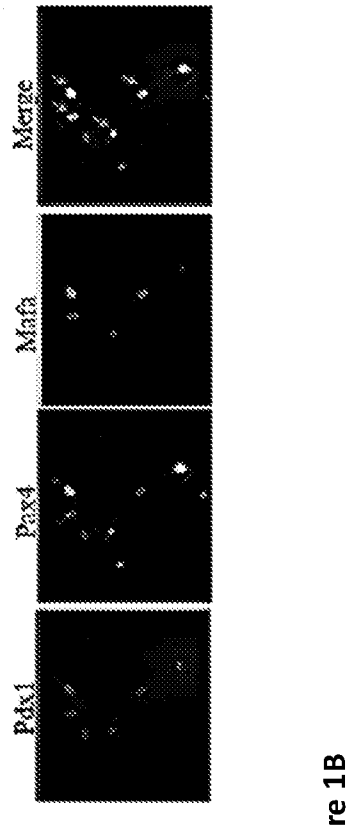
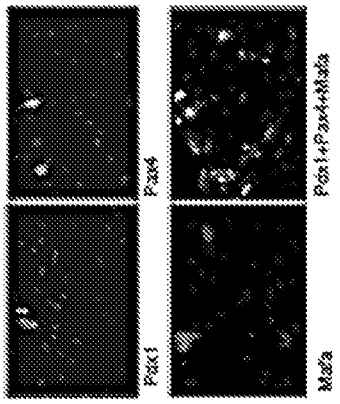


Figure 1A



Treatment	% insulin + cells
Ad-Pdx1	4.01±0.88
Ad-Pax4	3.65±0.42
Ad-Mafa	5.97±0.85
Ad-Pdx1+Ad-Pax4+Ad-Mafa (B)	14.03±1.92

Figure 1C

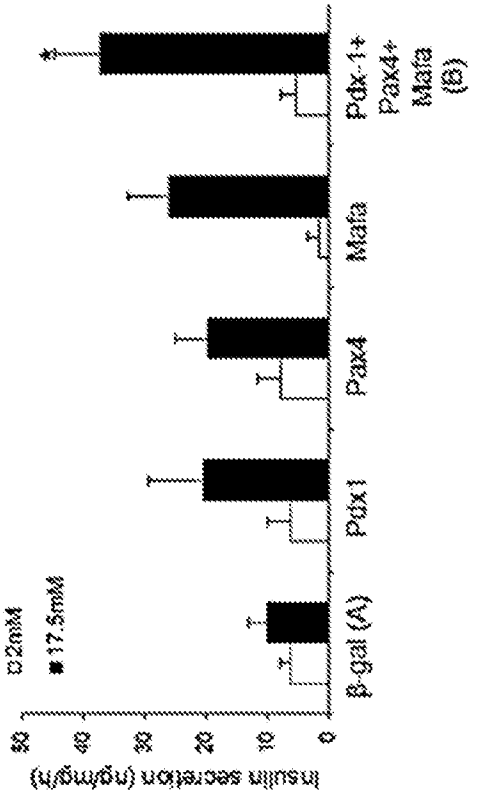


Figure 1D

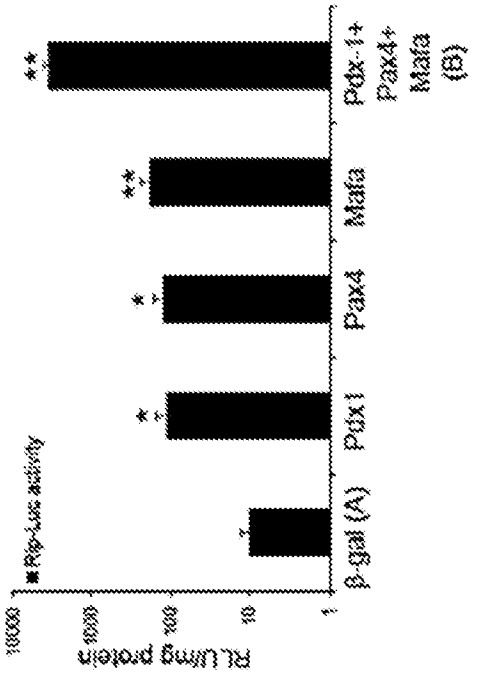
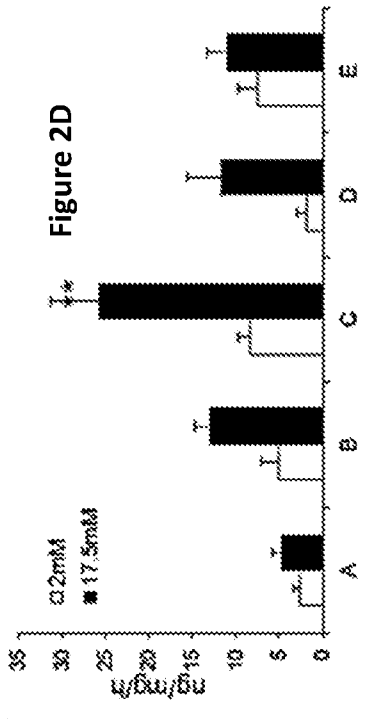
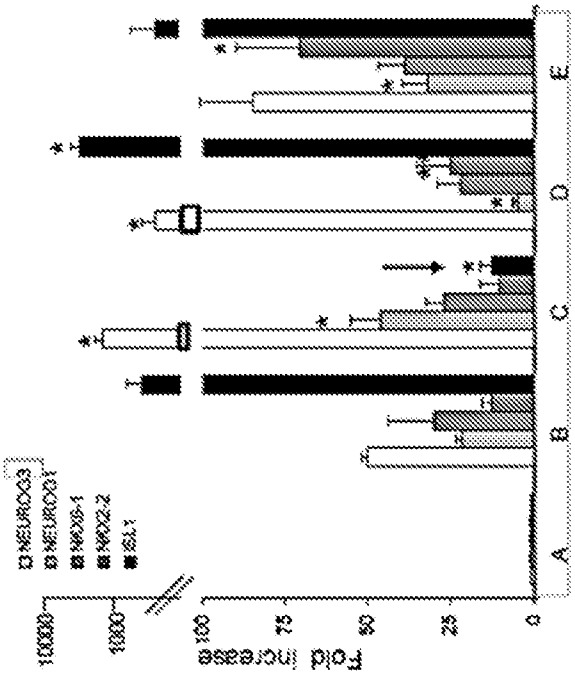


Figure 1B





	Day1	Day2	Day3	Day4	Day5	Day6
A	Ad-β-gal					Harvest
B	Ad-Pdx1+ Ad-Pax4+ Ad-Mafa					Harvest
C	Ad-Pdx1	Ad-Pax4	Ad-Mafa			Harvest
D	Ad-Mafa	Ad-Pax4	Ad-Pdx1			Harvest
E	Ad-Pdx1	Ad-Mafa	Ad-Pax4			Harvest

Figure 2A

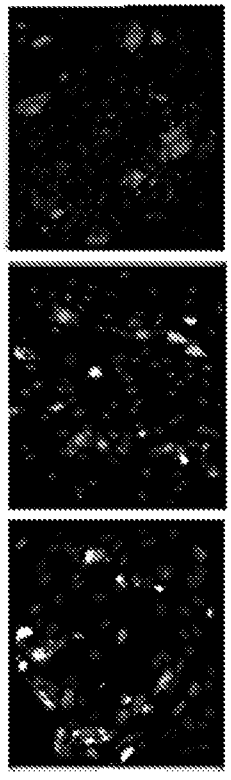


Figure 2B

Figure 2C

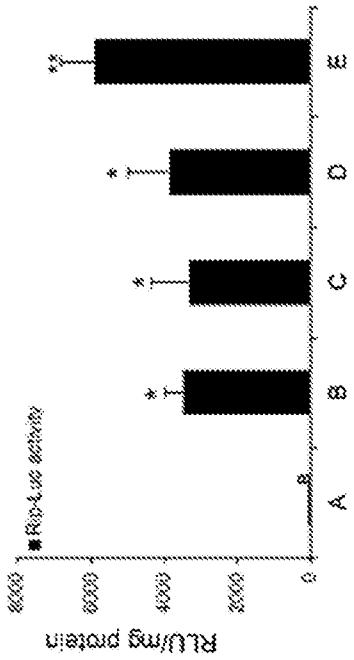


Figure 3A

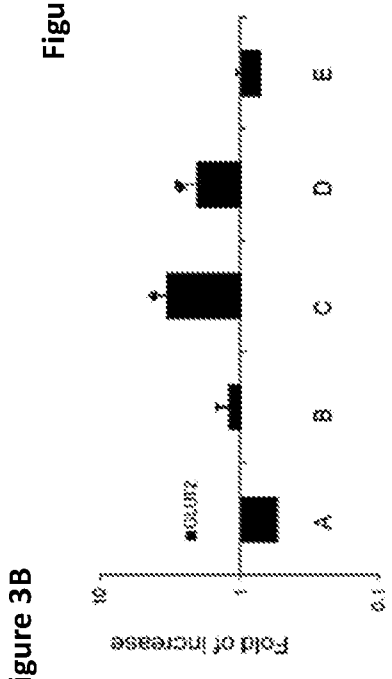


Figure 3B

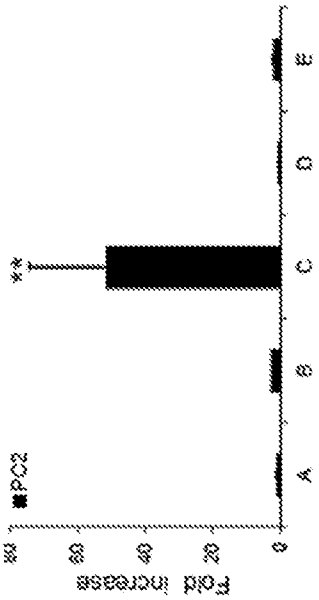


Figure 3C

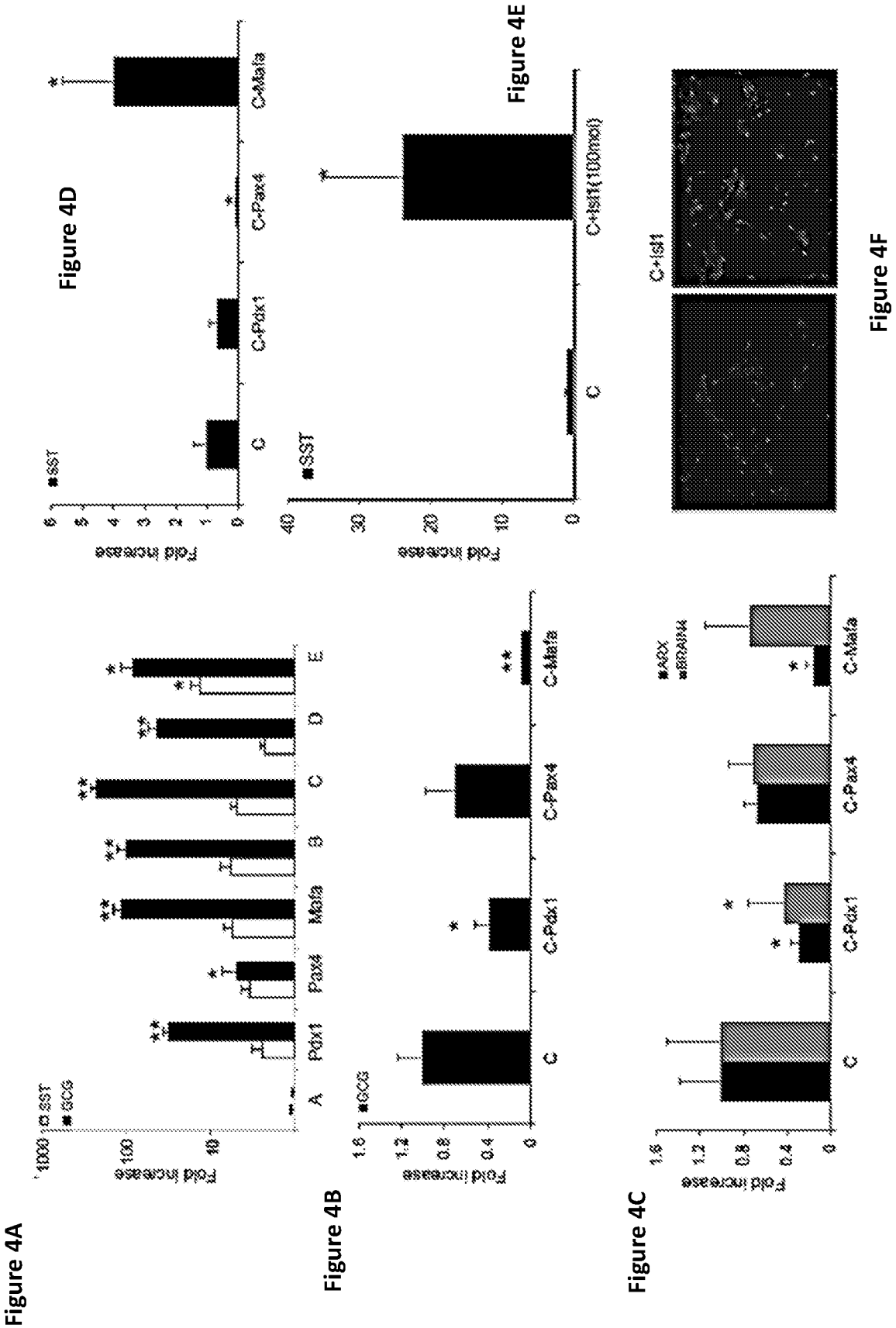

Figure 4A
Fold increase
1000
100
10
SST
GCG
A
Pdx1
Pax4
Mafa
B
C
D
E
Figure 4B
Fold increase
1.6
1.2
0.8
0.4
0
GCG
C
C-Pdx1
C-Pax4
C-Mafa
Figure 4C
Fold increase
1.6
1.2
0.8
0.4
0
ARX
PDX1
C
C-Pdx1
C-Pax4
C-Mafa
Figure 4D
Fold increase
6
5
4
3
2
1
0
SST
C
C-Pdx1
C-Pax4
C-Mafa
Figure 4E
Fold increase
40
30
20
10
0
SST
C
C+Ist1(100nM)
Figure 4F
C+Ist1

Figure 5

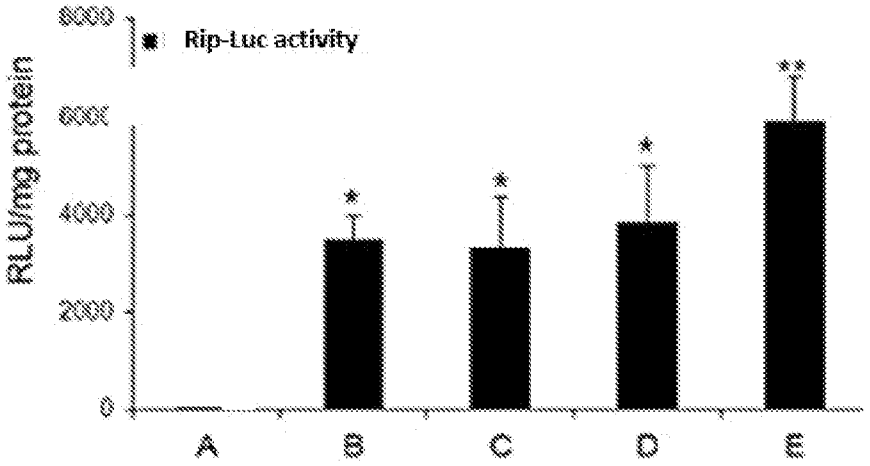


Figure 6A

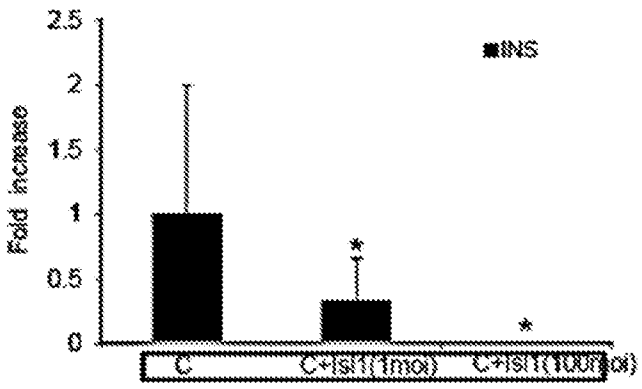


Figure 6B

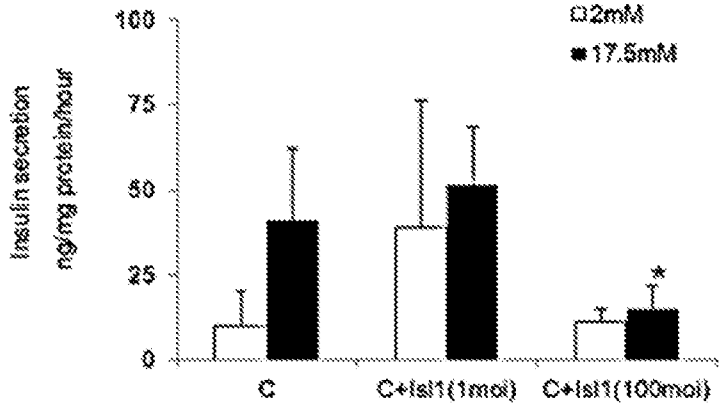
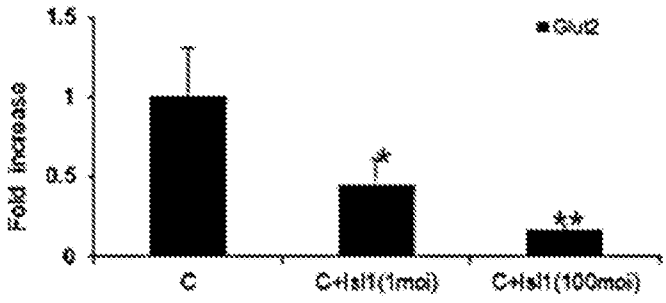


