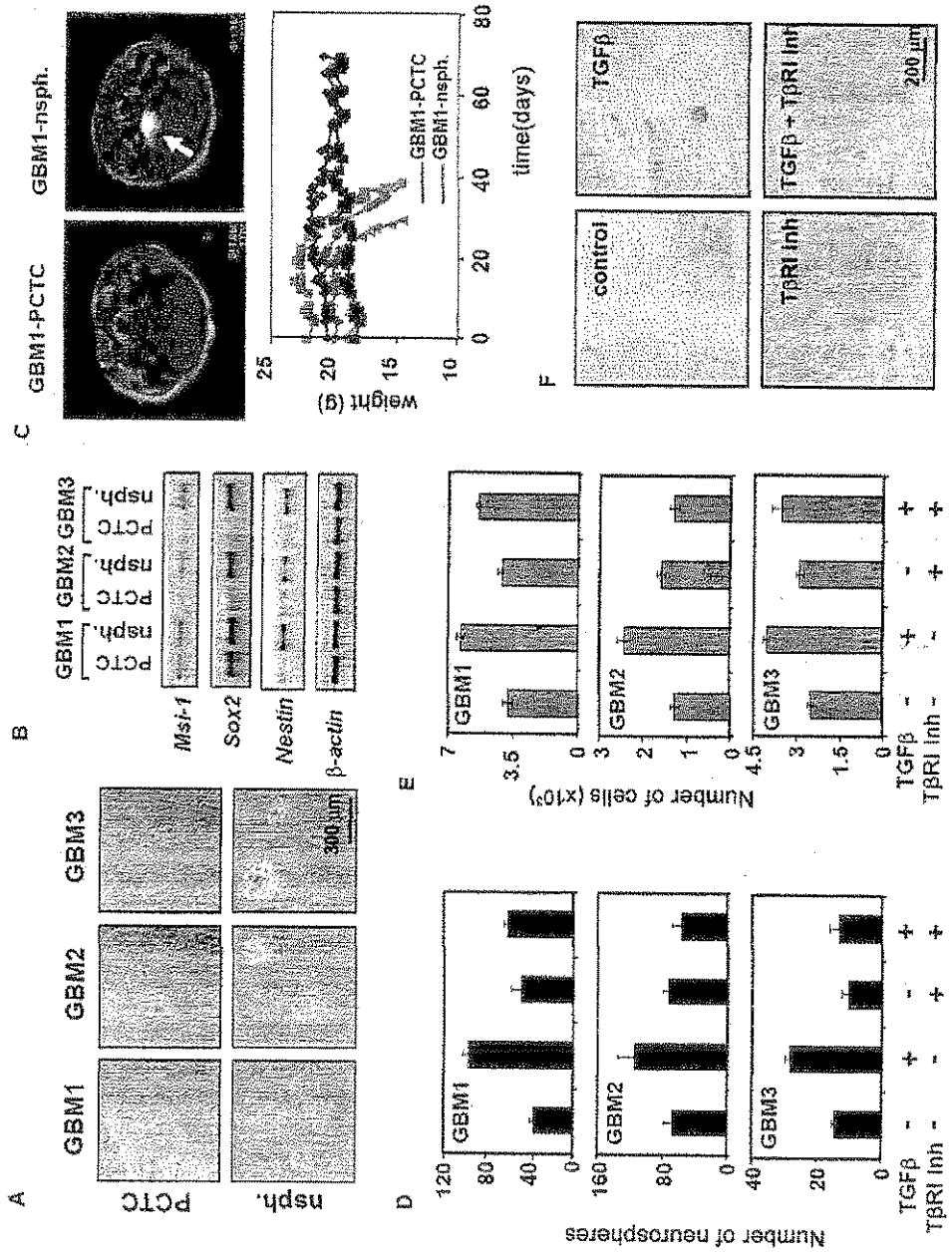

A
GBM1
GBM2
GBM3
PCTC
nsph.
300 µm
B
GBM1 GBM2 GBM3
PCTC
nsph.
Msi-1
Sox2
Nestin
β-actin
C
GBM1-PCTC
GBM1-nsph.
weight (g)
time(days)
GBM1-PCTC
GBM1-nsph.
D
Number of neurospheres
GBM1
GBM2
GBM3
TGFβ
TβRI Inh
E
Number of cells (x10³)
GBM1
GBM2
GBM3
TGFβ
TβRI Inh
F
control
TβRI inh
TGFβ
TGFβ + TβRI inh
200 µm

