FIG. 1

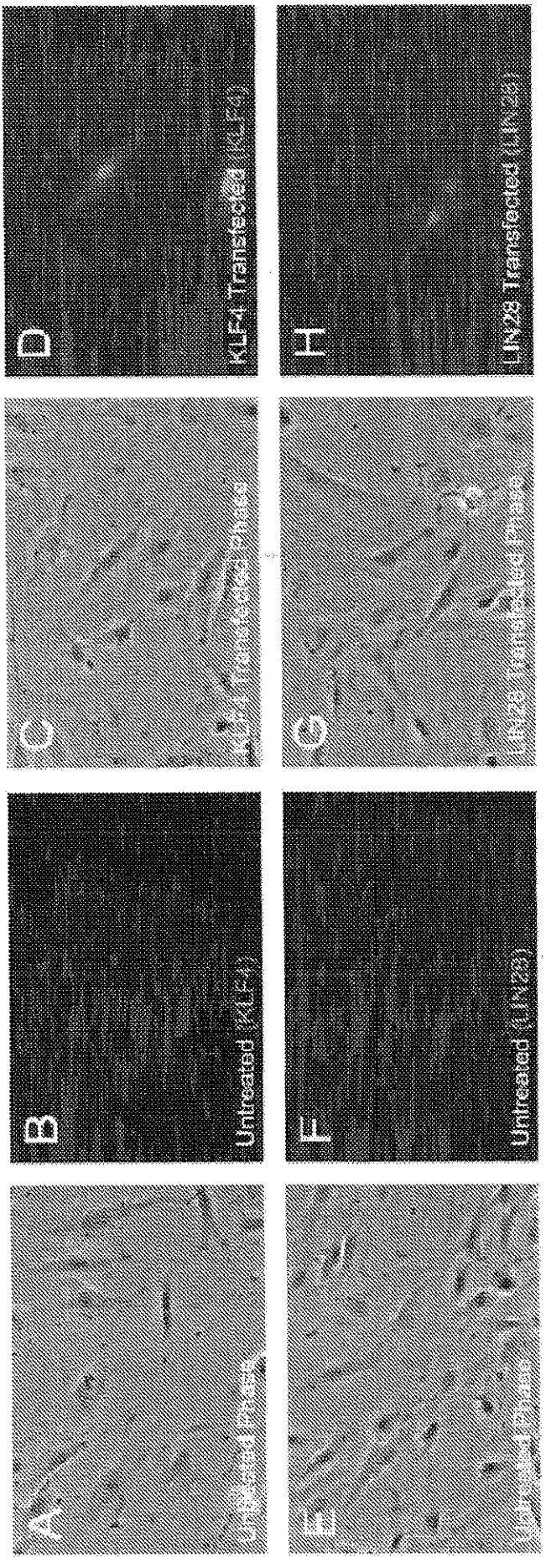

A
Untreated Phase
B
Untreated (KLF4)
C
KLF4 Transfected Phase
D
KLF4 Transfected (KLF4)
E
Untreated Phase
F
Untreated (LIN28)
G
LIN28 Transfected Phase
H
LIN28 Transfected (LIN28)

FIG. 1

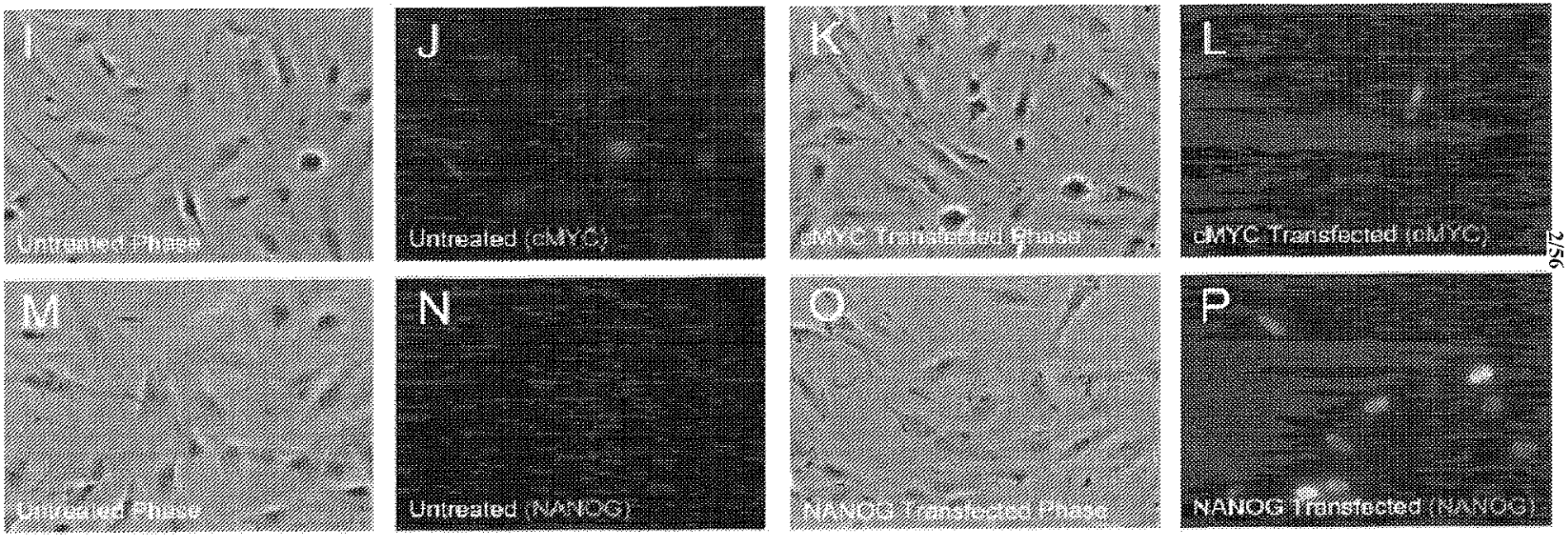

I
Untreated Phase
J
Untreated (cMYC)
K
cMYC Transfected Phase
L
cMYC Transfected (cMYC)
M
Untreated Phase
N
Untreated (NANOG)
O
NANOG Transfected Phase
P
NANOG Transfected (NANOG)

FIG. 1

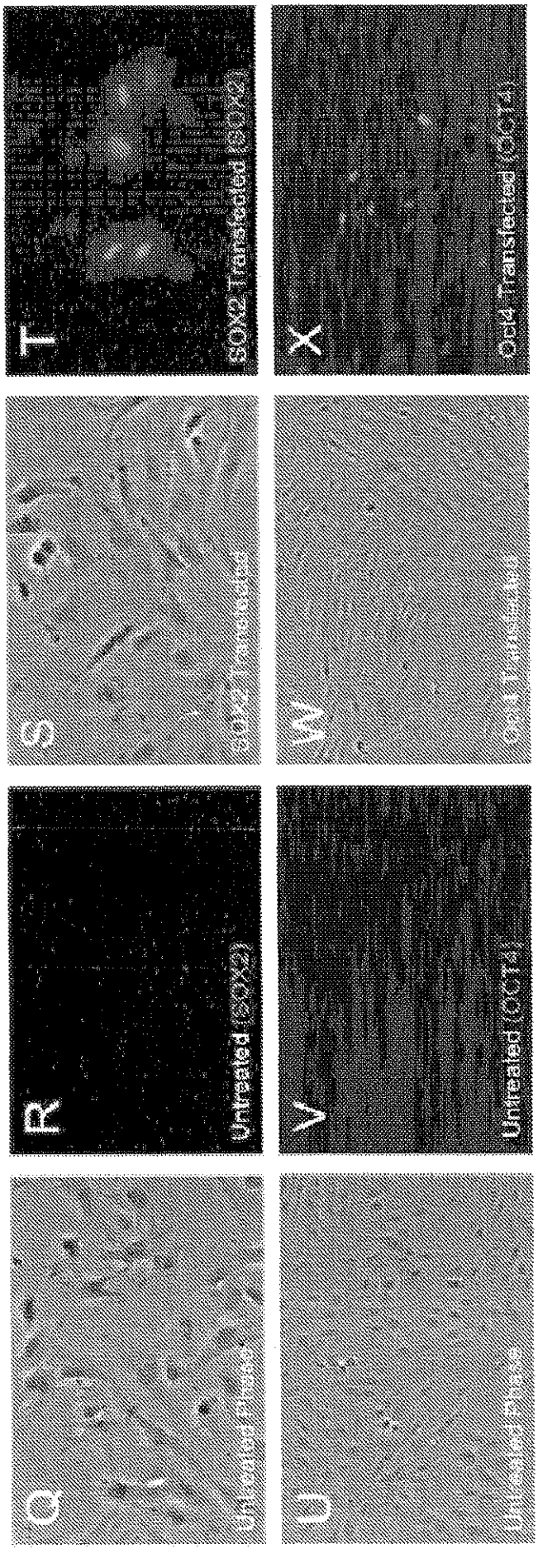
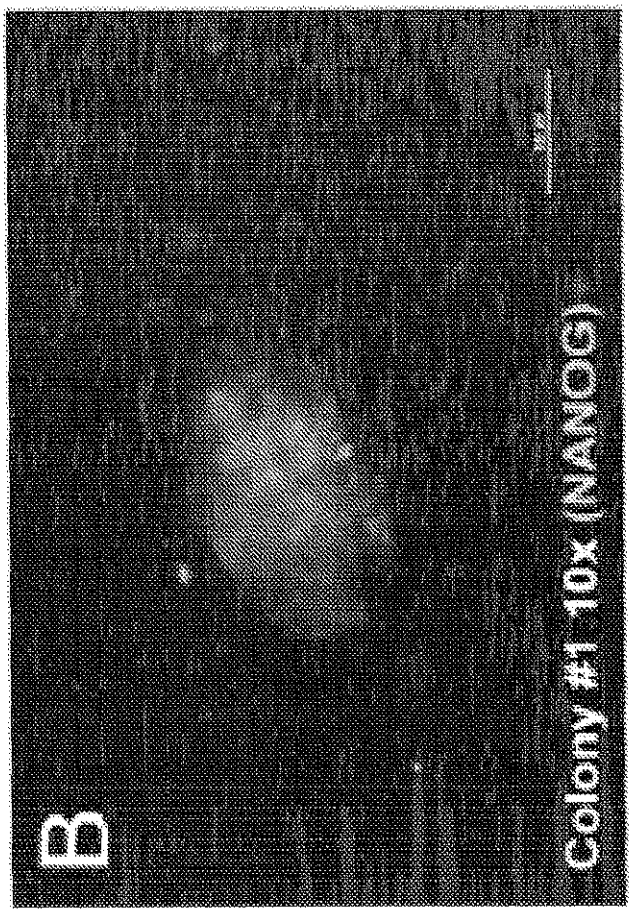

Q
Untreated (Phase)
R
Untreated (SOX2)
S
SOX2 Transfected
T
SOX2 Transfected (SOX2)
U
Untreated (Phase)
V
Untreated (OCT4)
W
OpN Transfected
X
Opt4 Transfected (OCT4)

FIG. 2



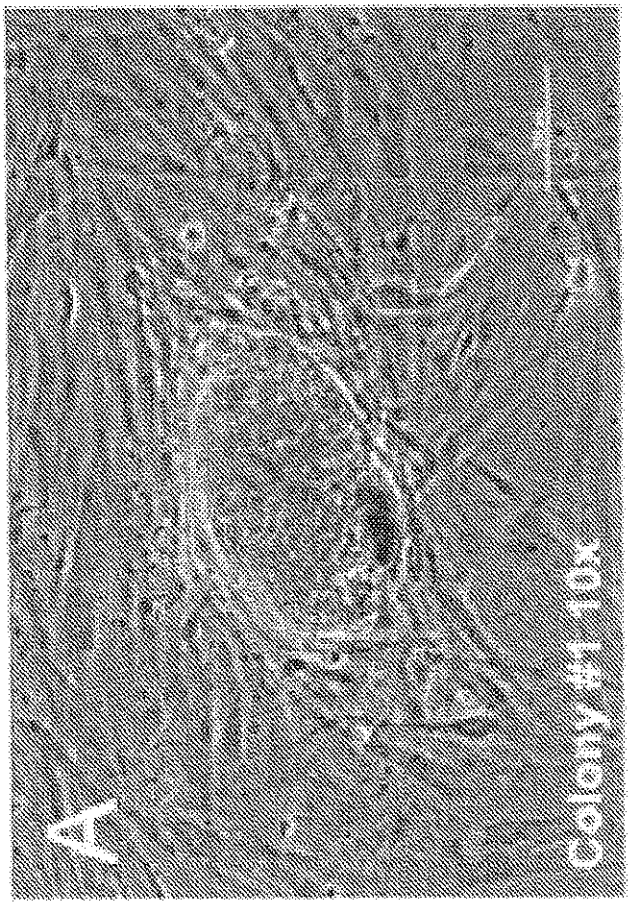
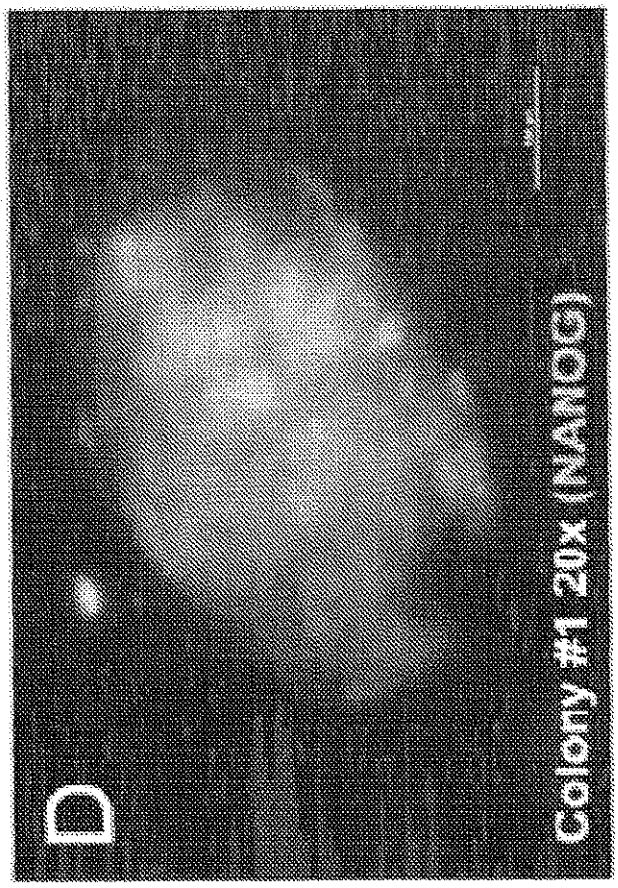