Figure 6C



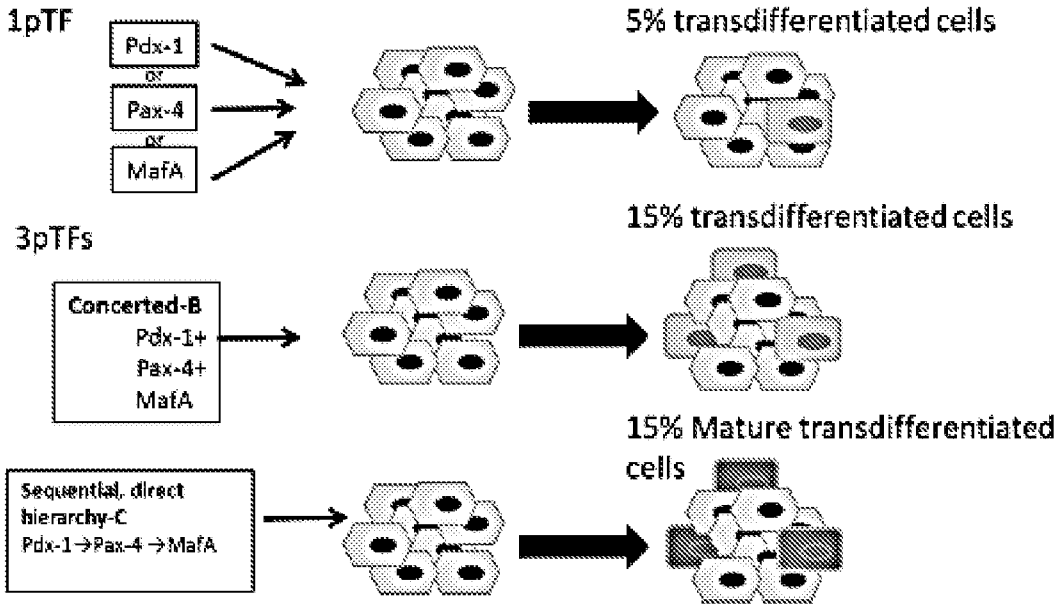
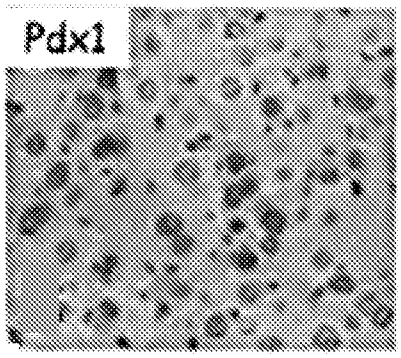


Figure 7

Figure 8A



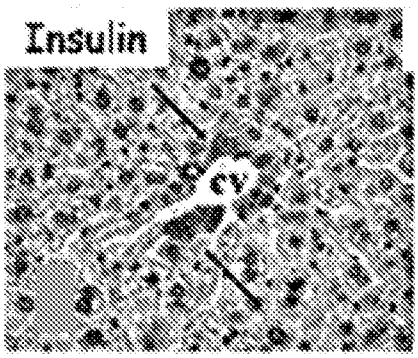
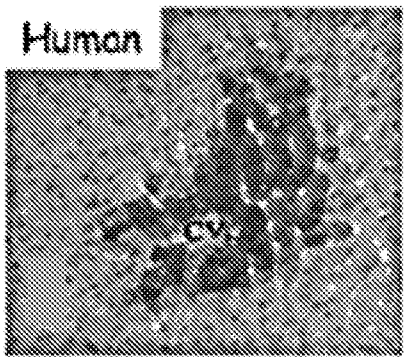


Figure 8B

Figure 8C



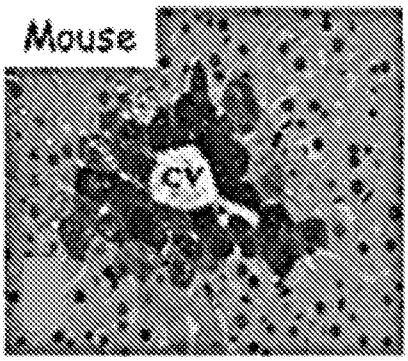


Figure 8D

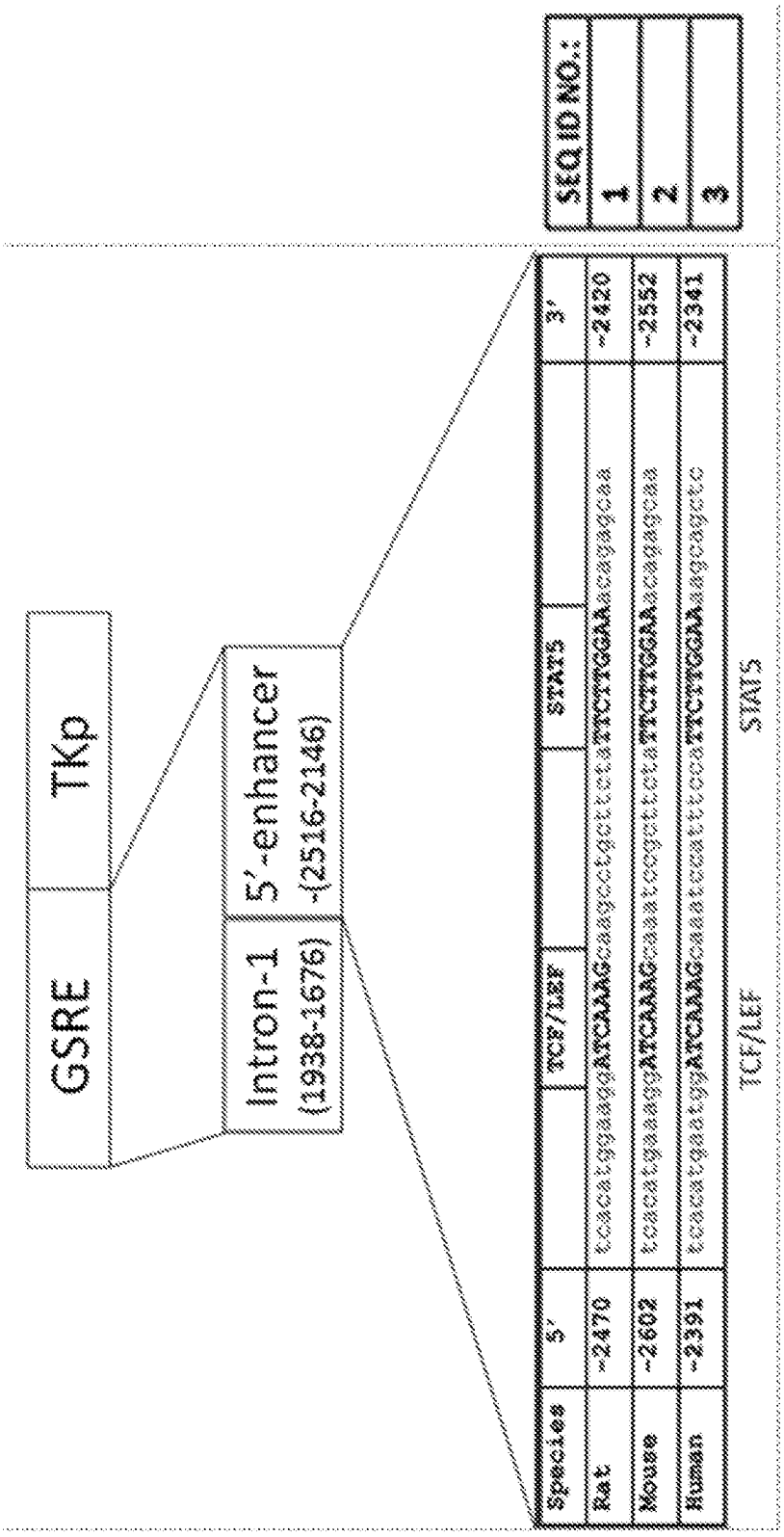

GSRE
TKp
Intron-1
(1938-1676)
5'-enhancer
-(2516-2146)
TCF/LEF
STAT5
TCF/LEF
STAT5
Species
5'
3'
SEQ ID NO.:
Rat
~2470
tcacatgaaggATCAAAGcaagcctgctcctaTTCTTGGAAacagagcaa
~2420
1
Mouse
~2602
tcacatgaaggATCAAAGcaaatccgcttcctaTTCTTGGAAacagagcaa
~2552
2
Human
~2391
tcacatgaatggATCAAAGcaaatccaattccaTTCTTGGAAaagcagctc
~2341
3

Figure 9

Figure 10A

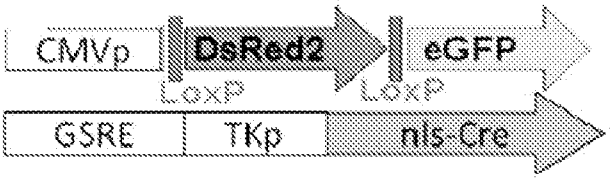


Figure 10B

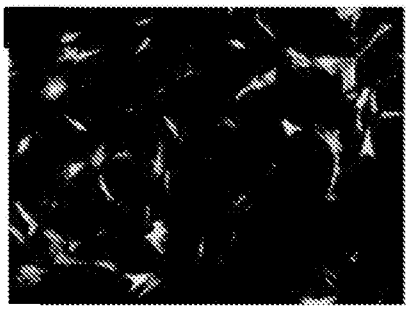


Figure 10C

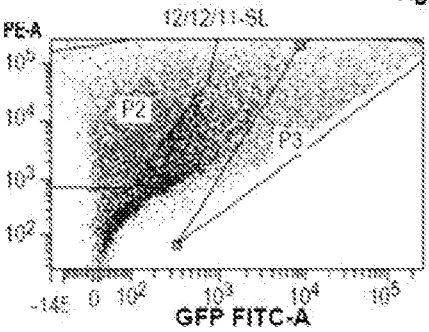


Figure 10D

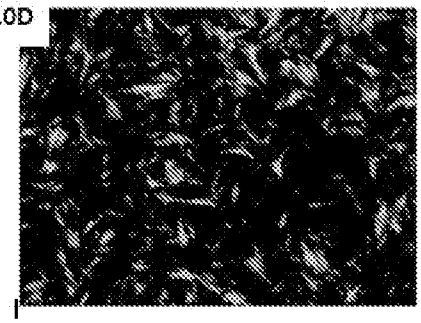
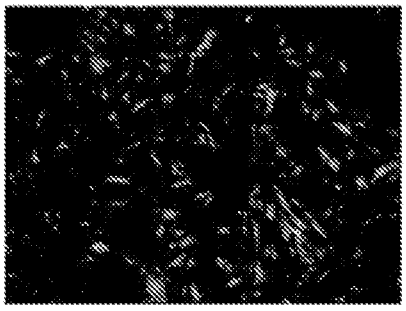


Figure 10E



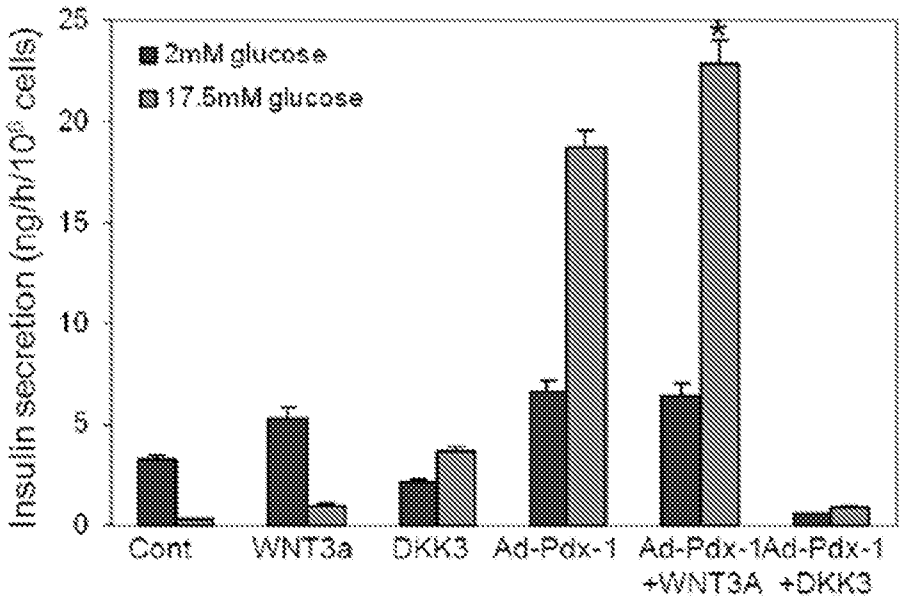


Figure 11

Figure 12A

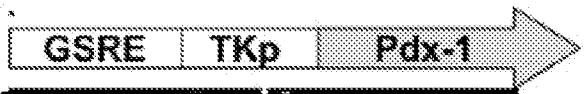


Figure 12B

Figure 12C

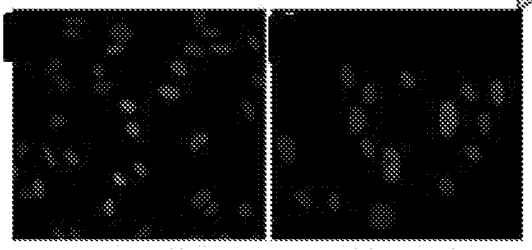


Figure 12D

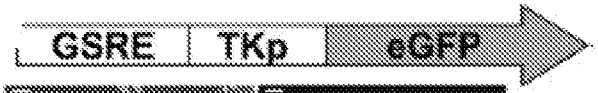


Figure 12E

Figure 12F

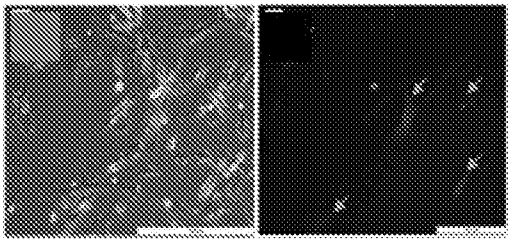


Figure 13A

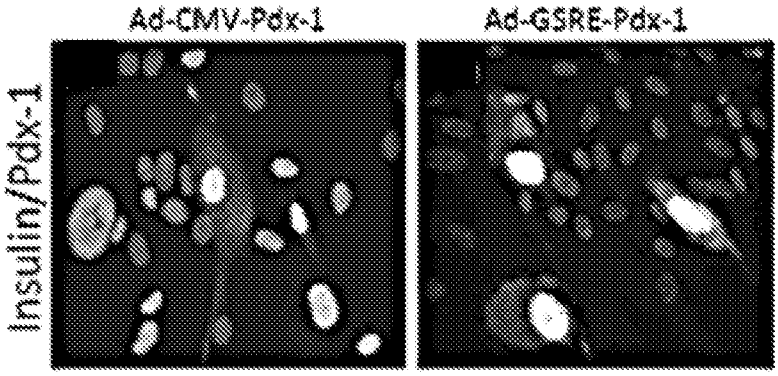


Figure 13B

Figure 13C

	INS+	Pdx-1+	INS+/Pdx-1+
Ad-CMV-Pdx-1	0.6%	60%	1%
Ad-GSRE-Pdx-1	4%	16%	25%

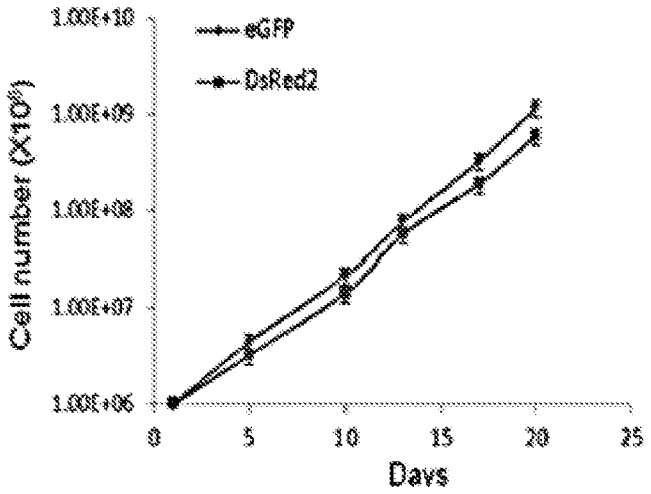

1.00E+10
1.00E+09
1.00E+08
1.00E+07
1.00E+06
Cell number (X10^6)
eGFP
DsRed2
0
5
10
15
20
25
Days