FIGURE 1

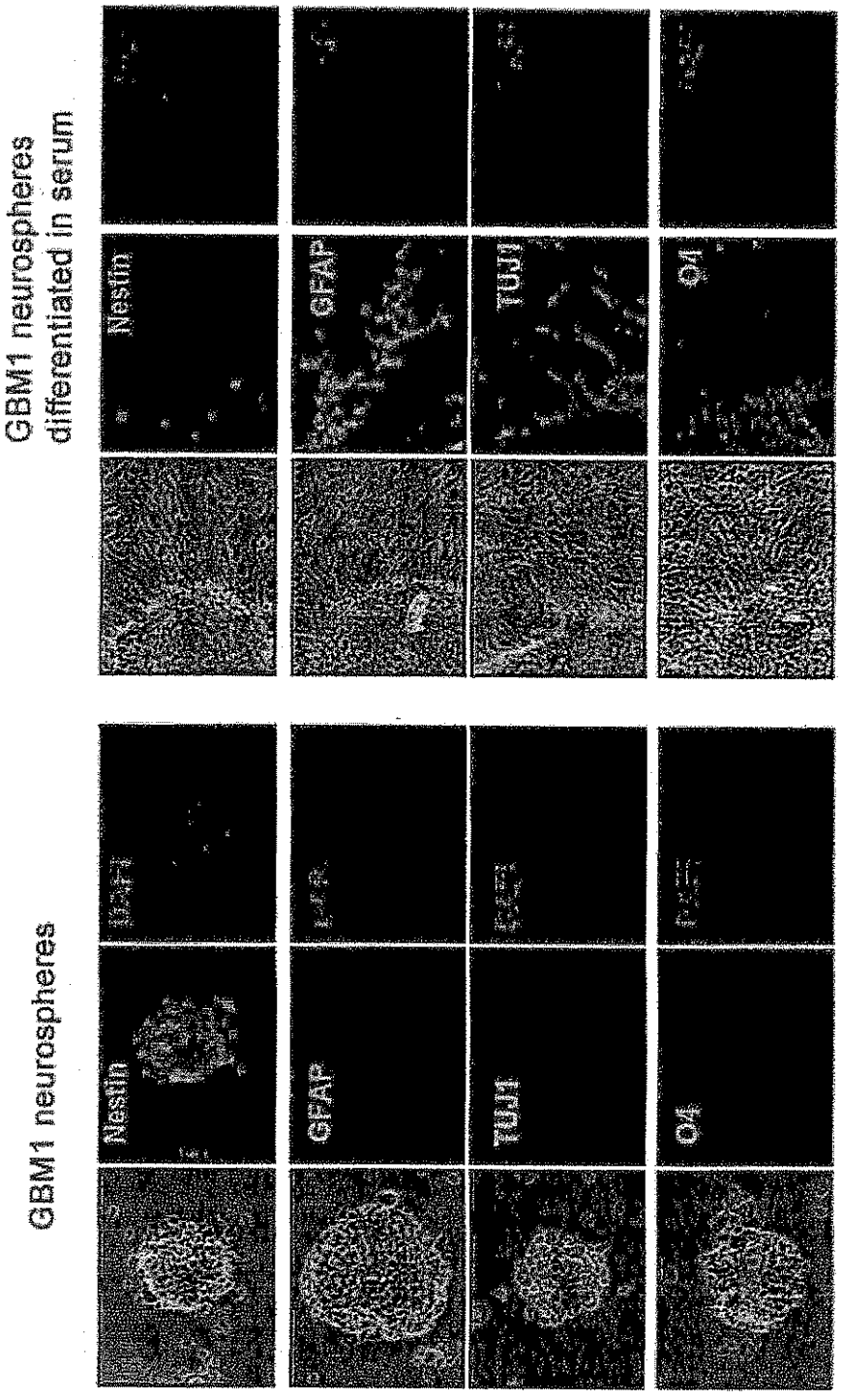

GBM1 neurospheres differentiated in serum
Nestin
GFAP
TUJ1
O4
GBM1 neurospheres
Nestin
GFAP
TUJ1
O4