FIG. 2



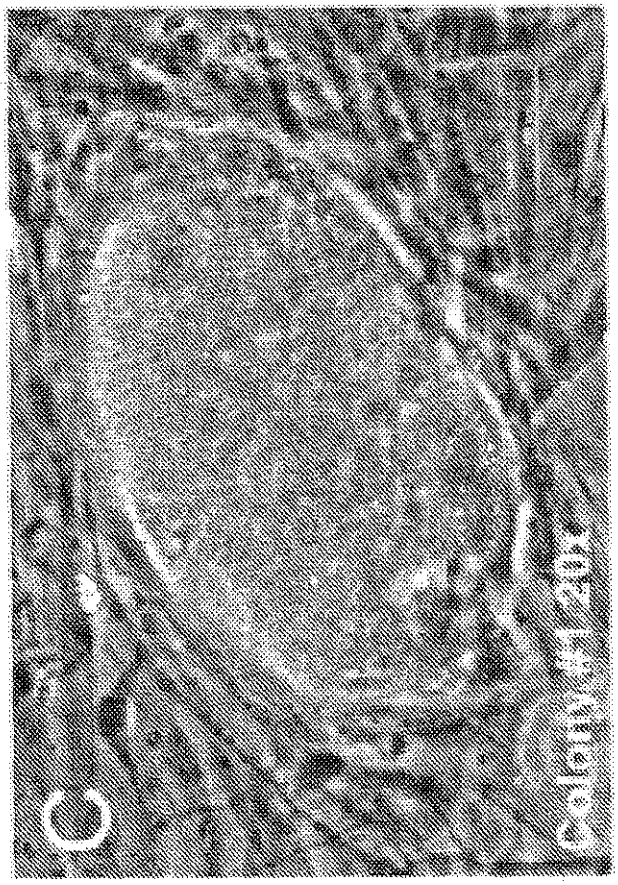


FIG. 3

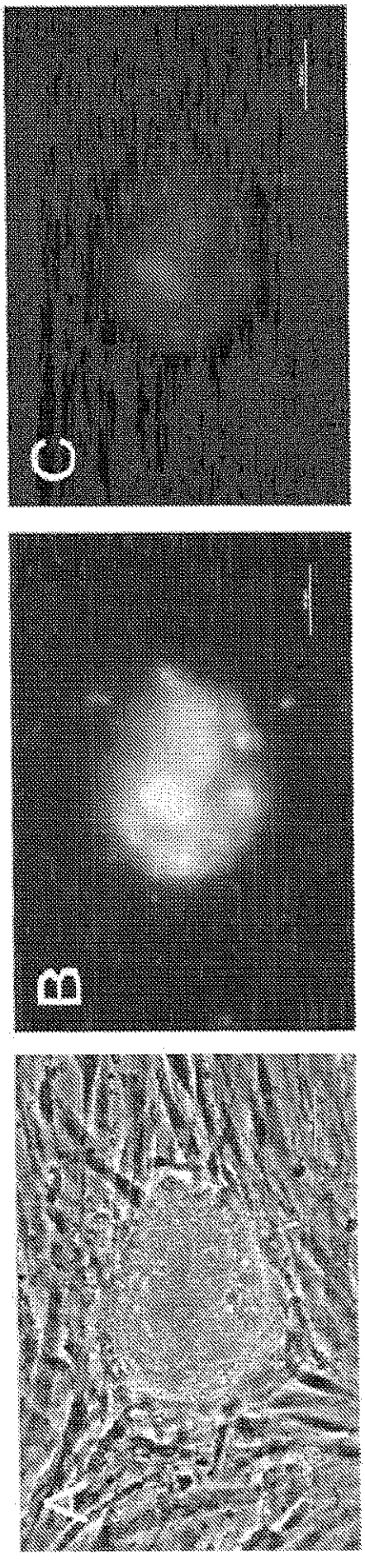


FIG. 3

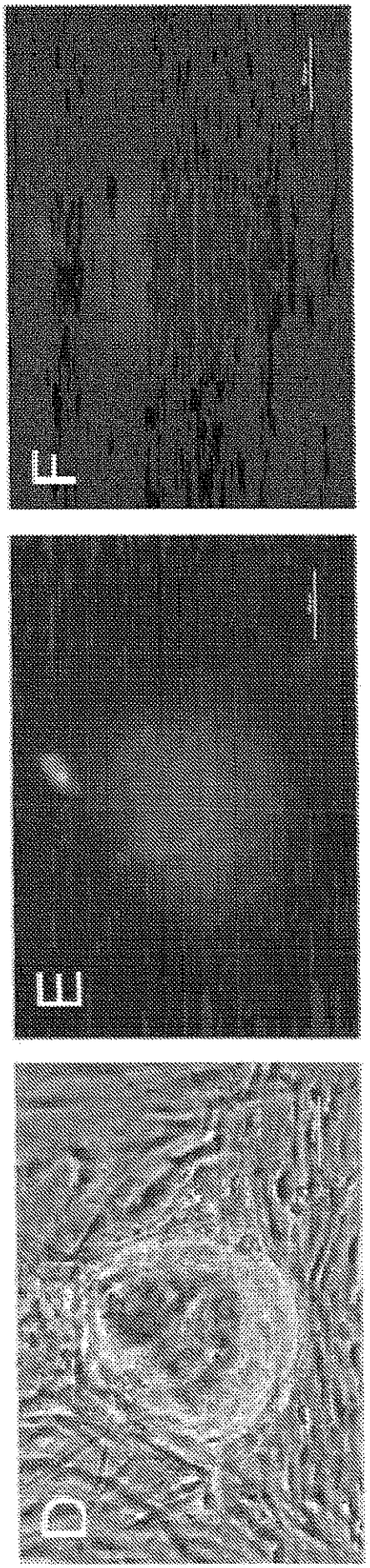


FIG. 3

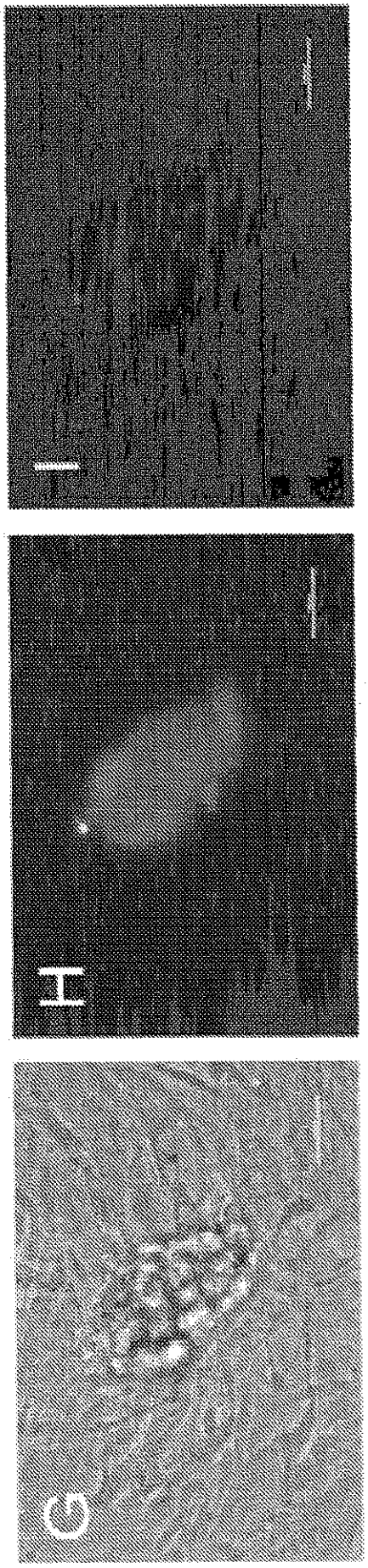


FIG. 4

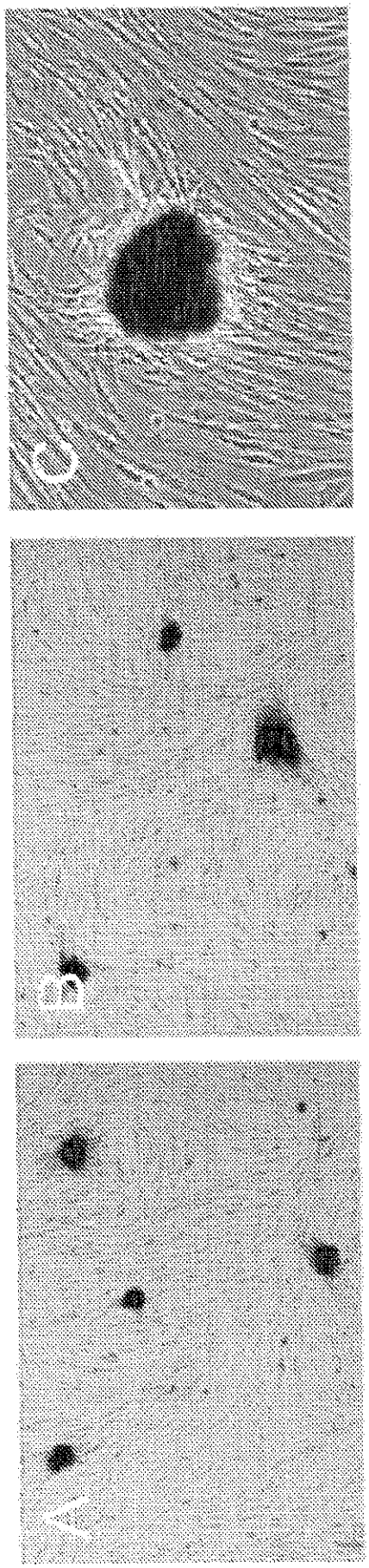


FIG. 4

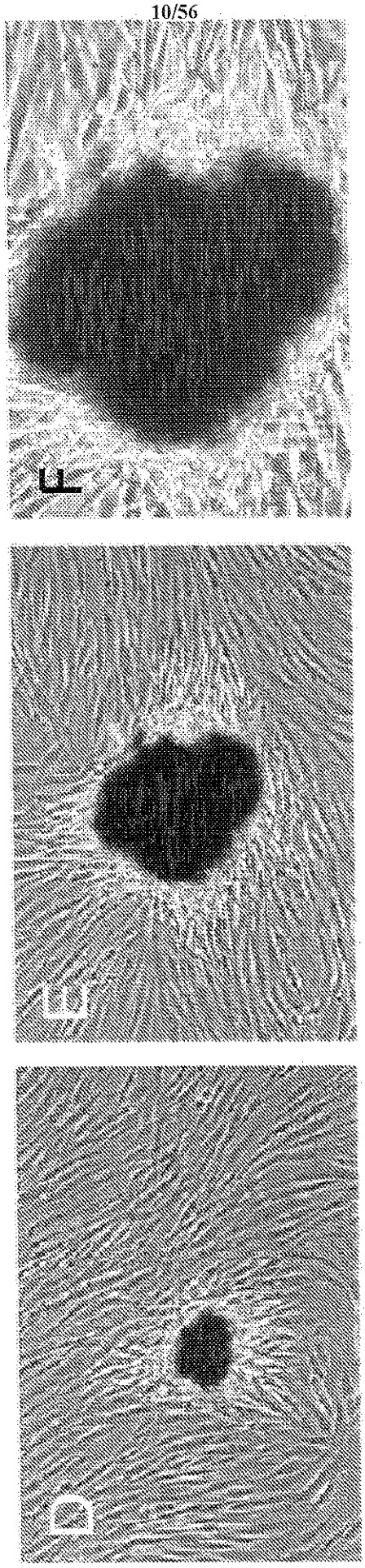


FIG. 4

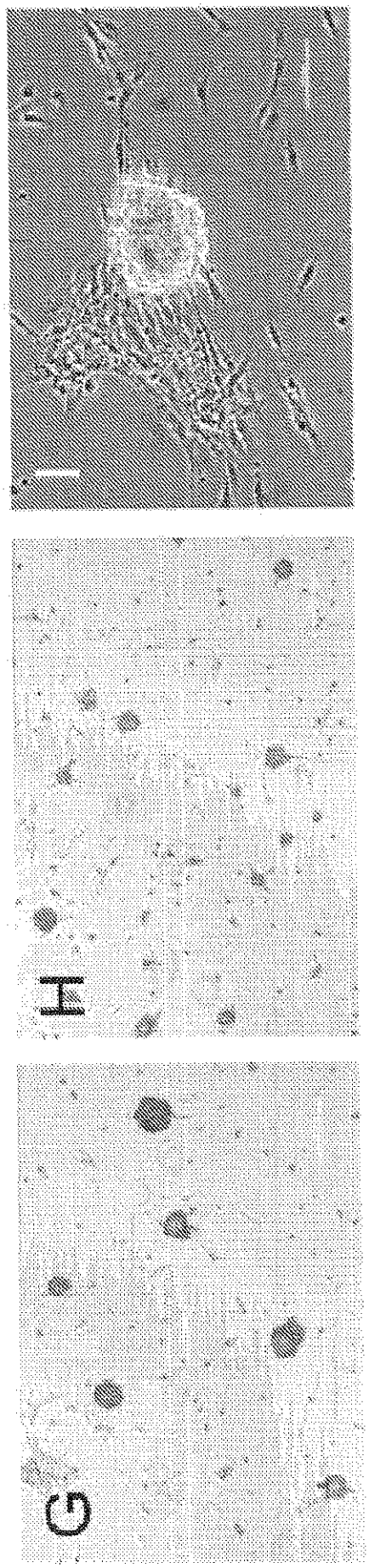


FIG. 5

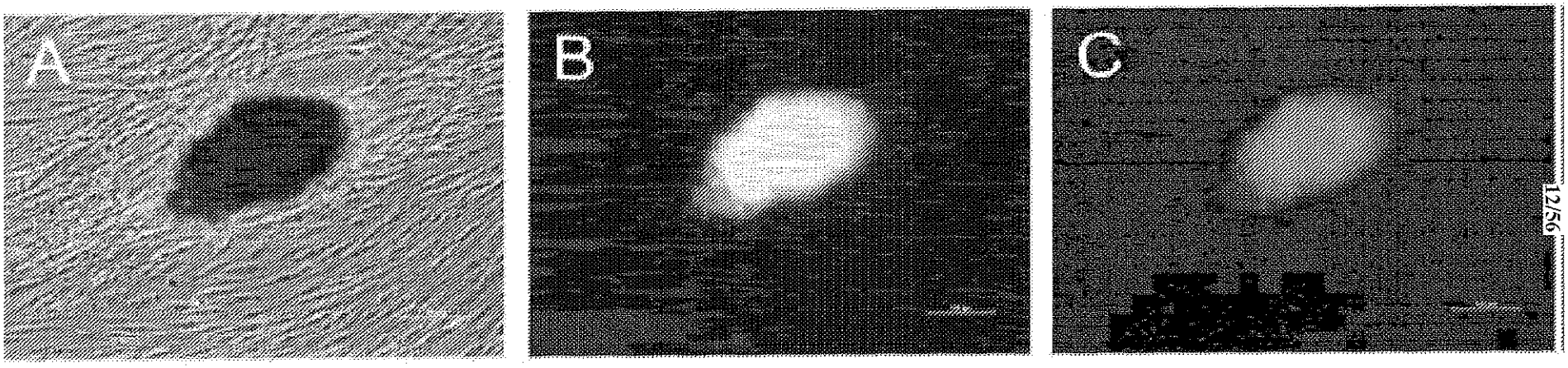


FIG. 5

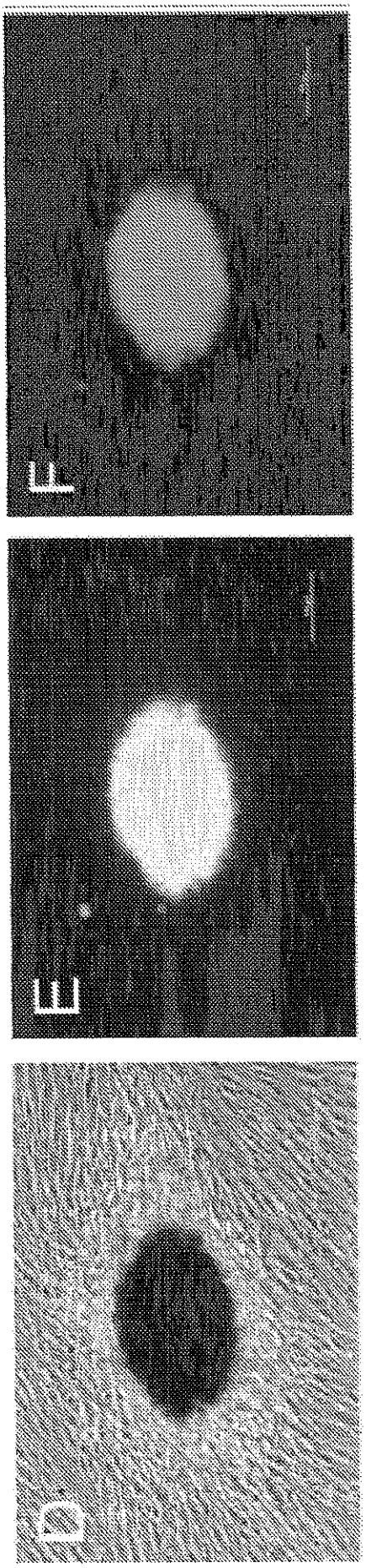
