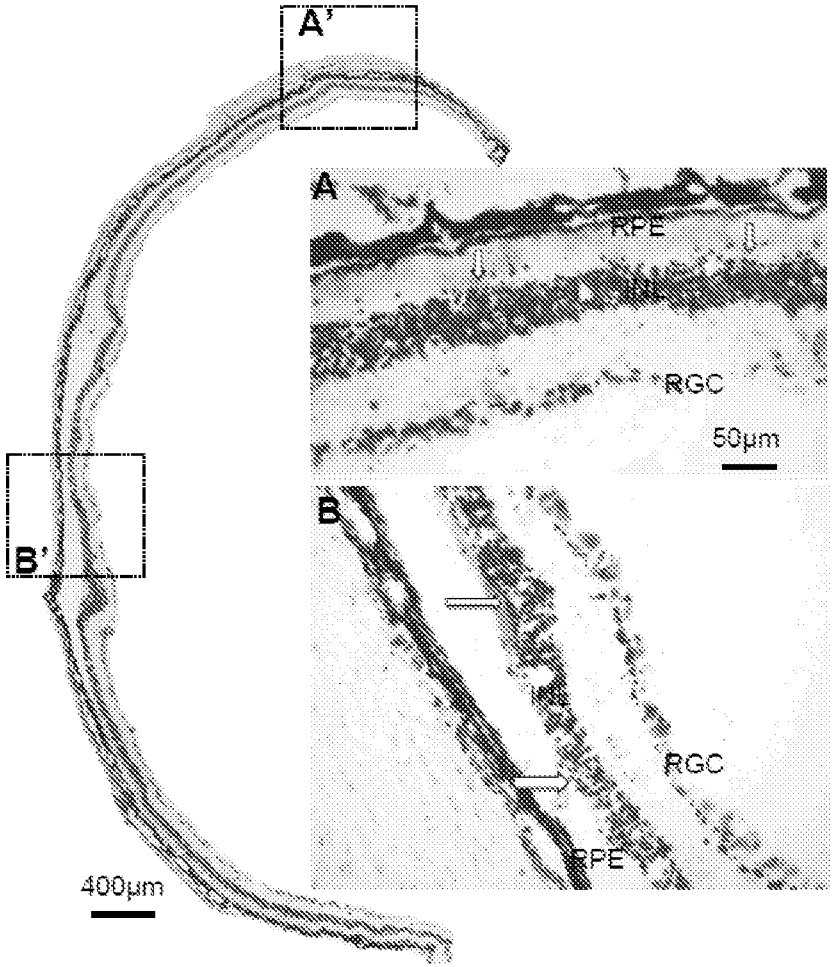
WO 2012/158910 PCT/US2012/038342



Intravitreal injection of RPC in RCS rat, viewed at P100. Left-montage image of cresyl violet stained section showing ONL rescue over the whole retinal. A: high power of outline A' showing 5-6 layers of ONL.B: high power image of outline B' showing ONL preservation.

FIGURE 52

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Intravitreal Injection of vehicle (sham)

No discernable rescue*

*(There will always be a nonspecific effect at initial needle entry point)

Intravitreal injection of carry medium in RCS rat, viewed at P100. Left-montage image of cresyl violet stained section. A&B: high power of outline A' &B' showing a single layer of photoreceptors (arrows)