FIGURE 2

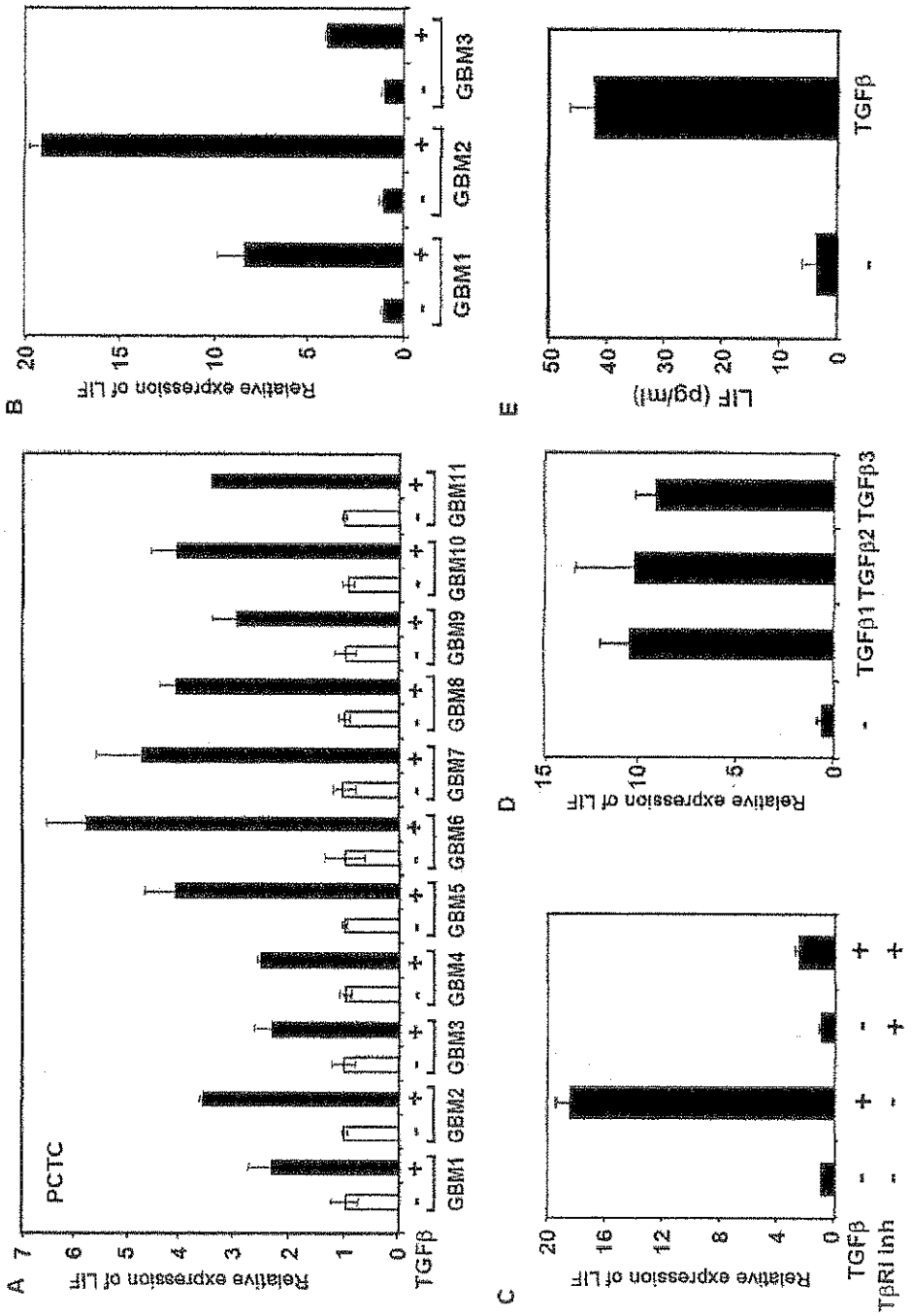

A
PCTC
Relative expression of LIF
TGFβ
GBM1 GBM2 GBM3 GBM4 GBM5 GBM6 GBM7 GBM8 GBM9 GBM10 GBM11
B
Relative expression of LIF
GBM1 GBM2 GBM3
C
Relative expression of LIF
TGFβ
TβRI inh
D
Relative expression of LIF
TGFβ1 TGFβ2 TGFβ3
E
LIF (pg/ml)
TGFβ

FIGURE 3

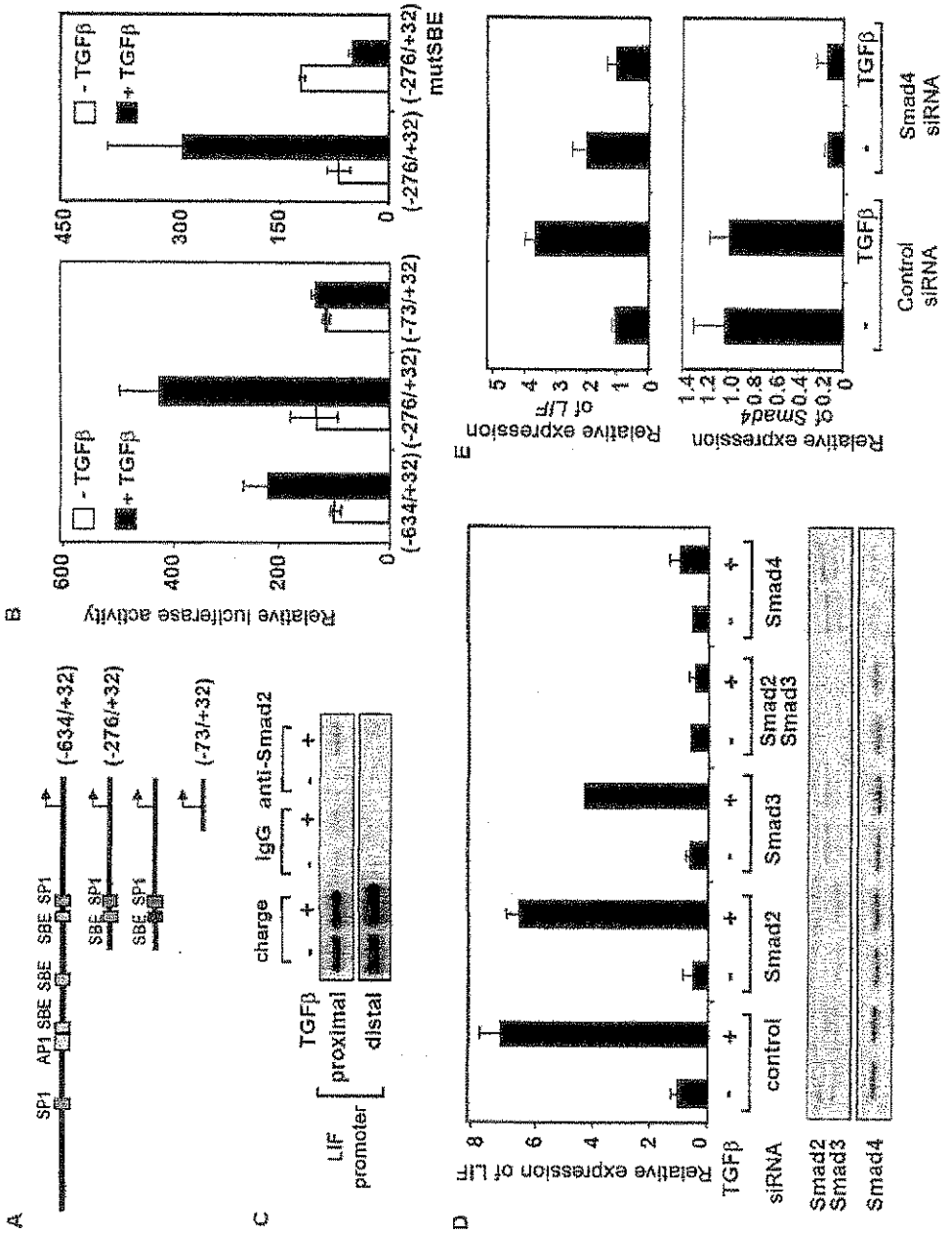

A
SP1
AP1
SBE
SBE
SBE
SP1
(-634/+32)
(-276/+32)
(-73/+32)
B
Relative luciferase activity
- TGFβ
+ TGFβ
(-634/+32)
(-276/+32)
(-73/+32)
(-276/+32)
(-276/+32)
mutSBE
C
charge
IgG
anti-Smad2
TGFβ
LIF promoter
proximal
distal
D
Relative expression of LIF
TGFβ
siRNA
control
Smad2
Smad3
Smad2
Smad3
Smad4
Smad4
E
Relative expression of LIF
Relative expression of Smad4
- TGFβ
+ TGFβ
Control siRNA
Smad4 siRNA