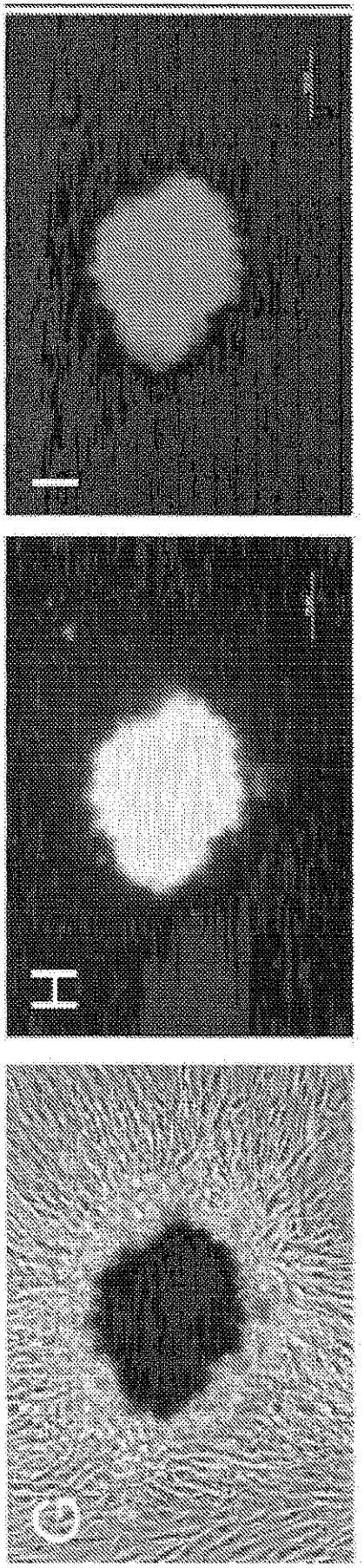


FIG. 5



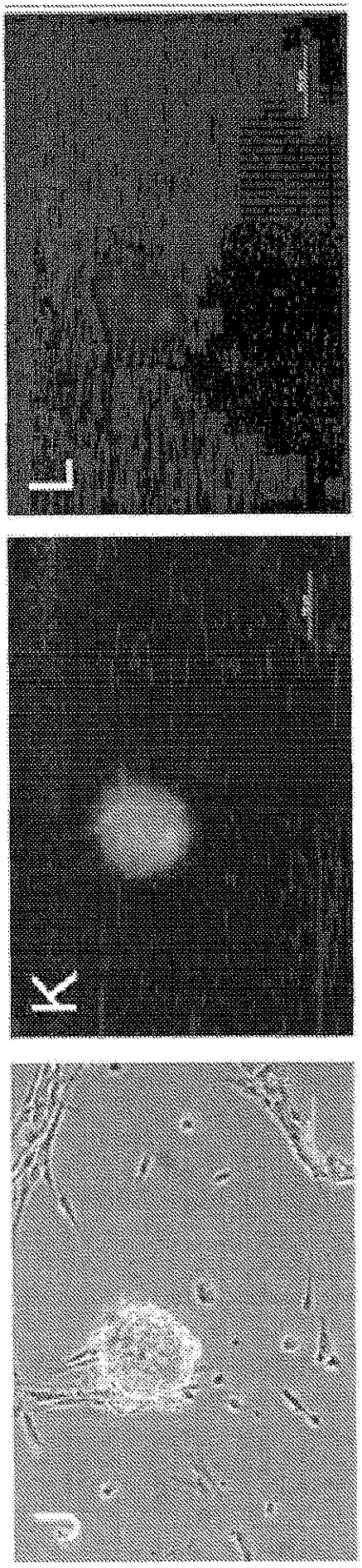


FIG. 5

FIG. 5

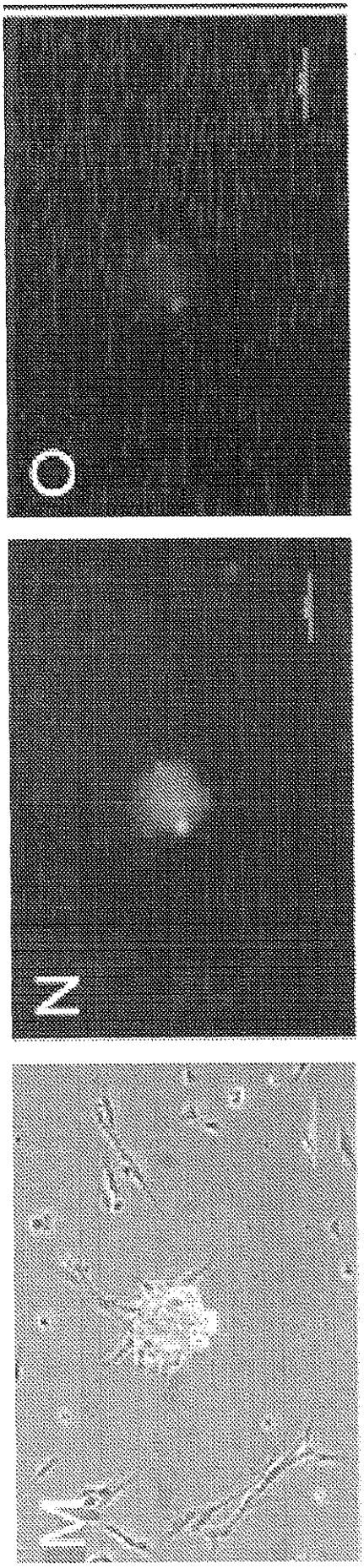


FIG. 6

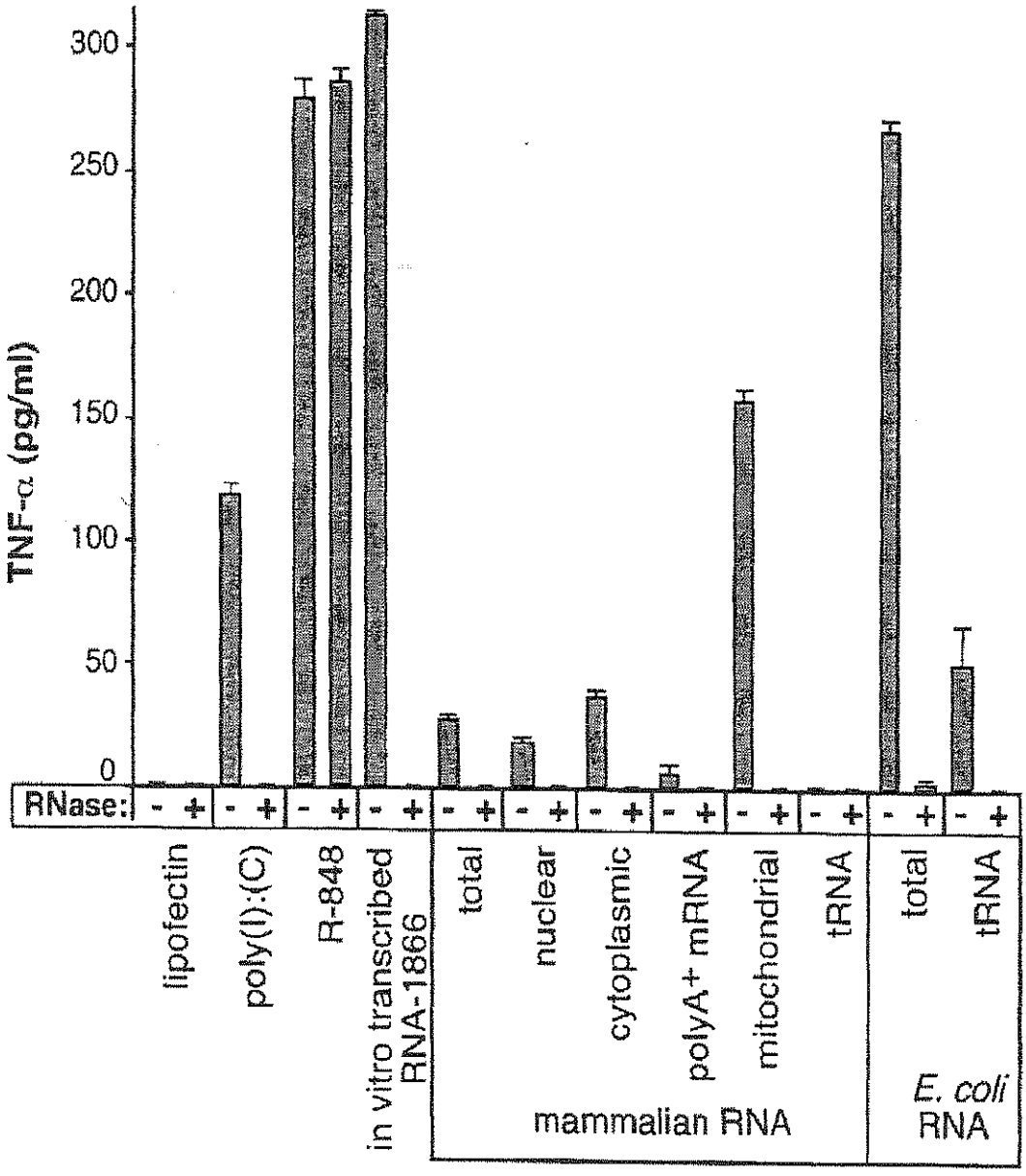

TNF-α (pg/ml)
300
250
200
150
100
50
0
RNase: - + - + - + - + - + - + - + - + - + - + - + - +
lipofectin
poly(I):(C)
R-848
in vitro transcribed RNA-1866
total
nuclear
cytoplasmic
polyA+ mRNA
mitochondrial
tRNA
mammalian RNA
total
tRNA
E. coli RNA