Figure 14

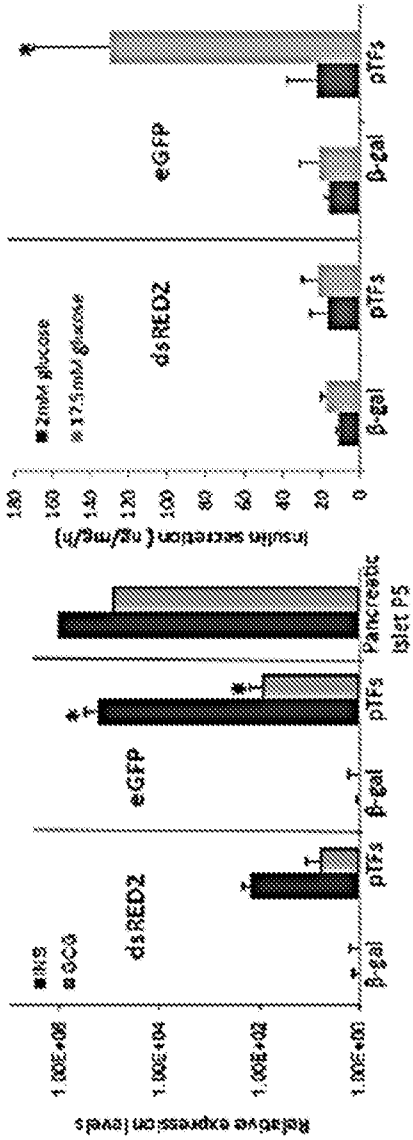


Figure 15A

Figure 15B

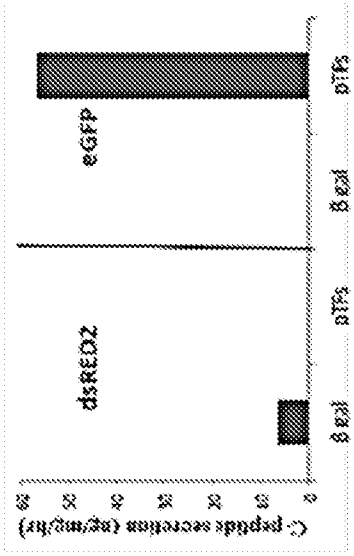


Figure 15C

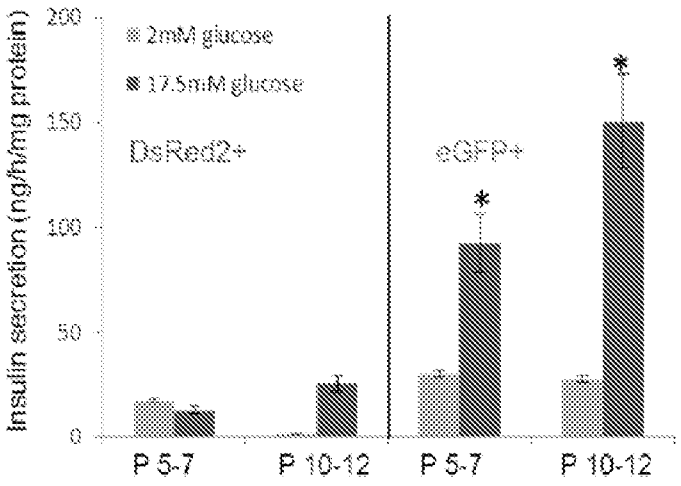


Figure 16

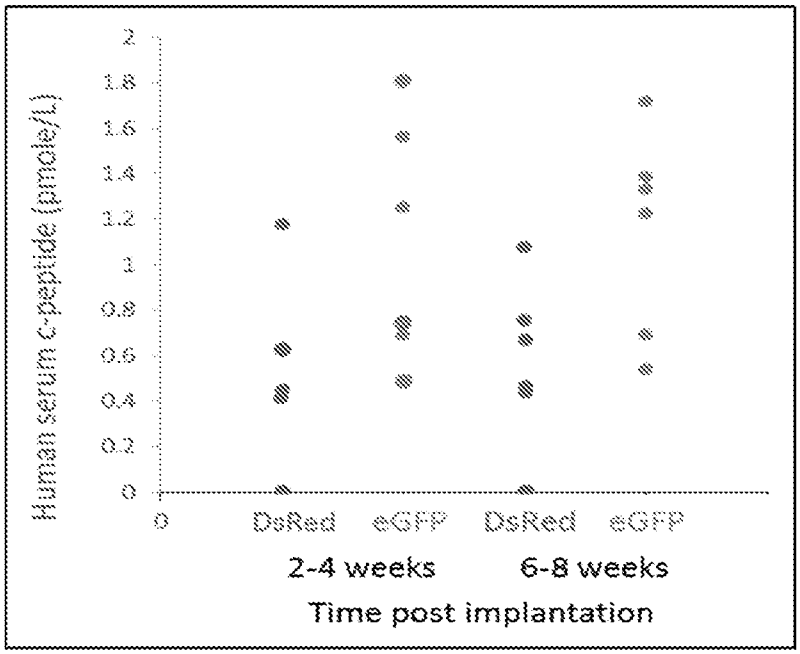


Figure 17A

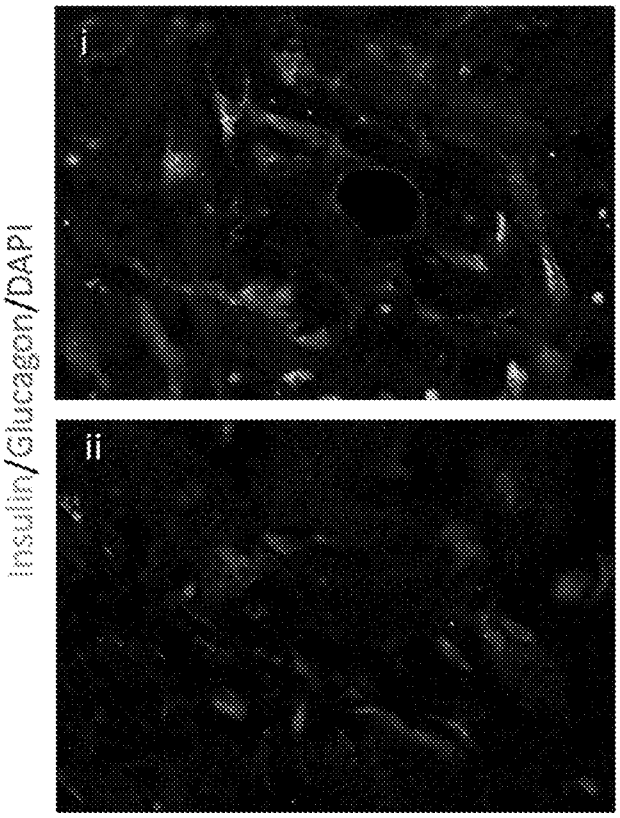


Figure 17B

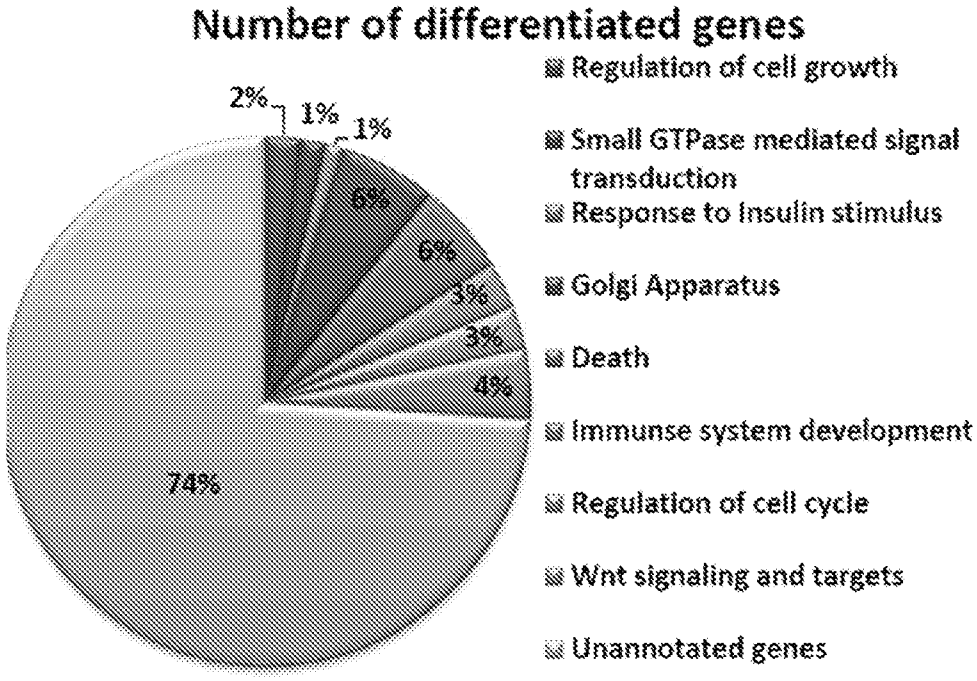


Figure 18

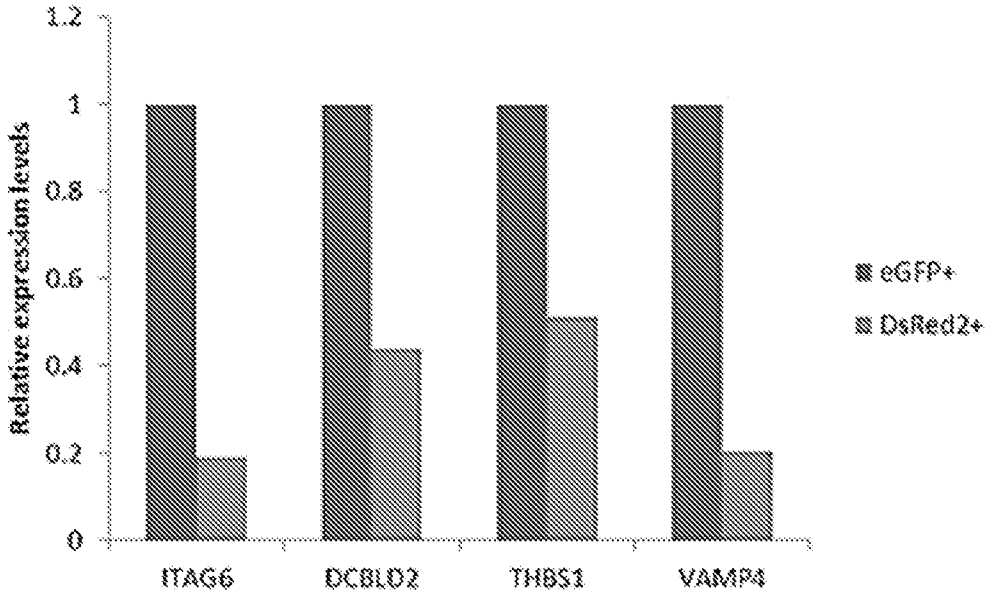


Figure 19

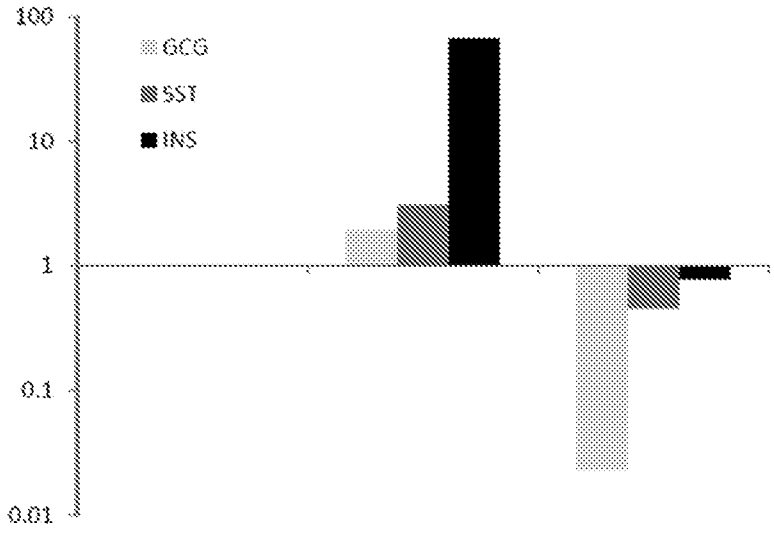


Figure 20

Figure 21A

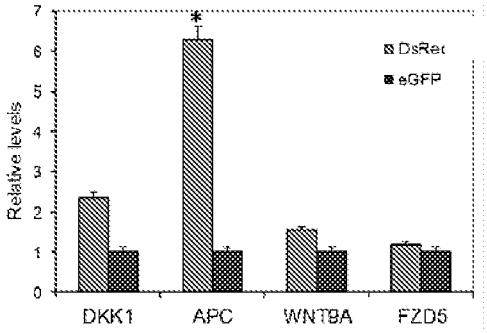


Figure 21B

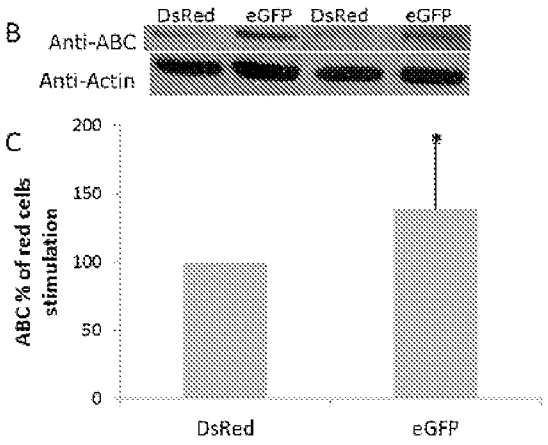


Figure 21C

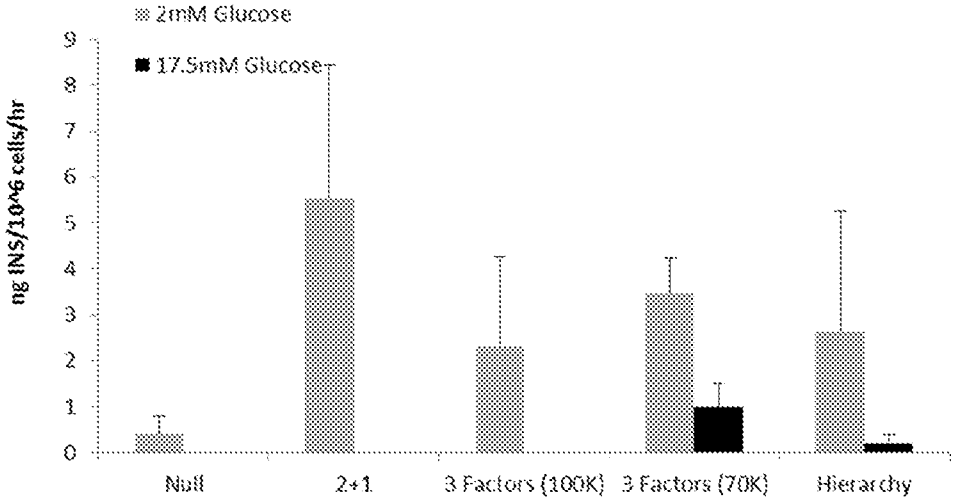


Figure 22A

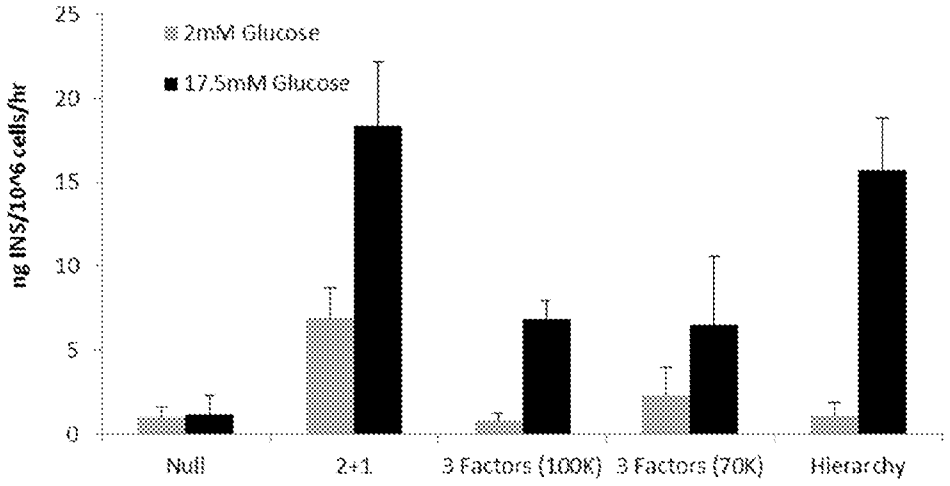


Figure 22B

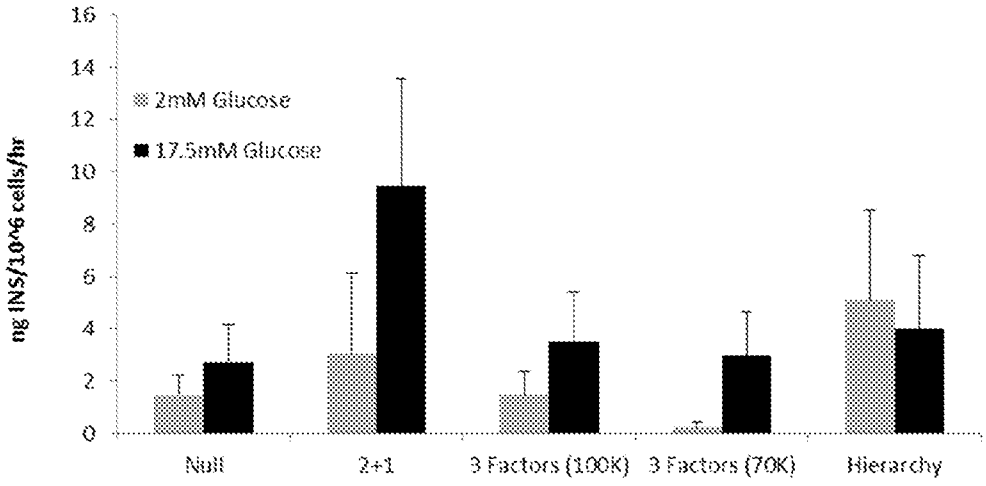


Figure 22C

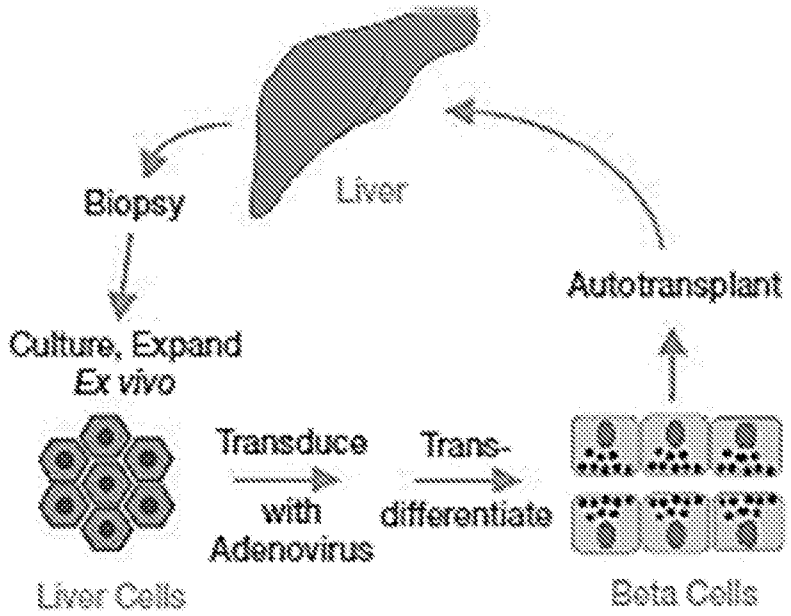


Figure 23

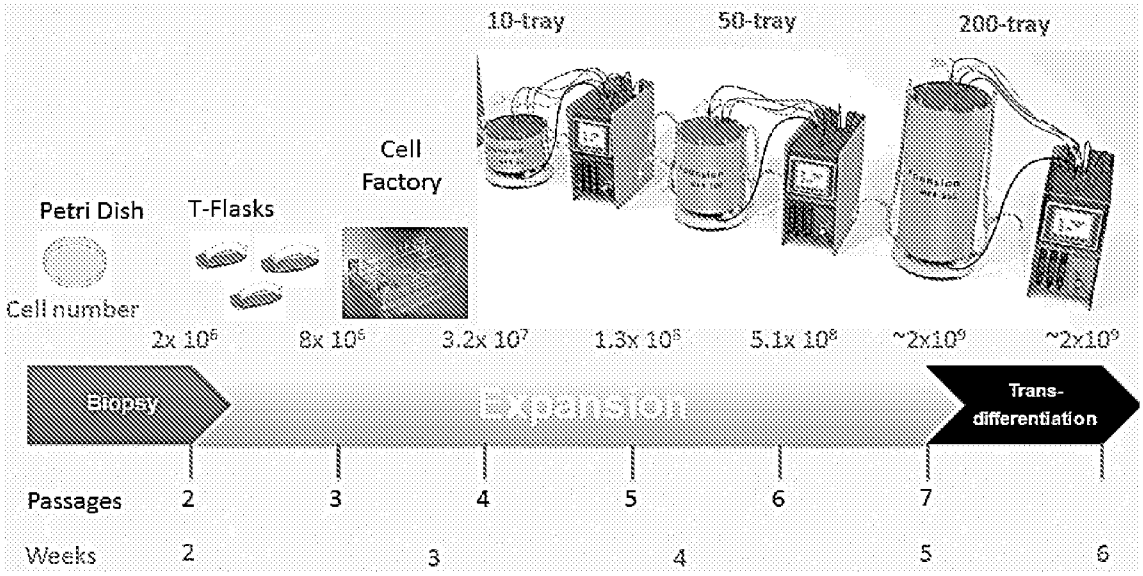


Figure 24

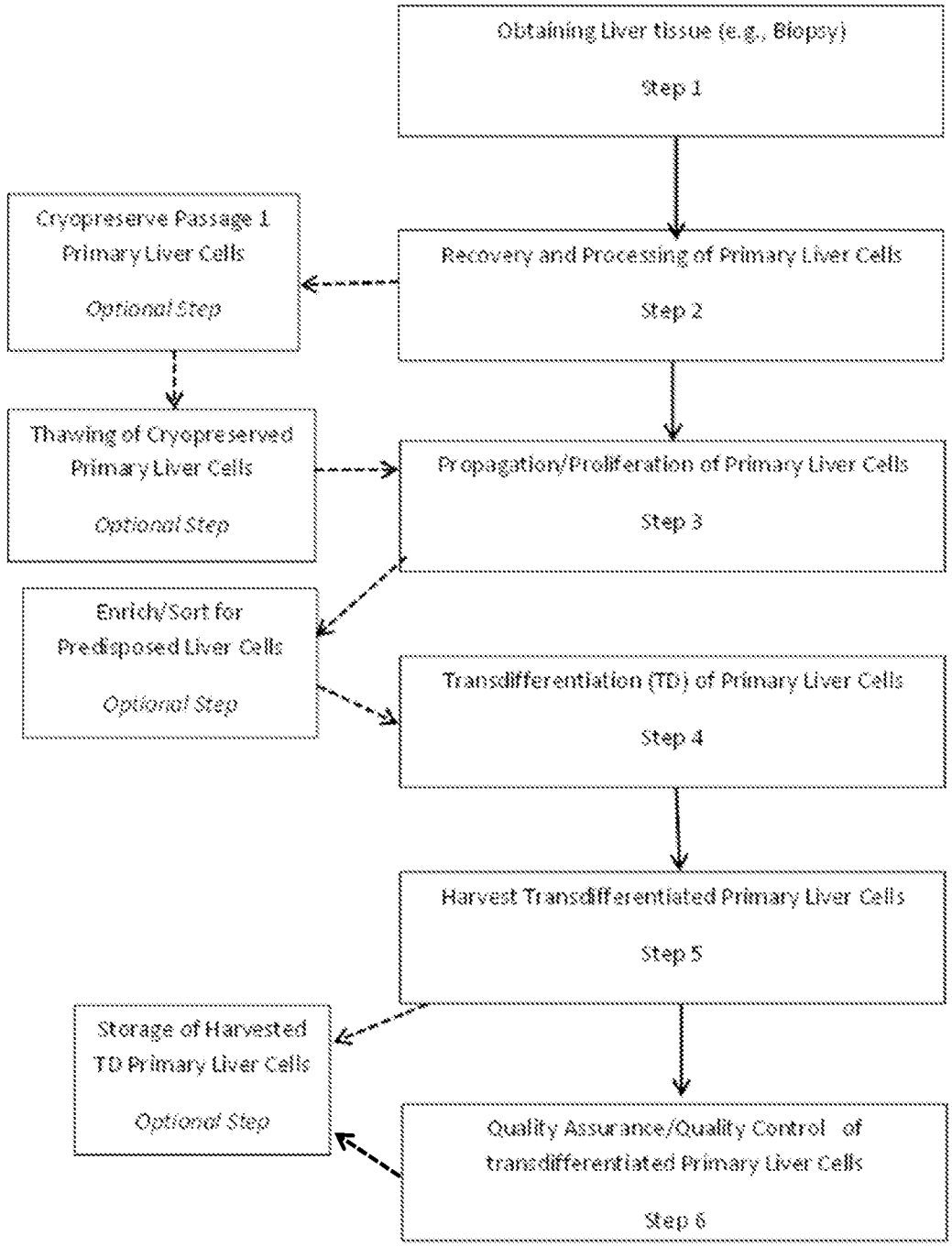


Figure 25

Run	Seeding density (cell/cm^2)	Harvest density (cell/cm^2)	Culture duration (days)
ORG-009	**4,000**	**17,500**	**8**
