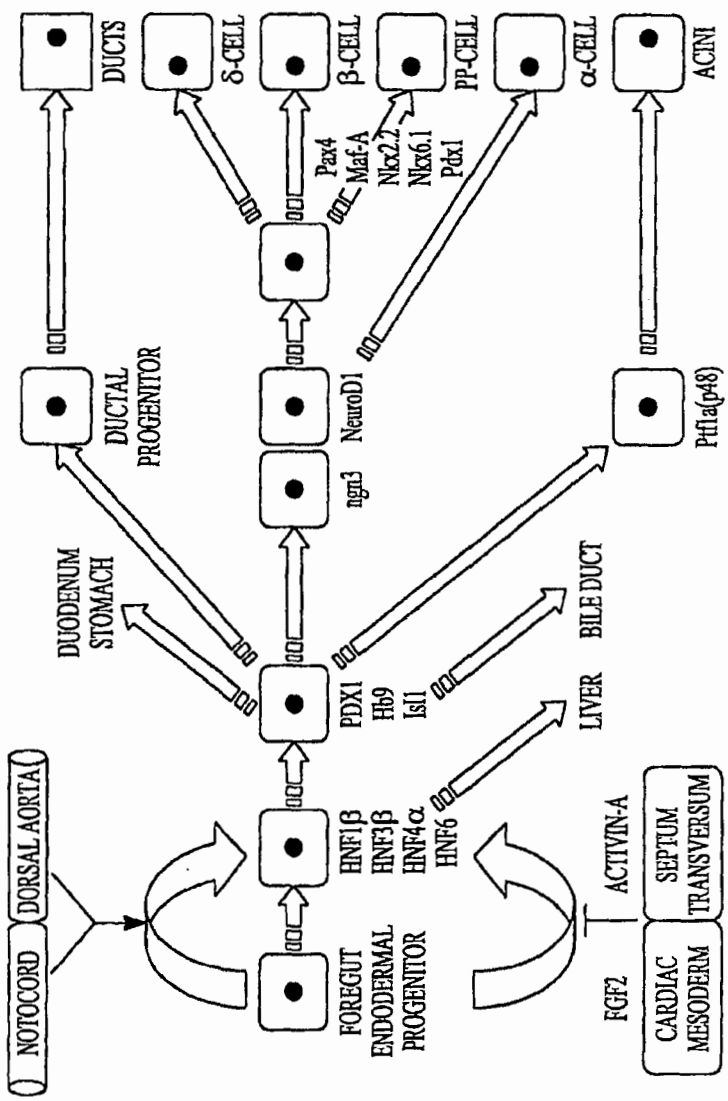

NOTOCORD
DORSAL AORTA
FOREGUT ENDODERMAL PROGENITOR
HNF1β HNF3β HNF4α HNF6
PDX1 Hb9 Isl1
LIVER
BILE DUCT
DUODENUM STOMACH
DUCTAL PROGENITOR
DUCTS
ngn3
NeuroD1
δ-CELL
Pax4 Maf-A
β-CELL
Nkx2.2 Nkx6.1
PP-CELL
Pdx1
α-CELL
Ptf1a(p48)
ACINI
FGF2
ACTIVIN-A
CARDIAC MESODERM
SEPTUM TRANSVERSUM

FIG. 1

Oct4 mRNA EXPRESSION MAPC
(RELATIVE TO GAPDH)

HIGH oct4 (HO)	0.3241 ± 0.333
LOW oct4 (LO)	0.0003 ± 0.00001

FIG. 2A

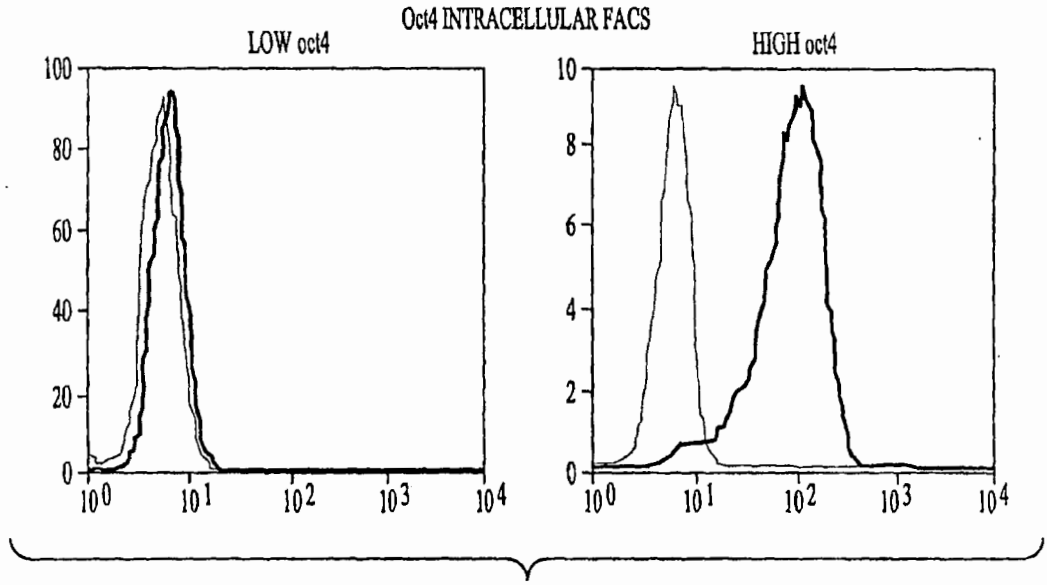


FIG. 2B

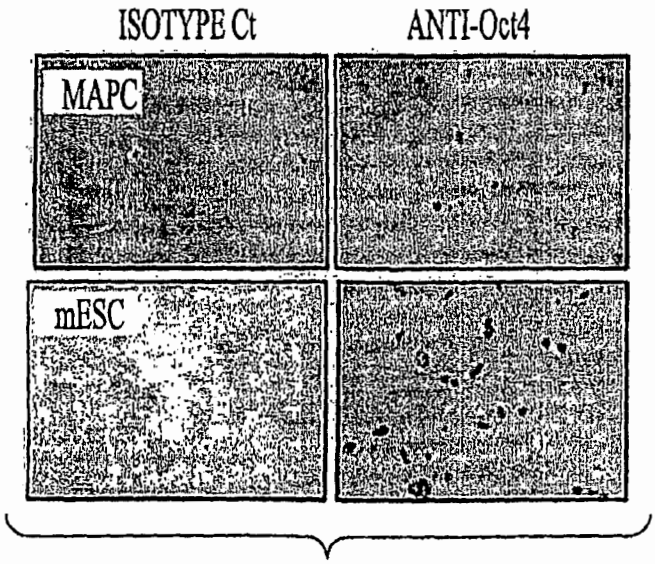


FIG. 2C

	HIGH Oct 4 mMAPC
Oct3/4	20-80
Rex1	10-100
Nanog	<0.01
Sox2	<0.001
Fgf4	<0.1
Fbx15	100
FoxD3	100
Utf1	<0.1
Eras	<0.01
Tcl1	<0.01
Tdgf1	<0.01
Ecat1	<0.1
Egs1	10-30
GDF3	<0.01
Dnmt31	80.-100
Ecat7	80-100