FIG. 7

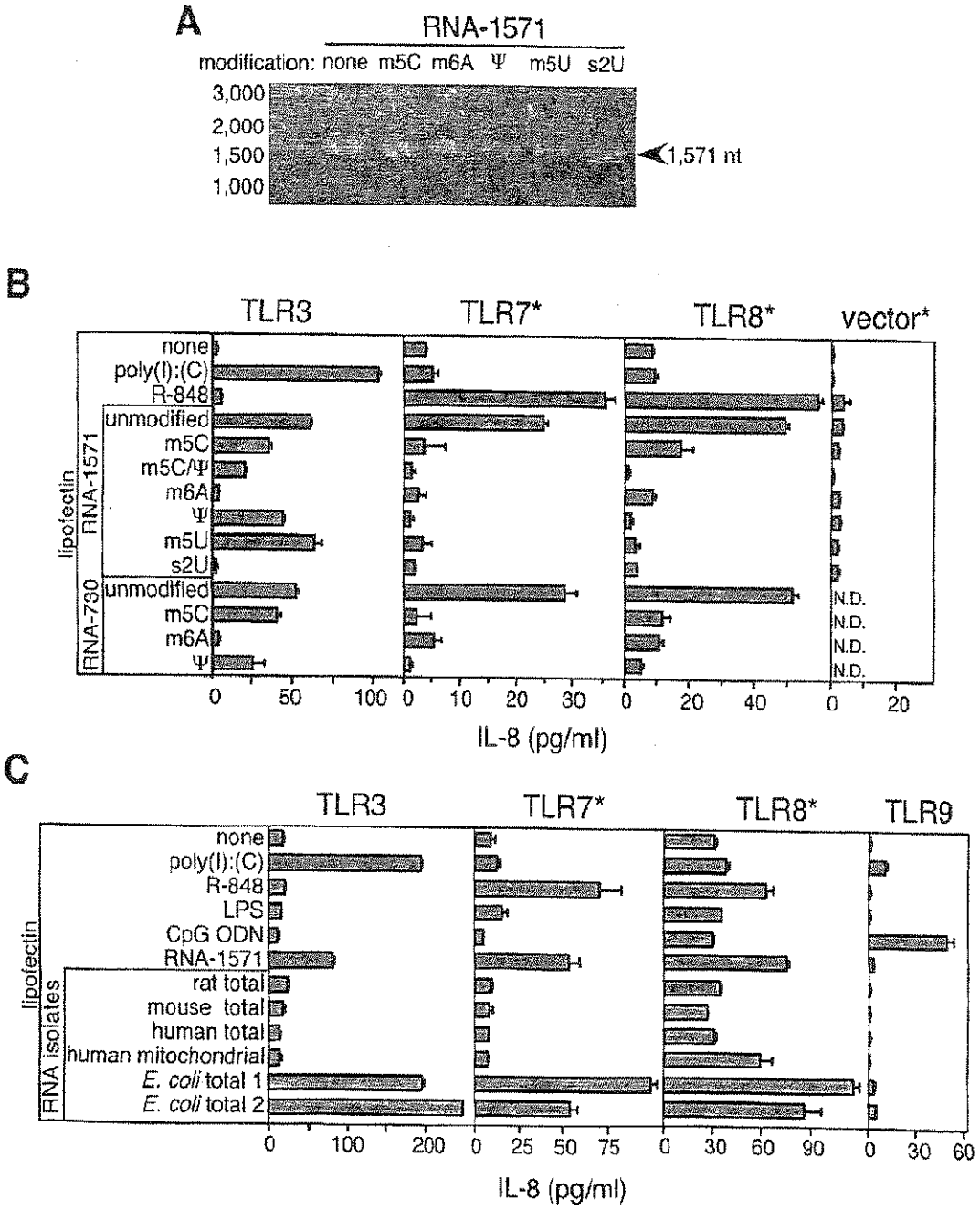

A
RNA-1571
modification: none m5C m6A Ψ m5U s2U
3,000
2,000
1,500
1,000
1,571 nt
B
TLR3
TLR7*
TLR8*
vector*
lipofectin
RNA-1571
RNA-730
none
poly(I):(C)
R-848
unmodified
m5C
m5C/Ψ
m6A
Ψ
m5U
s2U
unmodified
m5C
m6A
Ψ
N.D.
N.D.
N.D.
N.D.
0 50 100
0 10 20 30
0 20 40
0 20
IL-8 (pg/ml)
C
TLR3
TLR7*
TLR8*
TLR9
lipofectin
RNA isolates
none
poly(I):(C)
R-848
LPS
CpG ODN
RNA-1571
rat total
mouse total
human total
human mitochondrial
E. coli total 1
E. coli total 2
0 100 200
0 25 50 75
0 30 60 90
0 30 60
IL-8 (pg/ml)

FIG. 8

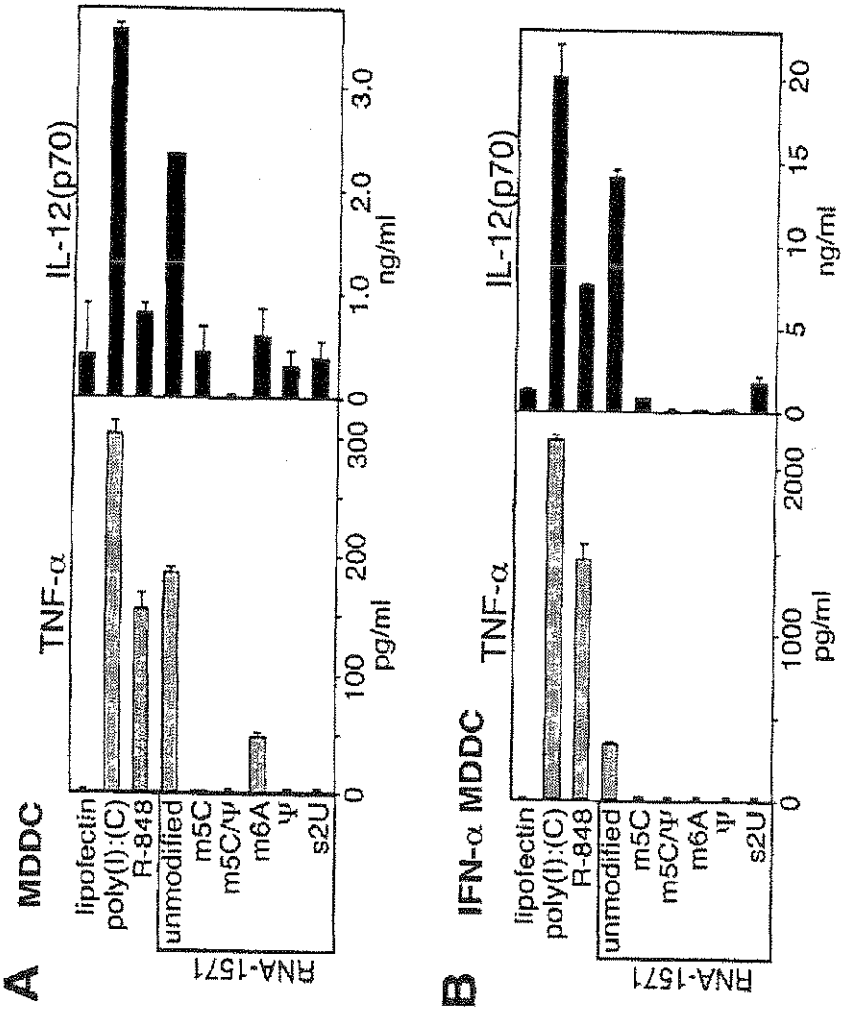

A
MDDC
TNF-α
IL-12(p70)
lipofectin
poly(I):(C)
R-848
unmodified
m5C
m5C/ψ
m6A
ψ
s2U
RNA-1571
0
100
200
300
1.0
2.0
3.0
pg/ml
ng/ml
B
IFN-α MDDC
TNF-α
IL-12(p70)
0
1000
2000
5
10
15
20
pg/ml
ng/ml
C
MDDC
TNF-α
lipofectin
poly(I):(C)
R-848
RNA-1866
RNA-1571
RNA-730
RNA-713
RNA-497
0
40
80
120
160
pg/ml

FIG. 8

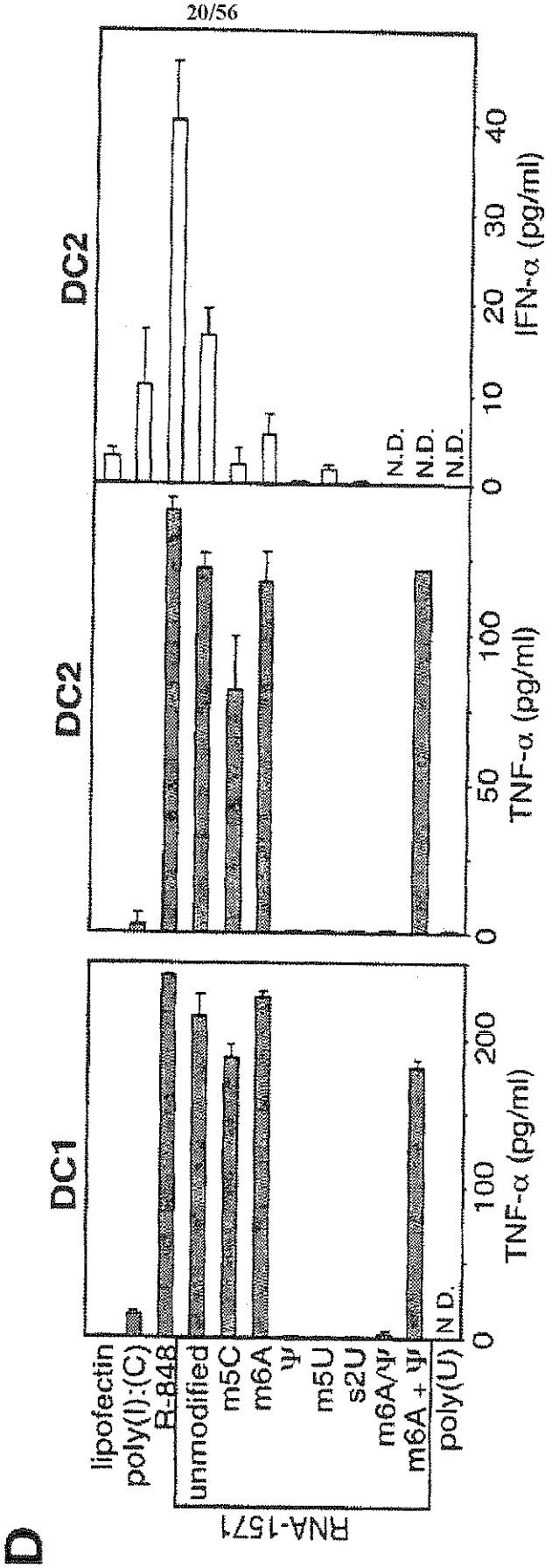

D
RNA-1571
lipofectin
poly(I):(C)
R-848
unmodified
m5C
m6A
ψ
m5U
s2U
m6A/ψ
m6A + ψ
poly(U)
N.D.
DC1
DC2
TNF-α (pg/ml)
0
100
200
50
IFN-α (pg/ml)
10
20
30
40

