FIG. 1a

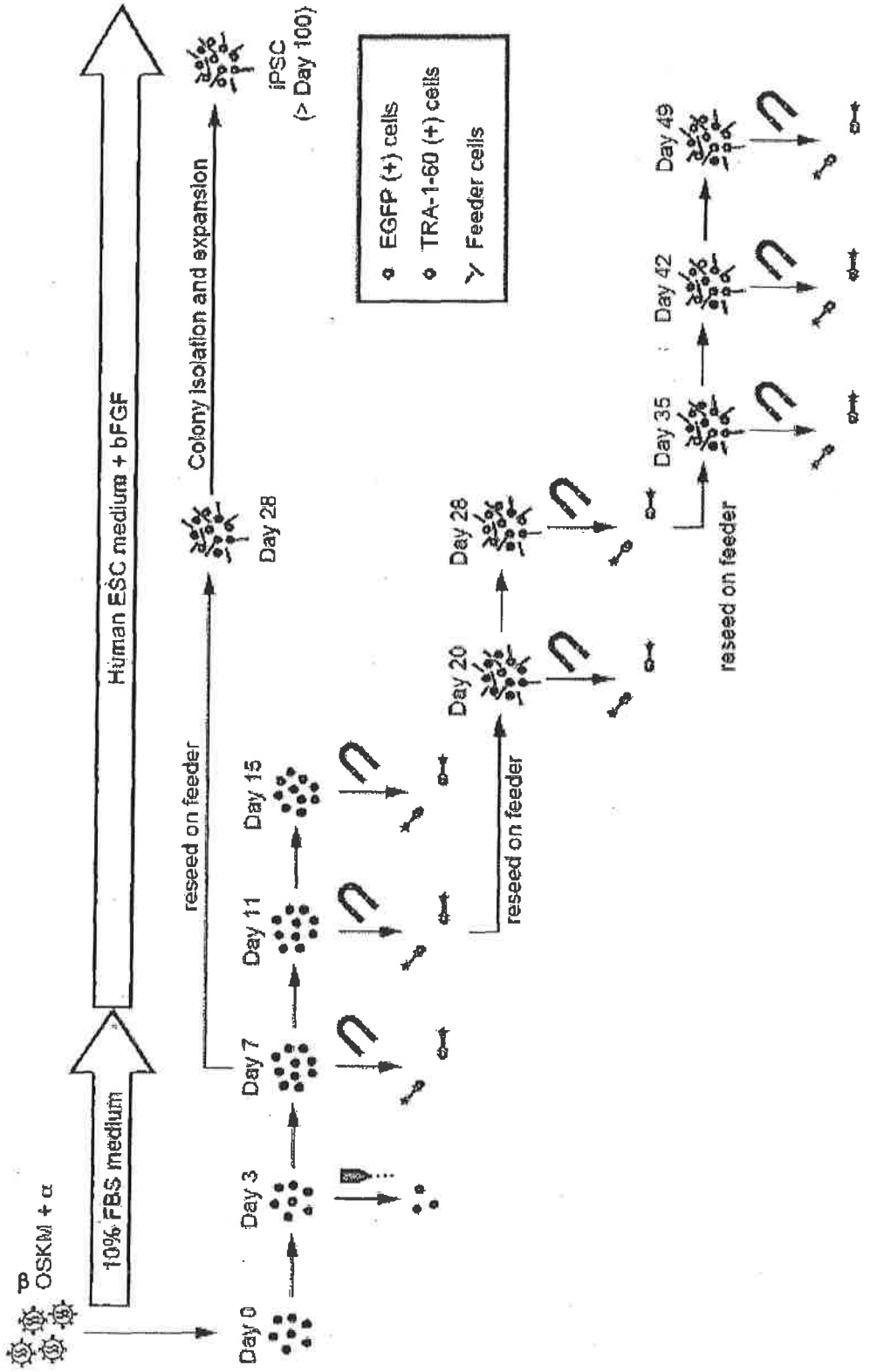

β
OSKM + α
10% FBS medium
Human ESC medium + bFGF
Day 0
Day 3
Day 7
Day 11
Day 15
reseed on feeder
Day 28
Colony isolation and expansion
iPSC
(> Day 100)
Day 20
reseed on feeder
Day 28
Day 35
reseed on feeder
Day 42
Day 49
EGFP (+) cells
TRA-1-60 (+) cells
Feeder cells

FIG. 1b

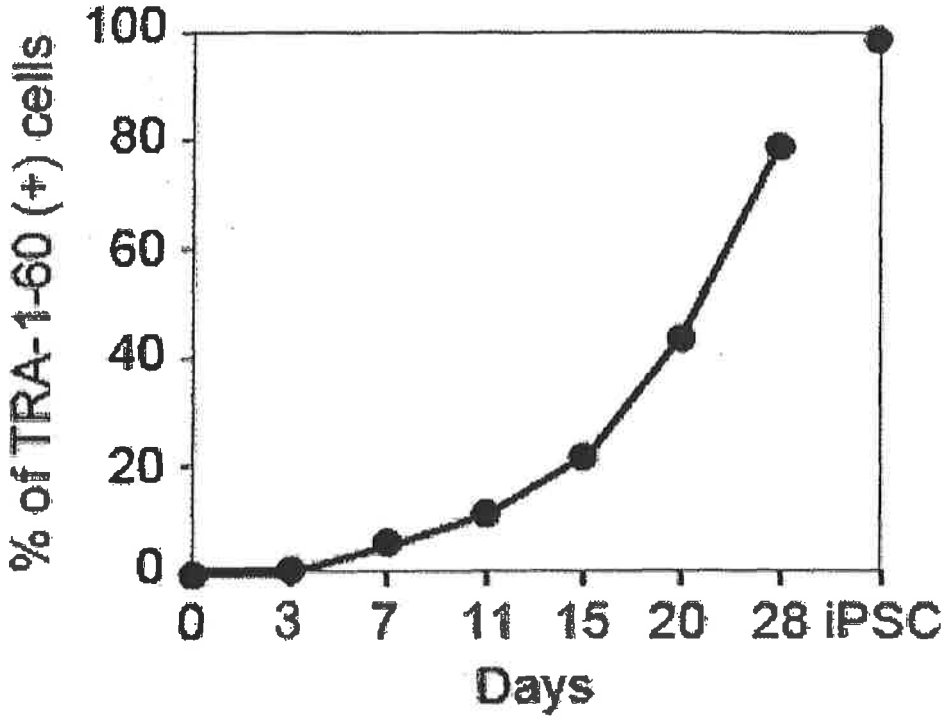


FIG. 1c

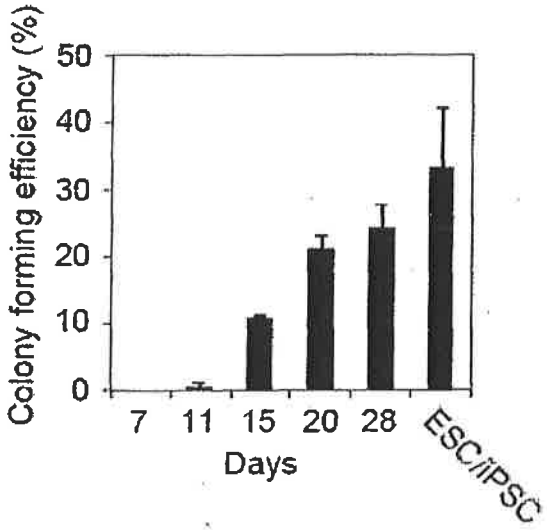


FIG. 1d

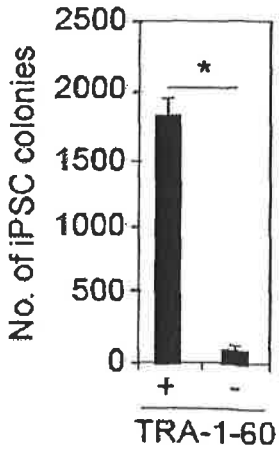


FIG. 1e

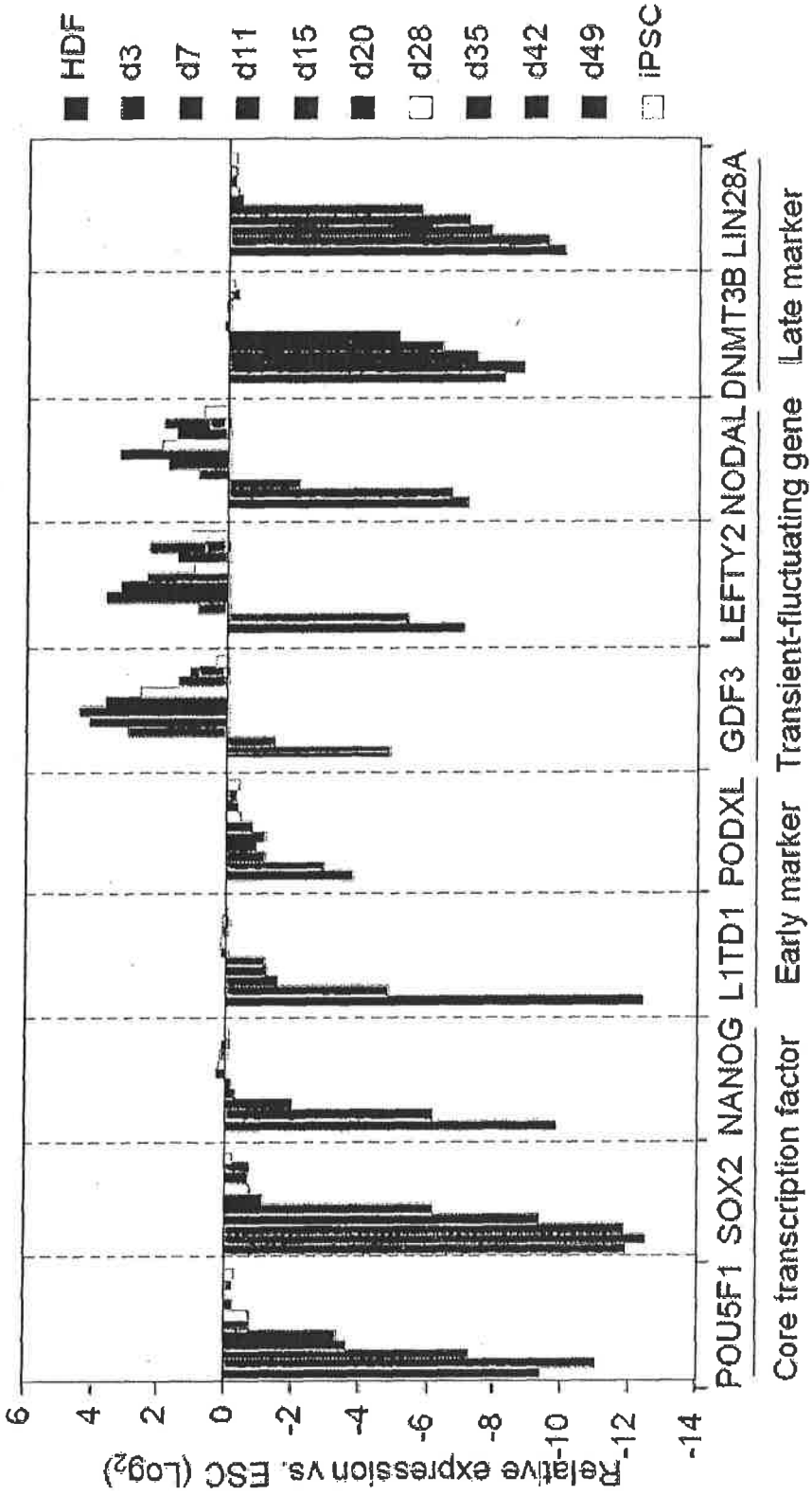

HDF
d3
d7
d11
d15
d20
d28
d35
d42
d49
iPSC
Relative expression vs. ESC (Log2)
6
4
2
0
-2
-4
-6
-8
-10
-12
-14
POU5F1
SOX2
NANOG
L1TD1
PODXL
GDF3
LEFTY2
NODAL
DNMT3B
LIN28A
Core transcription factor
Early marker
Transient-fluctuating gene
Late marker