FIG. 2D

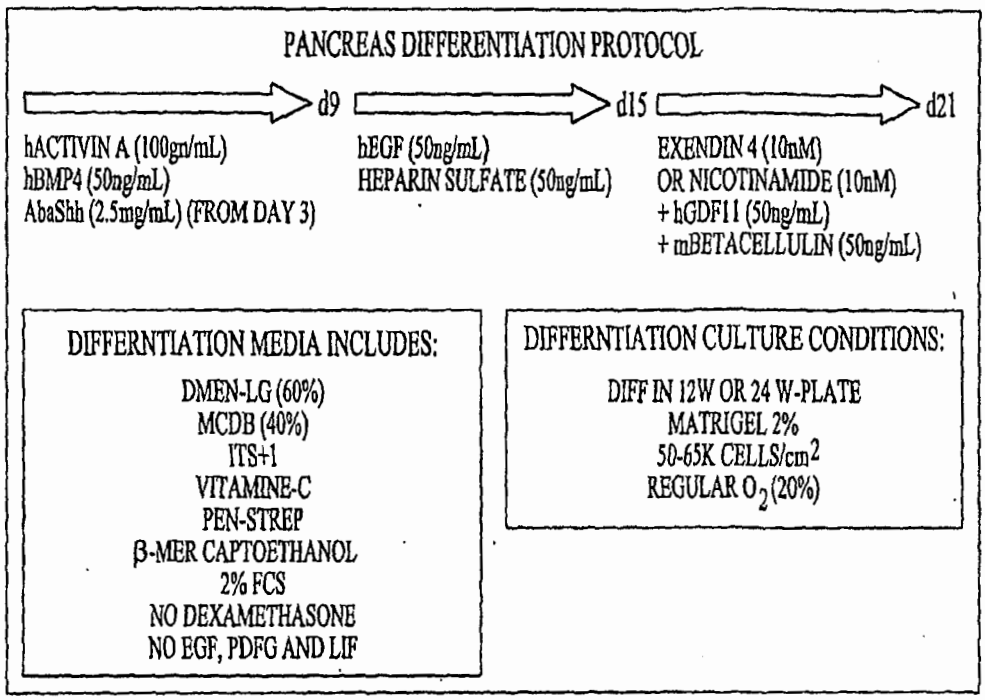

PANCREAS DIFFERENTIATION PROTOCOL
d9
d15
d21
hACTIVIN A (100gn/mL)
hBMP4 (50ng/mL)
AbaShh (2.5mg/mL) (FROM DAY 3)
hEGF (50ng/mL)
HEPARIN SULFATE (50ng/mL)
EXENDIN 4 (10nM)
OR NICOTINAMIDE (10nM)
+ hGDF11 (50ng/mL)
+ mBETACELLULIN (50ng/mL)
DIFFERNTIATION MEDIA INCLUDES:
DMEN-LG (60%)
MCDB (40%)
ITS+1
VITAMINE-C
PEN-STREP
β-MER CAPTOETHANOL
2% FCS
NO DEXAMETHASONE
NO EGF, PDFG AND LIF
DIFFERNTIATION CULTURE CONDITIONS:
DIFF IN 12W OR 24 W-PLATE
MATRIGEL 2%
50-65K CELLS/cm2
REGULAR O2 (20%)

FIG. 3A

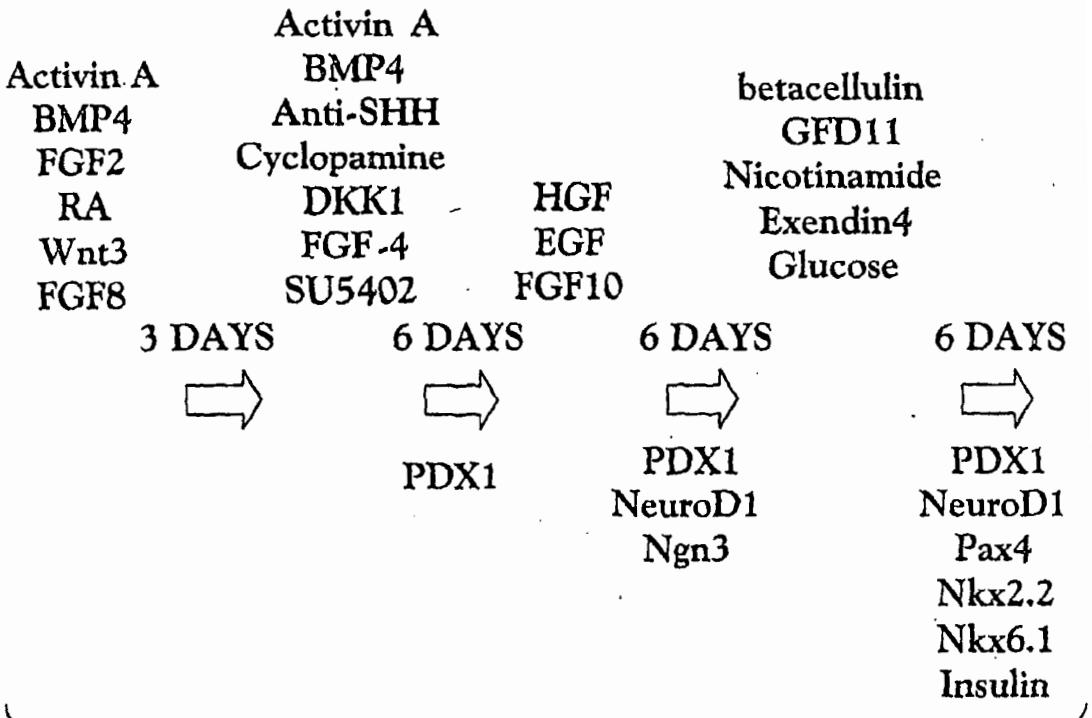

Activin A
BMP4
FGF2
RA
Wnt3
FGF8
Activin A
BMP4
Anti-SHH
Cyclopamine
DKK1
FGF-4
SU5402
HGF
EGF
FGF10
betacellulin
GFD11
Nicotinamide
Exendin4
Glucose
3 DAYS
6 DAYS
6 DAYS
6 DAYS
PDX1
PDX1
NeuroD1
Ngn3
PDX1
NeuroD1
Pax4
Nkx2.2
Nkx6.1
Insulin