ORG-014	**4,000**	**22,780**	**7**
ORG-017	**3,972**	**19,412**	**9**

Figure 26

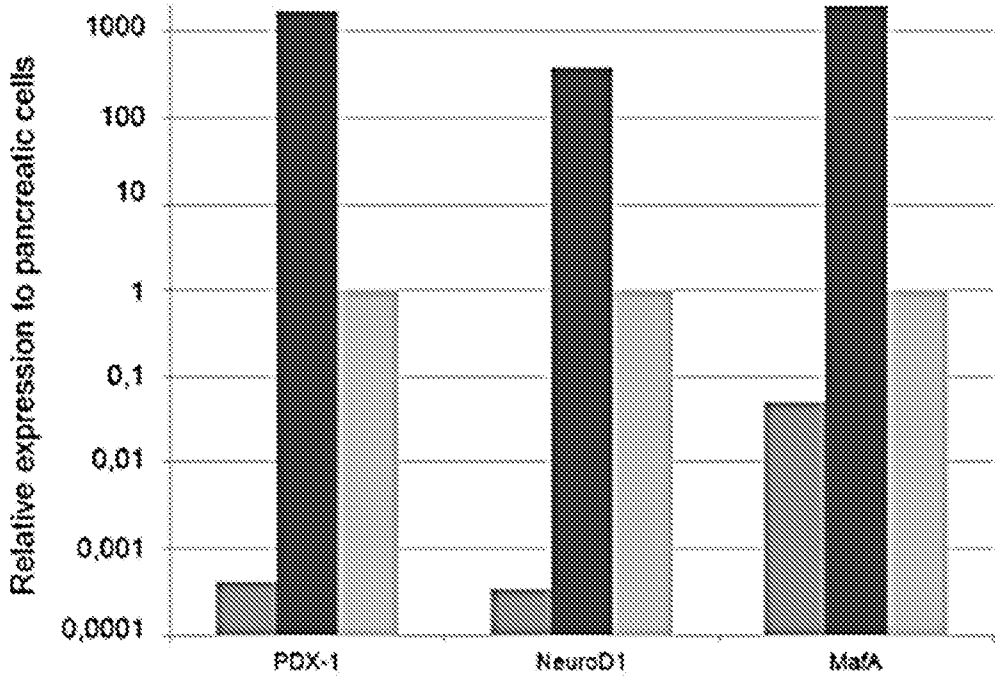
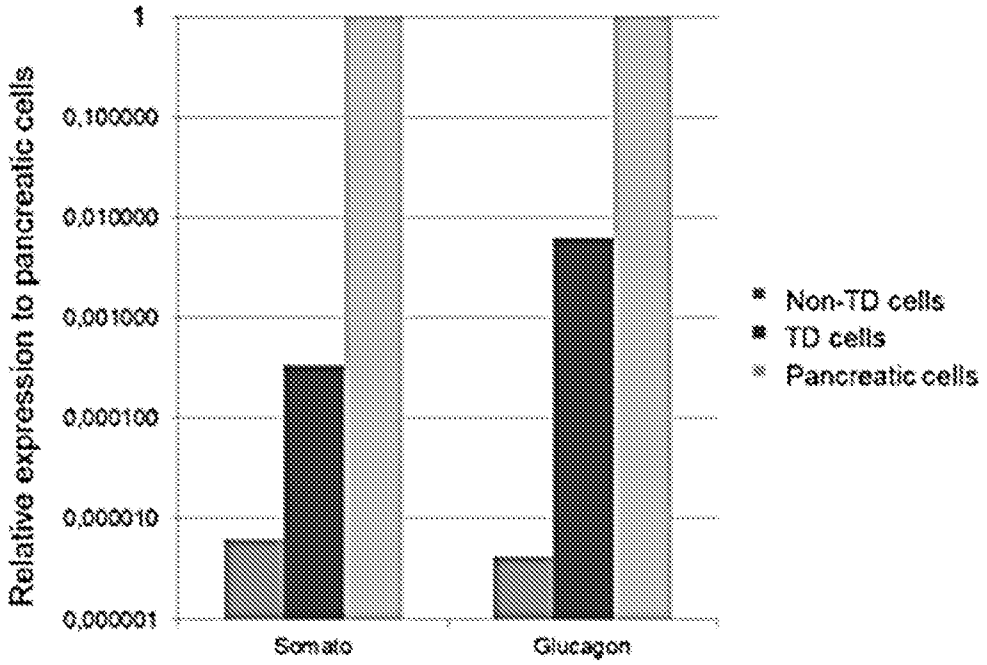


Figure 27A



0

Figure 27B

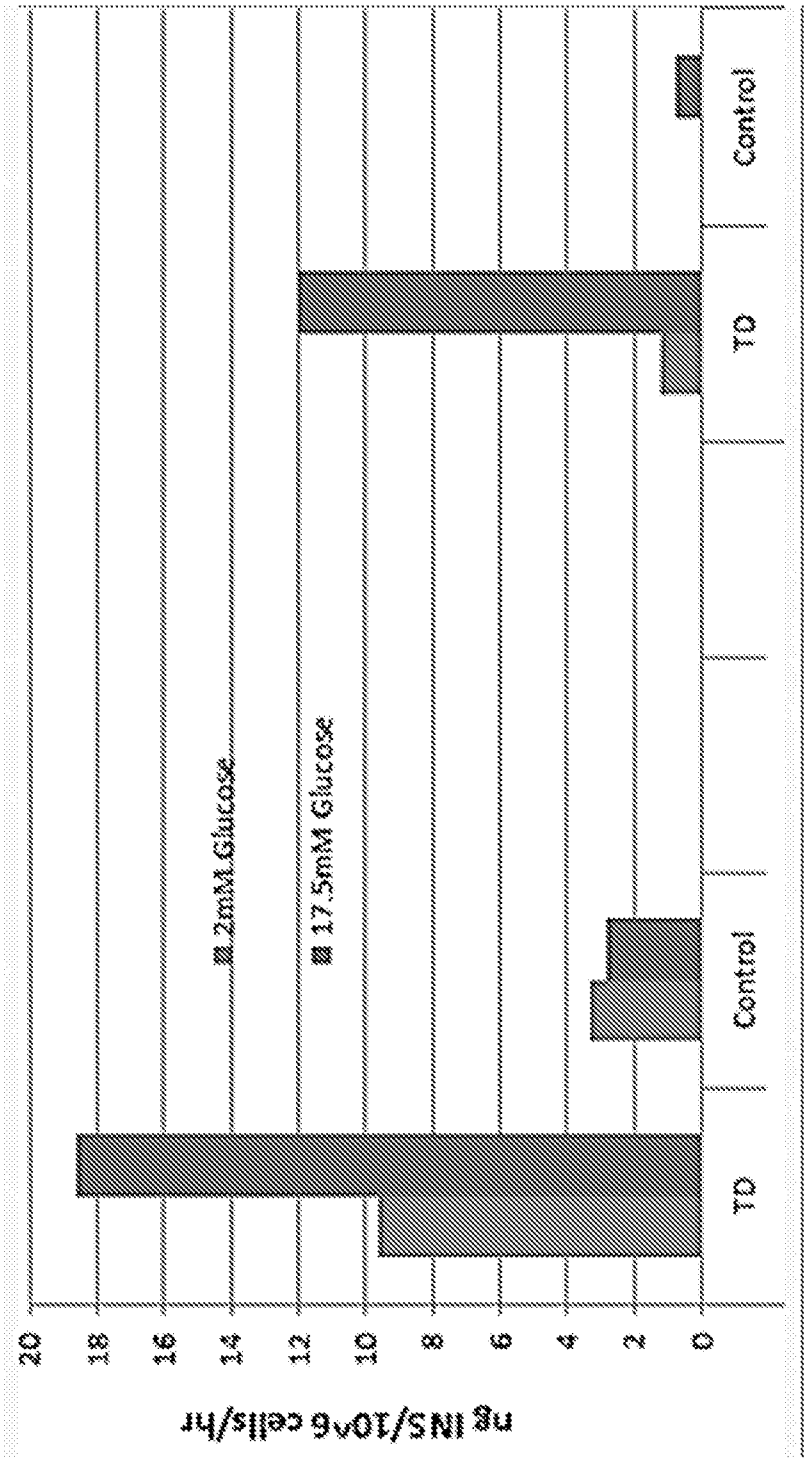

ng INS/10^6 cells/hr
20
18
16
14
12
10
8
6
4
2
0
2mM Glucose
17.5mM Glucose
TD
Control
TD
Control

Figure 28

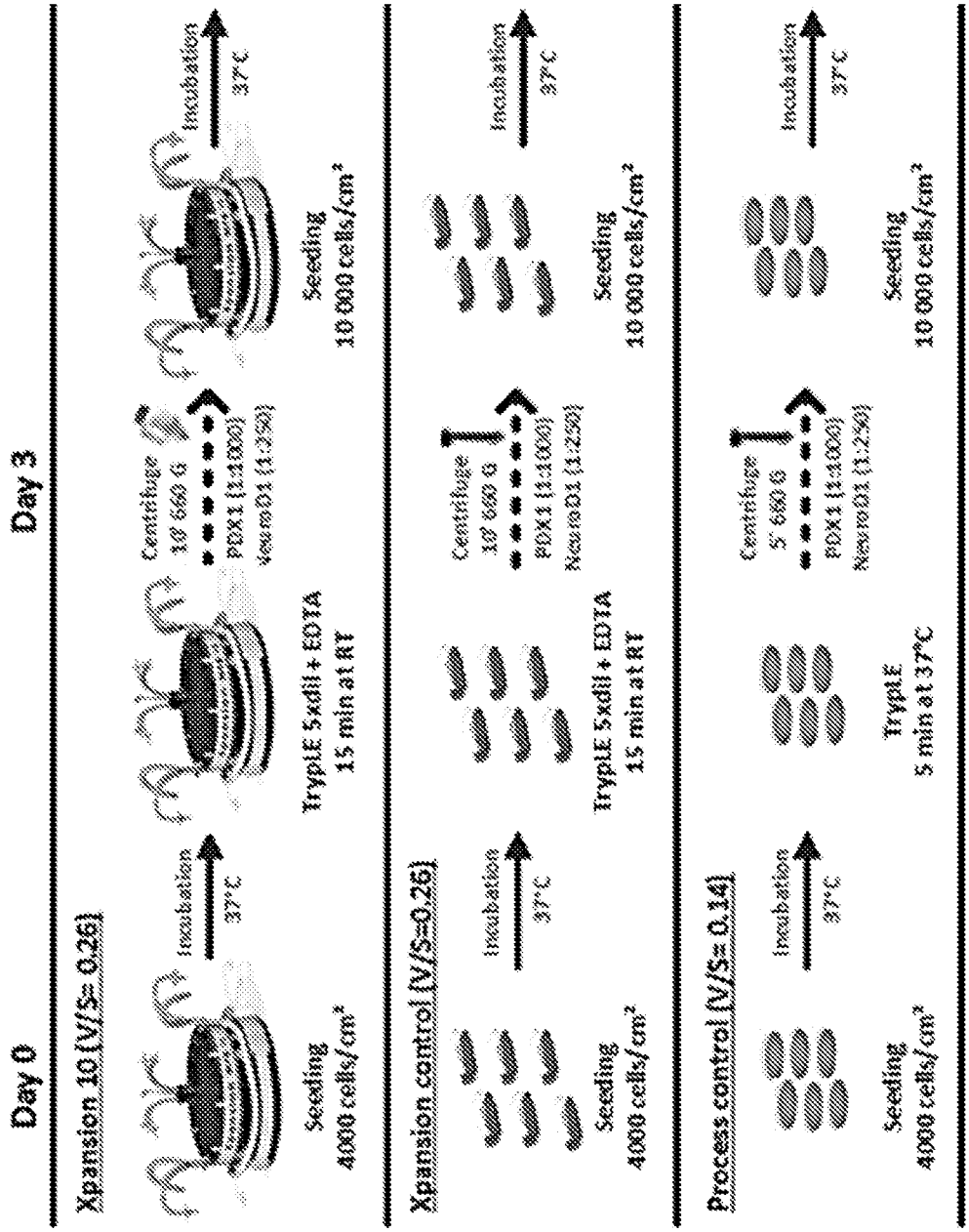

Day 0
Day 3
Xpansion 10 (V/S= 0.26)
Incubation
37°C
Seeding
4000 cells/cm²
TrypLE 5xdil + EDTA
15 min at RT
Centrifuge
10 660 G
PDX1 (1:1000)
Neuro D1 (1:250)
Incubation
37°C
Seeding
10 000 cells/cm²
Xpansion control (V/S=0.26)
Incubation
37°C
Seeding
4000 cells/cm²
TrypLE 5xdil + EDTA
15 min at RT
Centrifuge
10 660 G
PDX1 (1:1000)
Neuro D1 (1:250)
Incubation
37°C
Seeding
10 000 cells/cm²
Process control (V/S= 0.14)
Incubation
37°C
Seeding
4000 cells/cm²
TrypLE
5 min at 37°C
Centrifuge
5' 680 G
PDX1 (1:1000)
Neuro D1 (1:250)
Incubation
37°C
Seeding
10 000 cells/cm²
Seeding
First infection

Figure 29

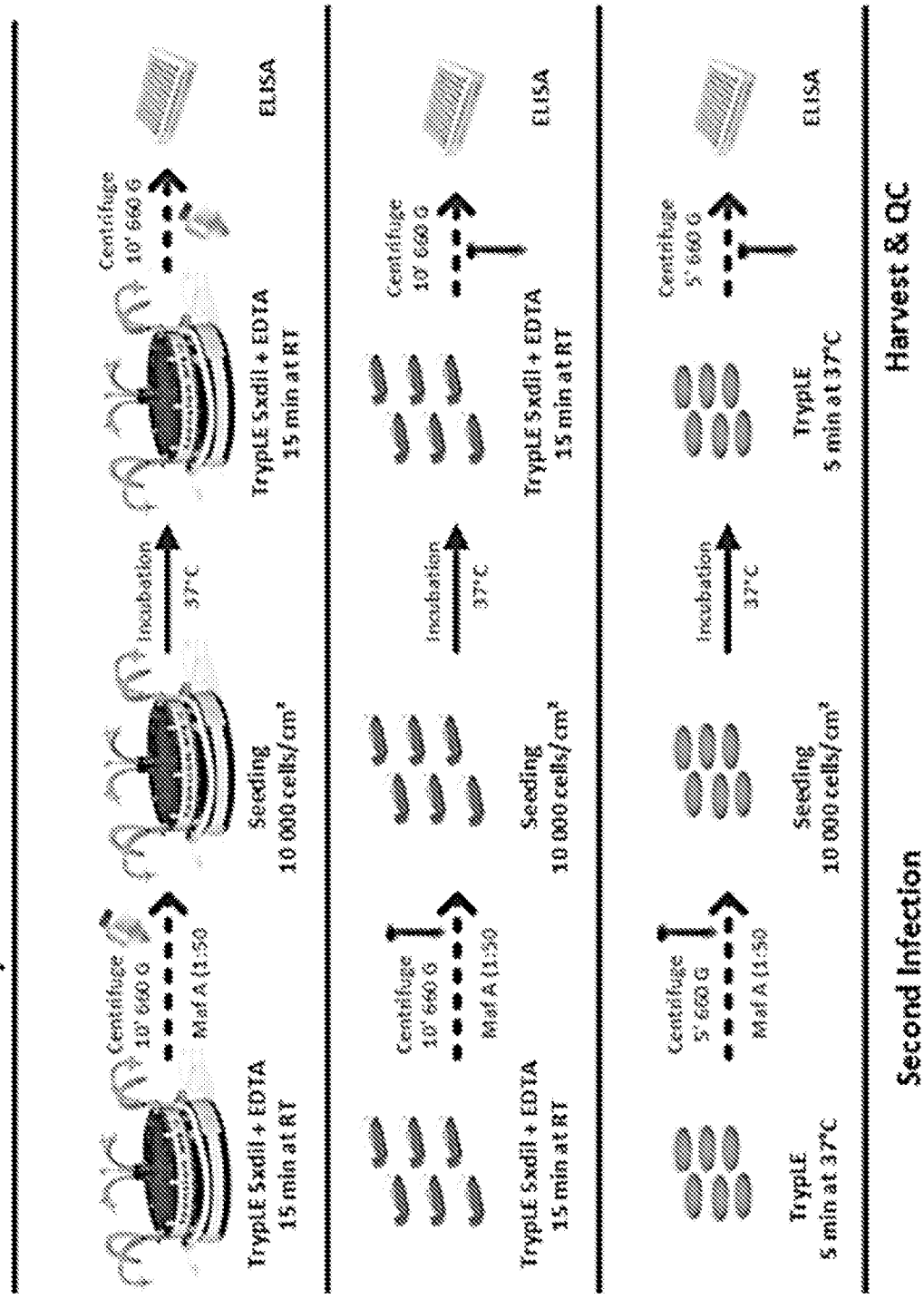


Figure 29 cont.