FIG. 2a

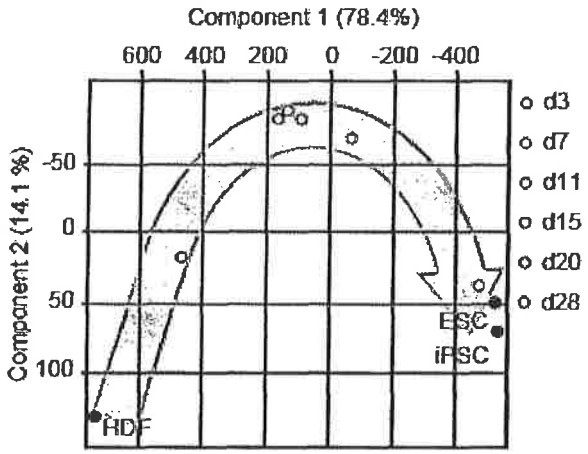

Component 1 (78.4%)
600 400 200 0 -200 -400
Component 2 (14.1 %)
-50
0
50
100
d3
d7
d11
d15
d20
d28
ESC
iPSC
HDF

FIG. 2b

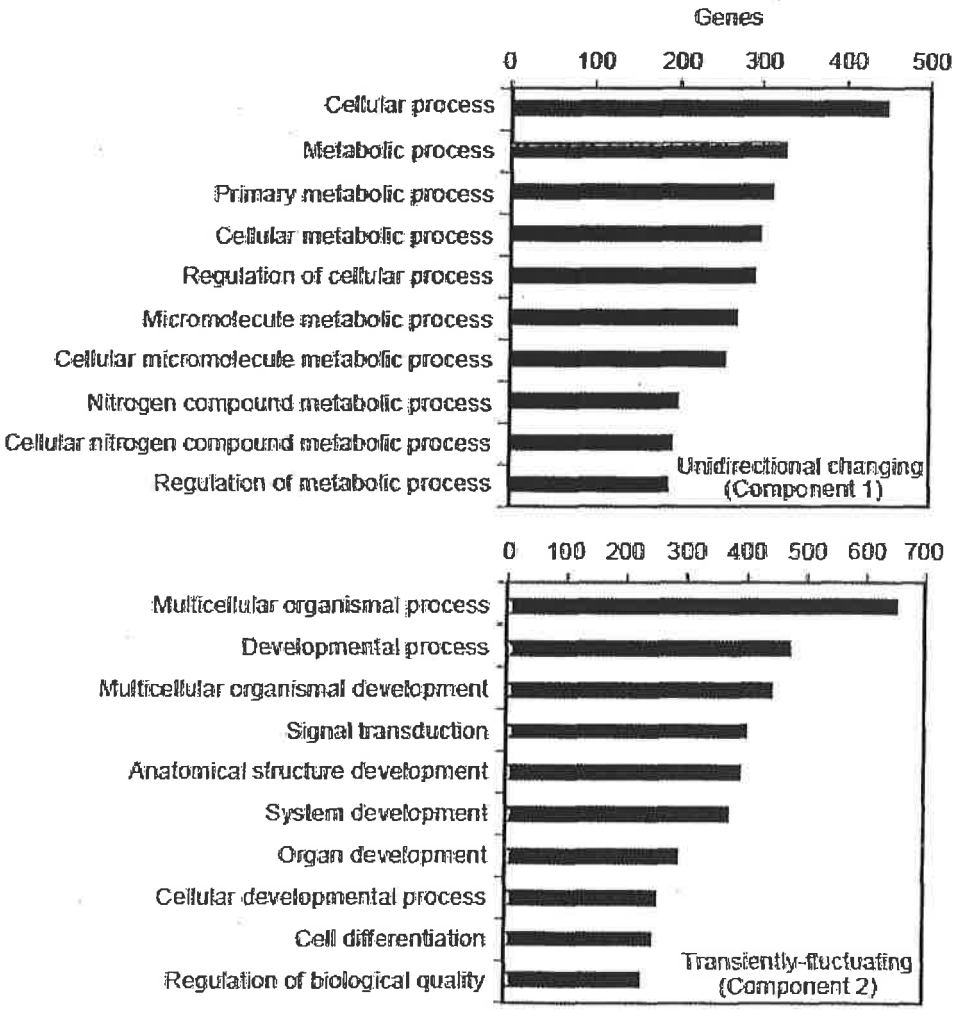

Genes
0 100 200 300 400 500
Cellular process
Metabolic process
Primary metabolic process
Cellular metabolic process
Regulation of cellular process
Micromolecule metabolic process
Cellular micromolecule metabolic process
Nitrogen compound metabolic process
Cellular nitrogen compound metabolic process
Regulation of metabolic process
Unidirectional changing (Component 1)
0 100 200 300 400 500 600 700
Multicellular organismal process
Developmental process
Multicellular organismal development
Signal transduction
Anatomical structure development
System development
Organ development
Cellular developmental process
Cell differentiation
Regulation of biological quality
Transiently-fluctuating (Component 2)

FIG. 2c

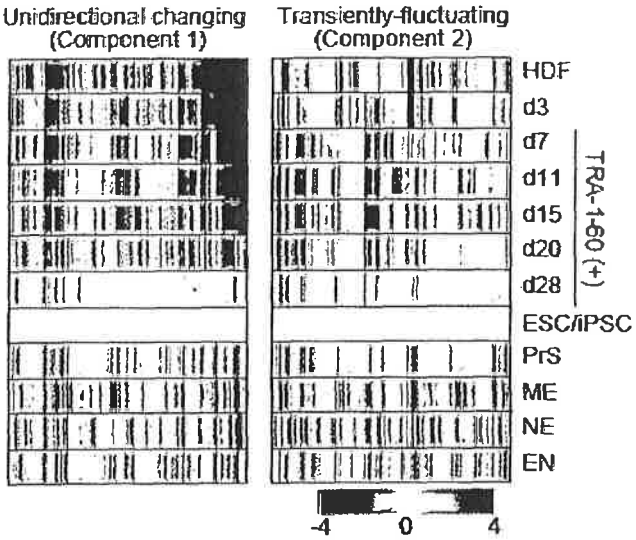


FIG. 2d

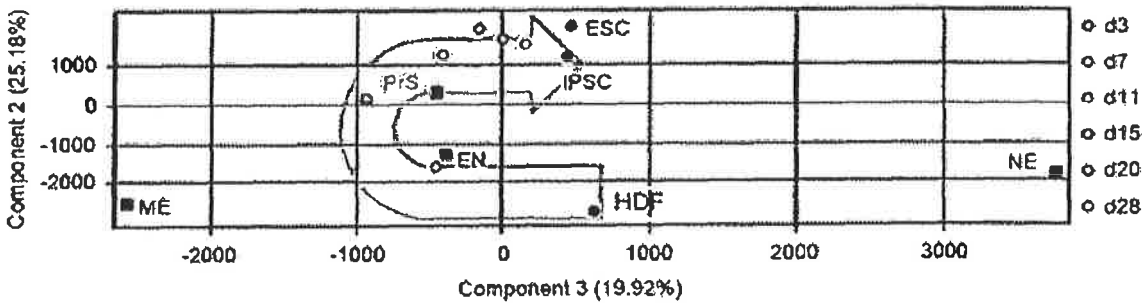


FIG. 2e

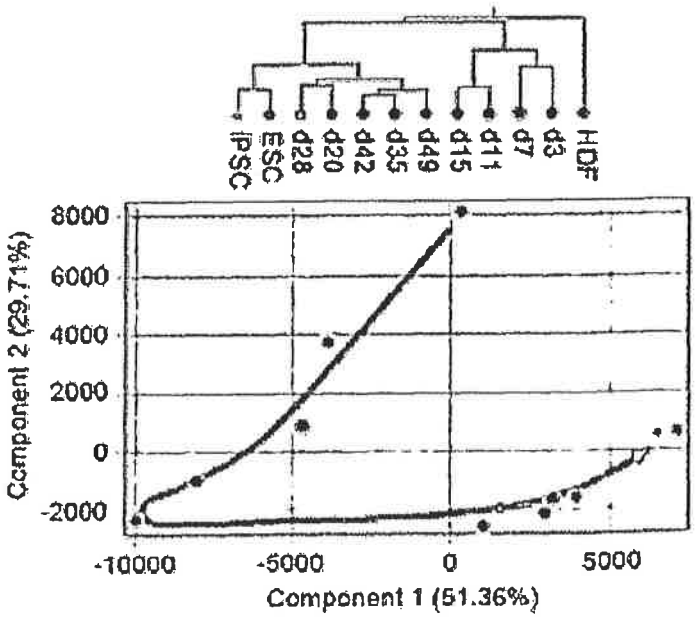


FIG. 2f

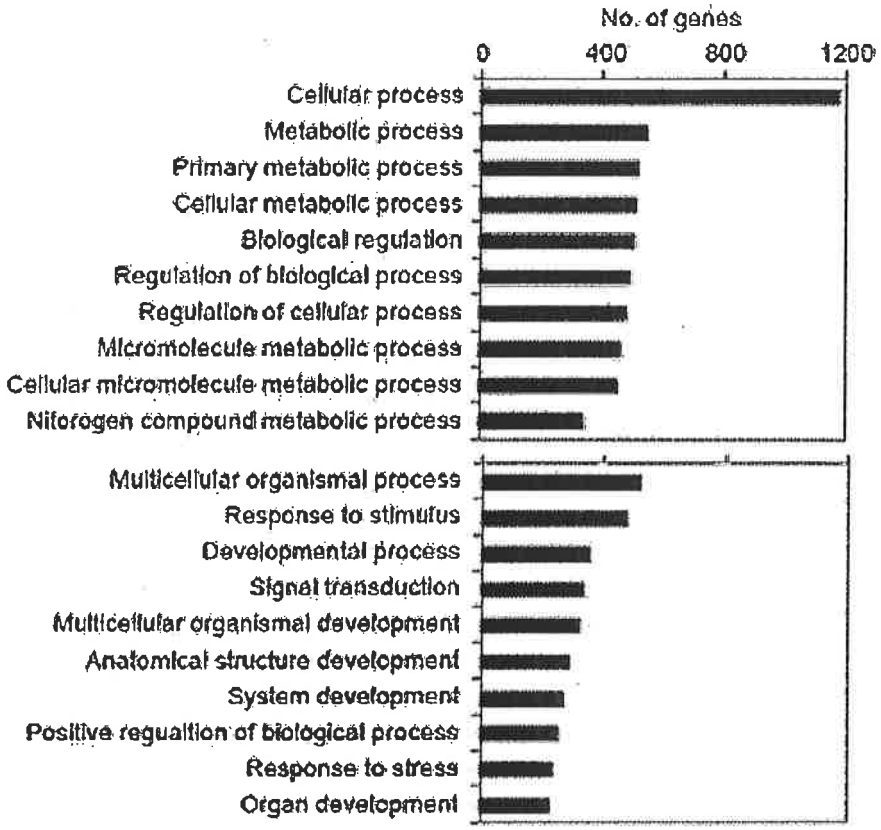

No. of genes
0
400
800
1200
Cellular process
Metabolic process
Primary metabolic process
Cellular metabolic process
Biological regulation
Regulation of biological process
Regulation of cellular process
Micromolecule metabolic process
Cellular micromolecule metabolic process
Nitorogen compound metabolic process
Multicellular organismal process
Response to stimulus
Developmental process
Signal transduction
Multicellular organismal development
Anatomical structure development
System development
Positive regualtion of biological process
Response to stress
Organ development