FIG. 8E

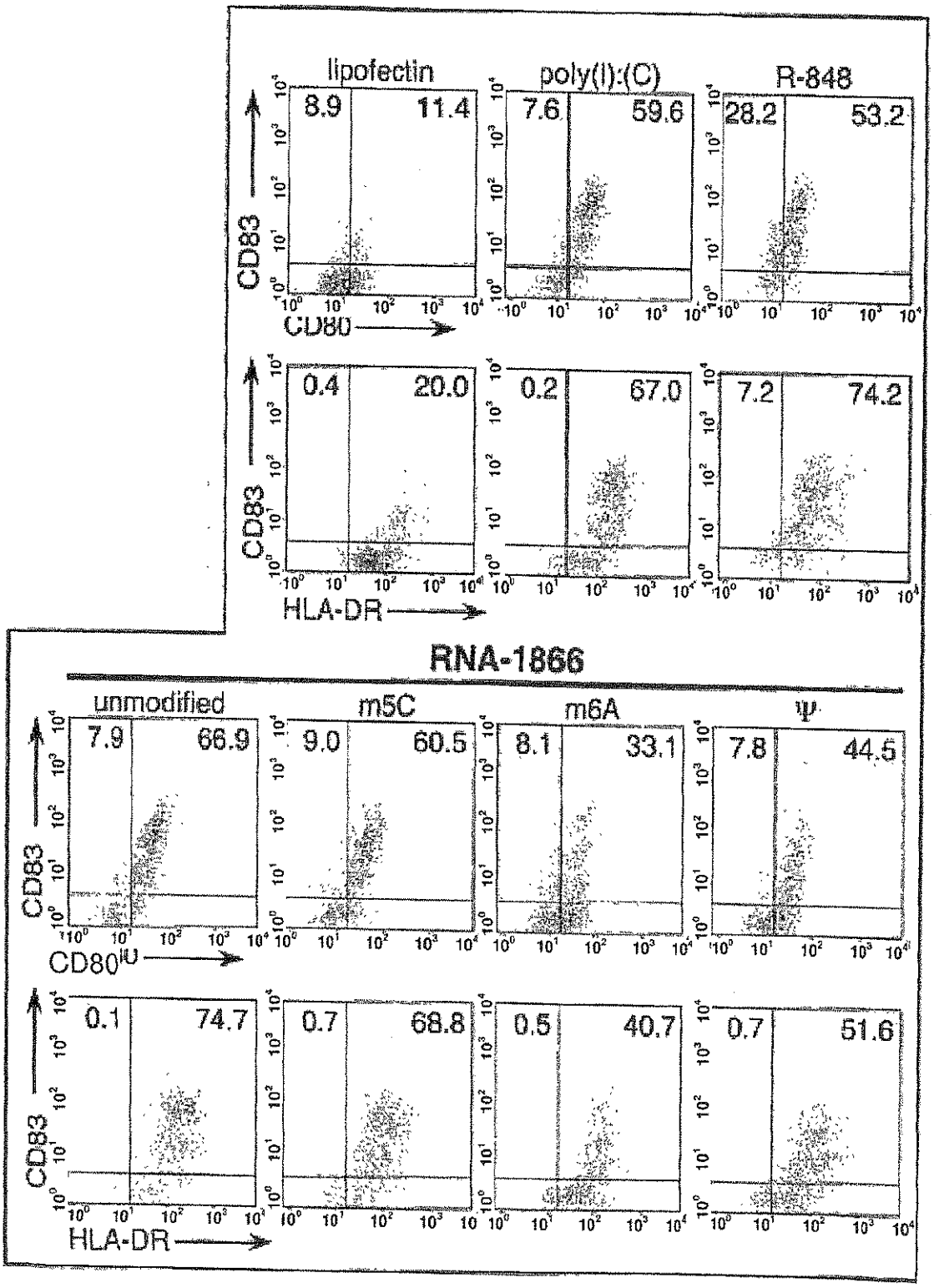

lipofectin
poly(I):(C)
R-848
8.9
11.4
7.6
59.6
28.2
53.2
CD83
CD80
0.4
20.0
0.2
67.0
7.2
74.2
HLA-DR
RNA-1866
unmodified
m5C
m6A
Ψ
7.9
66.9
9.0
60.5
8.1
33.1
7.8
44.5
CD80
0.1
74.7
0.7
68.8
0.5
40.7
0.7
51.6

FIG. 9

A

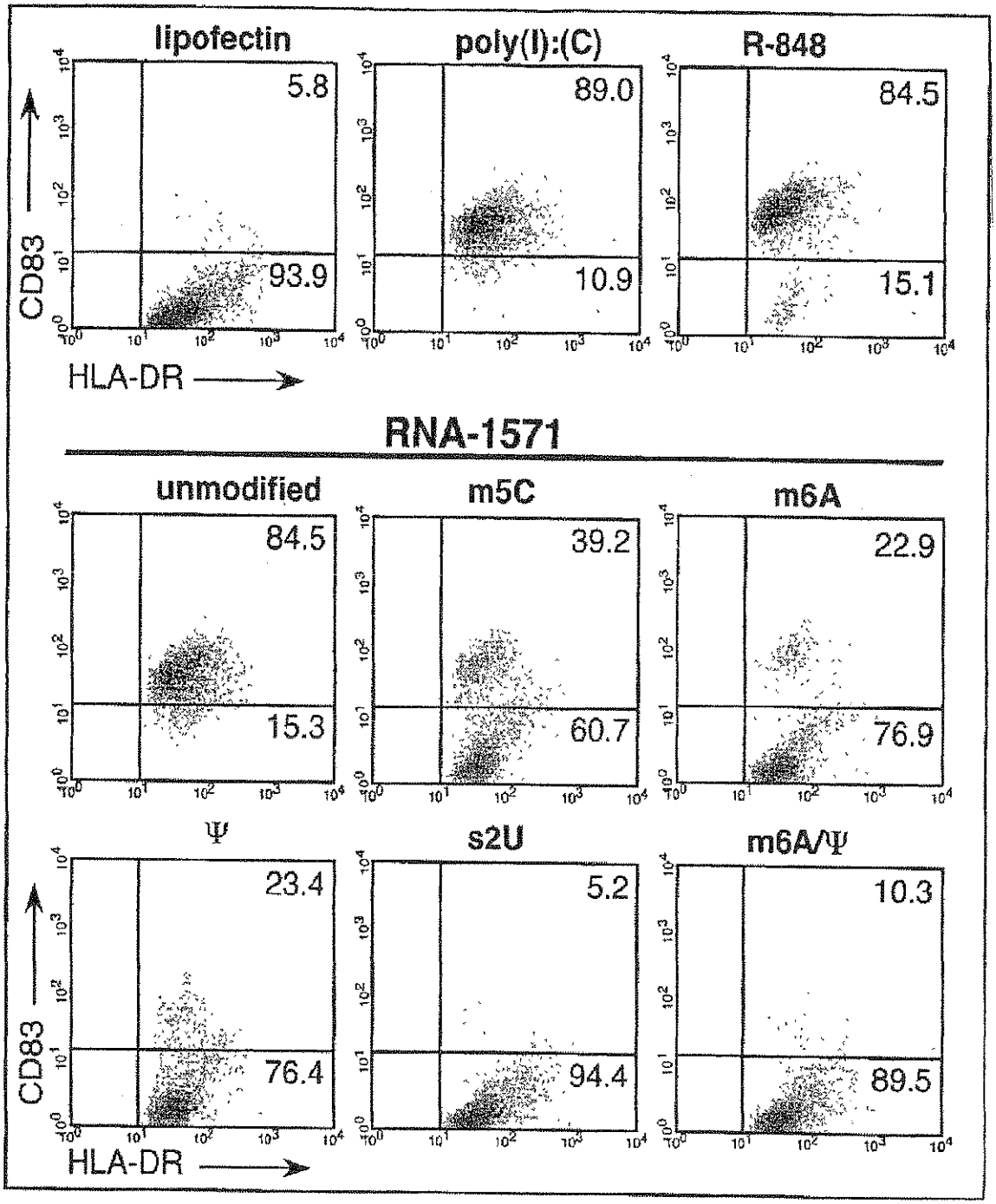

lipofectin
poly(I):(C)
R-848
5.8
93.9
89.0
10.9
84.5
15.1
CD83
HLA-DR
RNA-1571
unmodified
m5C
m6A
84.5
15.3
39.2
60.7
22.9
76.9
Ψ
s2U
m6A/Ψ
23.4
76.4
5.2
94.4
10.3
89.5
CD83
HLA-DR

FIG. 9

B

	TNF-α*	CD80	CD86
	pg/ml	mean fluorescence	
lipofectin	0	7.6	55.3
poly(I):(C)	45.6	59.4	257.4
R848	48.3	55.2	235.4
RNA-1866			
unmodified	26.7	52.7	246.4
m5C	0	16.4	108.6
m6A	0	12.4	78.4
Ψ	0	12.0	87.5
s2U	0	8.0	62.7
m6A/Ψ	0	8.6	68.4

FIG. 10

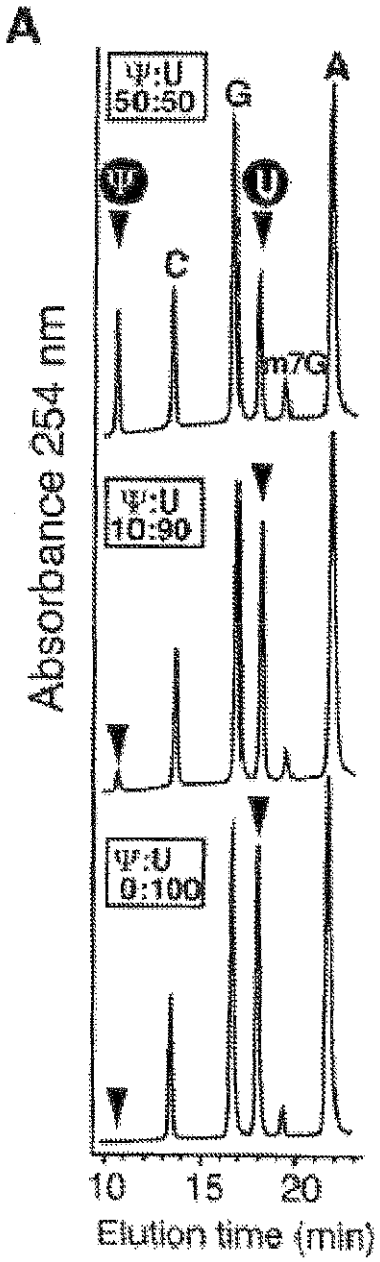

A
Ψ:U
50:50
G
A
Ψ
U
C
m7G
Ψ:U
10:90
Ψ:U
0:100
Absorbance 254 nm
10
15
20
Elution time (min)

FIG. 10

B

Modified nucleoside		m6A						Ψ						m5C					
in reaction[a] (%)	0	1	10	50	90	99	100	1	10	50	90	99	100	1	10	50	90	99	100
in RNA[b]																			
expected (%)	0	0.3	3.2	16	29	32	32	0.3	2.9	14	26	28	29	0.2	1.7	9	16	17	17
measured (%)	0	< 0.2	0.9	11	28	31	32	0.2	1.9	12	24	28	29	0.4	1.4	9	15	17	17
measured (number)	0	< 3	14	176	443	490	505	3	29	193	381	441	451	6	23	135	230	270	273

FIG. 10

C

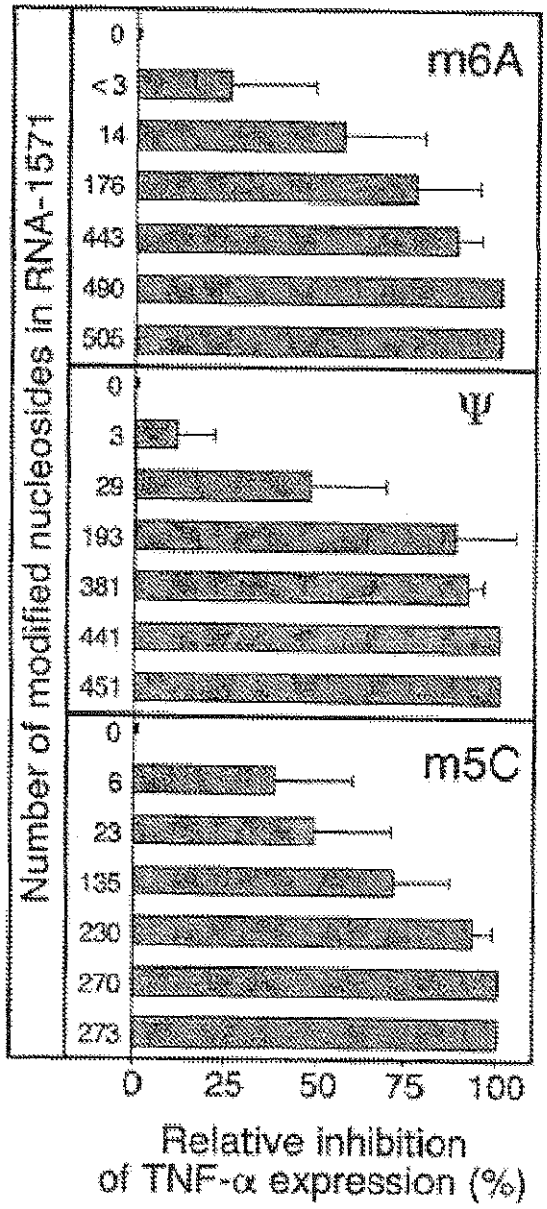

m6A
0
< 3
14
176
443
490
505
Ψ
0
3
29
193
381
441
451
m5C
0
6
23
135
230
270
273
Number of modified nucleosides in RNA-1571
0
25
50
75
100
Relative inhibition
of TNF-α expression (%)

FIG. 11

A

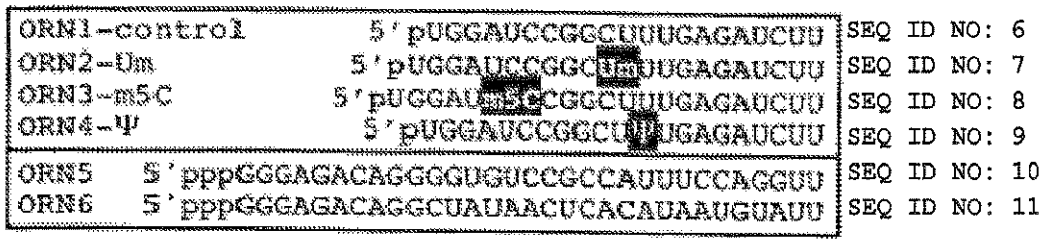

ORN1-control 5'pUGGAUCCGGCUUUGAGAUCUU SEQ ID NO: 6
ORN2-Um 5'pUGGAUCCGGCUUmUUGAGAUCUU SEQ ID NO: 7
ORN3-m5C 5'pUGGAUCCGGCUUUGAGAUCUU SEQ ID NO: 8
ORN4-Ψ 5'pUGGAUCCGGCUUΨUGAGAUCUU SEQ ID NO: 9
ORN5 5'pppGGGAGACAGGGGUGUCCGCCAUUUCCAGGUU SEQ ID NO: 10
ORN6 5'pppGGGAGACAGGCUAUAACUCACAUAAUGUAUU SEQ ID NO: 11