FIG. 3B

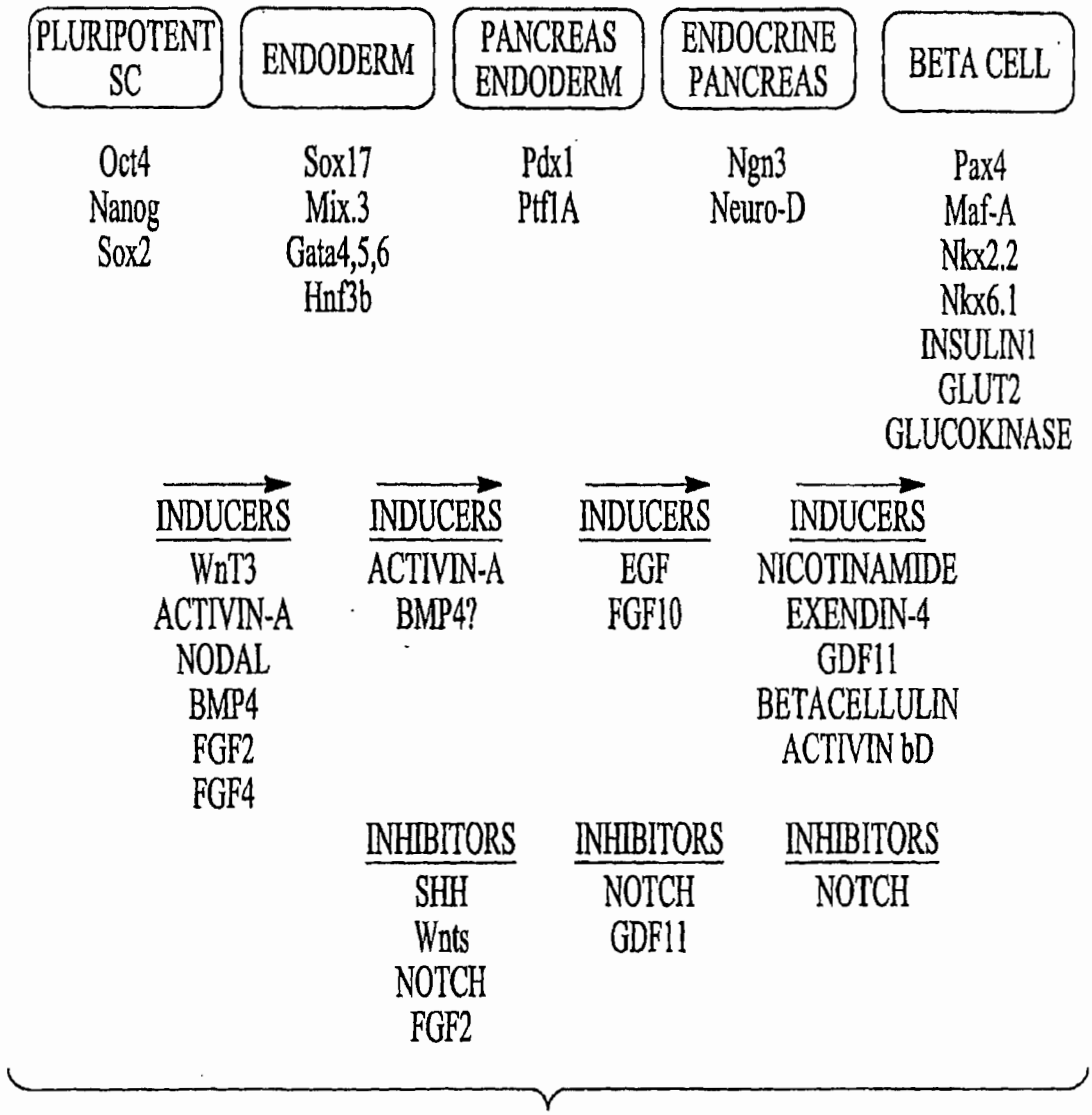

PLURIPOTENT SC
ENDODERM
PANCREAS ENDODERM
ENDOCRINE PANCREAS
BETA CELL
Oct4
Nanog
Sox2
Sox17
Mix.3
Gata4,5,6
Hnf3b
Pdx1
Ptf1A
Ngn3
Neuro-D
Pax4
Maf-A
Nkx2.2
Nkx6.1
INSULIN1
GLUT2
GLUCOKINASE
INDUCERS
WnT3
ACTIVIN-A
NODAL
BMP4
FGF2
FGF4
INDUCERS
ACTIVIN-A
BMP4?
INDUCERS
EGF
FGF10
INDUCERS
NICOTINAMIDE
EXENDIN-4
GDF11
BETACELLULIN
ACTIVIN bD
INHIBITORS
SHH
Wnts
NOTCH
FGF2
INHIBITORS
NOTCH
GDF11
INHIBITORS
NOTCH