Figure 30A

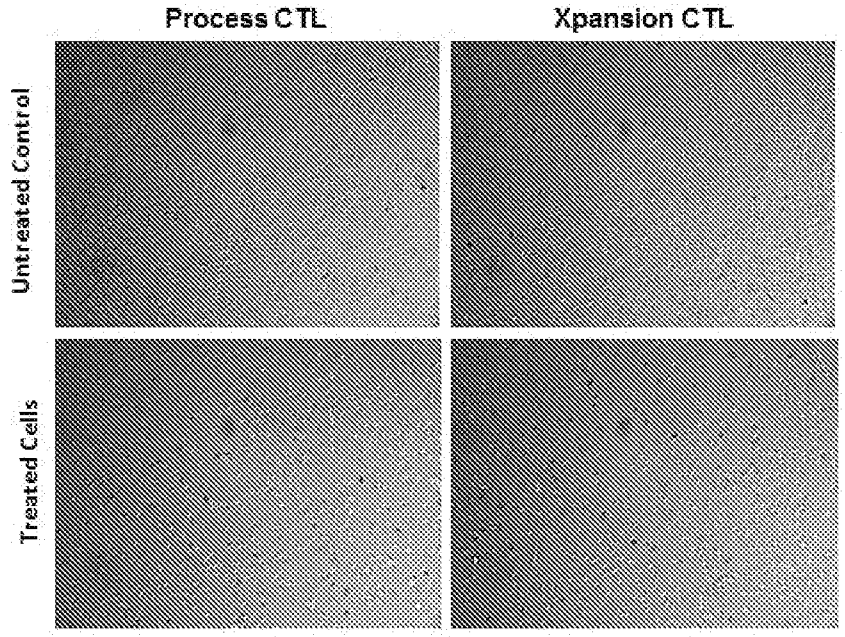


Figure 30B

Figure 30C

Figure 30D

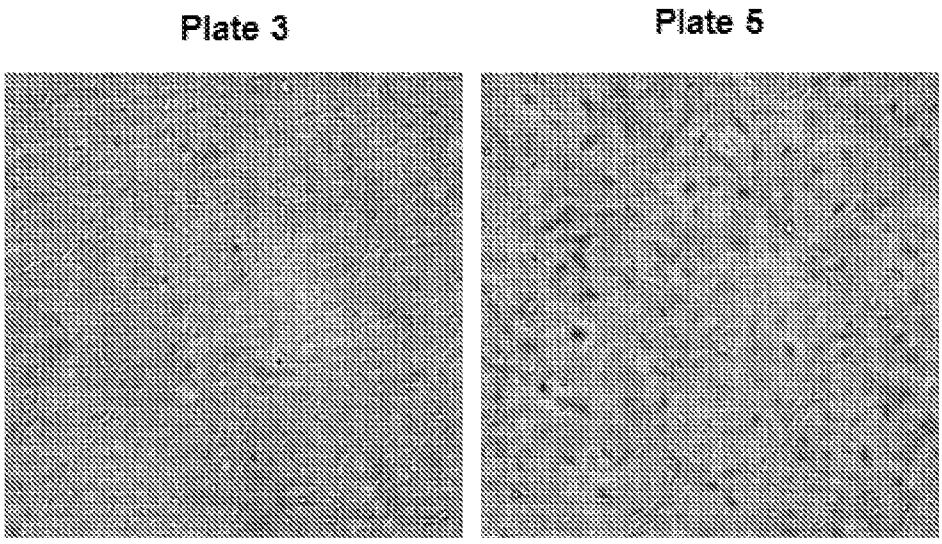


Figure 31A

Figure 31B

Figure 32A

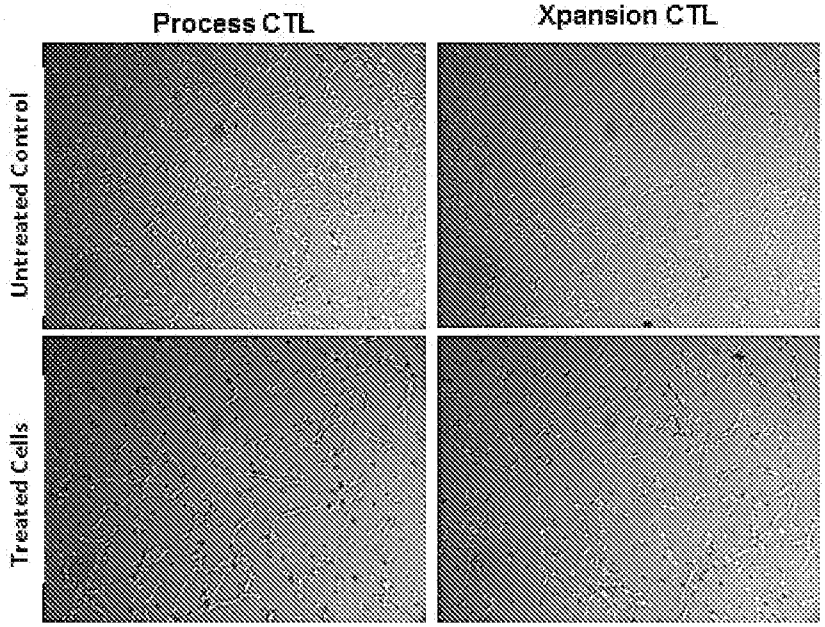


Figure 32B

Figure 32C

Figure 32D

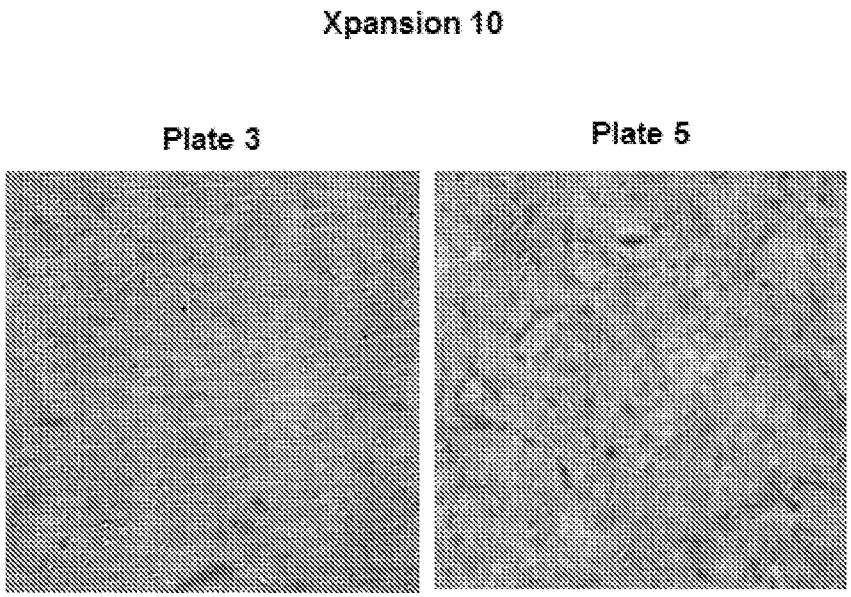


Figure 33A

Figure 33B

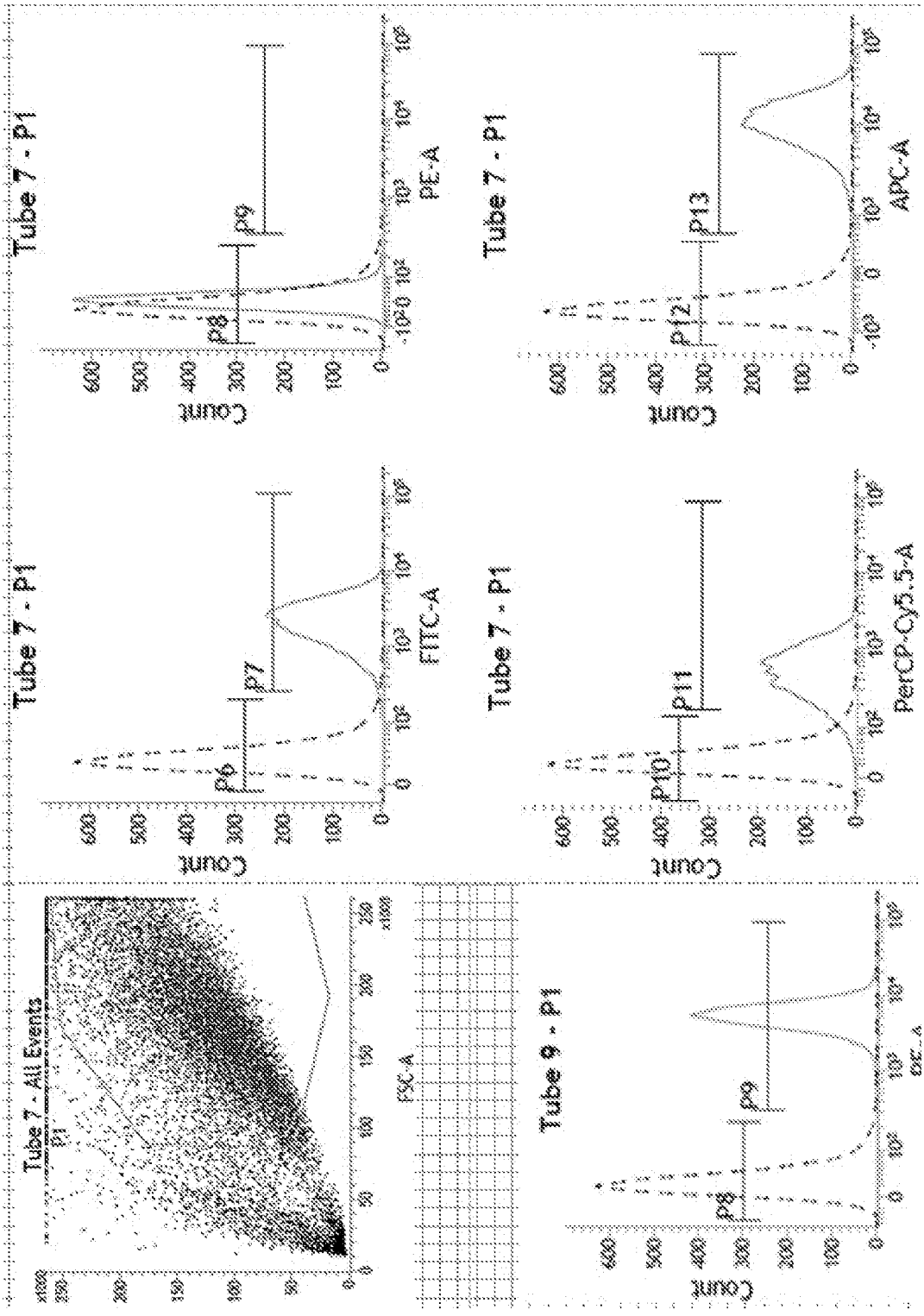

Tube 7 - All Events
P1
FSC-A
SSC-A
Tube 7 - P1
P6
P7
FITC-A
Count
Tube 7 - P1
P8
P9
PE-A
Count
Tube 7 - P1
P10
P11
PerCP-Cy5.5-A
Count
Tube 7 - P1
P12
P13
APC-A
Count
Tube 9 - P1
P8
P9
Count

Figure 34A

ORC_CIL	% CD105	% CD73	% CD90	% CD44	% Negative markers
P12	99,32	99,85	99,55	99,77	0,93
P13	98,75	99,71	99,67	99,70	0,73
P14	96,77	98,60	99,50	99,64	0,58
P16_AdV infection	89,77	99,41	99,22	99,91	0,44

Figure 34B

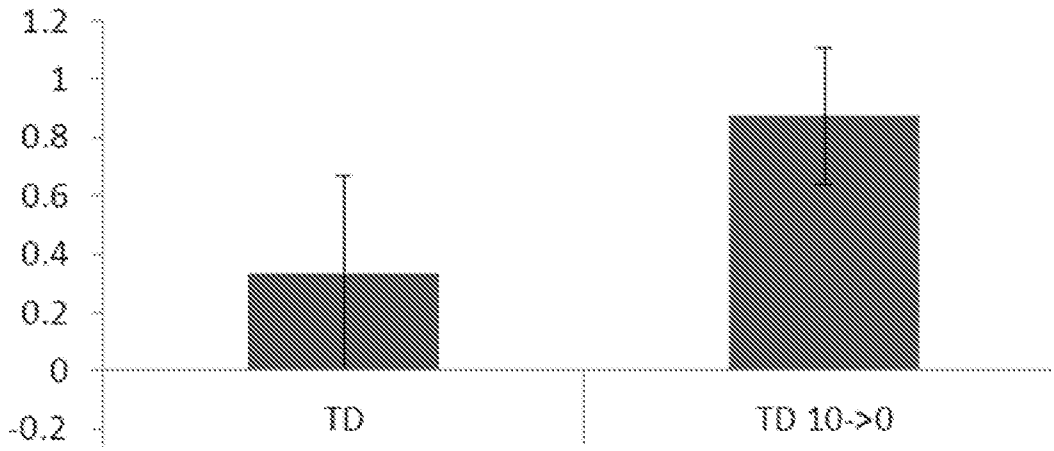


Figure 35A

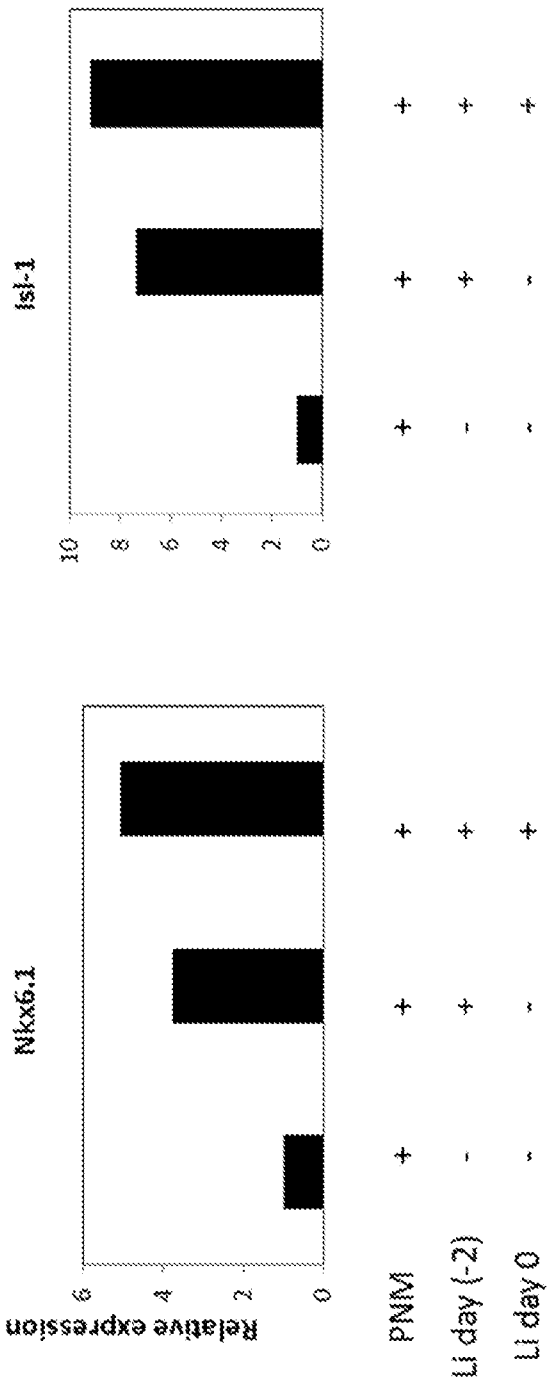

Isl-1
10
8
6
4
2
0
Nkx6.1
Relative expression
6
4
2
0
PNM
Li day (-2)
Li day 0 onward
+
-
+
+
+
+
+
+
+