FIG. 2g

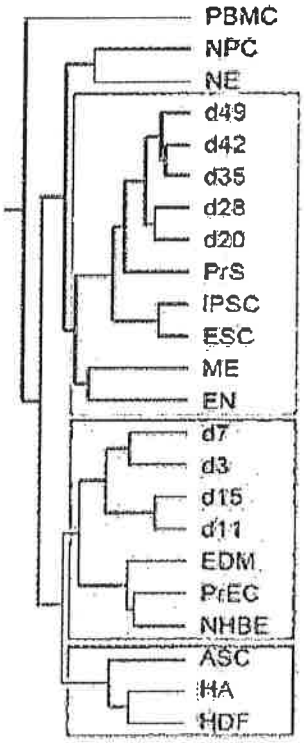

PBMC
NPC
NE
d49
d42
d35
d28
d20
PrS
IPSC
ESC
ME
EN
d7
d3
d15
d11
EDM
PrEC
NHBE
ASC
HA
HDF

FIG. 2h

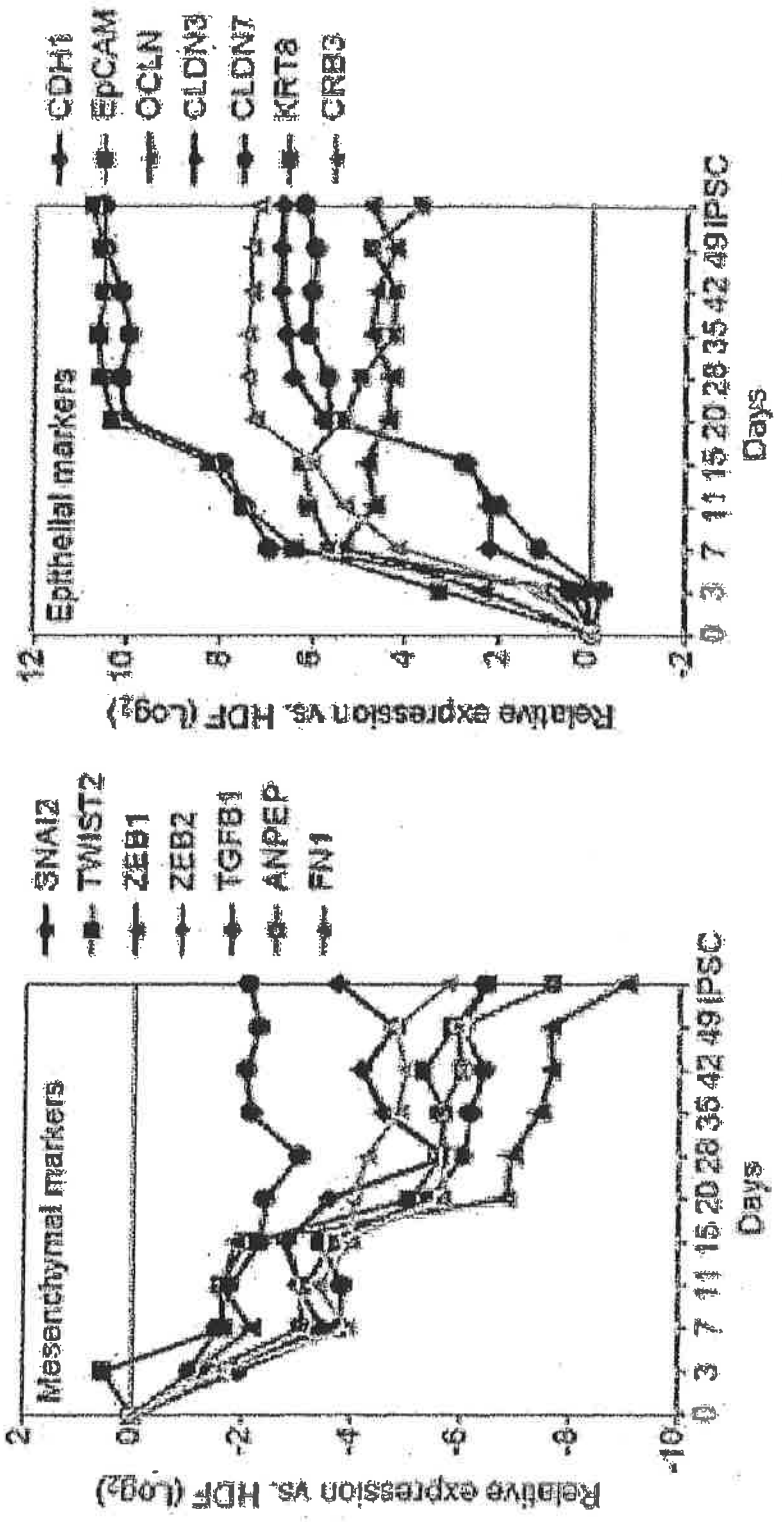

Epithelial markers
CDH1
EpCAM
OCLN
CLDN3
CLDN7
KRT8
CRB3
Relative expression vs. HDF (Log2)
Days
0 3 7 11 15 20 28 35 42 49 IPSC
Mesenchymal markers
SNAI2
TWIST2
ZEB1
ZEB2
TGFB1
ANPEP
FN1
Relative expression vs. HDF (Log2)
Days
0 3 7 11 15 20 28 35 42 49 IPSC