FIG. 3C

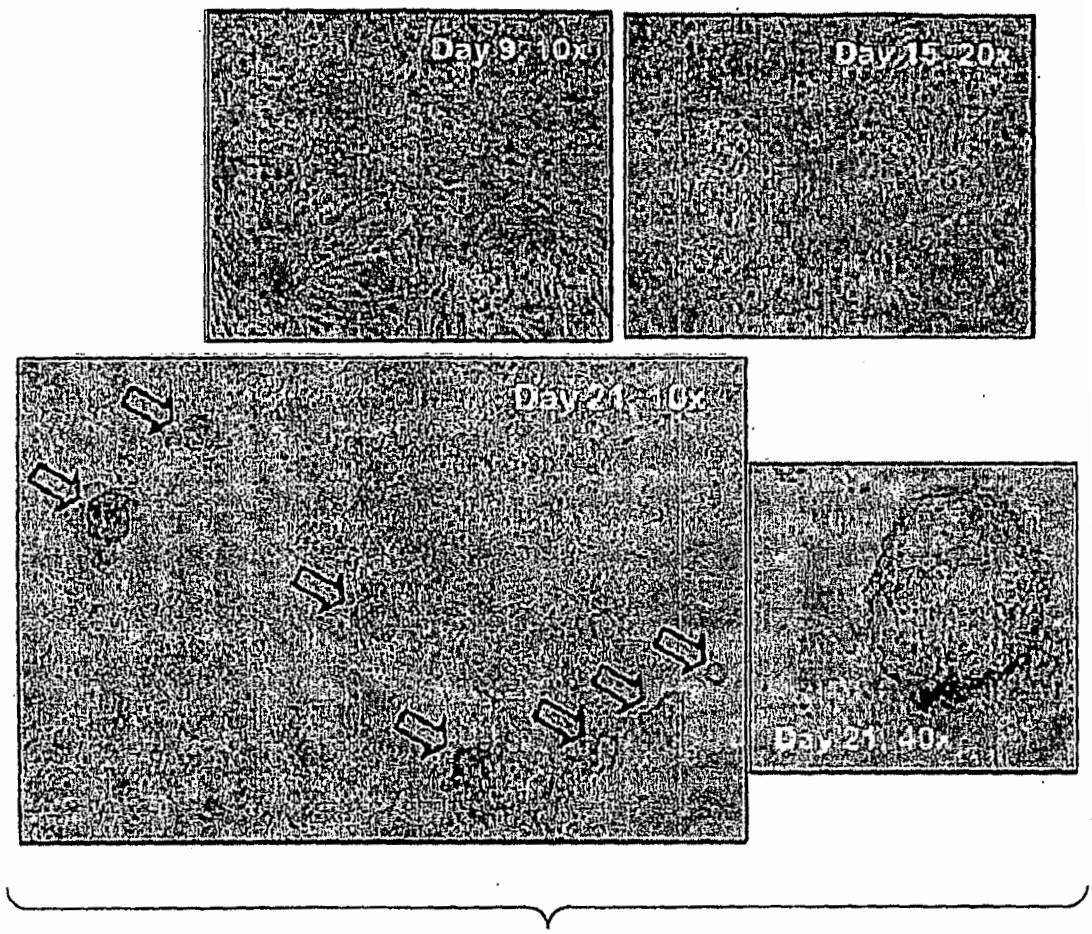


FIG. 4

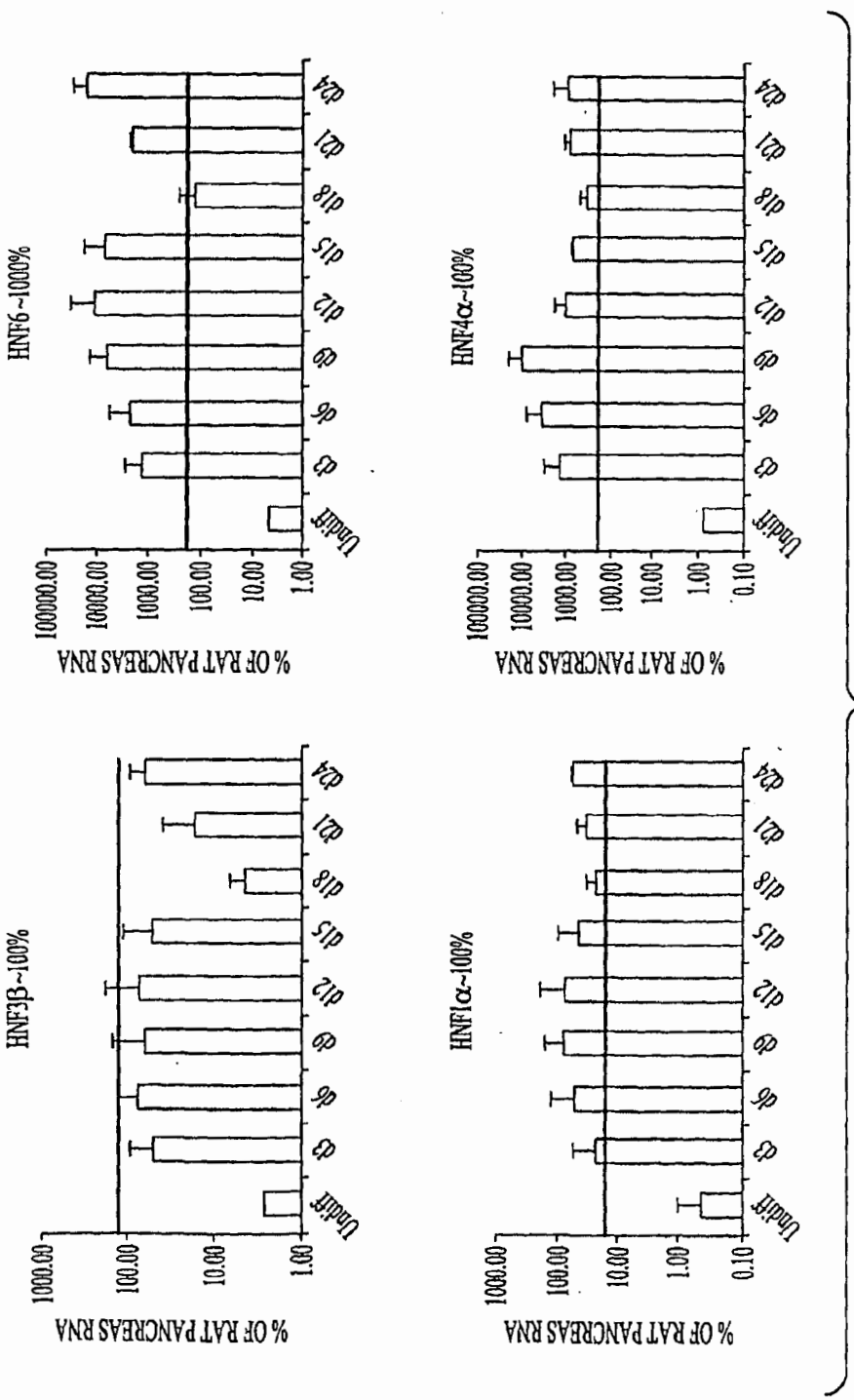

HNF6~100%
HNF4α~100%
HNF3β~100%
HNF1α~100%
% OF RAT PANCREAS RNA
Undiff
d3
d6
d9
d12
d15
d18
d21
d24