FIG. 11

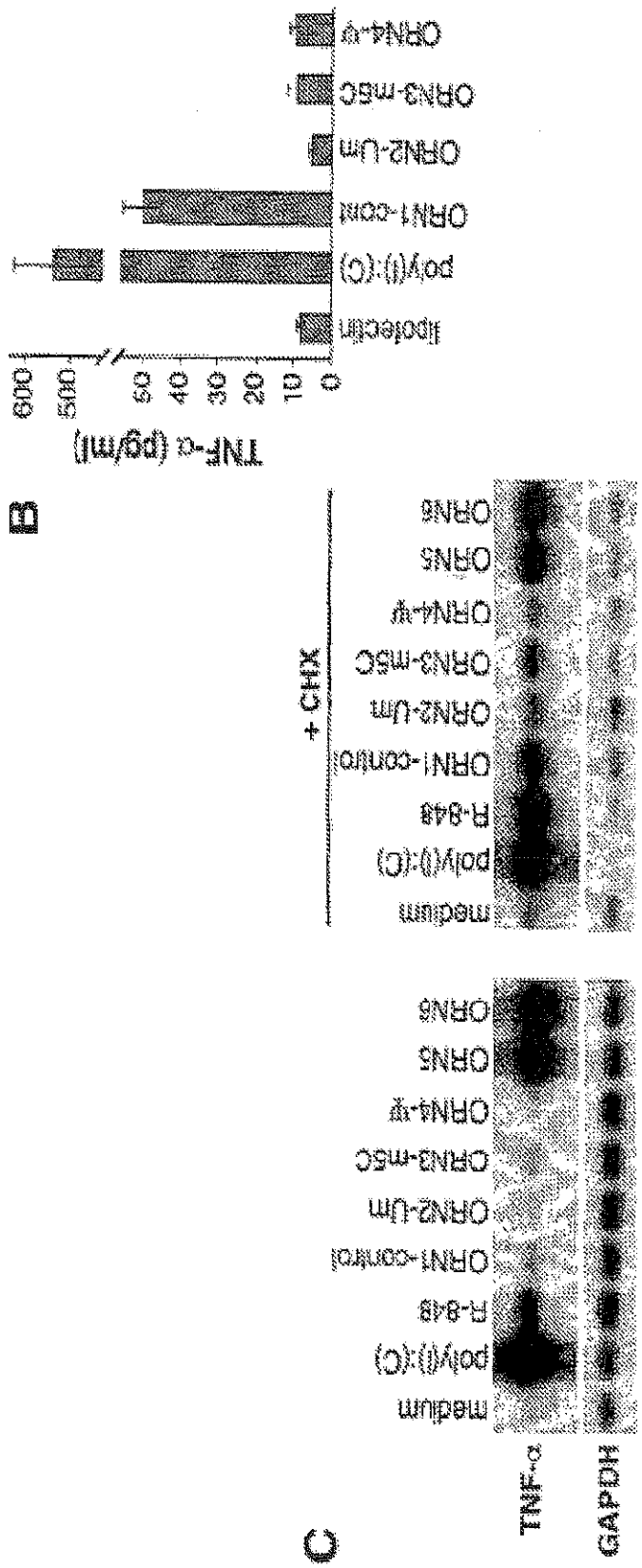
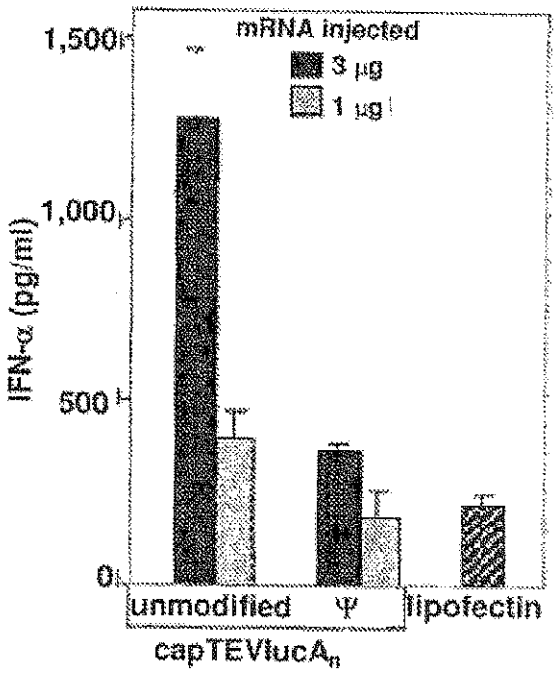

B
TNF-α (pg/ml)
0
10
20
30
40
50
500
600
lipofectin
poly(I):(C)
ORN1-control
ORN2-Um
ORN3-m5C
ORN4-ψ
C
TNF-α
GAPDH
medium
poly(I):(C)
R-848
ORN1-control
ORN2-Um
ORN3-m5C
ORN4-ψ
ORN5
ORN6
+ CHX

FIG. 12

A.


mRNA injected
3 µg
1 µg
1,500
1,000
500
0
IFN-α (pg/ml)
unmodified
Ψ
lipofectin
capTEVlucA$_n$

B.

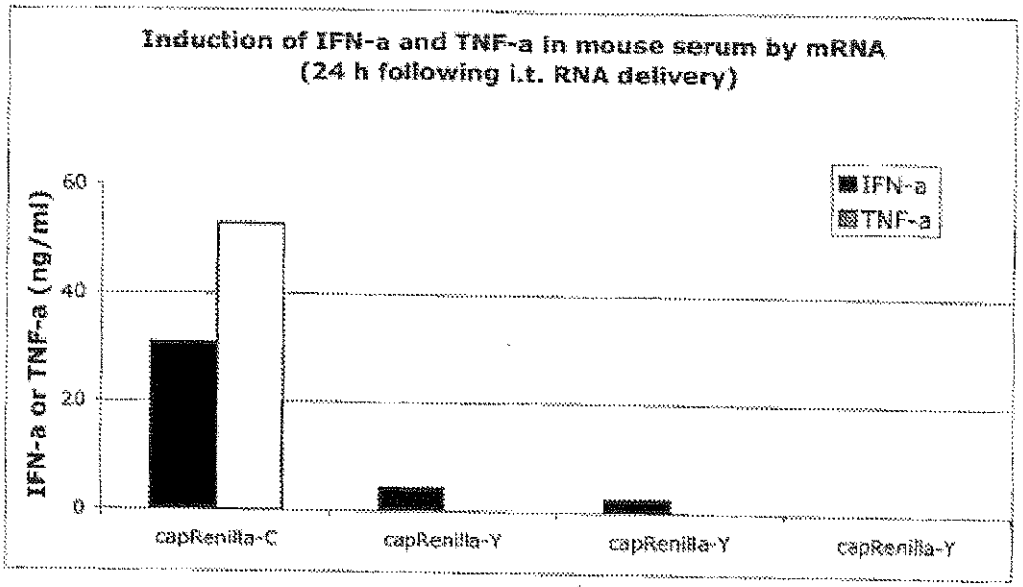

Induction of IFN-a and TNF-a in mouse serum by mRNA
(24 h following i.t. RNA delivery)
IFN-a
TNF-a
IFN-a or TNF-a (ng/ml)
60
40
20
0
capRenilla-C
capRenilla-Y
capRenilla-Y
capRenilla-Y

FIG. 13

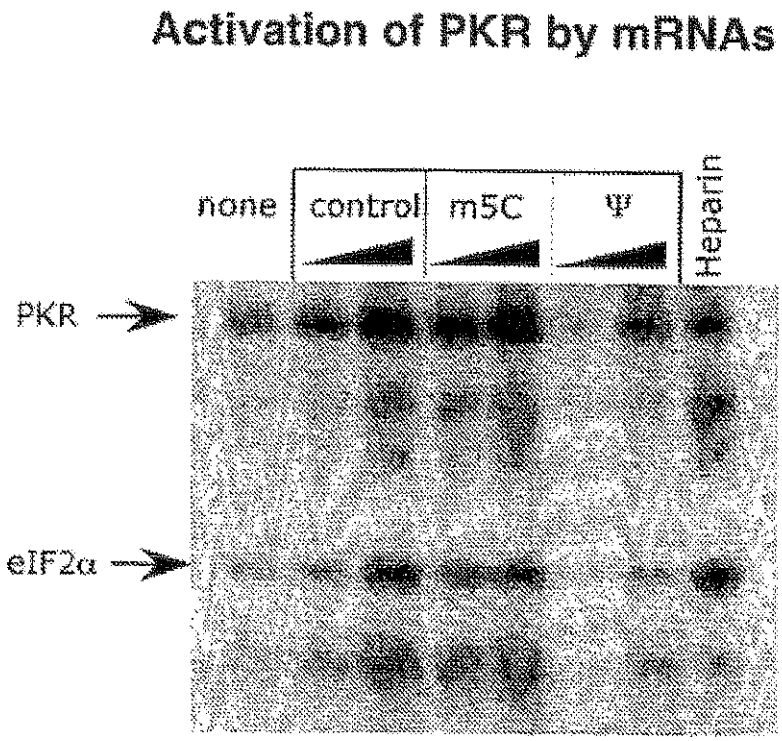

Activation of PKR by mRNAs
none
control
m5C
Ψ
Heparin
PKR
eIF2α

FIG. 14

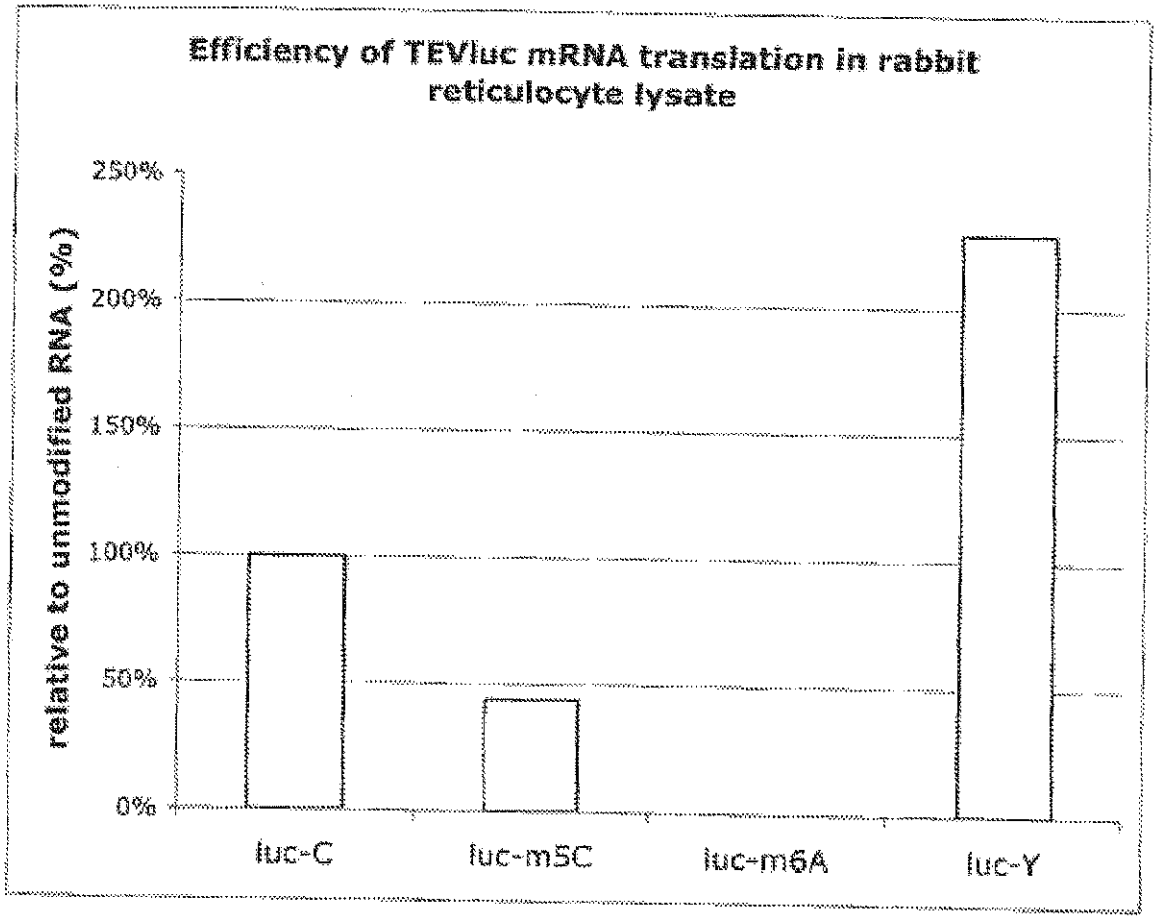
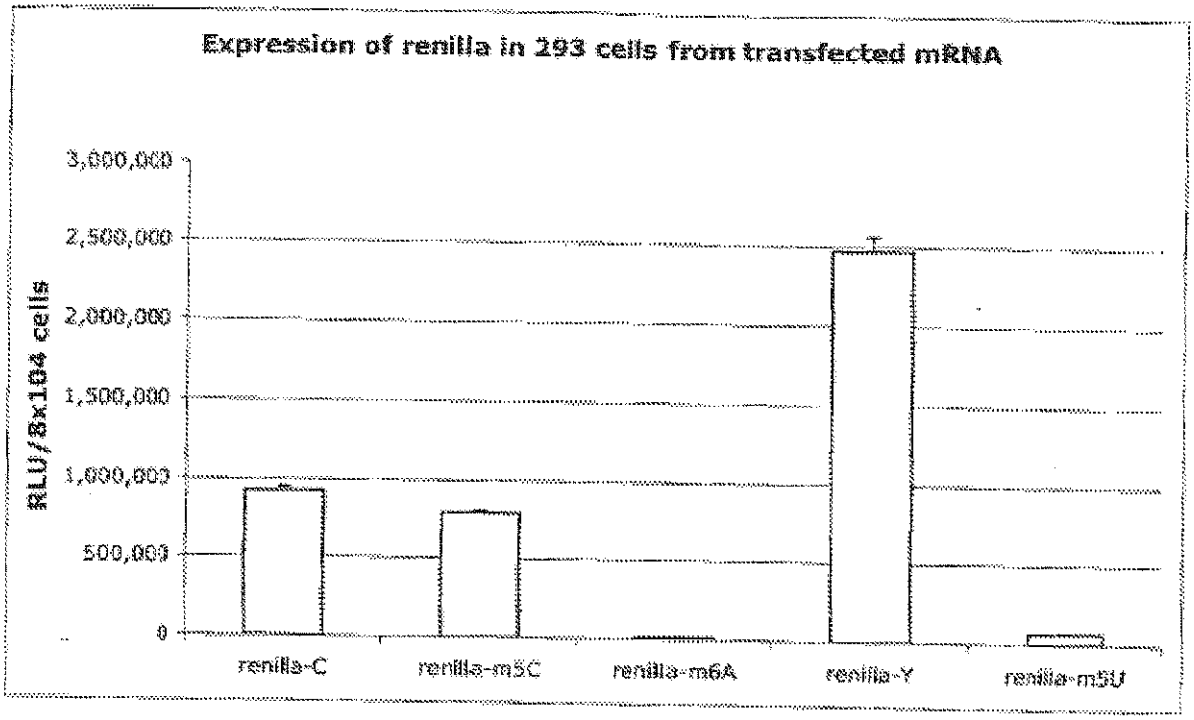