FIG. 3a

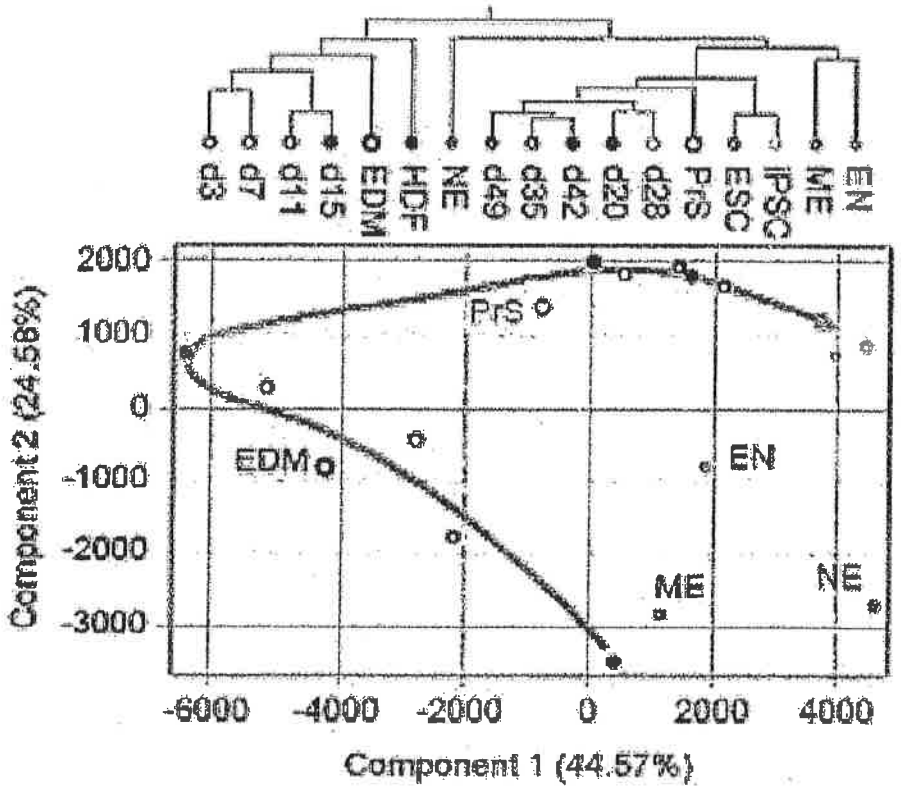


FIG. 3b

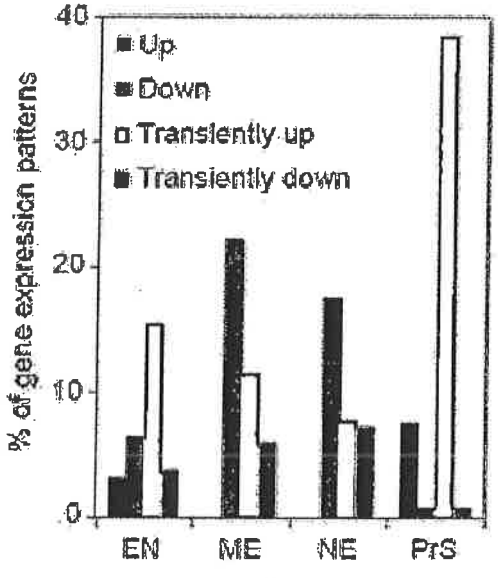


FIG. 3c

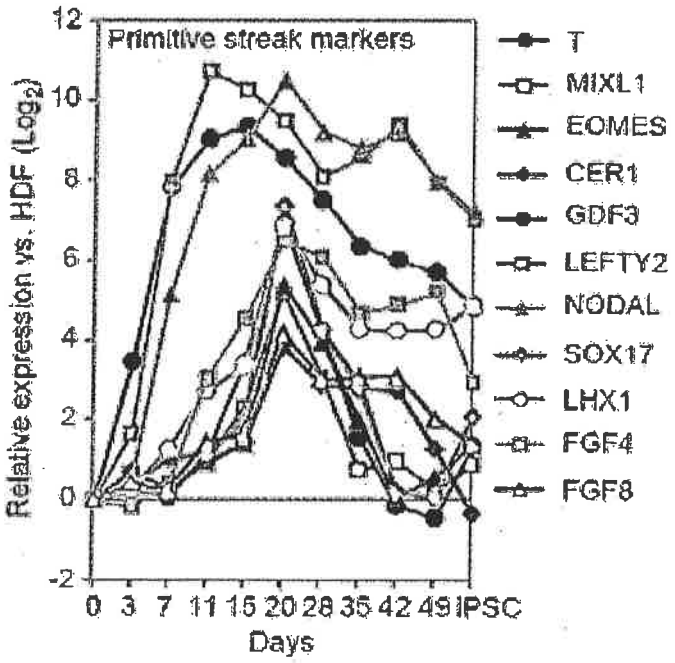


FIG. 3d

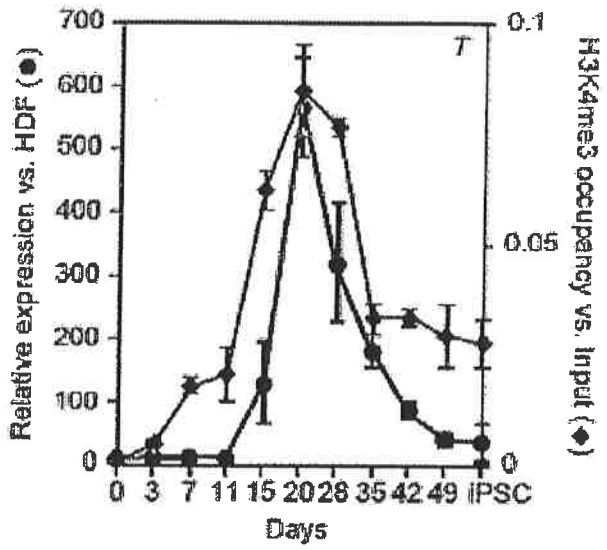


FIG. 3e

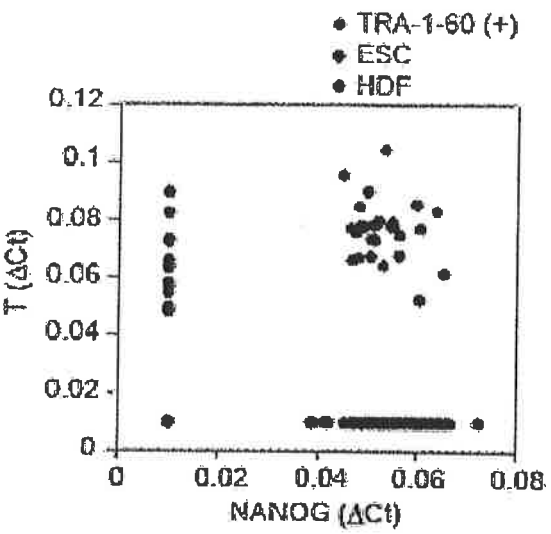


FIG. 3f

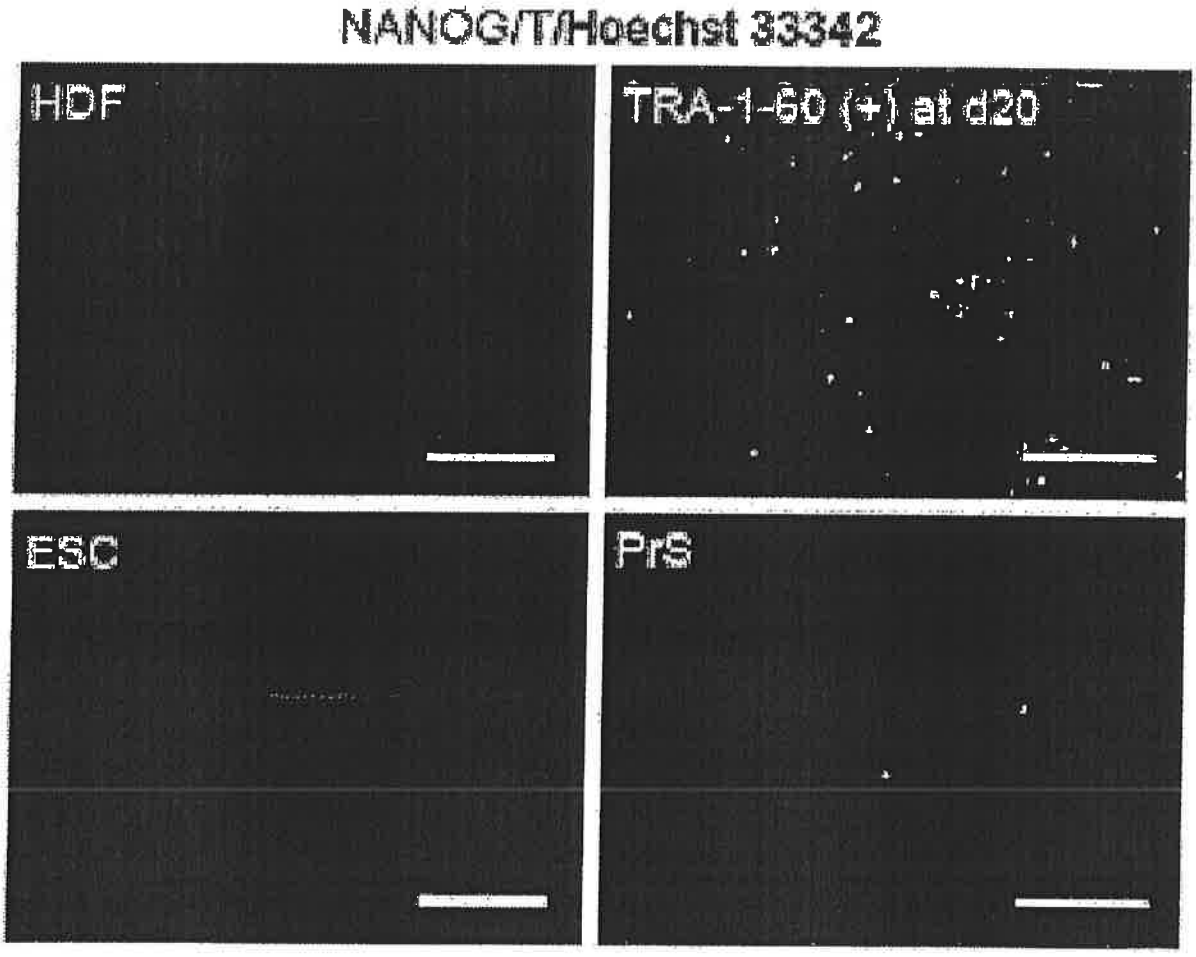


FIG. 3g

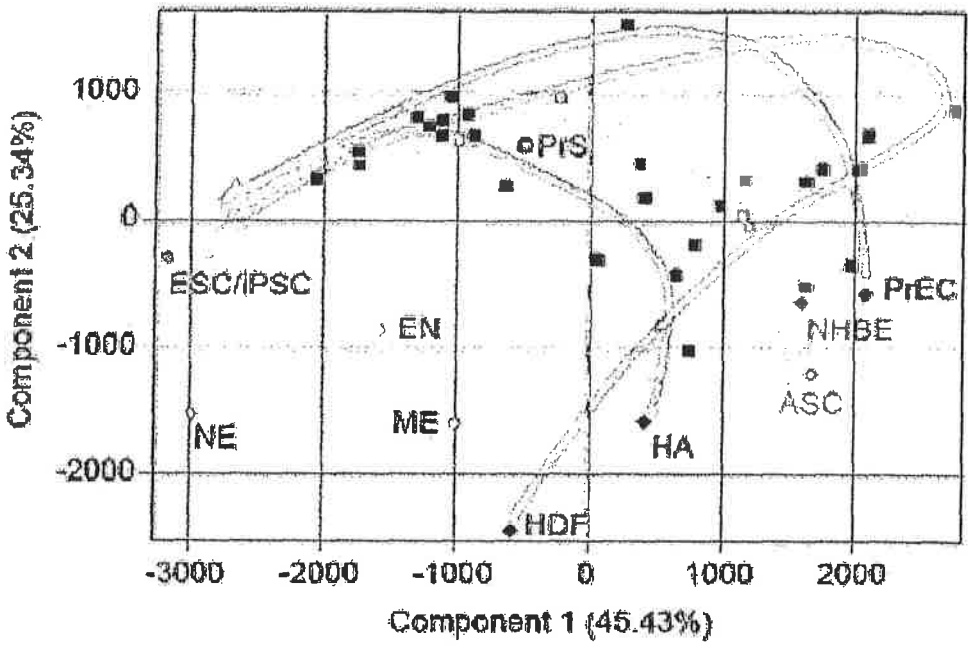

Component 2 (25.34%)
1000
0
-1000
-2000
PrS
ESC/IPSC
EN
NE
ME
HA
HDF
PrEC
NHBE
ASC
-3000
-2000
-1000
0
1000
2000
Component 1 (45.43%)

FIG. 4a

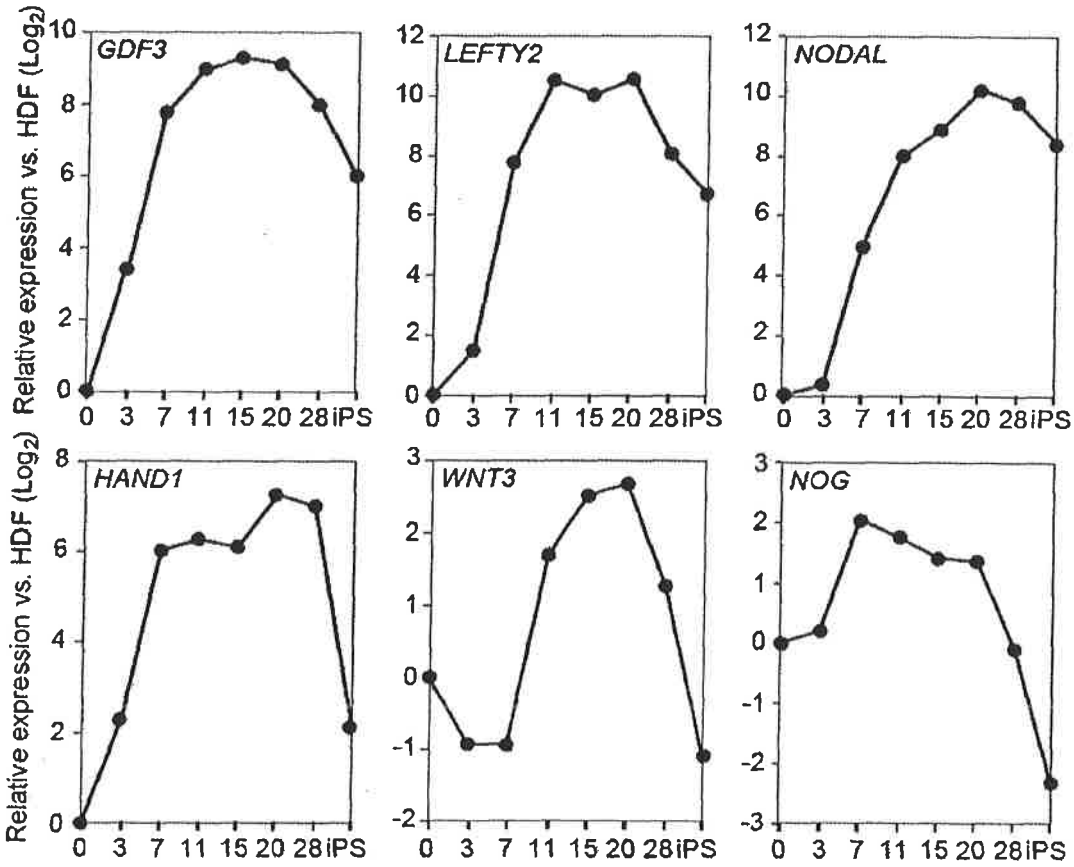

Relative expression vs. HDF (Log2)
GDF3
LEFTY2
NODAL
HAND1
WNT3
NOG
0 3 7 11 15 20 28iPS

FIG. 4b

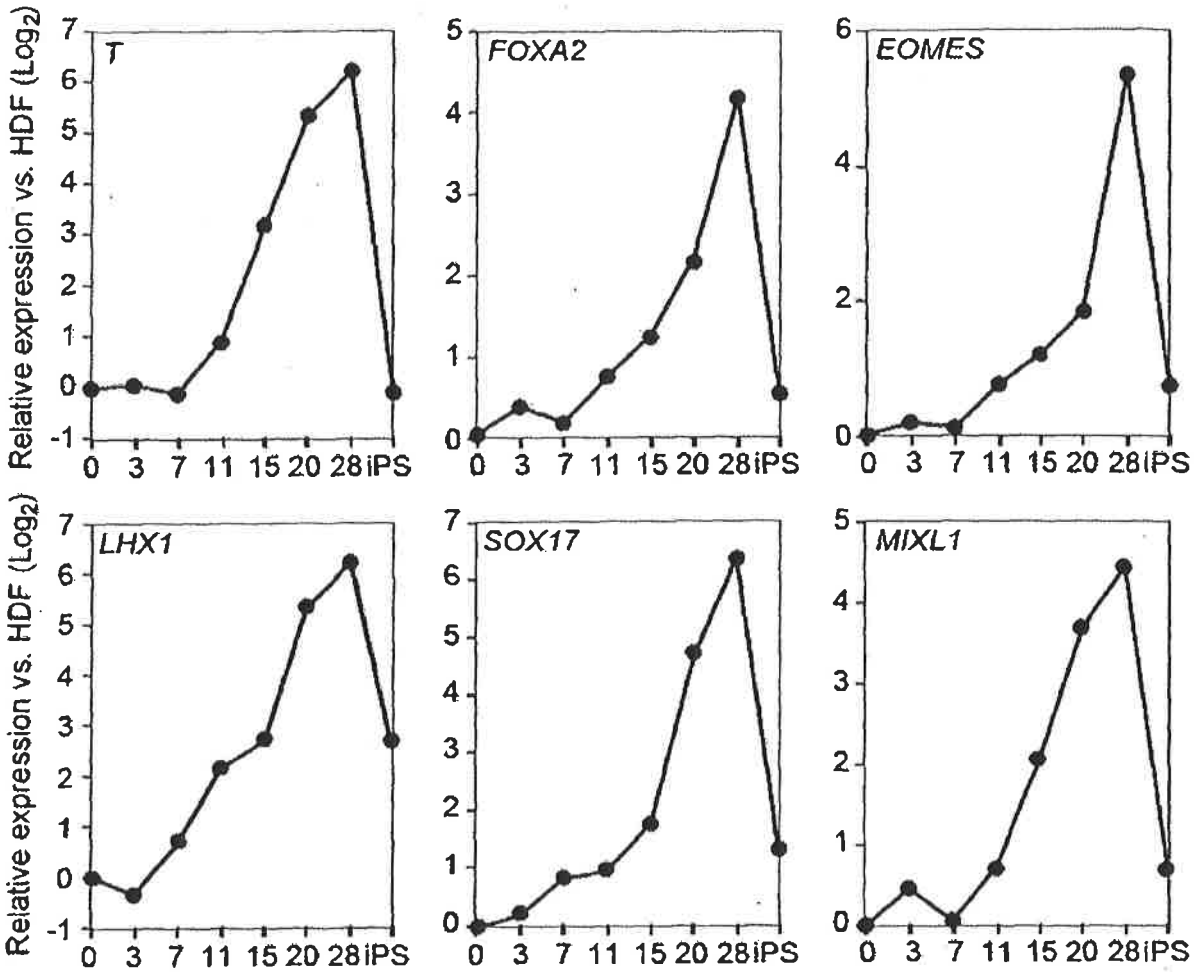

Relative expression vs. HDF (Log2)
T
FOXA2
EOMES
LHX1
SOX17
MIXL1
0 3 7 11 15 20 28iPS