FIG. 5A

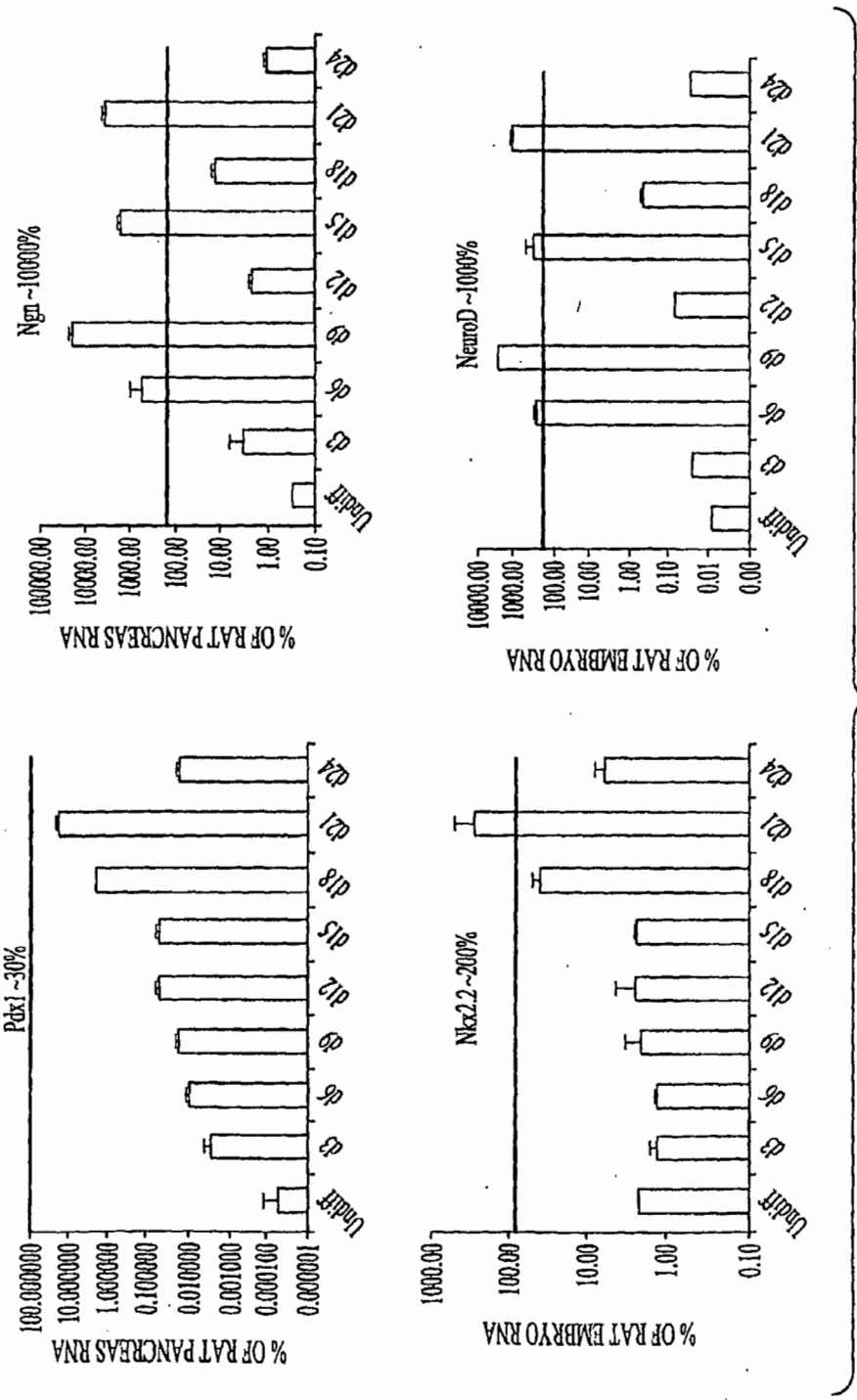

Ngn ~10000%
% OF RAT PANCREAS RNA
100000.00
10000.00
1000.00
100.00
10.00
1.00
0.10
Undiff
d3
d6
d9
d12
d15
d18
d21
d24
NeuroD ~1000%
% OF RAT EMBRYO RNA
10000.00
1000.00
100.00
10.00
1.00
0.10
0.01
0.00
Pdx1 ~30%
% OF RAT PANCREAS RNA
100.000000
10.000000
1.000000
0.100000
0.010000
0.001000
0.000100
0.000001
Nkx2.2 ~200%
% OF RAT EMBRYO RNA
1000.00
100.00
10.00
1.00
0.10

FIG. 5B

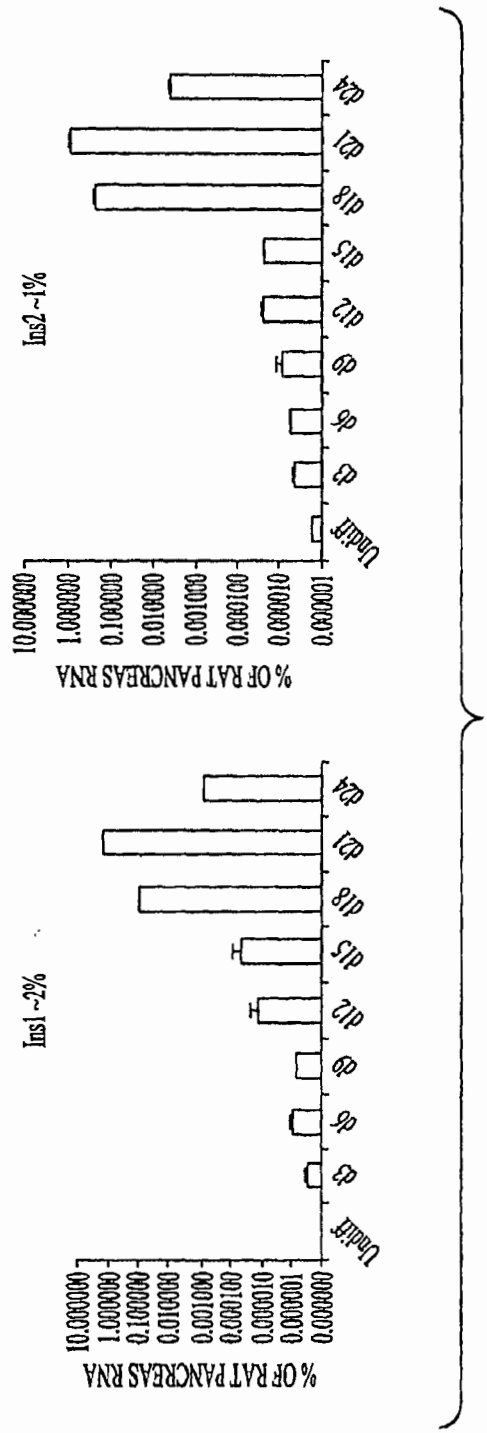

Ins1 ~2%
Ins2 ~1%
% OF RAT PANCREAS RNA
10.000000
1.000000
0.100000
0.010000
0.001000
0.000100
0.000010
0.000001
0.000000
Undiff
d3
d6
d9
d12
d15
d18
d21
d24