Figure 35B

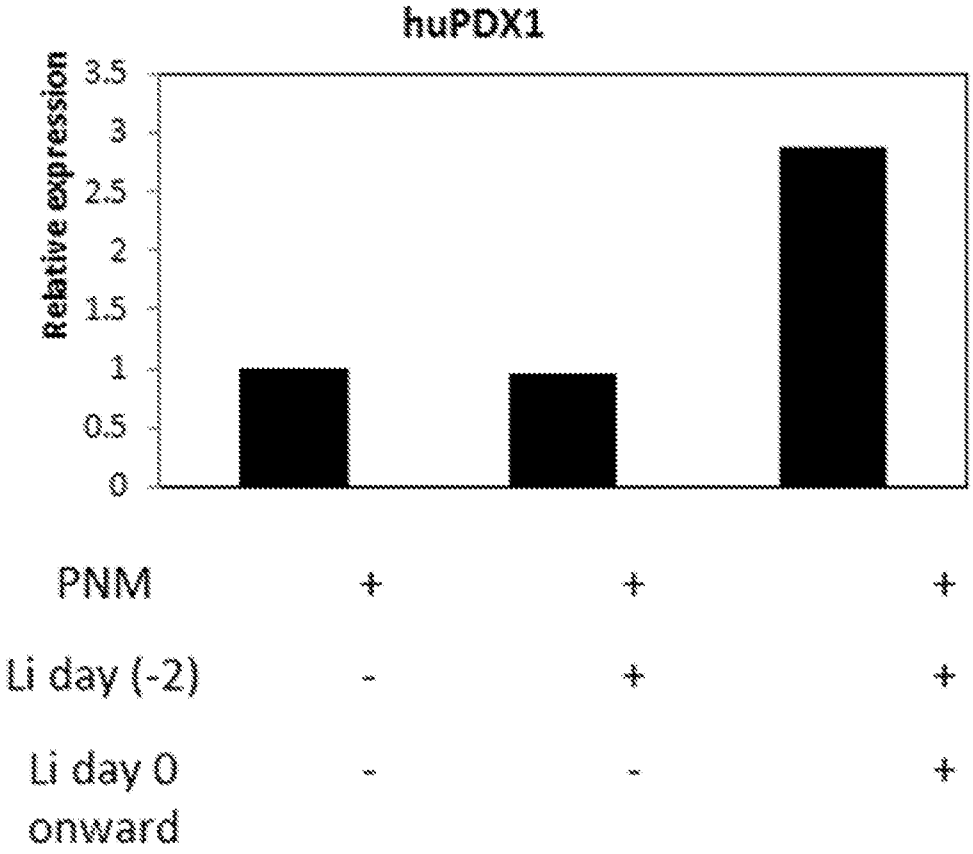


Figure 35C

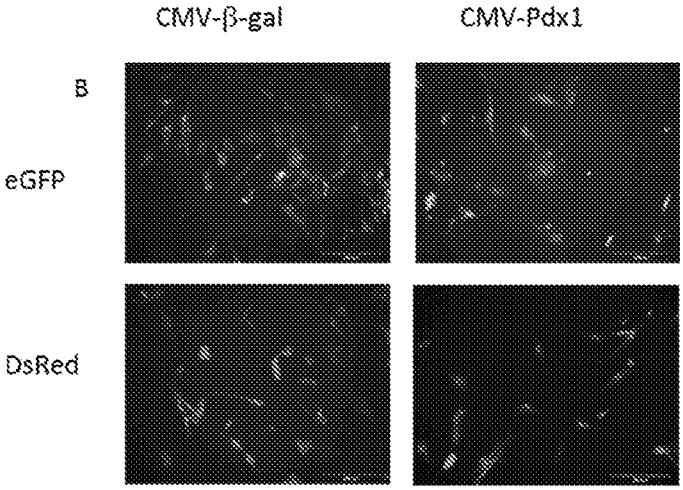


Figure 36

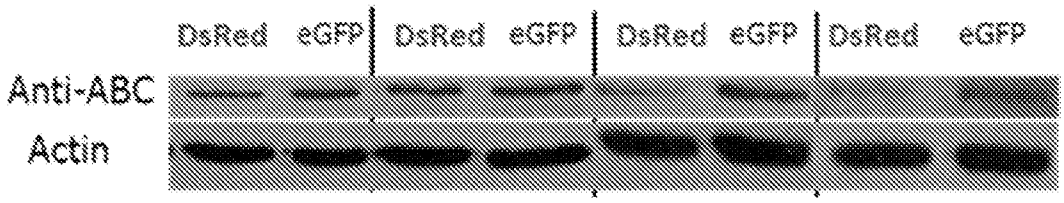


Figure 37A

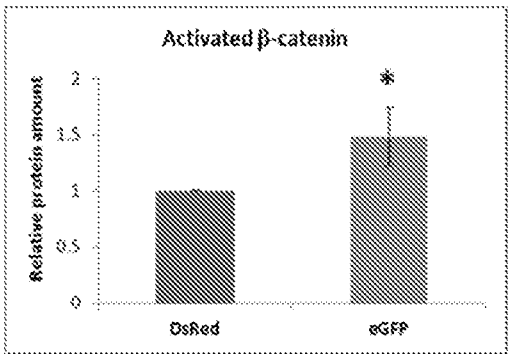


Figure 37B

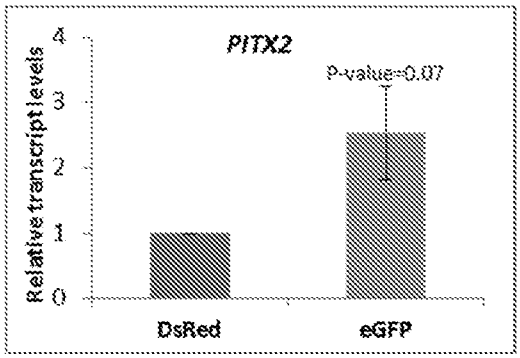


Figure 37C

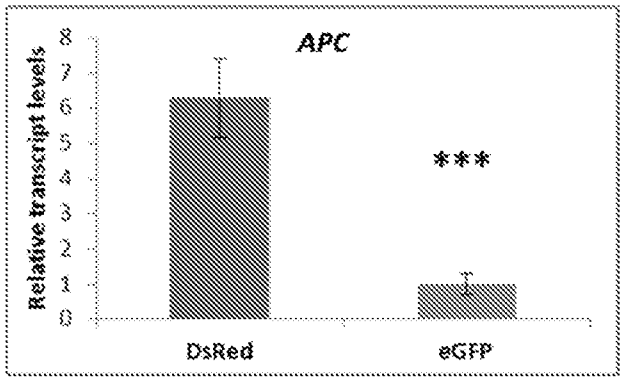


Figure 37D

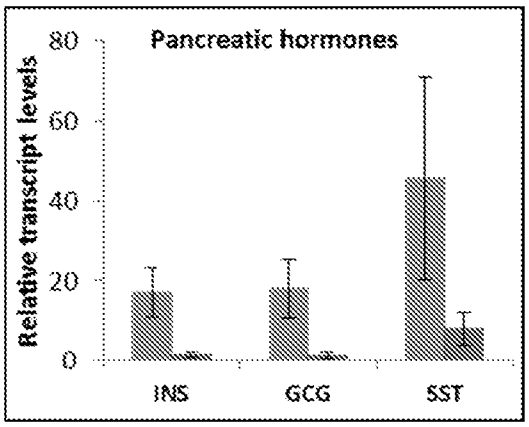


Figure 38A

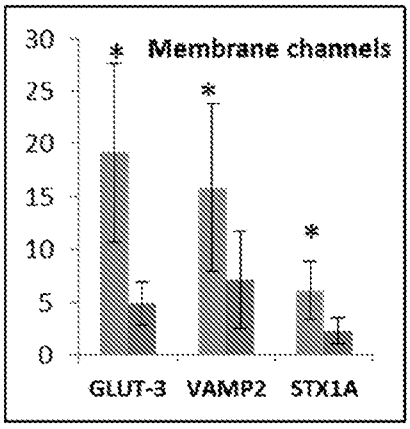


Figure 38B

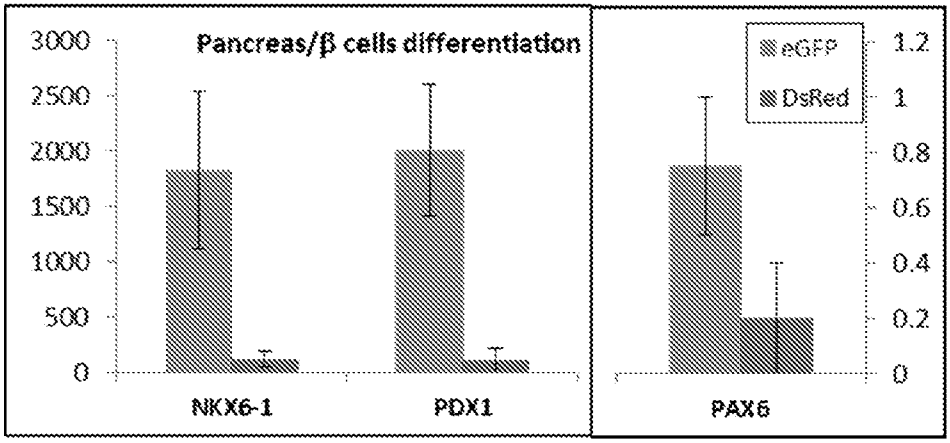


Figure 38C

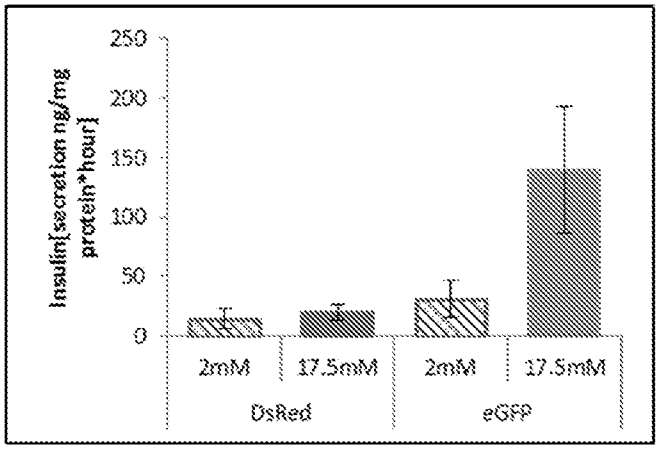


Figure 38D

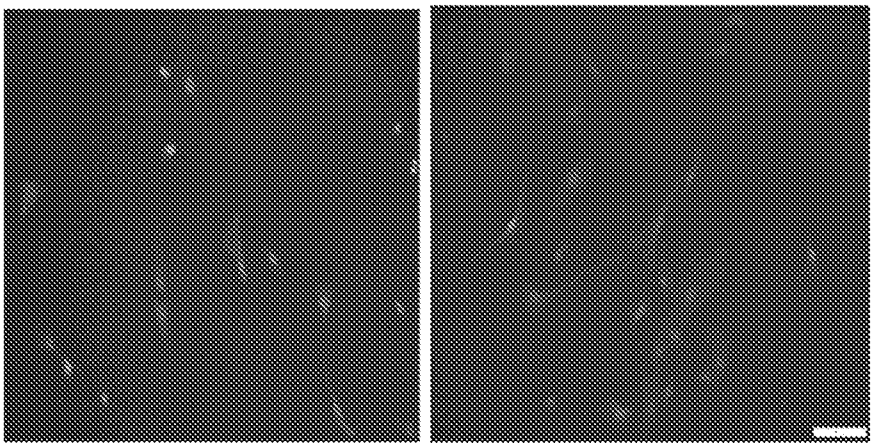


Figure 38E

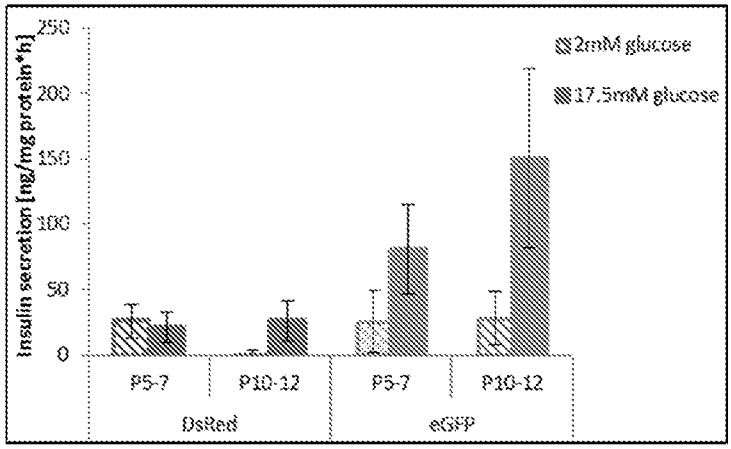


Figure 38F

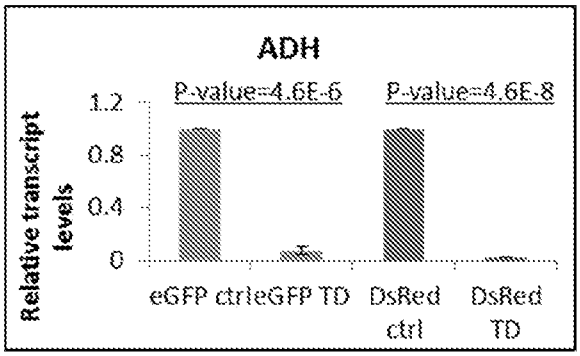


Figure 39A

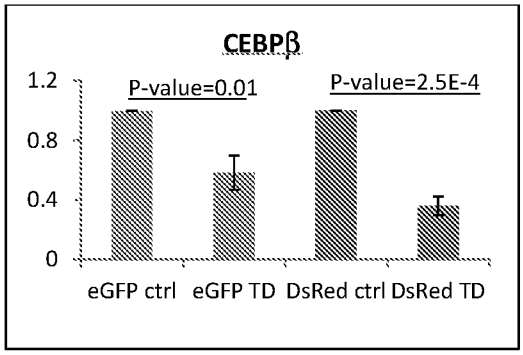


Figure 39B

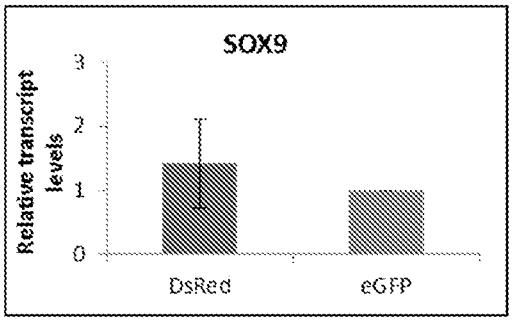


Figure 39C

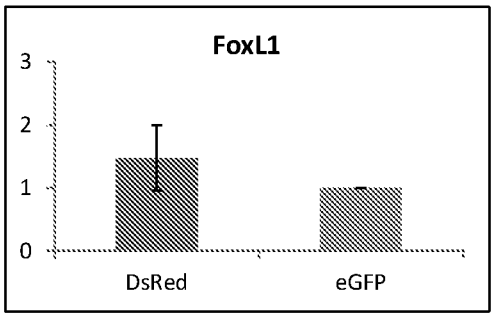


Figure 39D

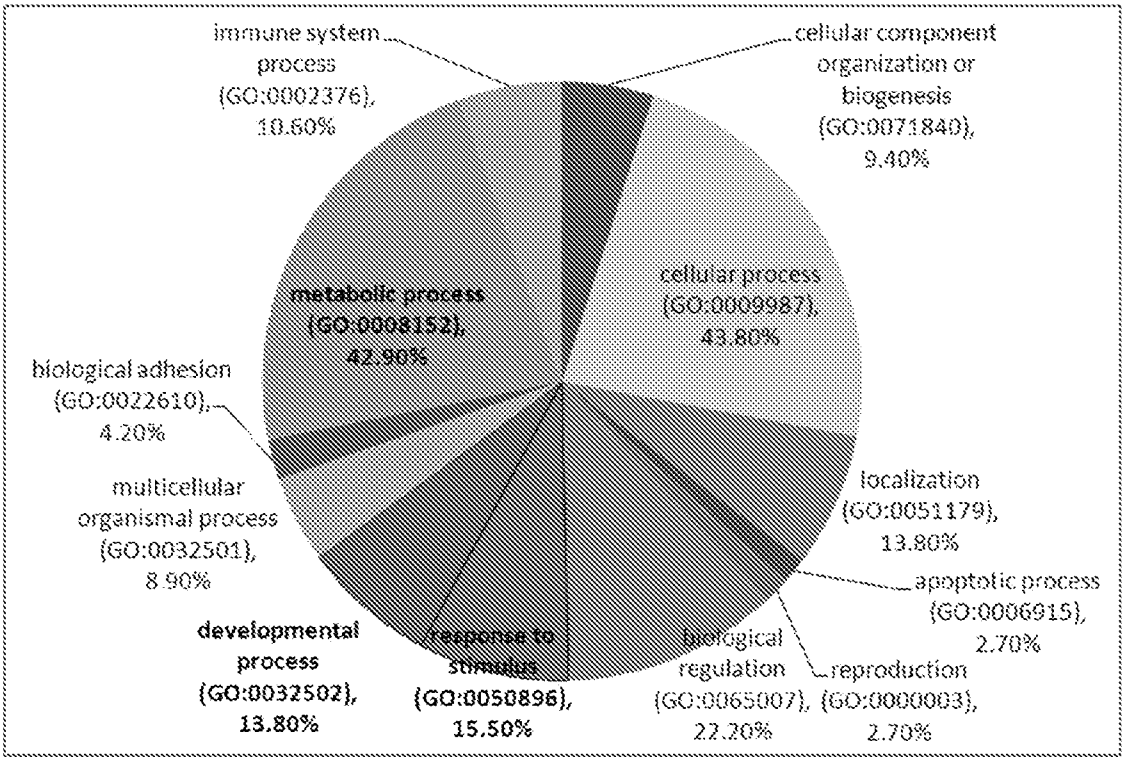
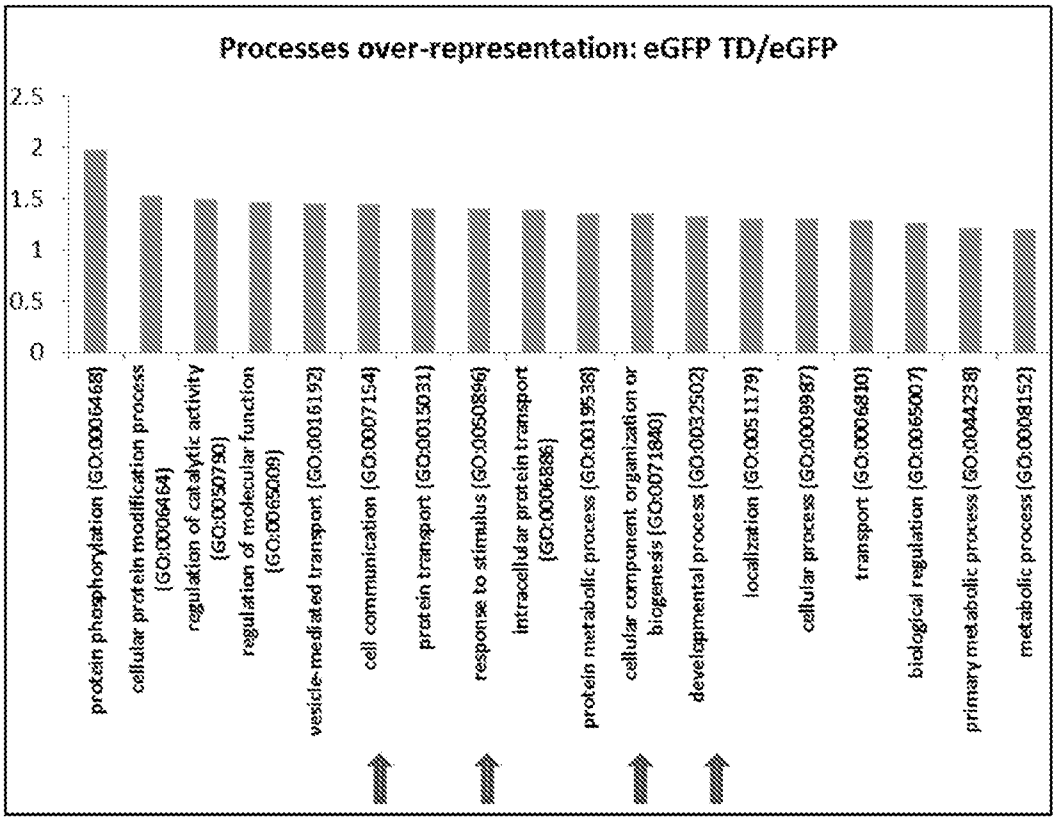