FIG. 4c

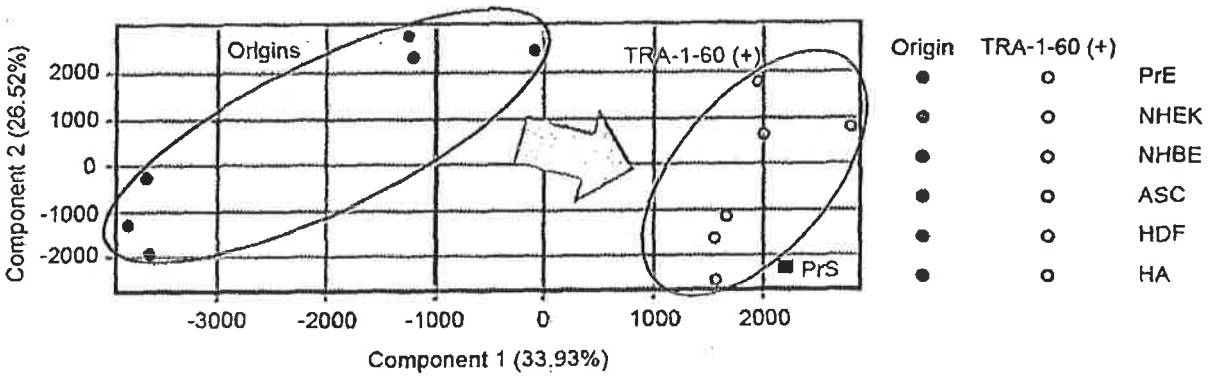

Origins
TRA-1-60 (+)
PrS
Component 2 (26.52%)
Component 1 (33.93%)
Origin
TRA-1-60 (+)
PrE
NHEK
NHBE
ASC
HDF
HA

FIG. 5a

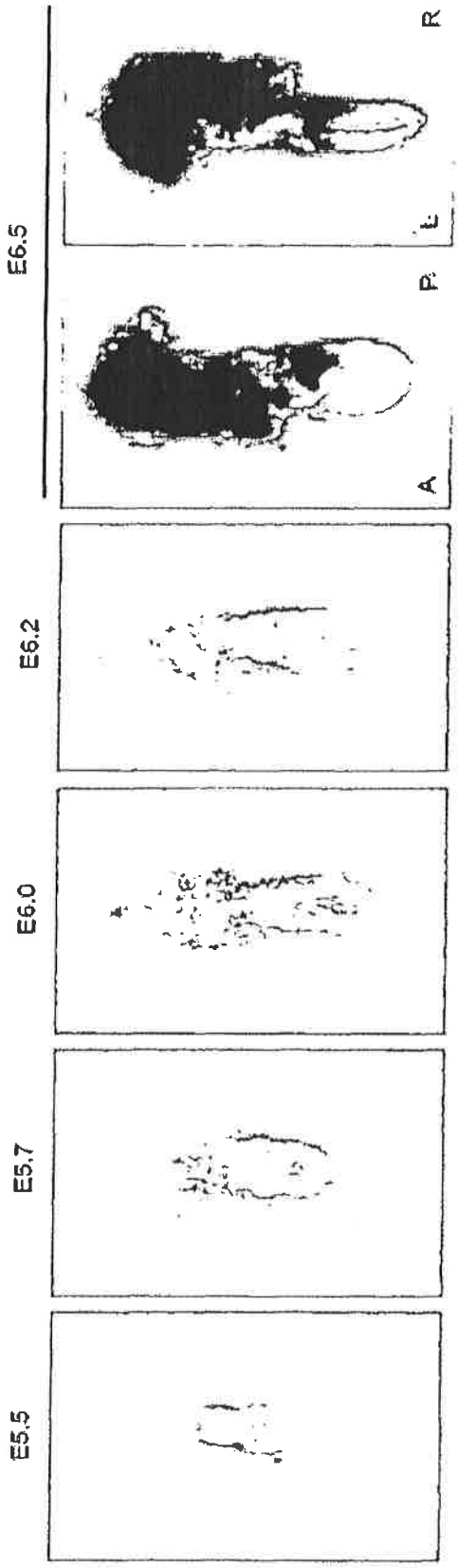


FIG. 5b

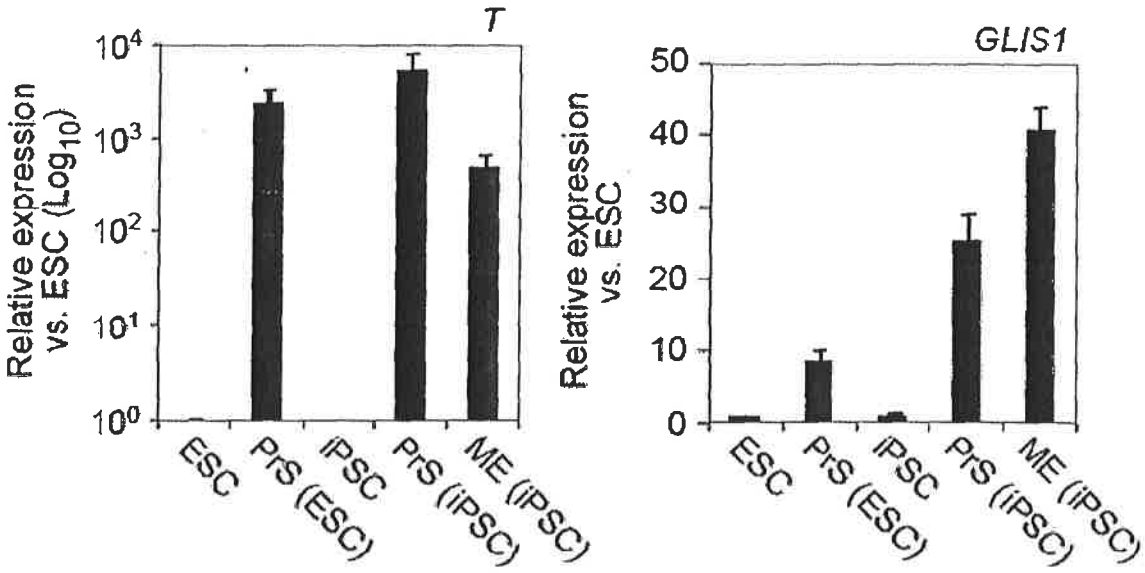

T
Relative expression vs. ESC (Log10)
10^4
10^3
10^2
10^1
10^0
ESC
PrS (ESC)
iPSC
PrS (iPSC)
ME (iPSC)
GLIS1
Relative expression vs. ESC
50
40
30
20
10
0
ESC
PrS (ESC)
iPSC
PrS (iPSC)
ME (iPSC)

FIG. 5c

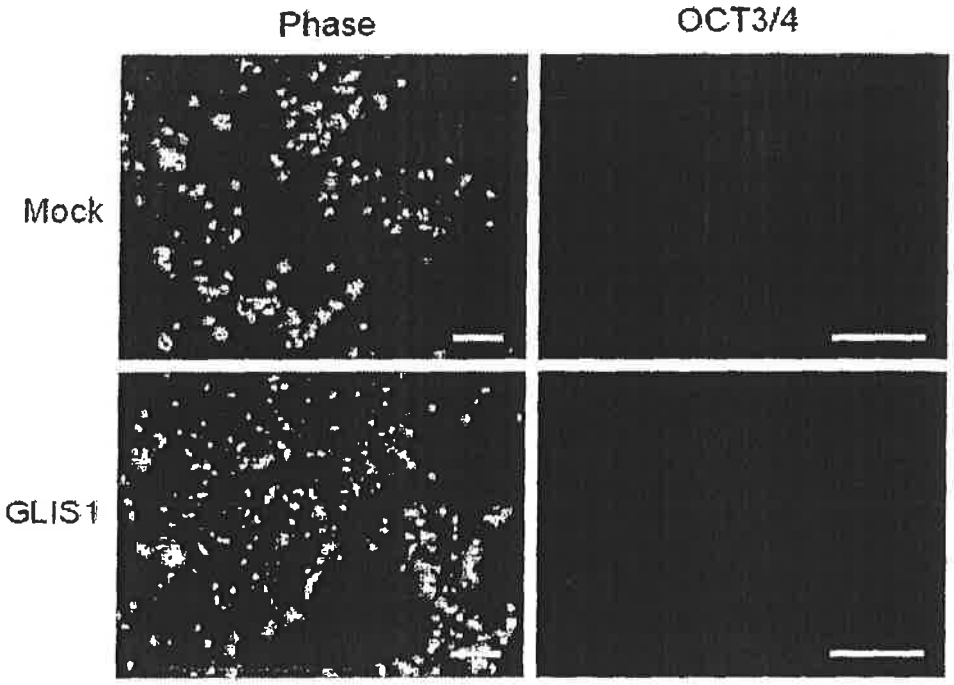

Phase
OCT3/4
Mock
GLIS1

FIG. 5d

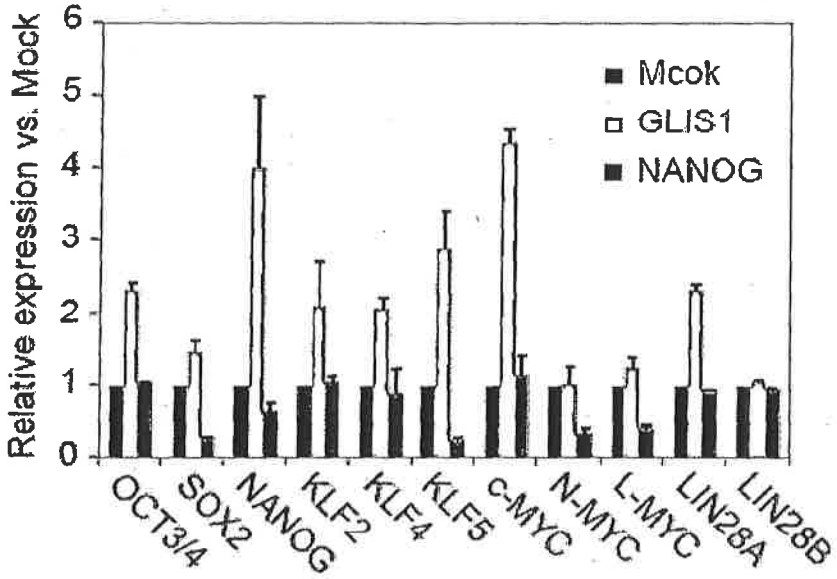

Relative expression vs. Mock
0
1
2
3
4
5
6
Mcok
GLIS1
NANOG
OCT3/4
SOX2
NANOG
KLF2
KLF4
KLF5
c-MYC
N-MYC
L-MYC
LIN28A
LIN28B