FIG. 5C

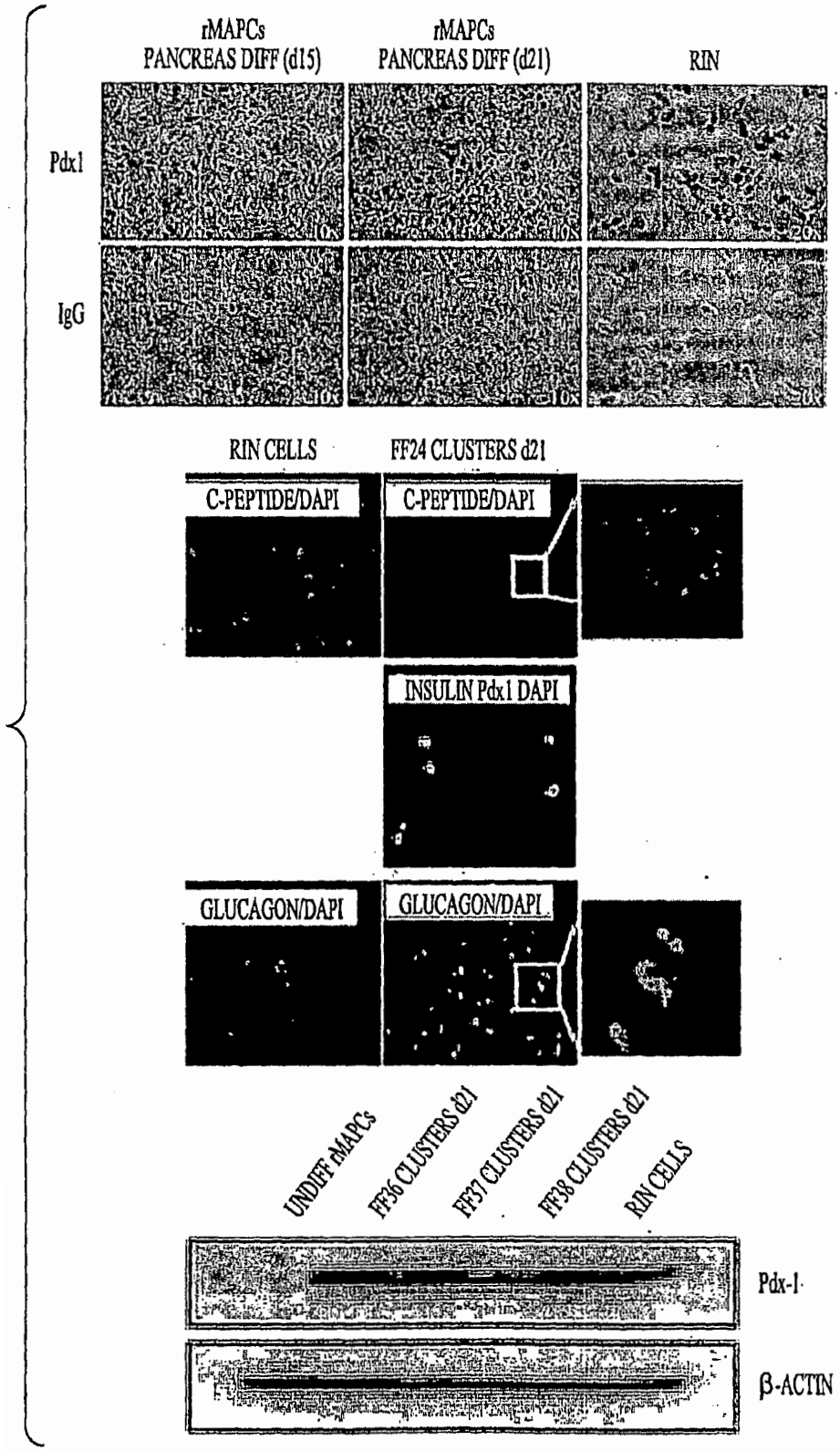

rMAPCs
PANCREAS DIFF (d15)
rMAPCs
PANCREAS DIFF (d21)
RIN
Pdx1
IgG
RIN CELLS
FF24 CLUSTERS d21
C-PEPTIDE/DAPI
C-PEPTIDE/DAPI
INSULIN Pdx1 DAPI
GLUCAGON/DAPI
GLUCAGON/DAPI
UNDIFF rMAPCs
FF36 CLUSTERS d21
FF37 CLUSTERS d21
FF38 CLUSTERS d21
RIN CELLS
Pdx-1
β-ACTIN

FIG. 6

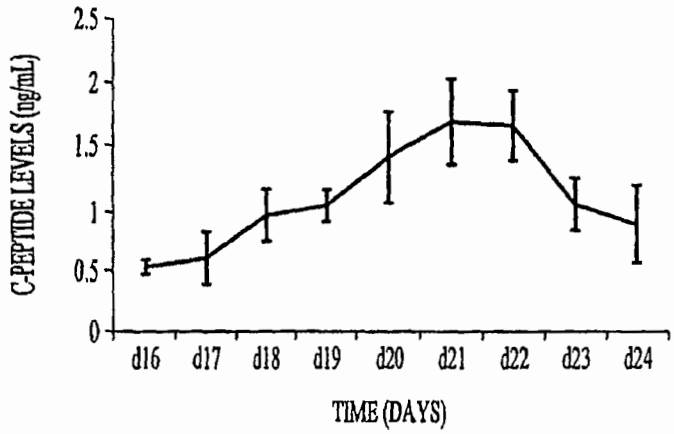

C-PEPTIDE LEVELS (ng/mL)
2.5
2
1.5
1
0.5
0
d16
d17
d18
d19
d20
d21
d22
d23
d24
TIME (DAYS)

FIG. 7

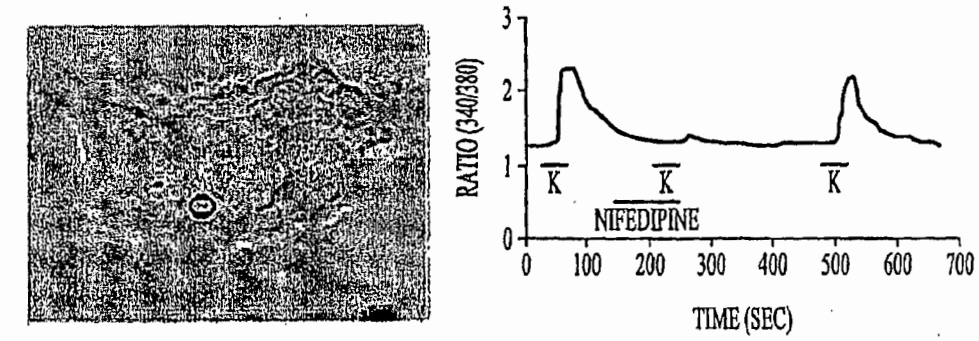

RATIO (340/380)
3
2
1
0
K
K
K
NIFEDIPINE
0
100
200
300
400
500
600
700
TIME (SEC)