FIGURE 4

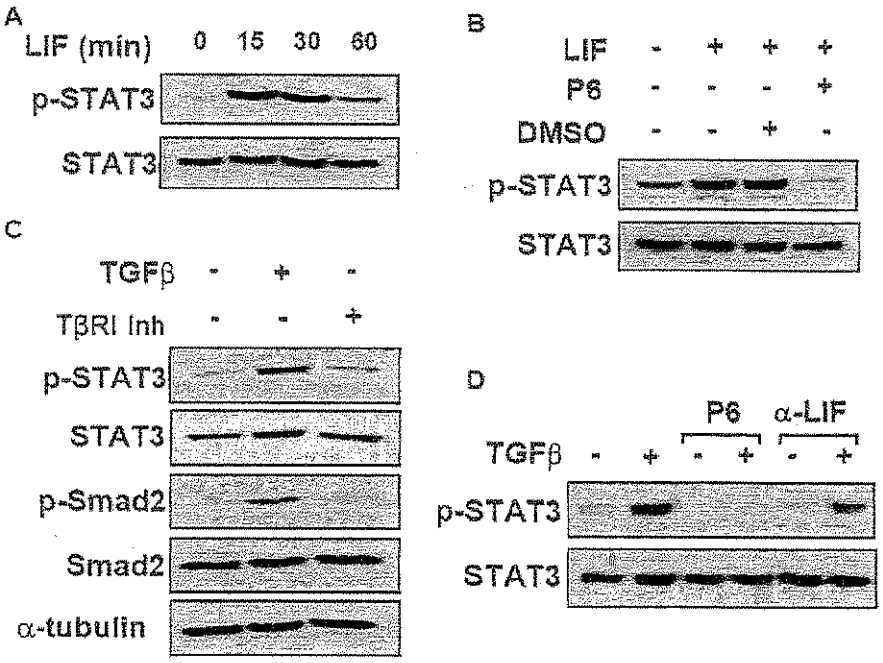

A
LIF (min) 0 15 30 60
p-STAT3
STAT3
B
LIF - + + +
P6 - - - +
DMSO - - + -
p-STAT3
STAT3
C
TGFβ - + -
TβRI Inh - - +
p-STAT3
STAT3
p-Smad2
Smad2
α-tubulin
D
P6 α-LIF
TGFβ - + - + - +
p-STAT3
STAT3