FIG. 5e

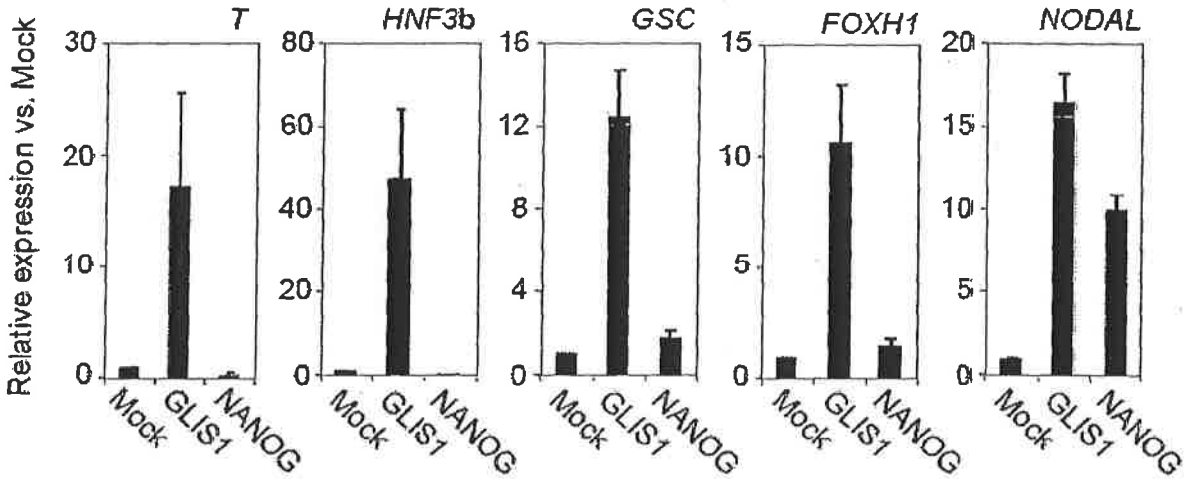

Relative expression vs. Mock
T
HNF3b
GSC
FOXH1
NODAL
Mock
GLIS1
NANOG

FIG. 5f

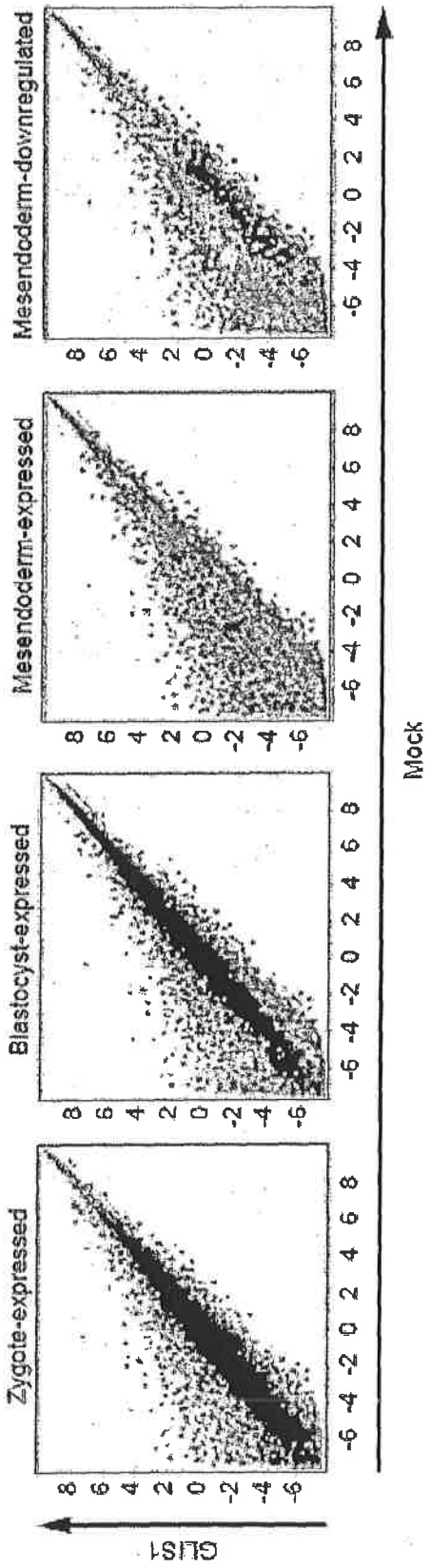

Mesendoderm-downregulated
Mesendoderm-expressed
Blastocyst-expressed
Zygote-expressed
Mock
Gli3

FIG. 5g

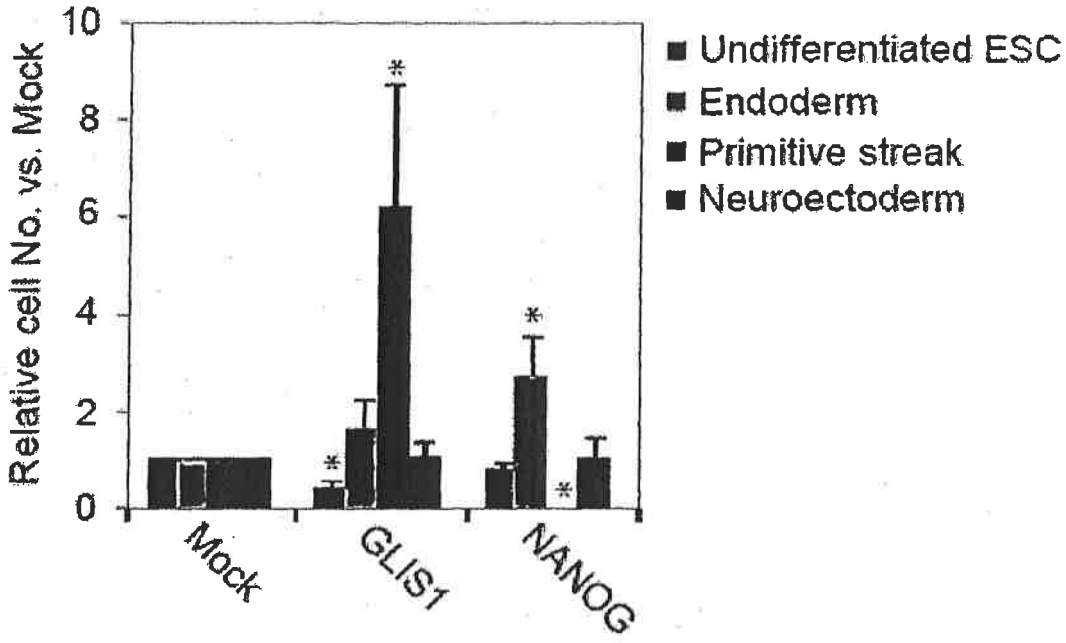


FIG. 6a

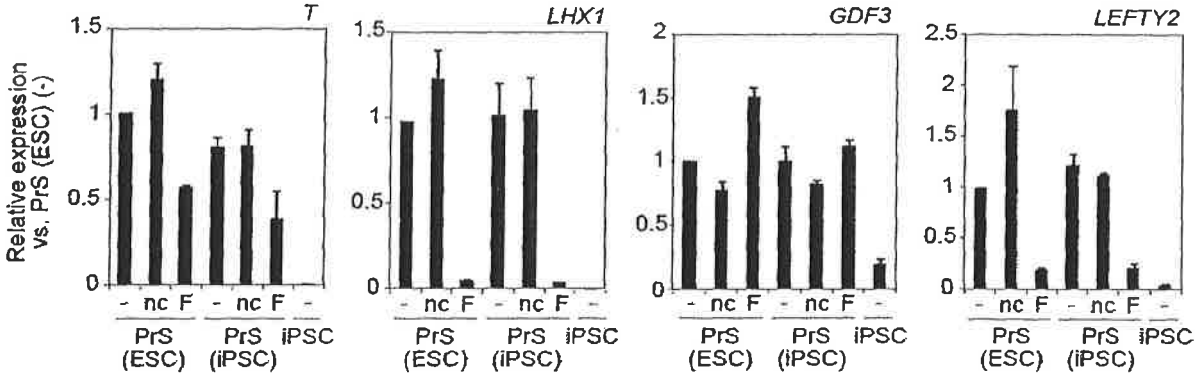


FIG. 6b

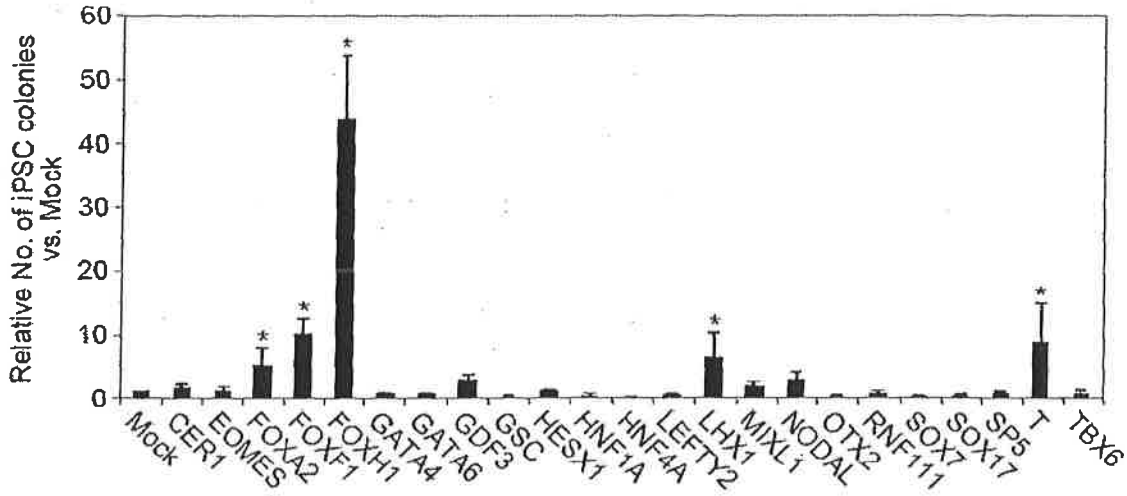


FIG. 6c

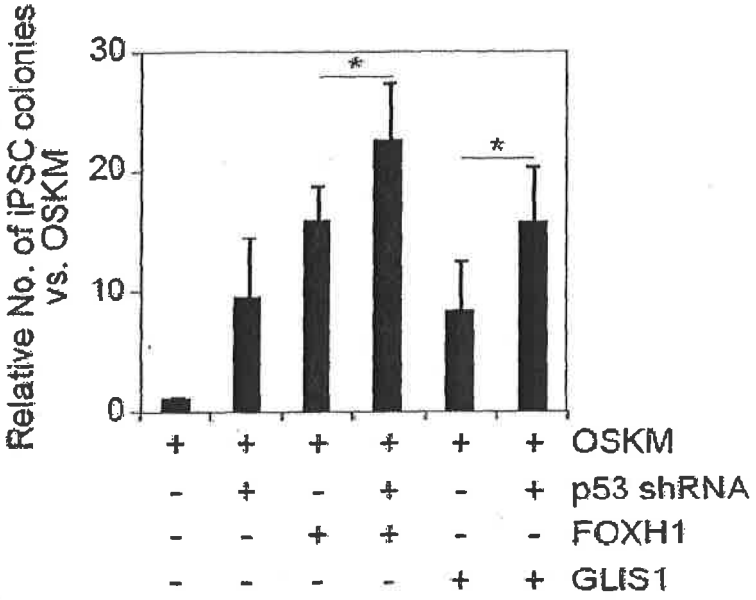

Relative No. of iPSC colonies vs. OSKM
30
20
10
0
*
*
+ + + + + + OSKM
- + - + - + p53 shRNA
- - + + - - FOXH1
- - - - + + GLIS1