FIG. 8

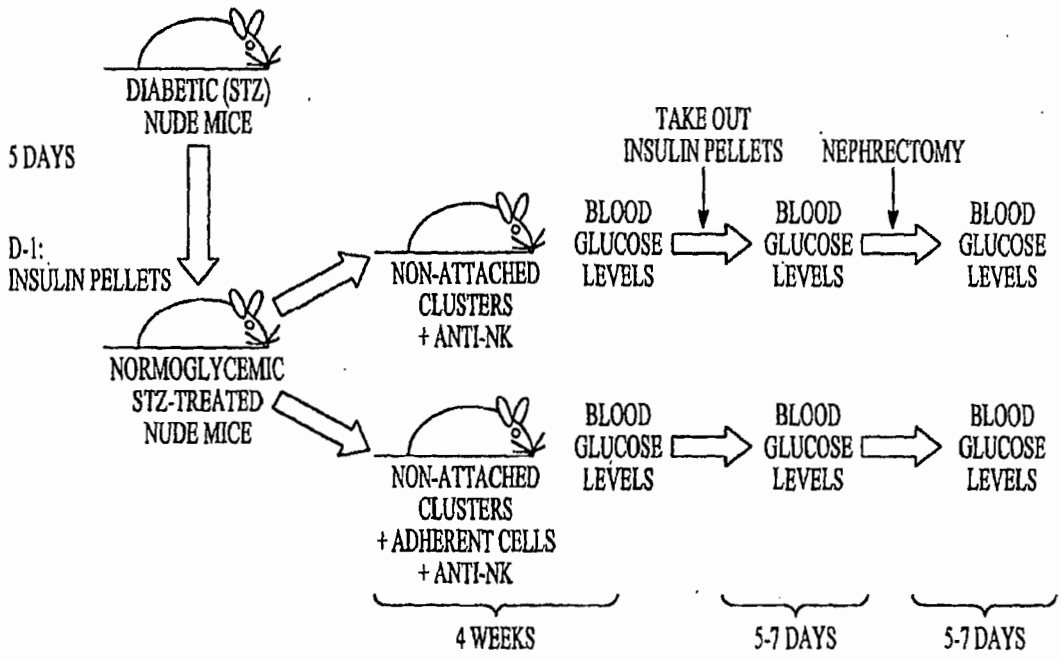

DIABETIC (STZ)
NUDE MICE
5 DAYS
D-1:
INSULIN PELLETS
NORMOGLYCEMIC
STZ-TREATED
NUDE MICE
NON-ATTACHED
CLUSTERS
+ ANTI-NK
NON-ATTACHED
CLUSTERS
+ ADHERENT CELLS
+ ANTI-NK
TAKE OUT
INSULIN PELLETS
NEPHRECTOMY
BLOOD
GLUCOSE
LEVELS
BLOOD
GLUCOSE
LEVELS
BLOOD
GLUCOSE
LEVELS
BLOOD
GLUCOSE
LEVELS
BLOOD
GLUCOSE
LEVELS
BLOOD
GLUCOSE
LEVELS
4 WEEKS
5-7 DAYS
5-7 DAYS

FIG. 9A

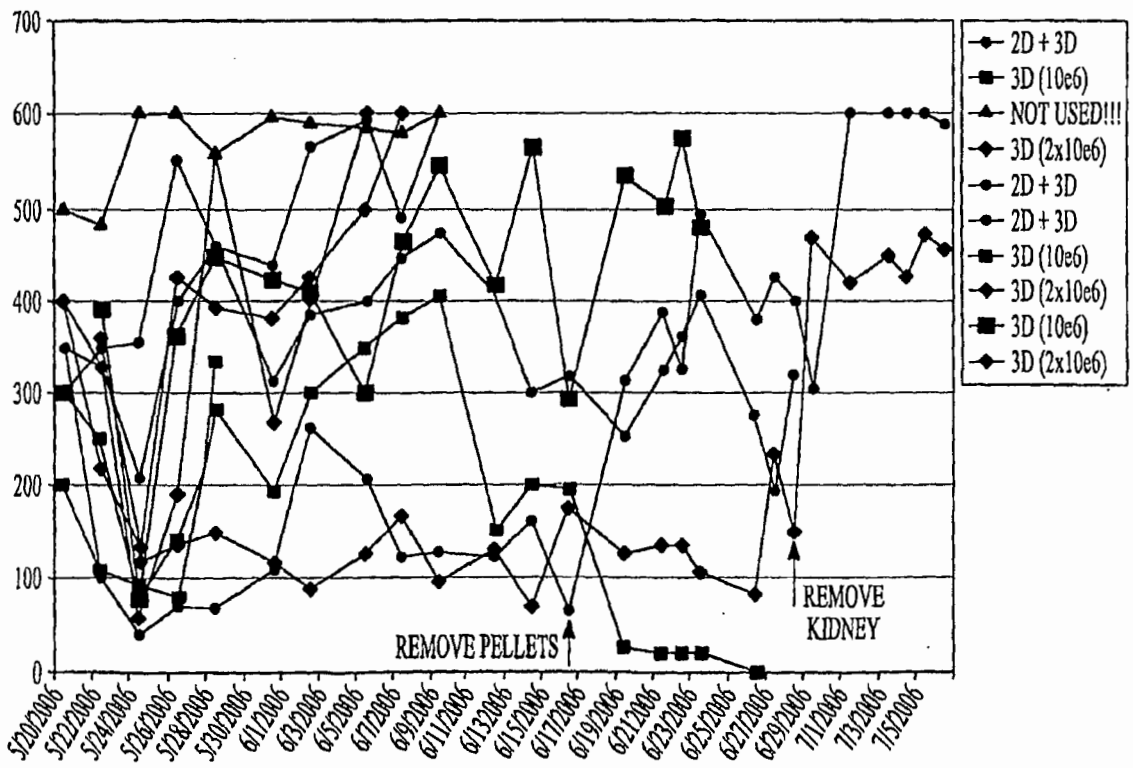

700
600
500
400
300
200
100
0
2D + 3D
3D (10e6)
NOT USED!!!
3D (2x10e6)
2D + 3D
2D + 3D
3D (10e6)
3D (2x10e6)
3D (10e6)
3D (2x10e6)
REMOVE PELLETS
REMOVE KIDNEY
5/20/2006
5/22/2006
5/24/2006
5/26/2006
5/28/2006
5/30/2006
6/1/2006
6/3/2006
6/5/2006
6/7/2006
6/9/2006
6/11/2006
6/13/2006
6/15/2006
6/17/2006
6/19/2006
6/21/2006
6/23/2006
6/25/2006
6/27/2006
6/29/2006
7/1/2006
7/3/2006
7/5/2006