FIGURE 5

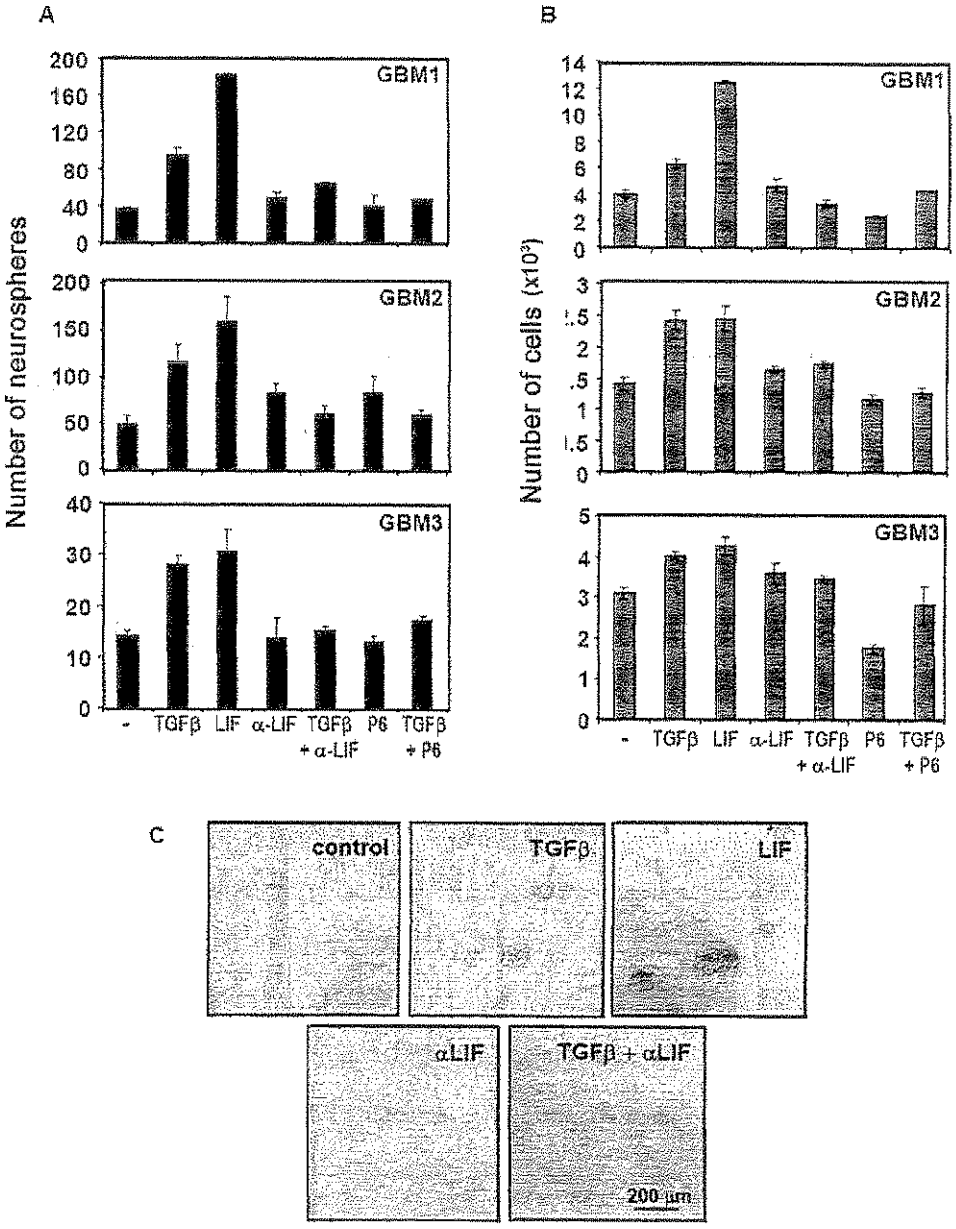

A
B
C
Number of neurospheres
Number of cells (x10³)
GBM1
GBM2
GBM3
- TGFβ LIF α-LIF TGFβ + α-LIF P6 TGFβ + P6
control
TGFβ
LIF
αLIF
TGFβ + αLIF
200 µm

FIGURE 6

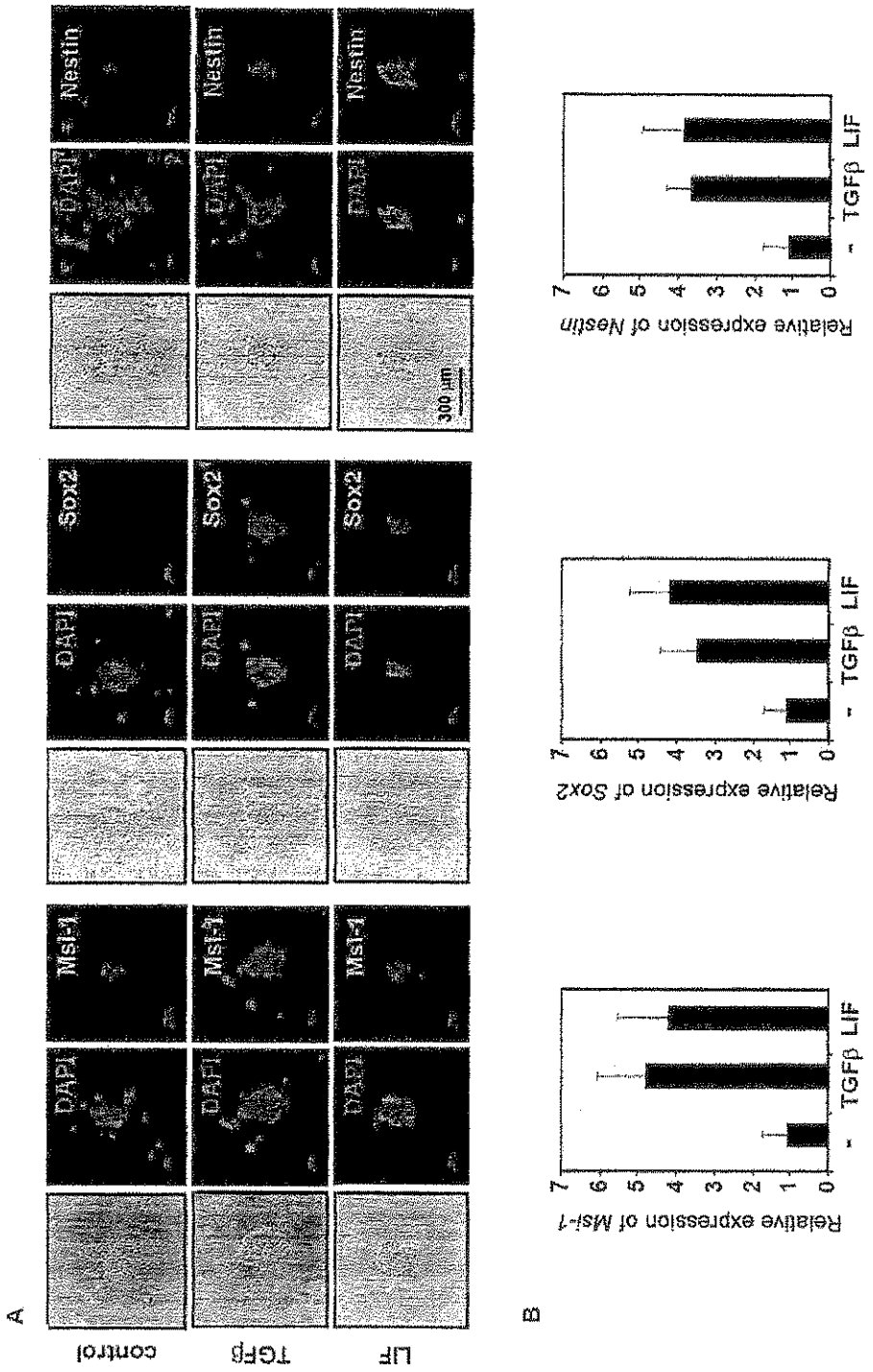

A
control
TGFβ
LIF
Msi1
Msi-1
Sox2
Nestin
DAPI
300 µm
B
Relative expression of Msi-1
Relative expression of Sox2
Relative expression of Nestin
- TGFβ LIF
0
1
2
3
4
5
6
7