FIG. 6d

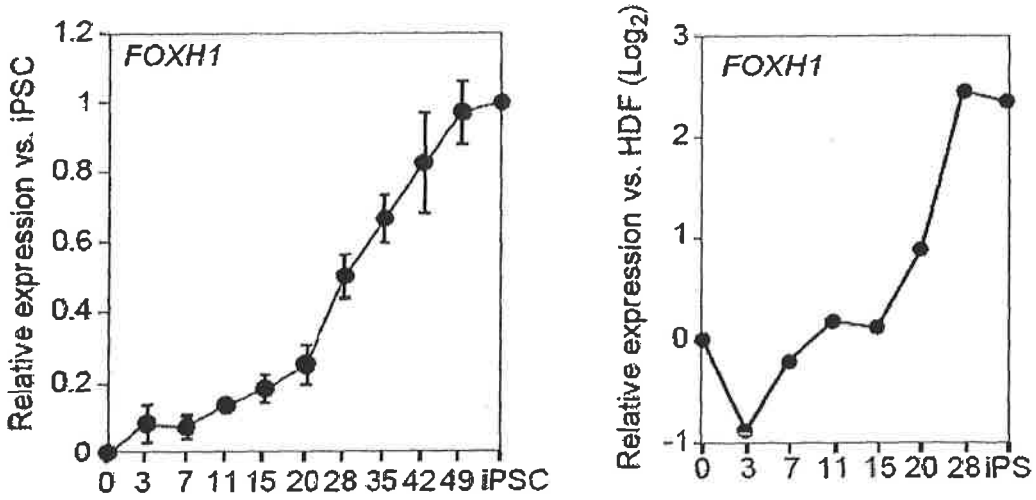

FOXH1
Relative expression vs. iPSC
1.2
1
0.8
0.6
0.4
0.2
0
0 3 7 11 15 20 28 35 42 49 iPSC
FOXH1
Relative expression vs. HDF (Log2)
3
2
1
0
-1
0 3 7 11 15 20 28 iPS