FIG. 9B

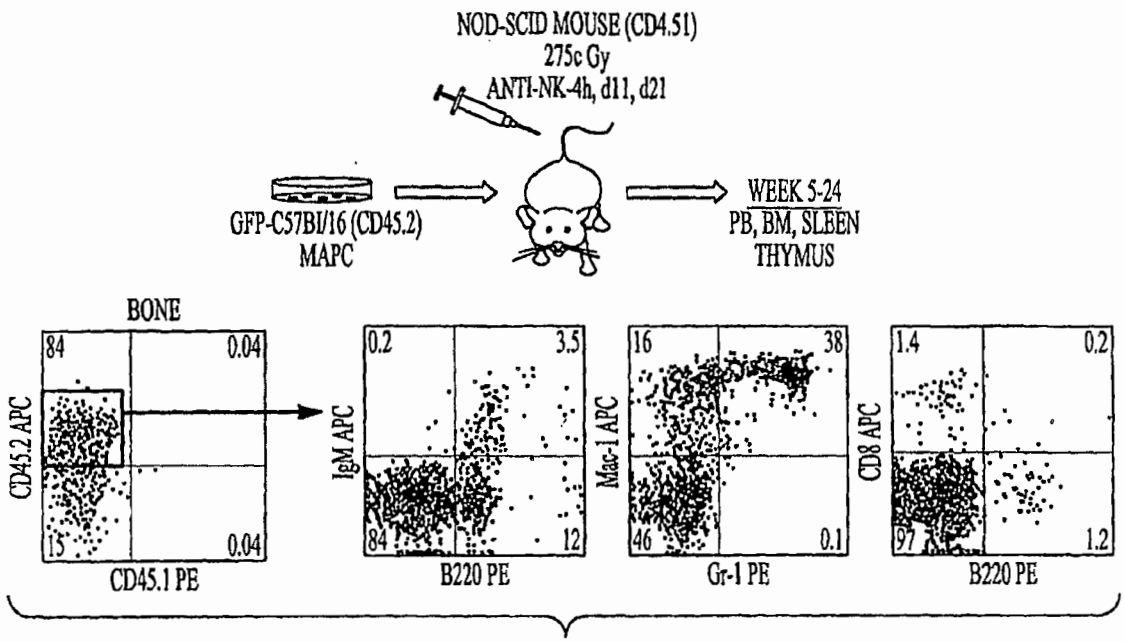


FIG. 10A

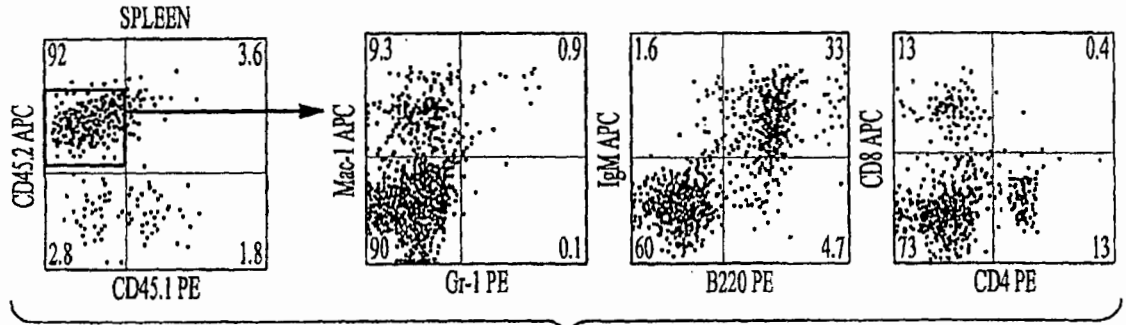


FIG. 10B

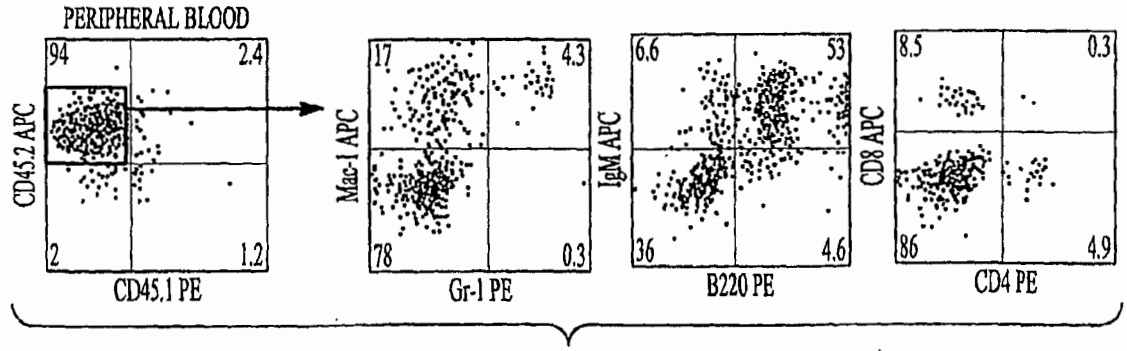


FIG. 10C

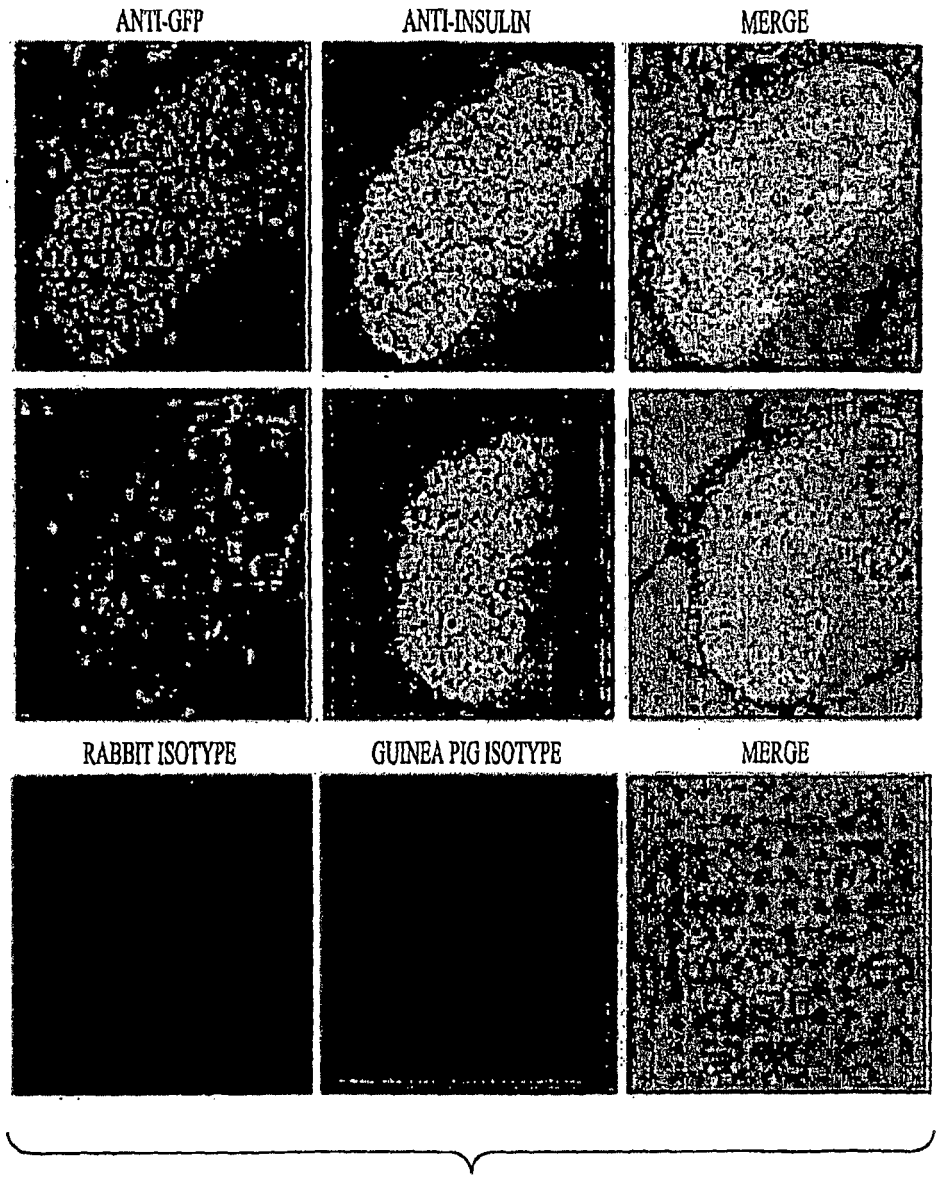

ANTI-GFP
ANTI-INSULIN
MERGE
RABBIT ISOTYPE
GUINEA PIG ISOTYPE
MERGE

FIG. 11