FIGURE 7

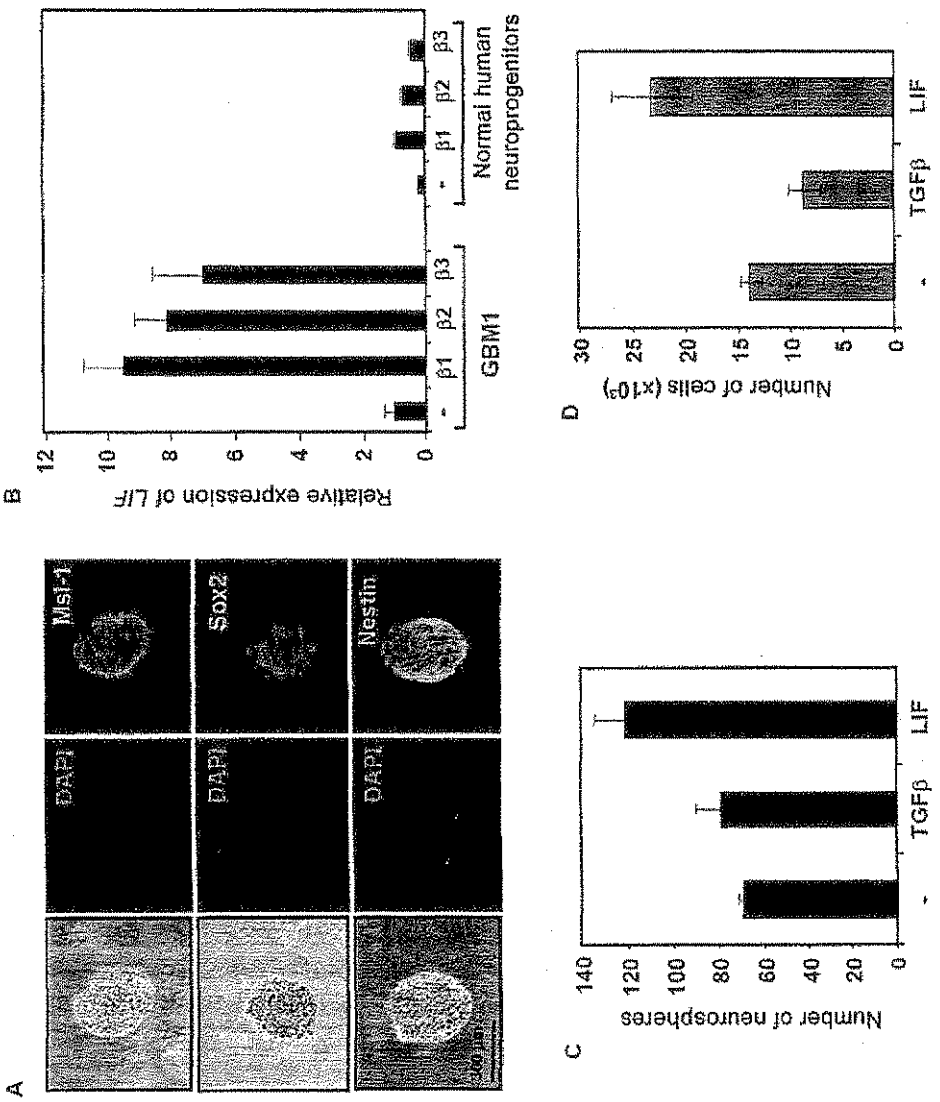

A
Msi-1
DAPI
Sox2
DAPI
Nestin
DAPI
B
Relative expression of LIF
0
2
4
6
8
10
12
-
β1
β2
β3
GBM1
-
β1
β2
β3
Normal human neuroprogenitors
C
Number of neurospheres
0
20
40
60
80
100
120
140
-
TGFβ
LIF
D
Number of cells (x10³)
0
5
10
15
20
25
30
-
TGFβ
LIF