FIG. 6e

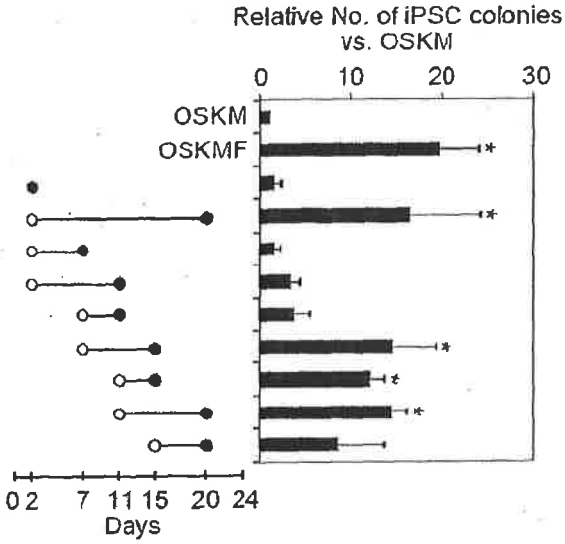


FIG. 6f

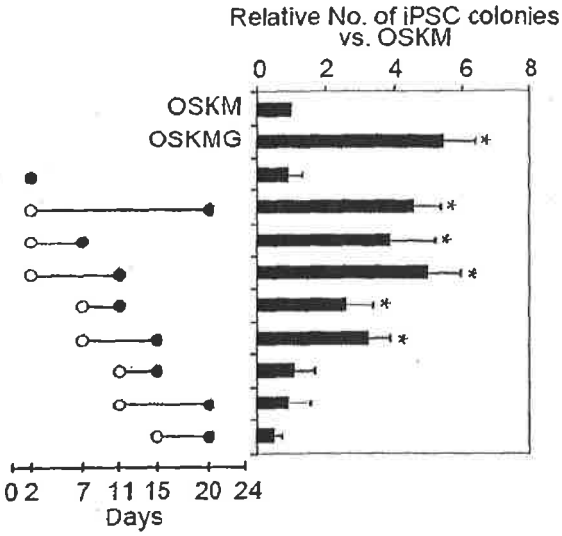


FIG. 6g

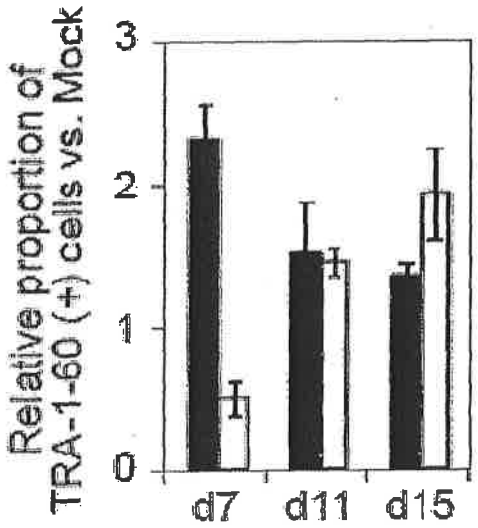


FIG. 6h

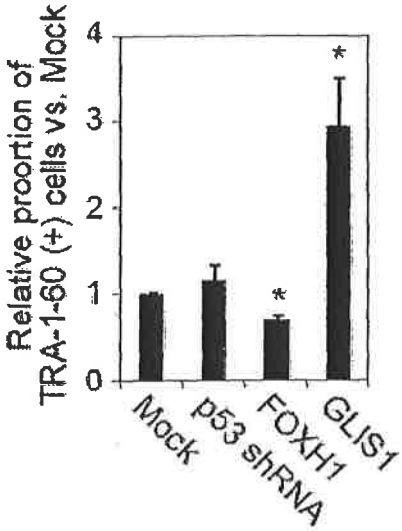


FIG. 6i

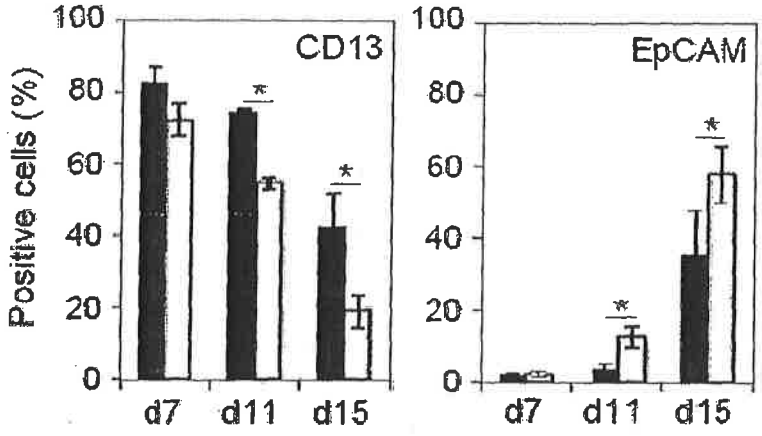


FIG. 6j

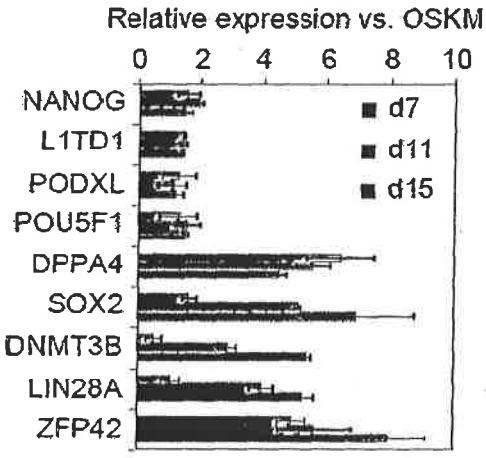


FIG. 6k

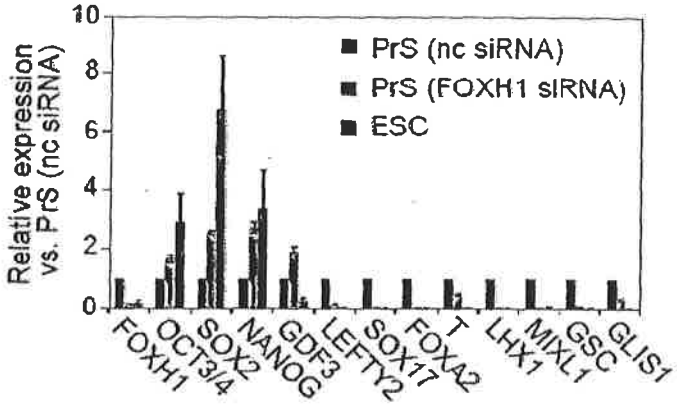


FIG. 6l

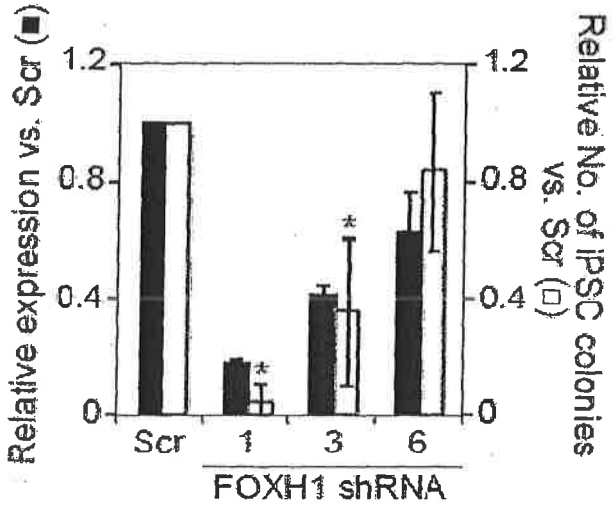


FIG. 6m

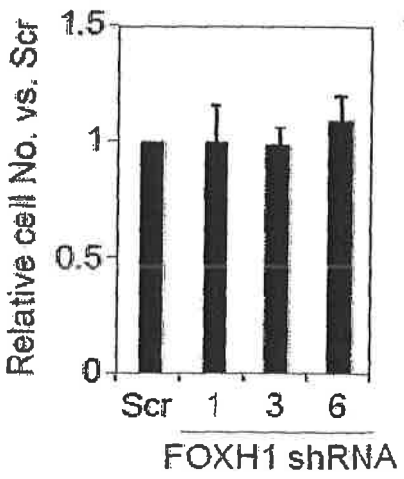


FIG. 7a

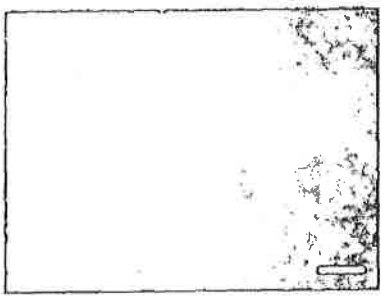


FIG. 7b

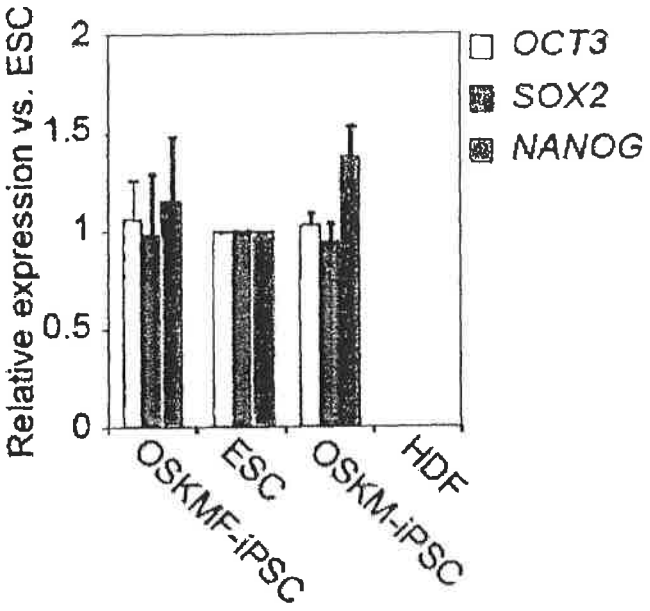


FIG. 7C

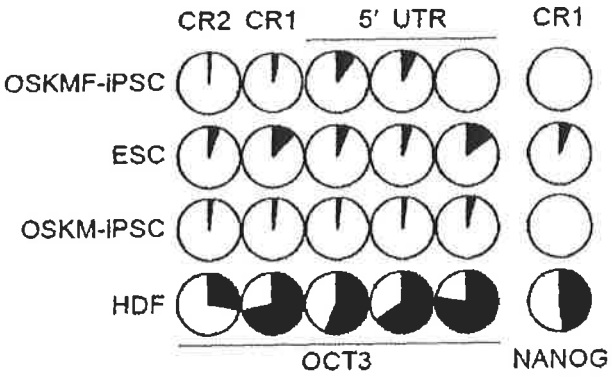


FIG. 7d

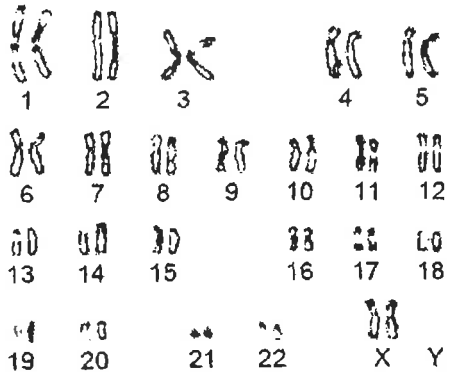


FIG. 7e

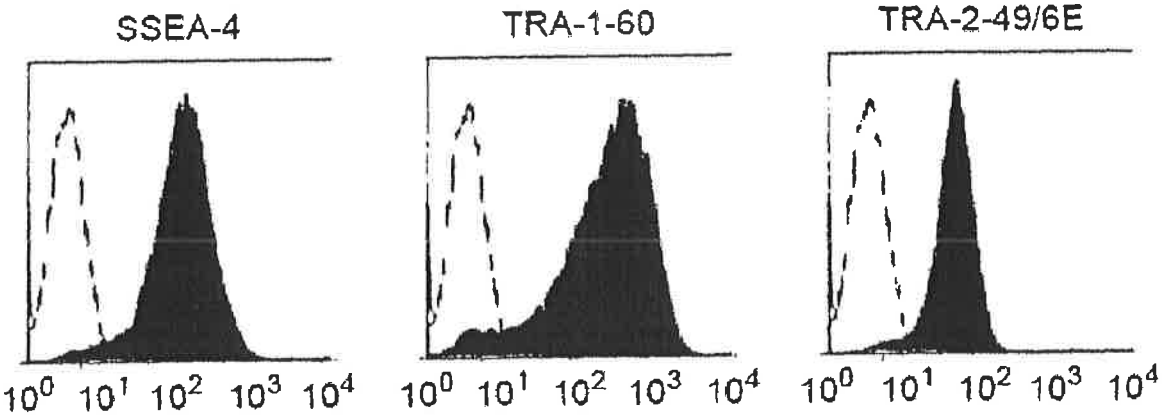


FIG. 7f

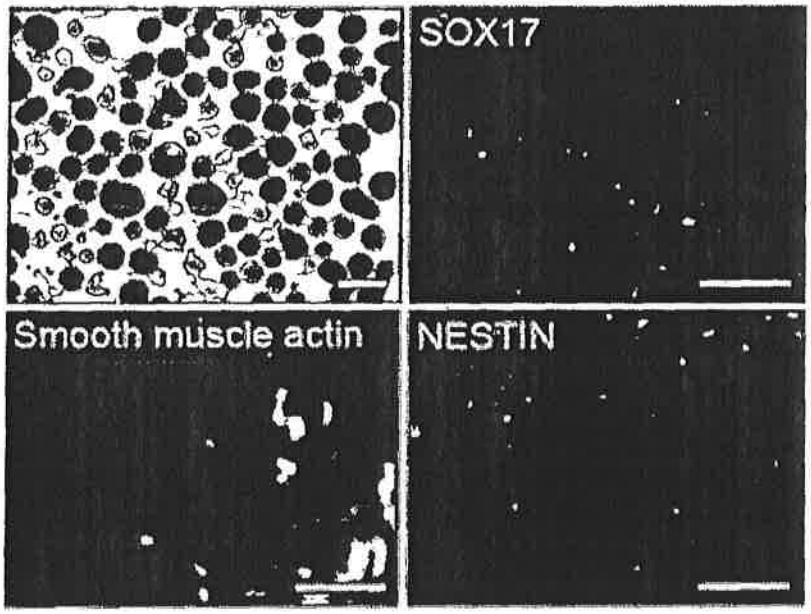

SOX17
Smooth muscle actin
NESTIN

FIG. 7g

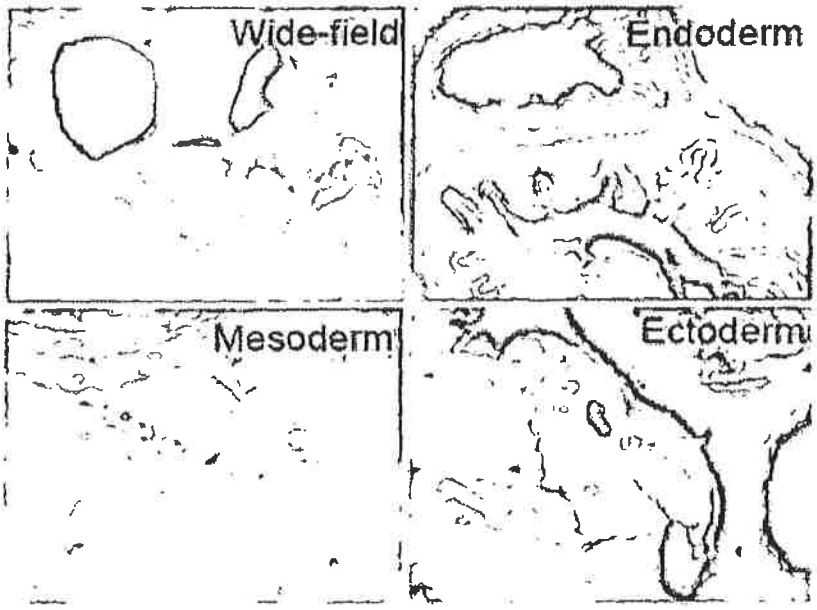

Wide-field
Endoderm
Mesoderm
Ectoderm

FIG. 8

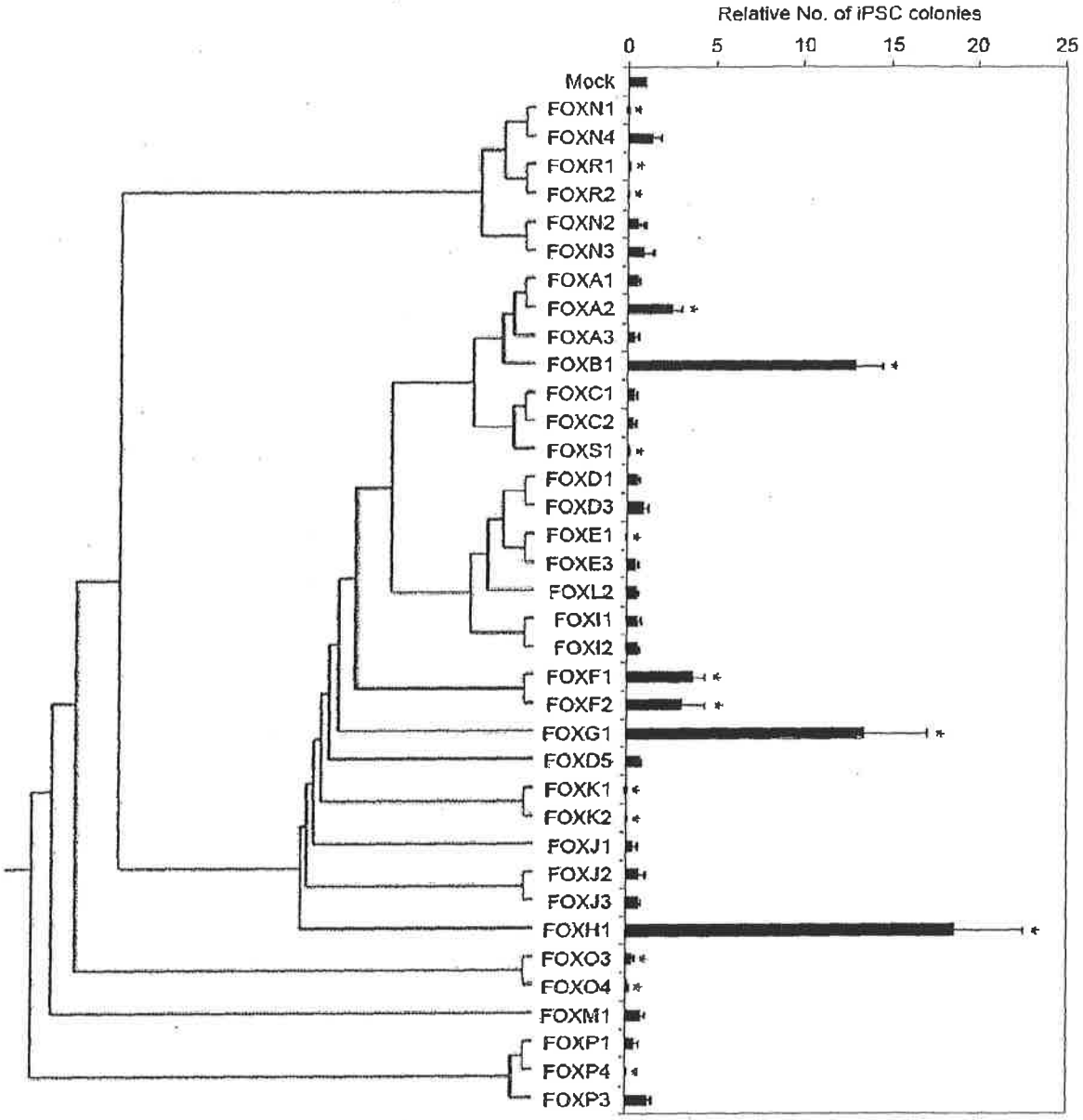
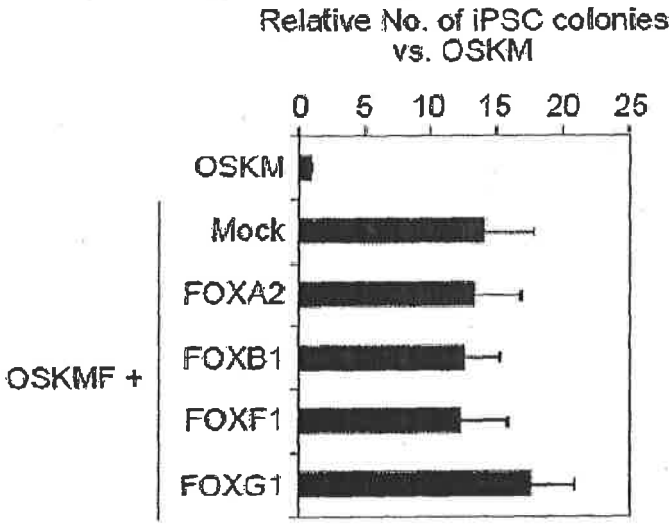

Relative No. of iPSC colonies
0
5
10
15
20
25
Mock
FOXN1
FOXN4
FOXR1
FOXR2
FOXN2
FOXN3
FOXA1
FOXA2
FOXA3
FOXB1
FOXC1
FOXC2
FOXS1
FOXD1
FOXD3
FOXE1
FOXE3
FOXL2
FOXI1
FOXI2
FOXF1
FOXF2
FOXG1
FOXD5
FOXK1
FOXK2
FOXJ1
FOXJ2
FOXJ3
FOXH1
FOXO3
FOXO4
FOXM1
FOXP1
FOXP4
FOXP3

FIG. 9


Relative No. of iPSC colonies vs. OSKM
0
5
10
15
20
25
OSKM
Mock
FOXA2
FOXB1
FOXF1
FOXG1
OSKMF +