Efficiency of TEVluc mRNA translation in rabbit reticulocyte lysate
relative to unmodified RNA (%)
250%
200%
150%
100%
50%
0%
luc-C
luc-m5C
luc-m6A
luc-Y

FIG. 15

A.


Expression of renilla in 293 cells from transfected mRNA
RLU/8x104 cells
3,000,000
2,500,000
2,000,000
1,500,000
1,000,000
500,000
0
renilla-C
renilla-m5C
renilla-m6A
renilla-Y
renilla-m5U

B.

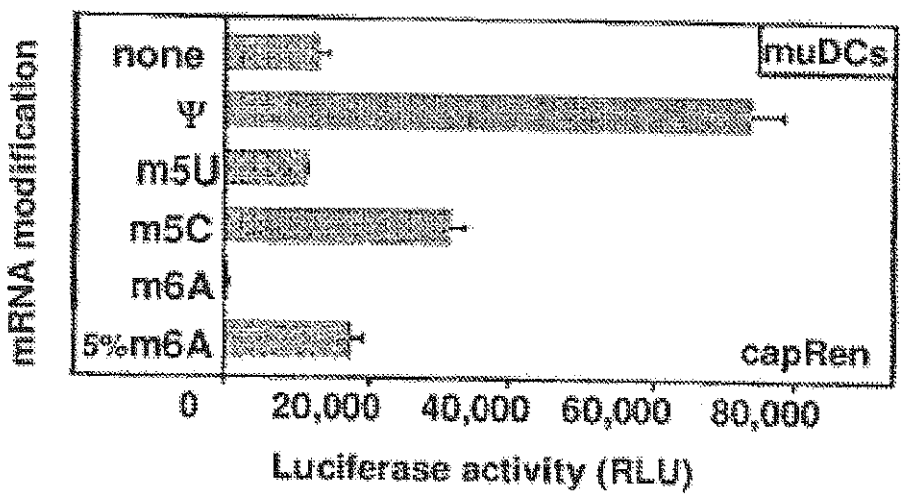
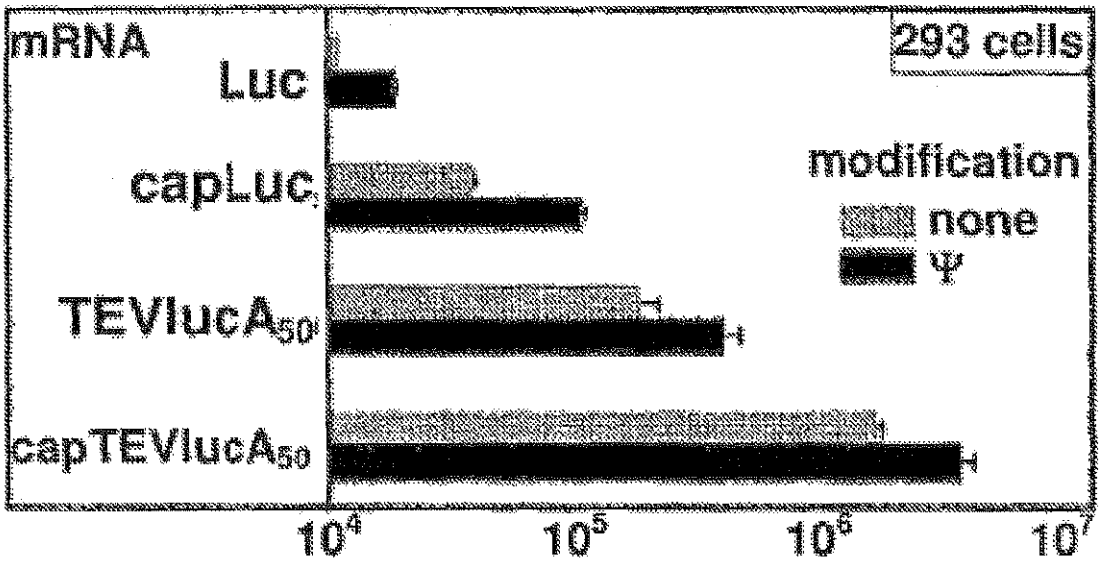

mRNA modification
none
Ψ
m5U
m5C
m6A
5%m6A
muDCs
capRen
0
20,000
40,000
60,000
80,000
Luciferase activity (RLU)

FIG. 16

A.


mRNA
293 cells
Luc
capLuc
TEVlucA50
capTEVlucA50
modification
none
Ψ
10^4
10^5
10^6
10^7

B.

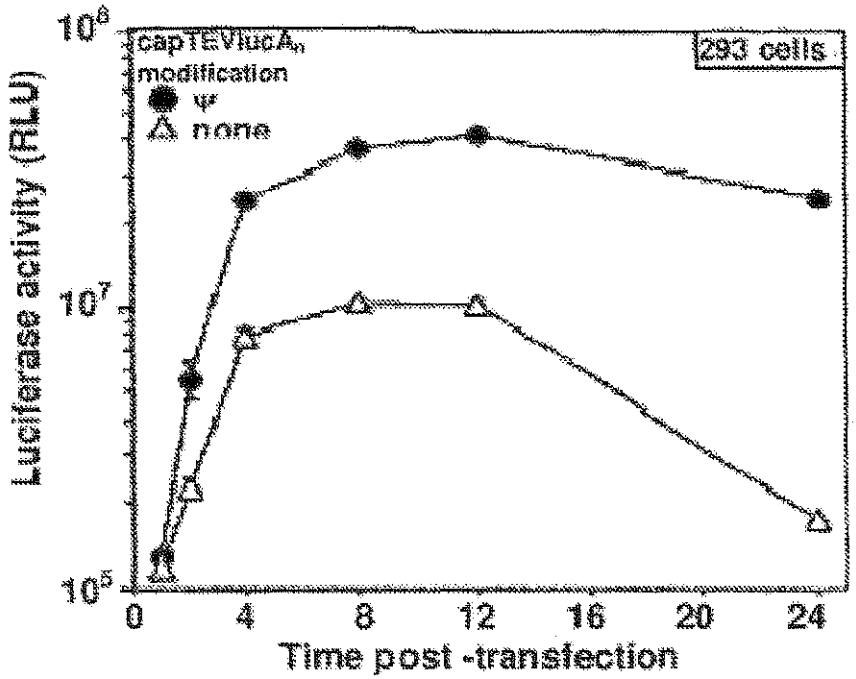

capTEVlucA50
modification
Ψ
none
293 cells
Luciferase activity (RLU)
10^8
10^7
10^5
0
4
8
12
16
20
24
Time post -transfection

FIG. 16

C.

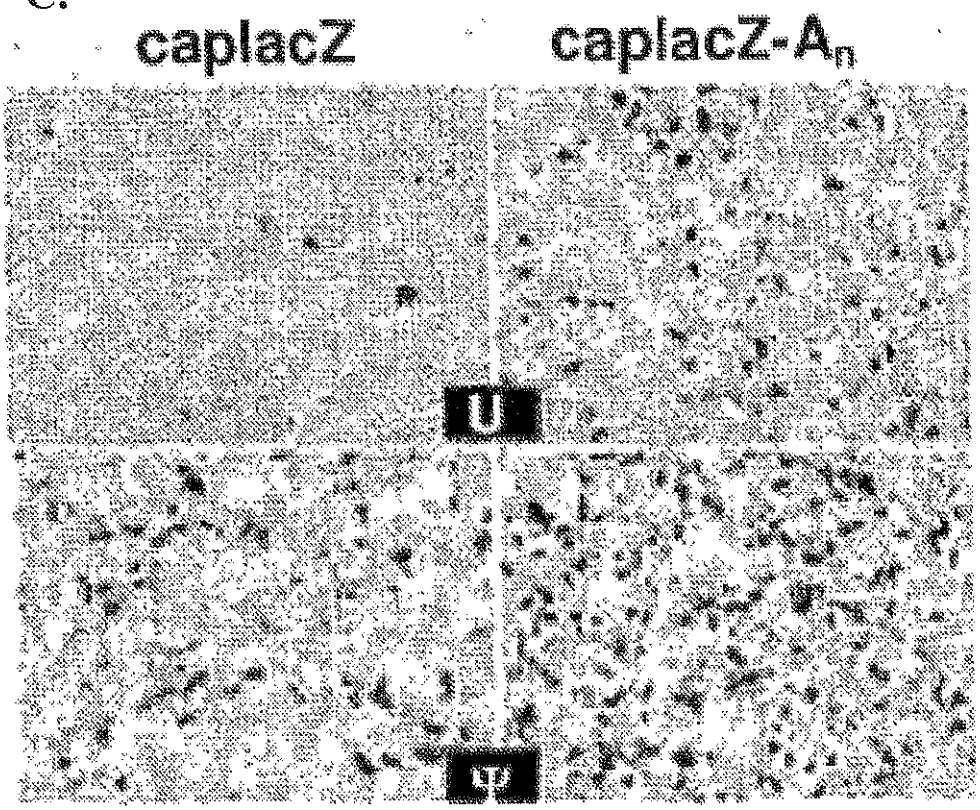
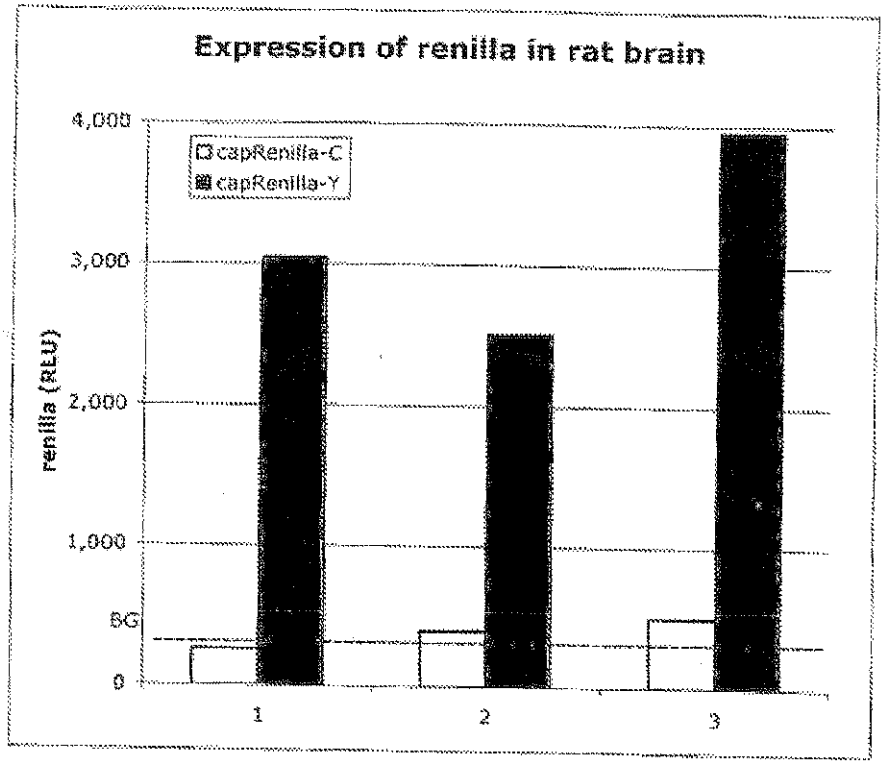


FIG. 17

A.