Figure 40A


Processes over-representation: eGFP TD/eGFP
2.5
2
1.5
1
0.5
0
protein phosphorylation (GO:0006468)
cellular protein modification process (GO:0006464)
regulation of catalytic activity (GO:0030790)
regulation of molecular function (GO:0065009)
vesicle-mediated transport (GO:0016192)
cell communication (GO:0007154)
protein transport (GO:0015031)
response to stimulus (GO:0050896)
intracellular protein transport (GO:0006886)
protein metabolic process (GO:0019538)
cellular component organization or biogenesis (GO:0071840)
developmental process (GO:0032502)
localization (GO:0051179)
cellular process (GO:0009987)
transport (GO:0006810)
biological regulation (GO:0065007)
primary metabolic process (GO:0044238)
metabolic process (GO:0008152)

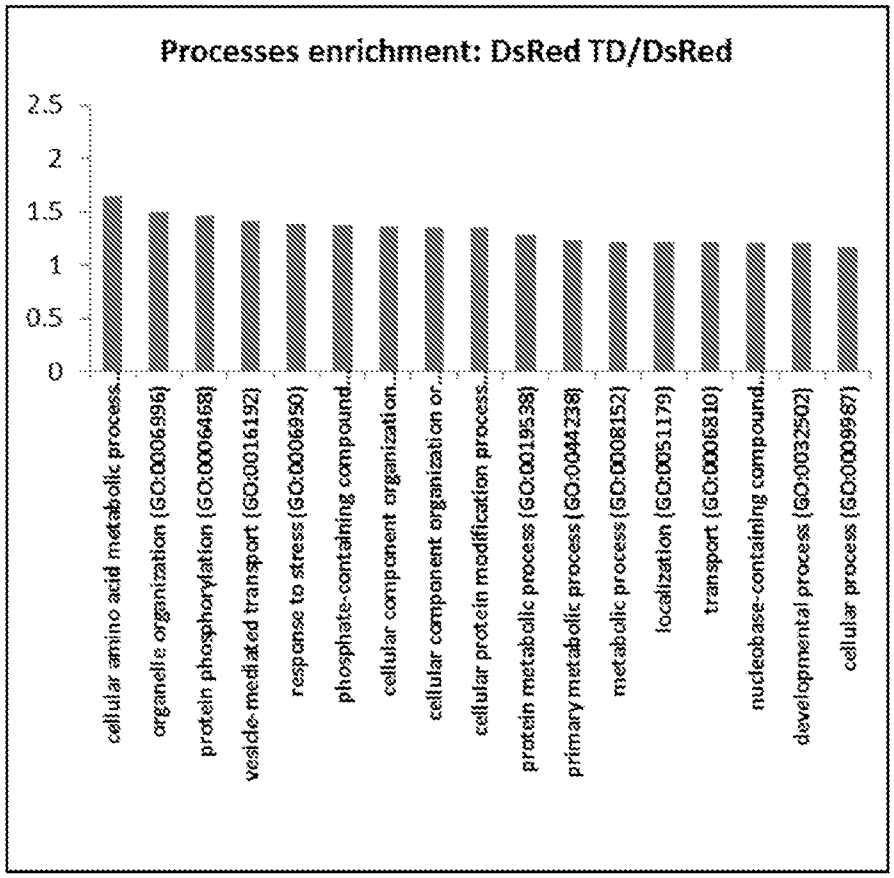

Processes enrichment: DsRed TD/DsRed
2.5
2
1.5
1
0.5
0
cellular amino acid metabolic process...
organelle organization (GO:0006996)
protein phosphorylation (GO:0006468)
vesicle-mediated transport (GO:0016192)
response to stress (GO:0006950)
phosphate-containing compound...
cellular component organization...
cellular component organization or...
cellular protein modification process...
protein metabolic process (GO:0019538)
primary metabolic process (GO:0044238)
metabolic process (GO:0008152)
localization (GO:0051179)
transport (GO:0006810)
nucleobase-containing compound...
developmental process (GO:0032502)
cellular process (GO:0009987)