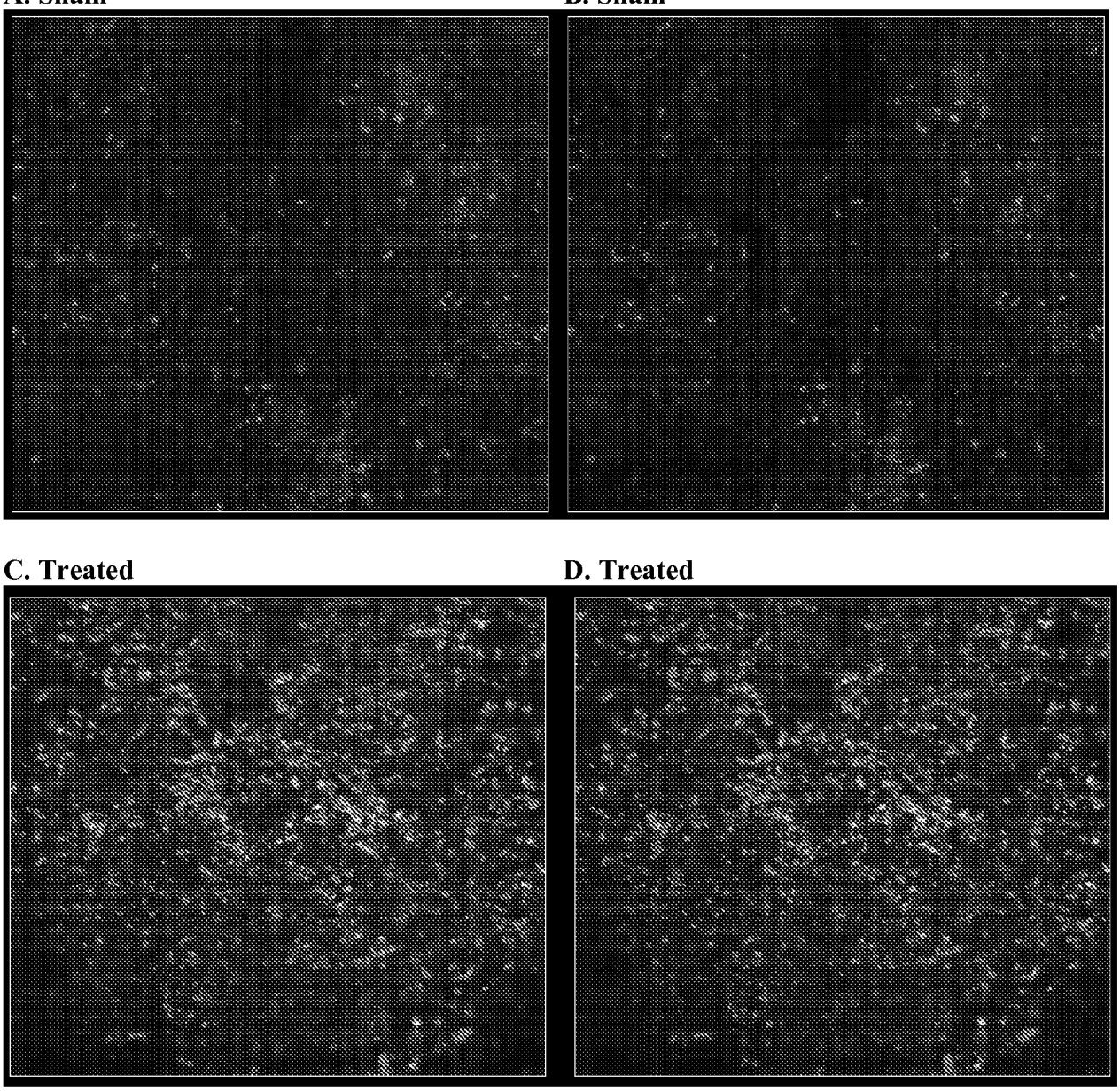
FIGURE 53

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FIG. 54/55

A. Sham **B. Sham**

C. Treated **D. Treated**



Red: Rod opsin; Green: M-cone opsin; Blue: PNA (M-&S-cone sheaths)

FIGURE 54

FIG. 55/55

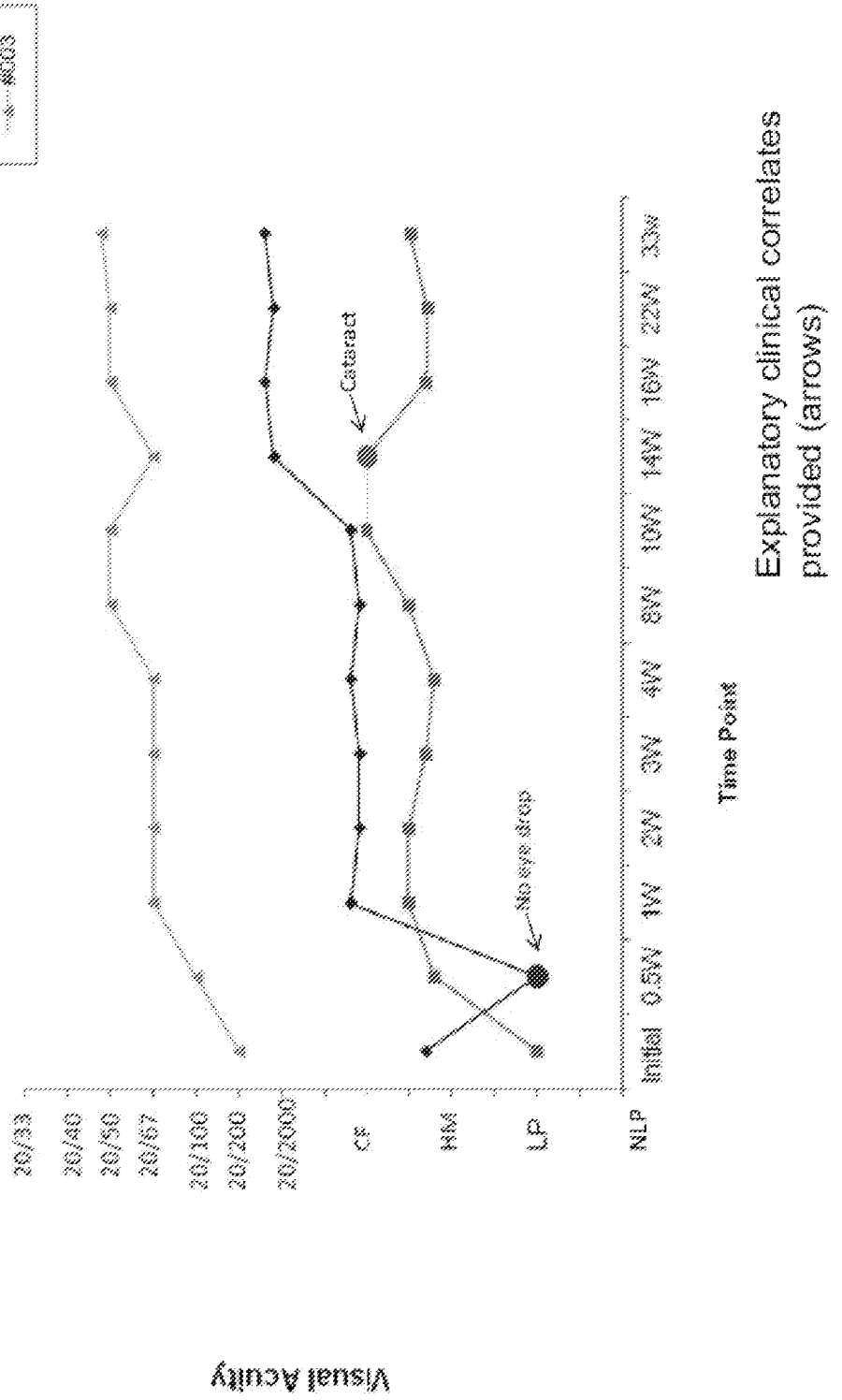


FIGURE 55