FIGURE 8

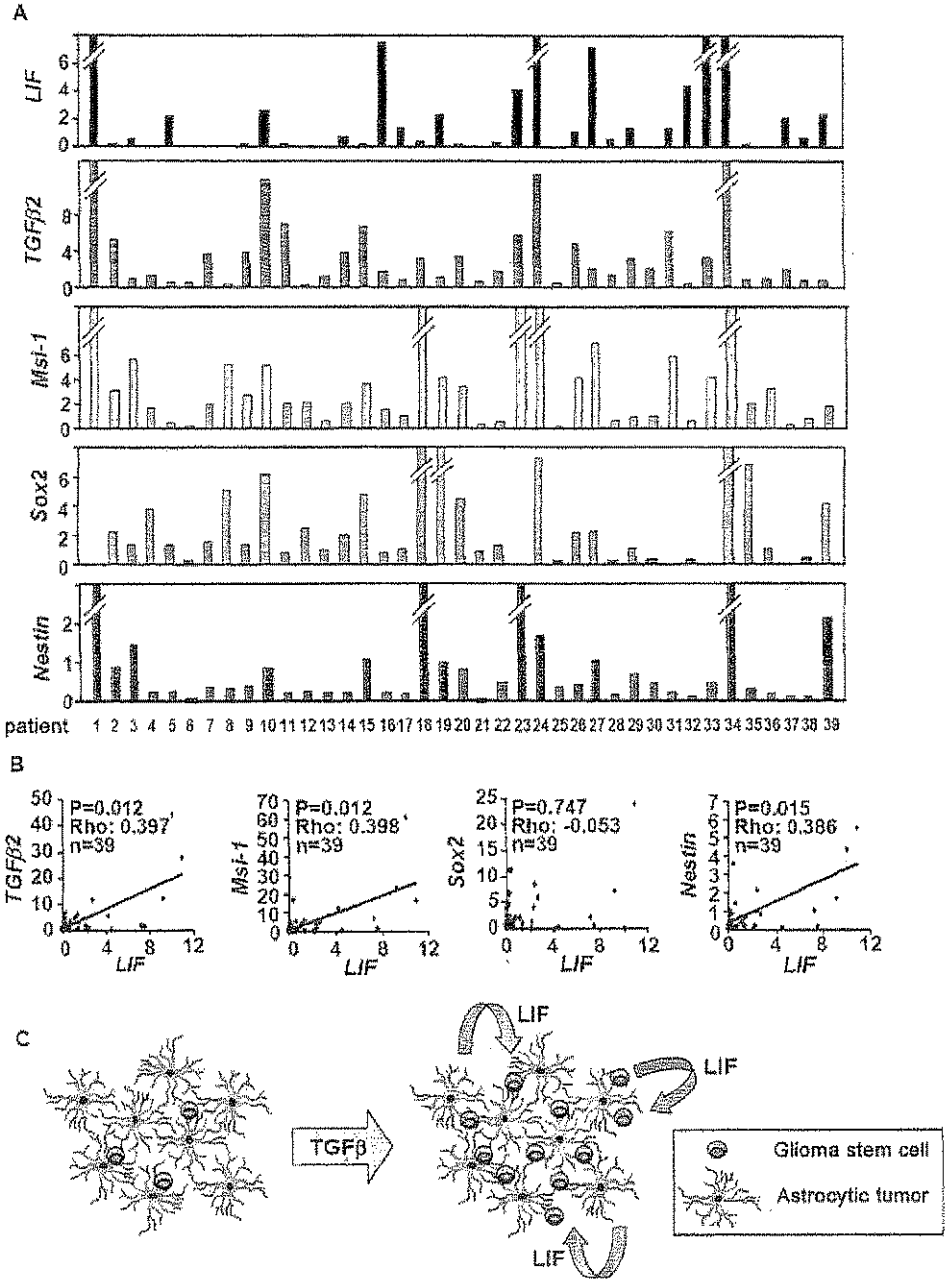

A
LIF
TGFβ2
Msi-1
Sox2
Nestin
patient 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39
B
TGFβ2 P=0.012 Rho: 0.397 n=39
Msi-1 P=0.012 Rho: 0.398 n=39
Sox2 P=0.747 Rho: -0.053 n=39
Nestin P=0.015 Rho: 0.386 n=39
LIF
C
TGFβ
LIF
Glioma stem cell
Astrocytic tumor

FIGURE 9

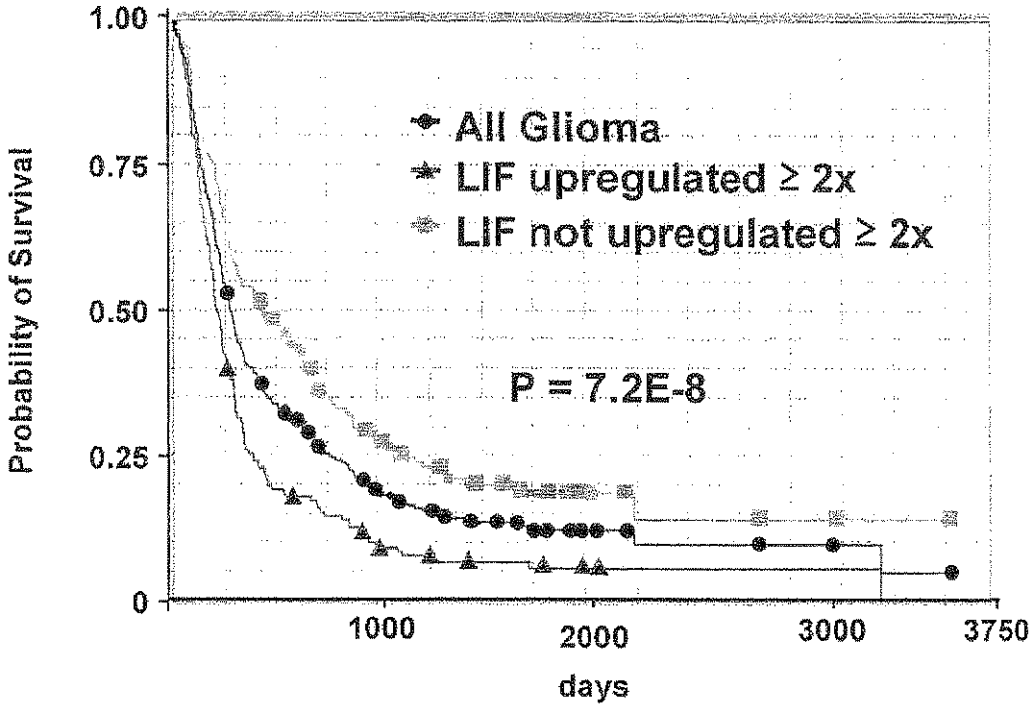

1.00
0.75
0.50
0.25
0
Probability of Survival
All Glioma
LIF upregulated ≥ 2x
LIF not upregulated ≥ 2x
P = 7.2E-8
1000
2000
3000
3750
days