Figure 40B

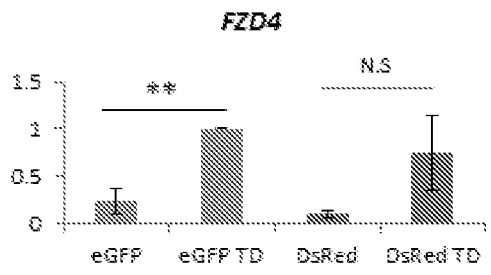


Figure 40C

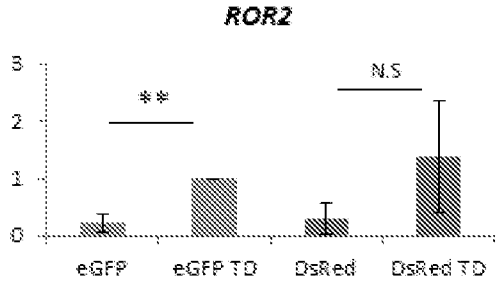


Figure 40D

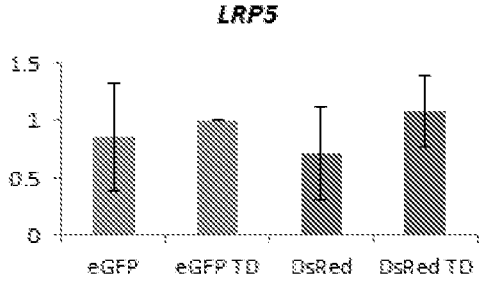


Figure 40E

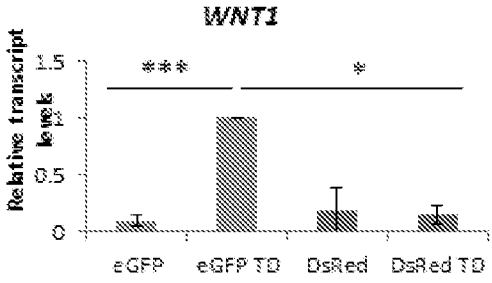


Figure 40F

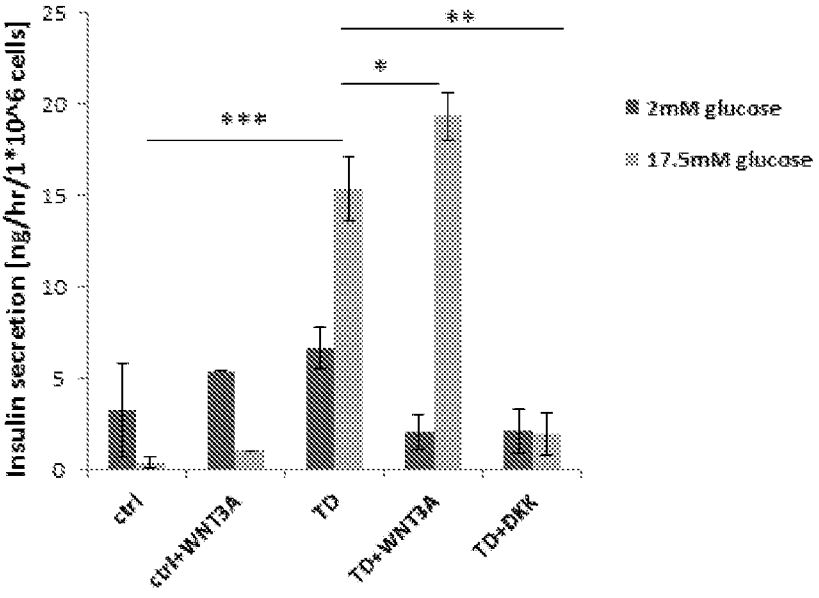


Figure 41A

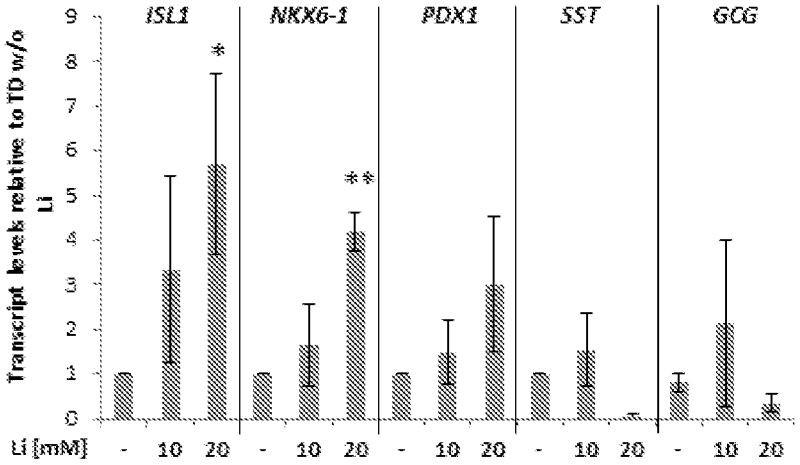


Figure 41B

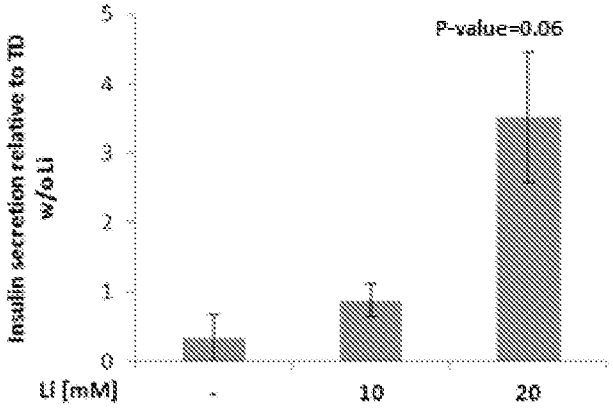


Figure 41C

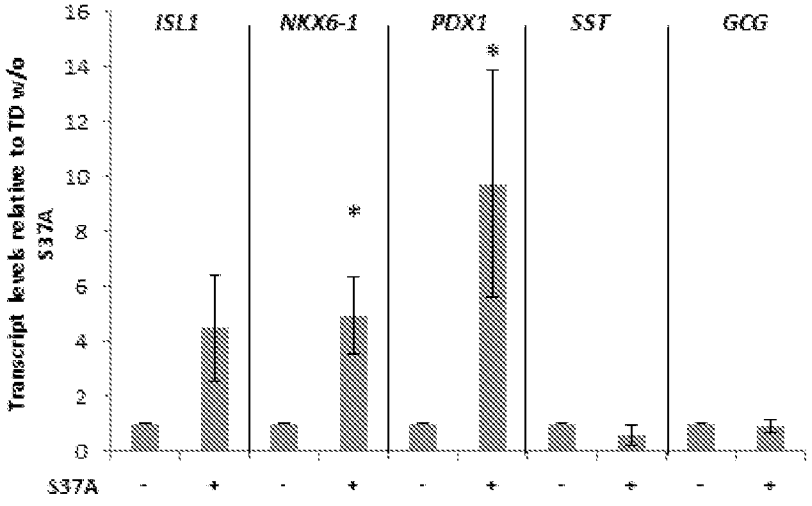


Figure 41D

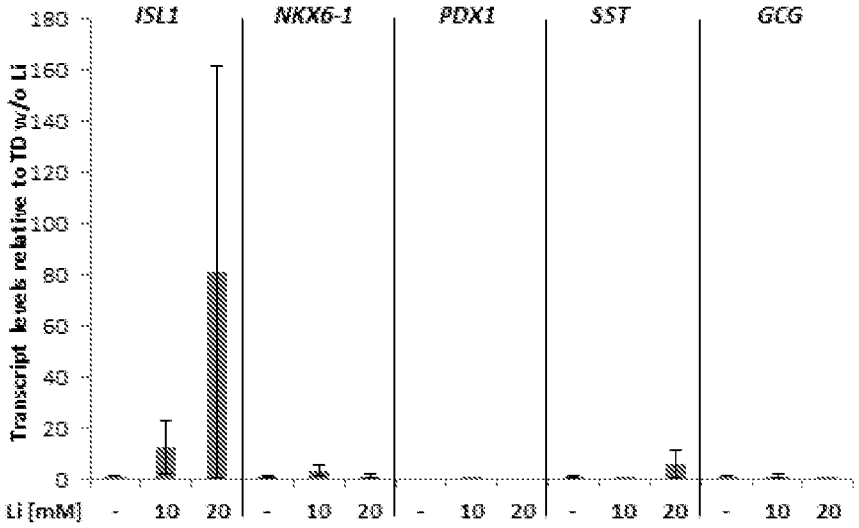


Figure 41E

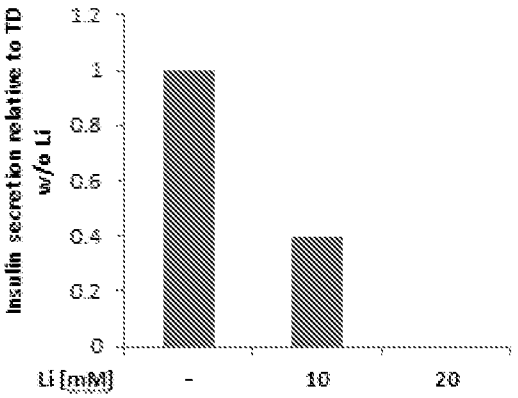


Figure 41F

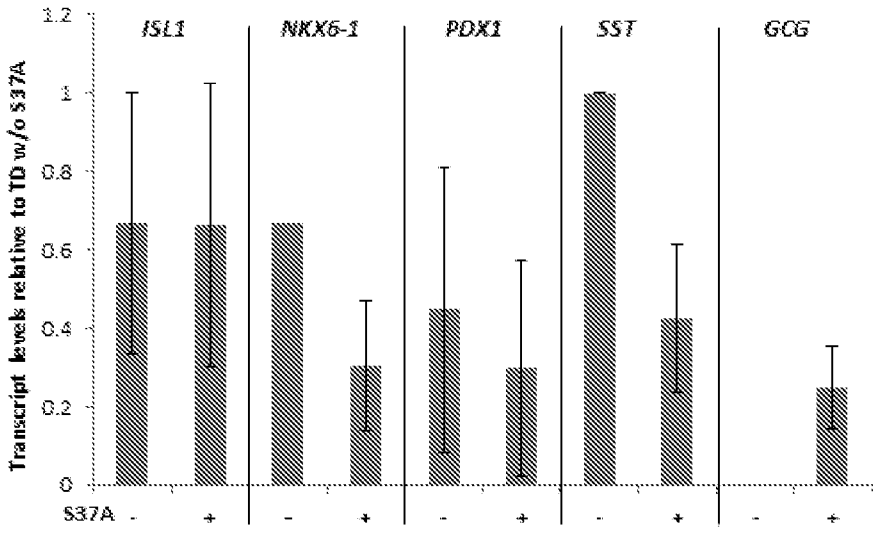


Figure 41G

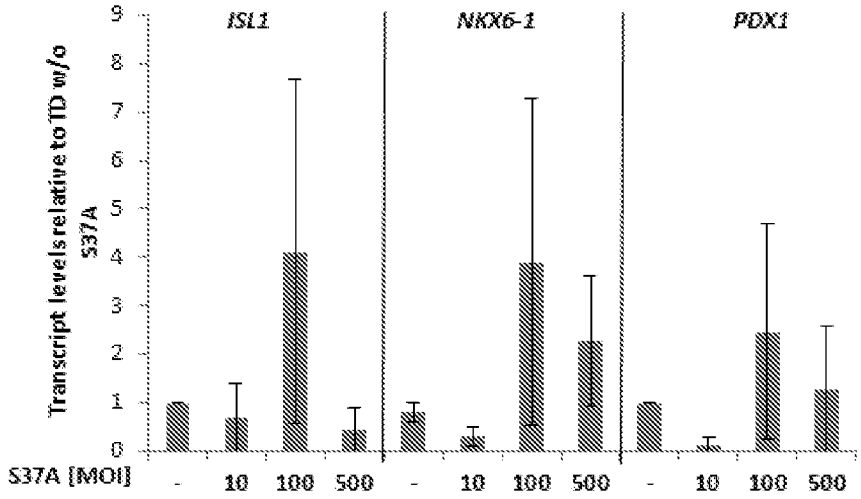


Figure 42

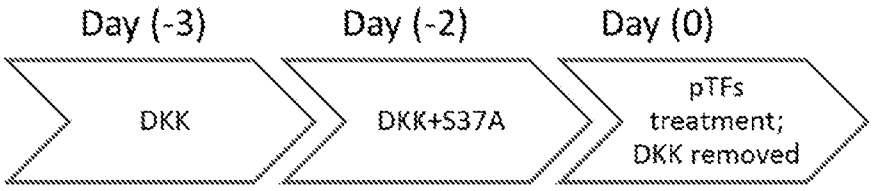


Figure 43A

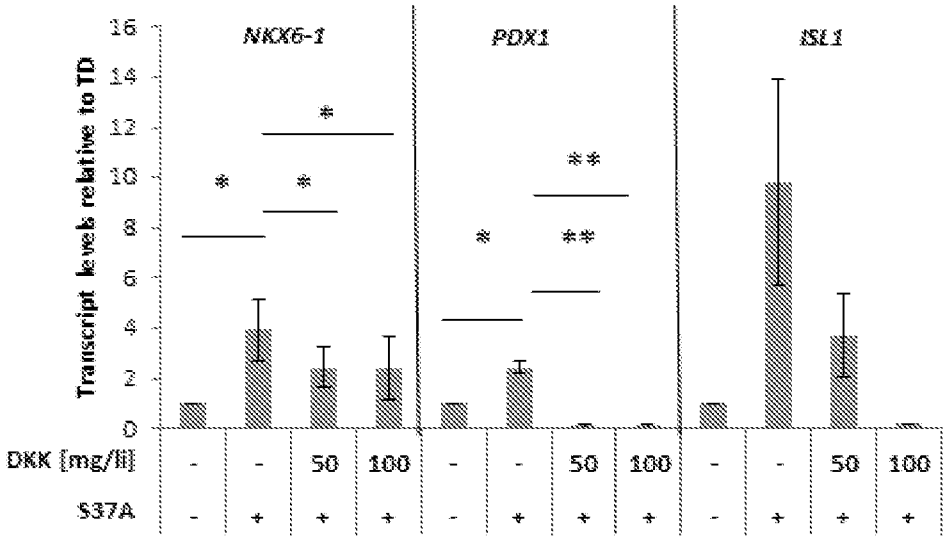


Figure 43B

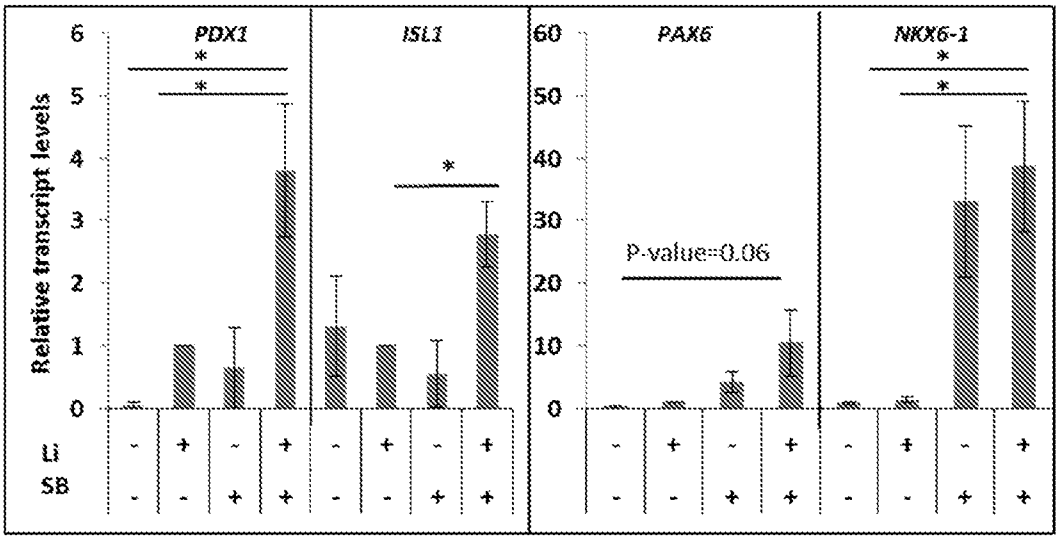


Figure 44A

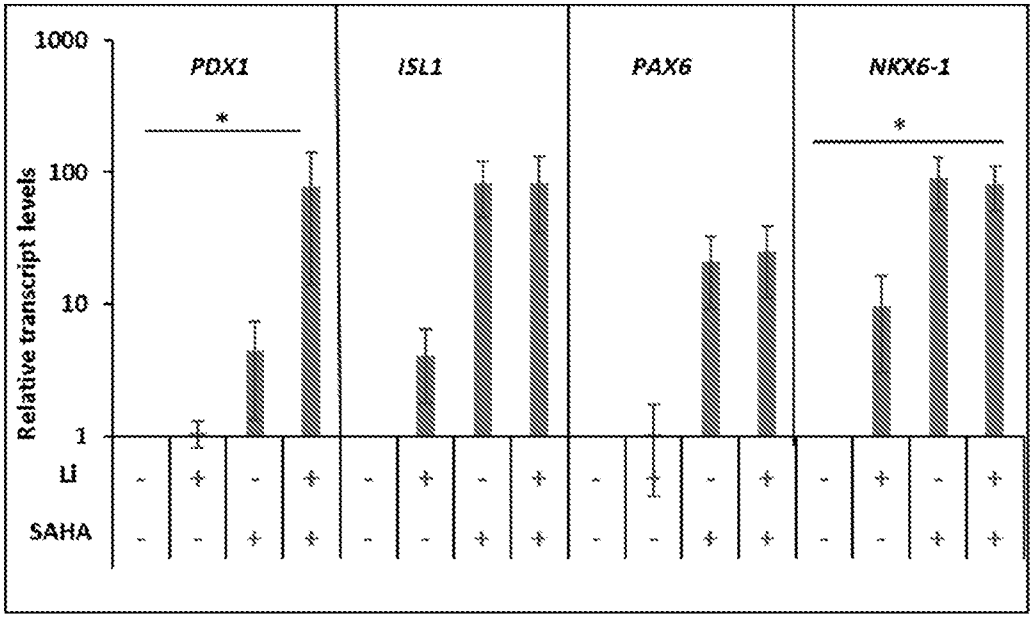


Figure 44B

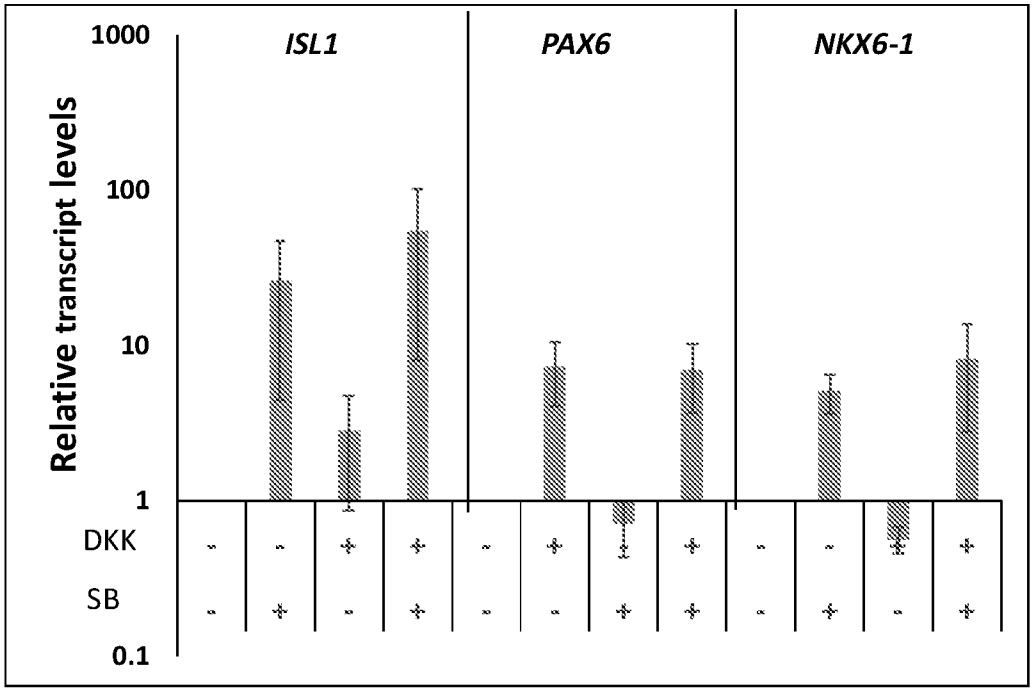

Relative transcript levels
1000
100
10
1
0.1
ISL1
PAX6
NKX6-1
DKK
SB

Figure 44C

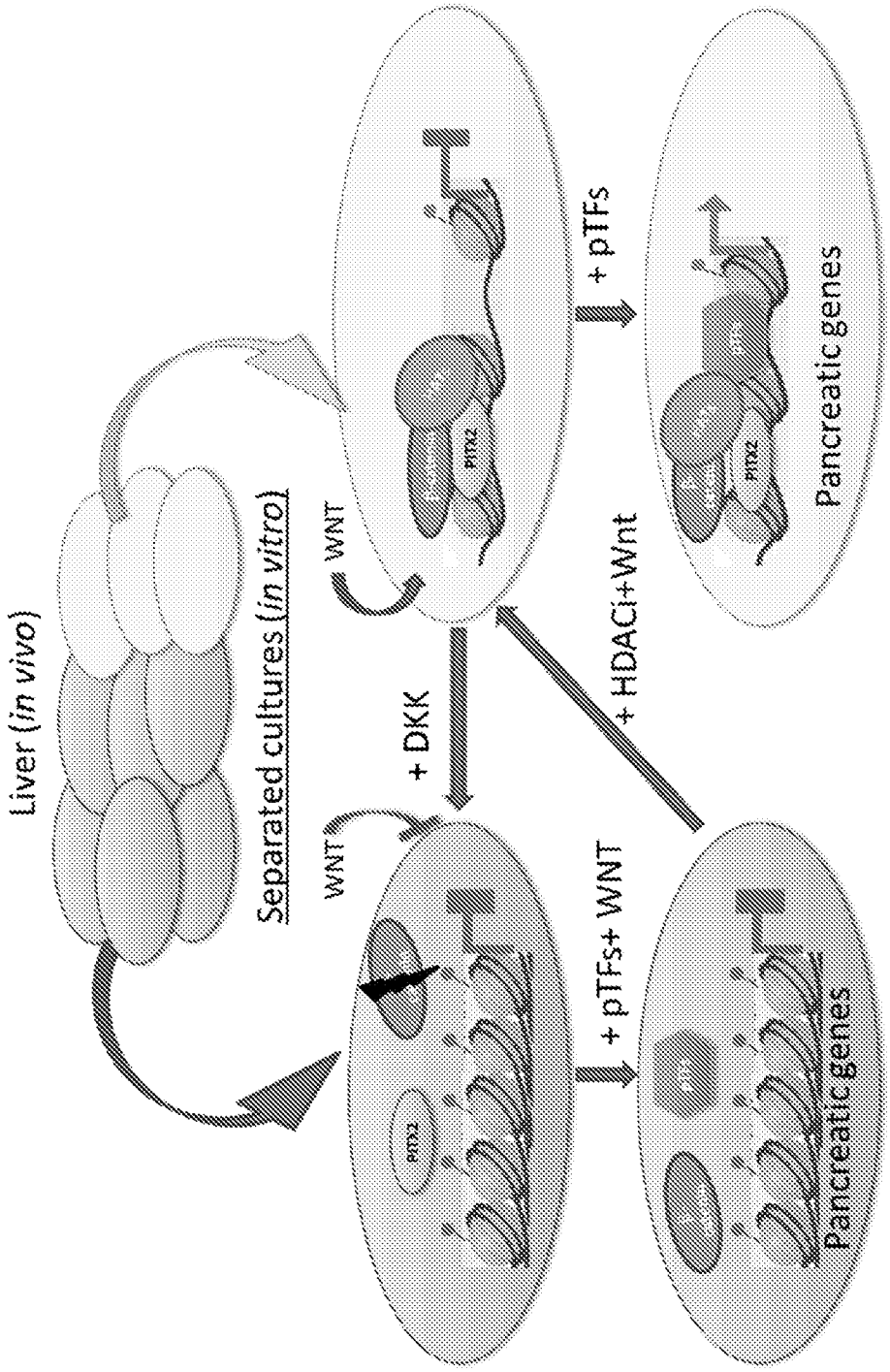

Liver (in vivo)
Separated cultures (in vitro)
WNT
WNT
+ DKK
+ pTFs
+ HDACi+Wnt
+ pTFs+ WNT
PITX2
PITX2
PITX2
Pancreatic genes
Pancreatic genes

Figure 45

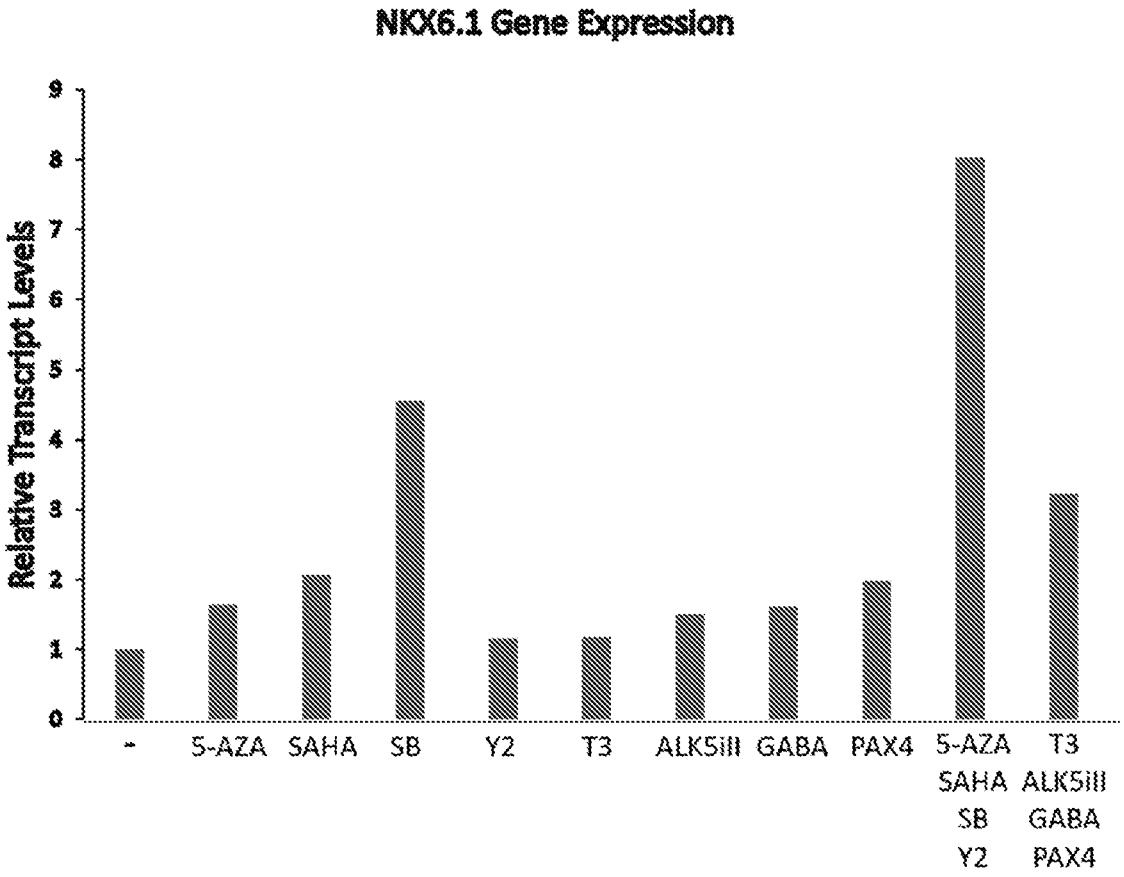

NKX6.1 Gene Expression
Relative Transcript Levels
0
1
2
3
4
5
6
7
8
9
-
5-AZA
SAHA
SB
Y2
T3
ALK5iII
GABA
PAX4
5-AZA SAHA SB Y2
T3 ALK5iII GABA PAX4

Figure 46

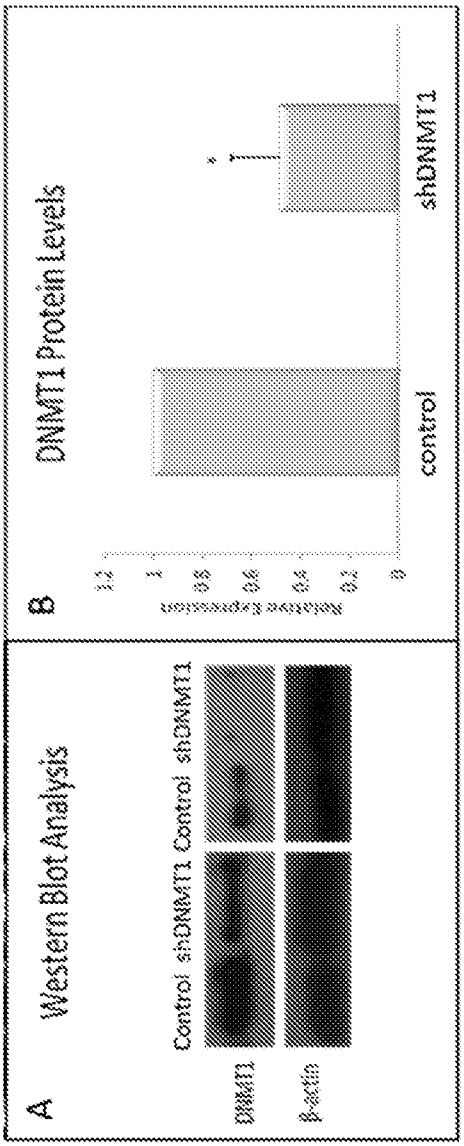


Figure 47A

Figure 47B

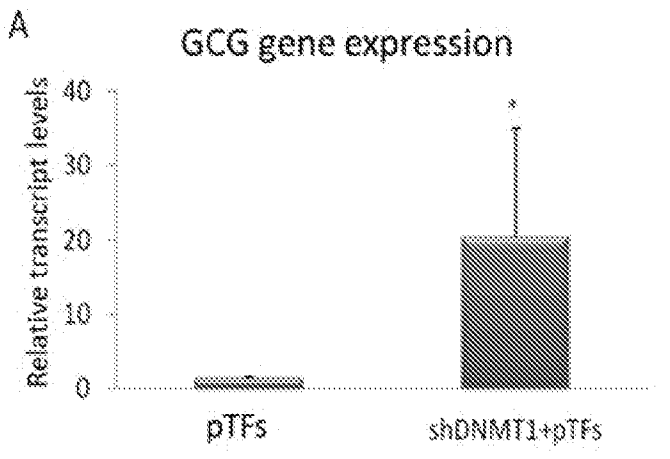


Figure 48A

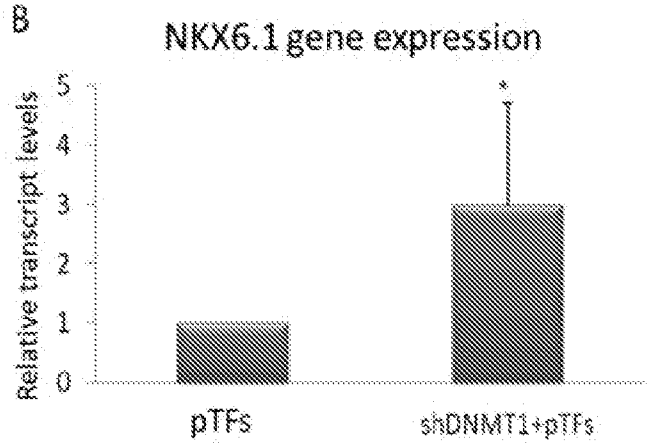


Figure 48B

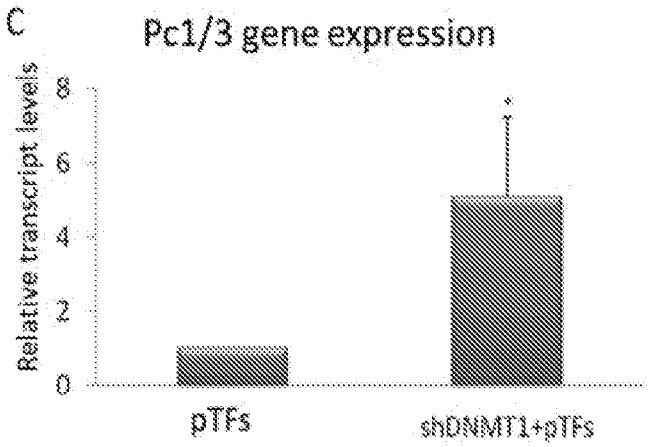


Figure 48C

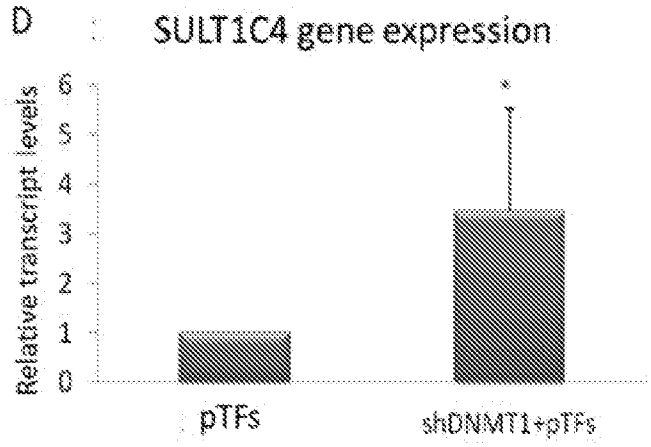


Figure 48D