FIGURE 10

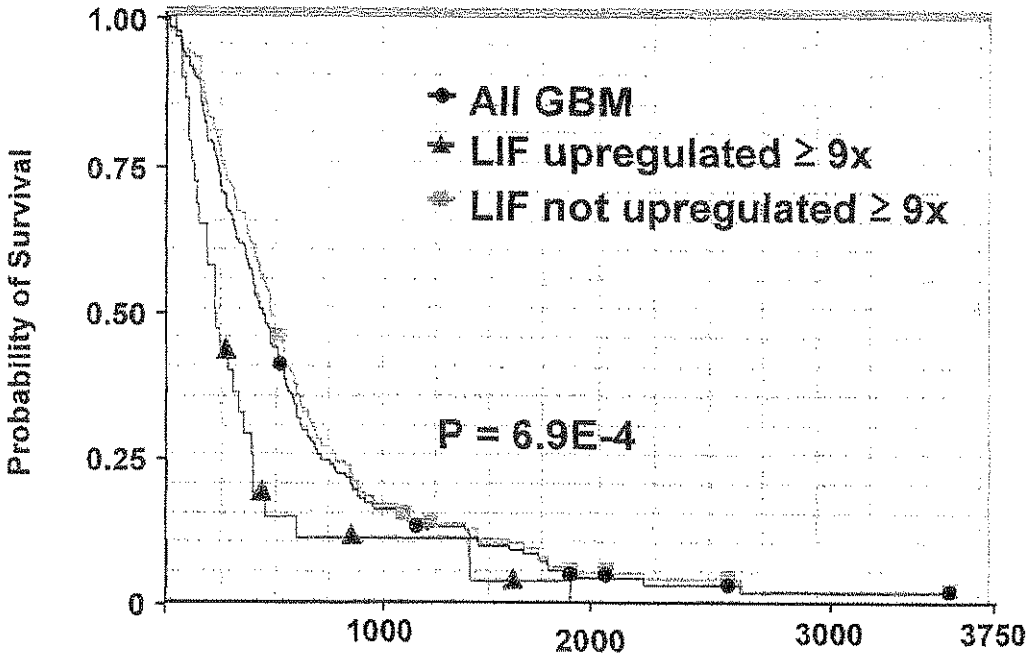

1.00
0.75
0.50
0.25
0
Probability of Survival
All GBM
LIF upregulated ≥ 9x
LIF not upregulated ≥ 9x
P = 6.9E-4
1000
2000
3000
3750

FIGURE 11

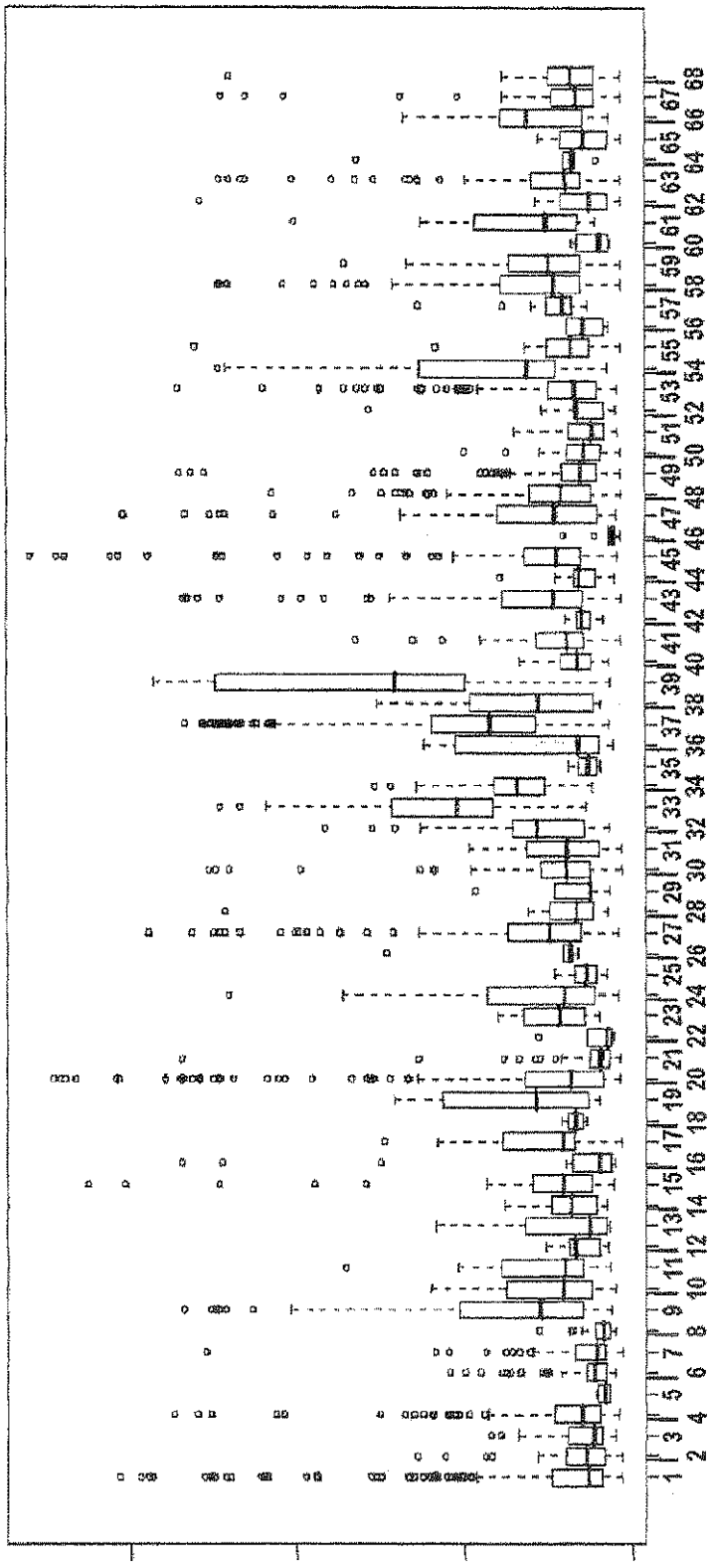


FIGURE 12