Expression of renilla in rat brain
4,000
3,000
2,000
1,000
BG
0
renilla (RLU)
capRenilla-C
capRenilla-Y
1
2
3

B.

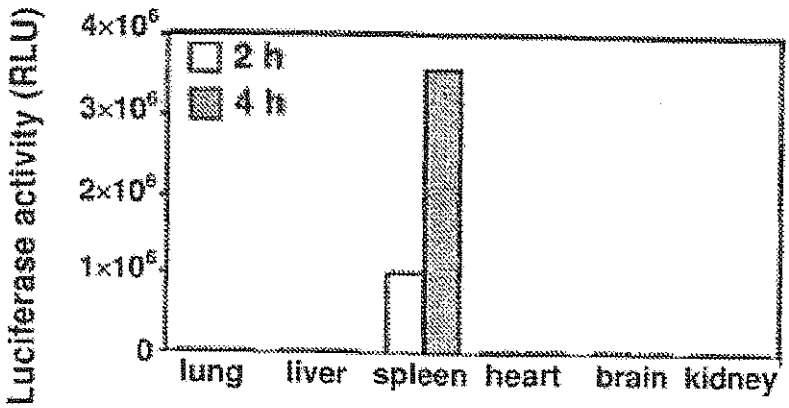
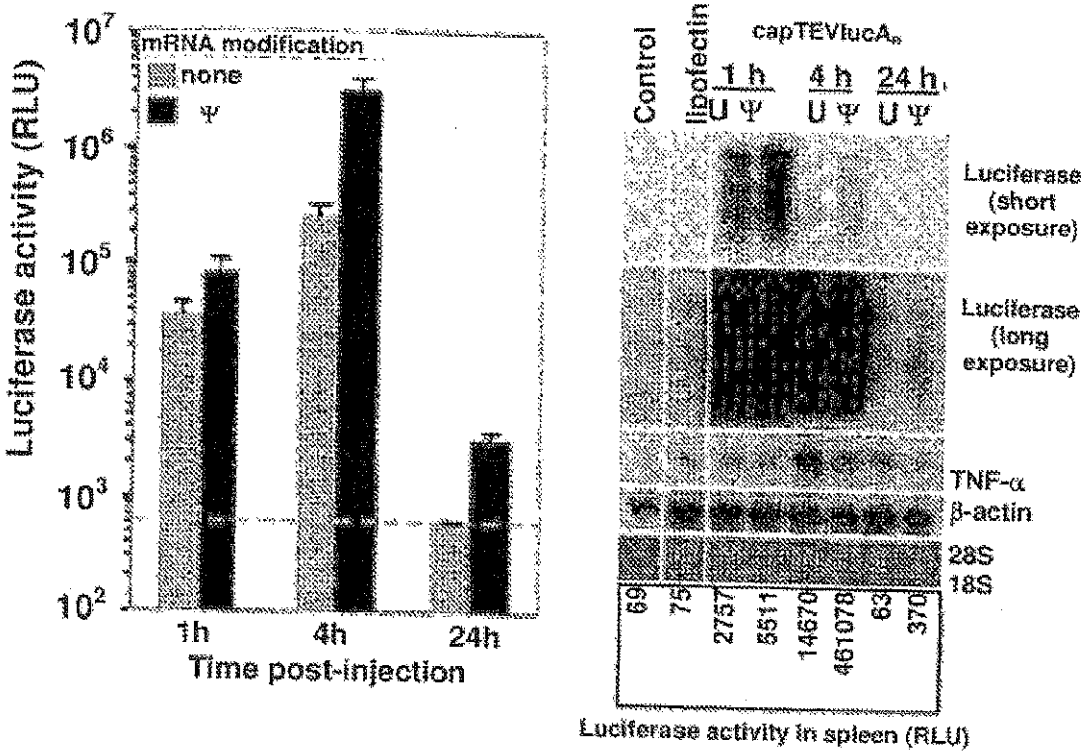

Luciferase activity (RLU)
4×10^6
3×10^6
2×10^6
1×10^6
0
2 h
4 h
lung
liver
spleen
heart
brain
kidney

FIG. 17

C.


Luciferase activity (RLU)
mRNA modification
none
Ψ
1h
4h
24h
Time post-injection
Control
lipofectin
capTEVlucA60
1 h
4 h
24 h
U Ψ
Luciferase (short exposure)
Luciferase (long exposure)
TNF-α
β-actin
28S
18S
69
75
2757
8511
14670
461078
63
370
Luciferase activity in spleen (RLU)

D.

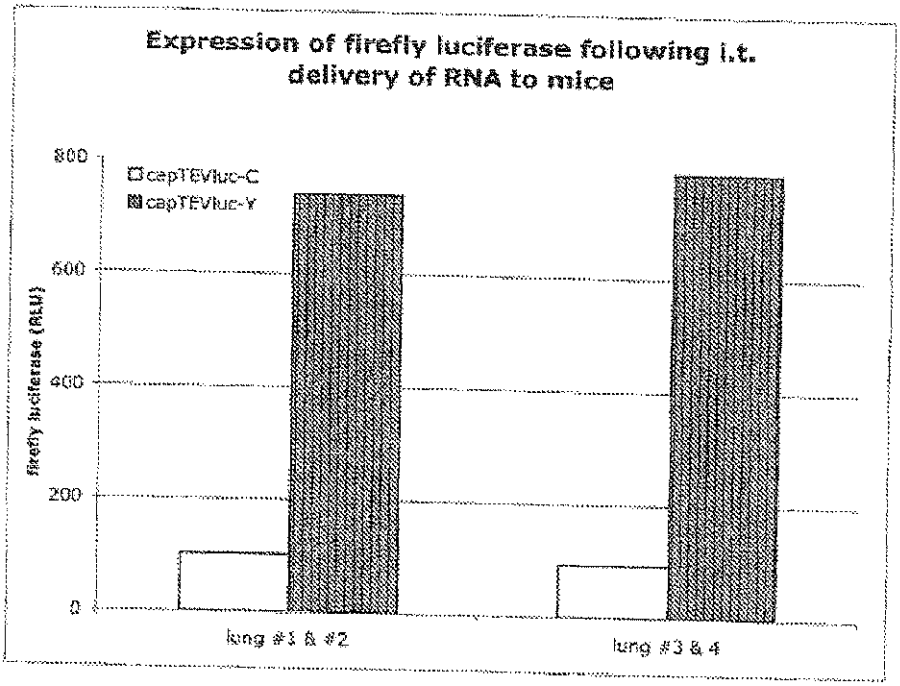

Expression of firefly luciferase following i.t. delivery of RNA to mice
capTEVluc-C
capTEVluc-Y
firefly luciferase (RLU)
800
600
400
200
0
lung #1 & #2
lung #3 & 4

FIG. 18

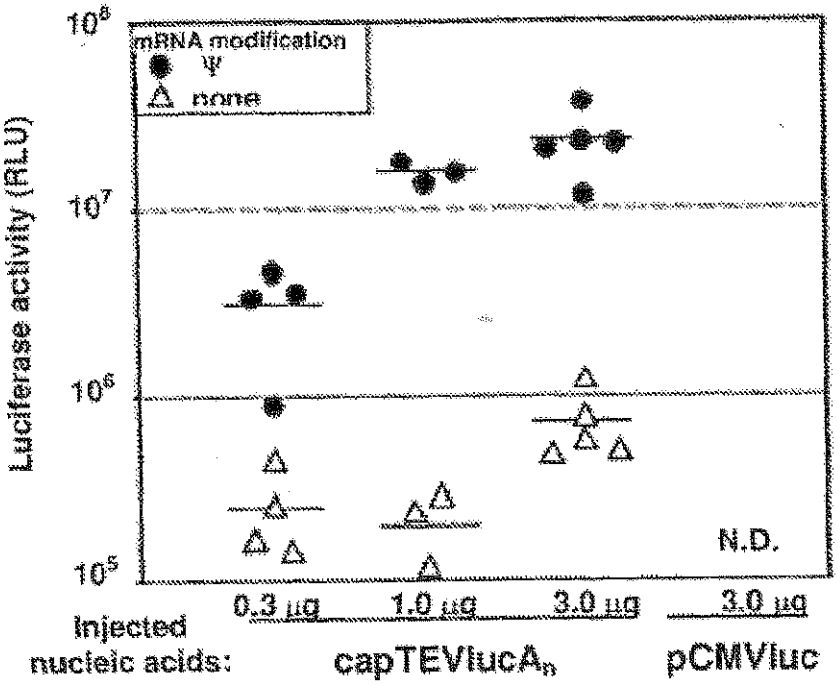

mRNA modification
Ψ
none
Luciferase activity (RLU)
10^8
10^7
10^6
10^5
N.D.
0.3 μg
1.0 μg
3.0 μg
3.0 μg
Injected nucleic acids:
capTEVlucA$_n$
pCMVluc

FIG. 19

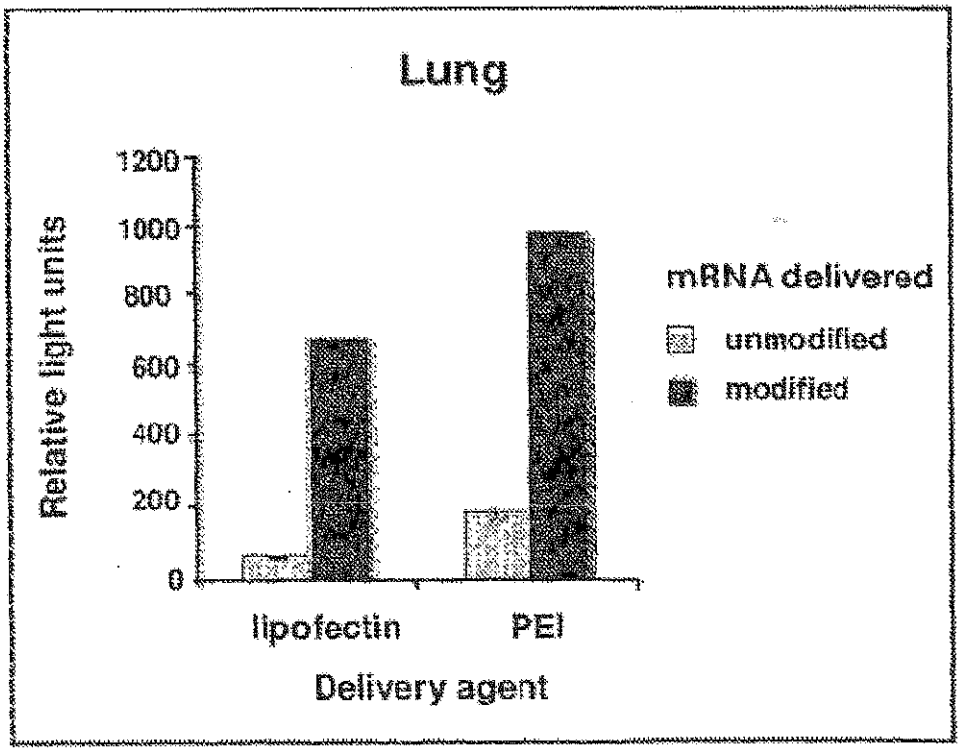

Lung
Relative light units
1200
1000
800
600
400
200
0
lipofectin
PEI
Delivery agent
mRNA delivered
unmodified
modified

FIG. 20

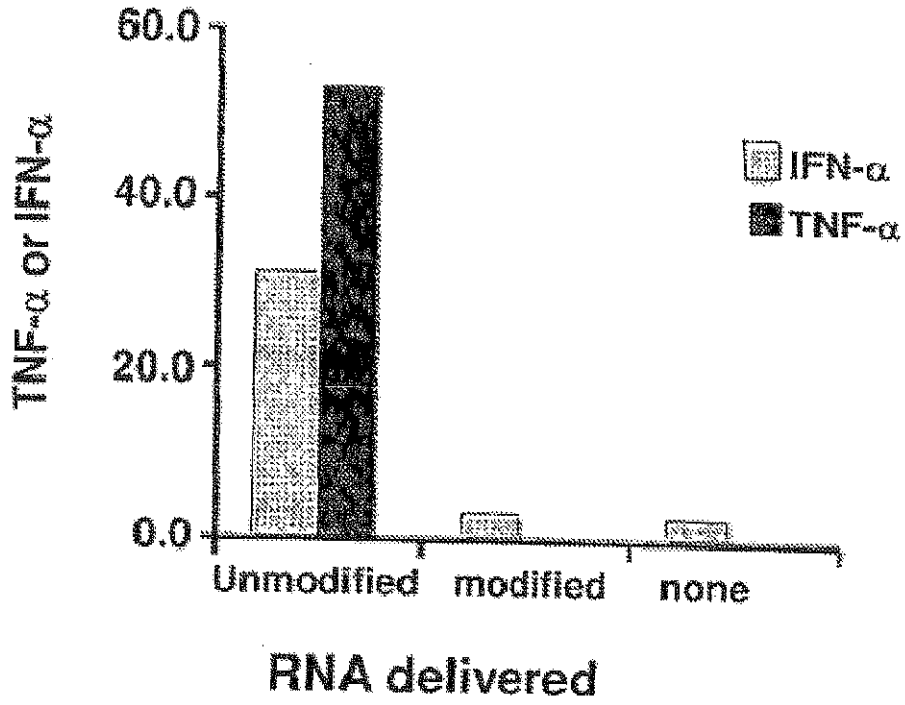

60.0
40.0
20.0
0.0
TNF-α or IFN-α
IFN-α
TNF-α
Unmodified
modified
none
RNA delivered

FIG. 21

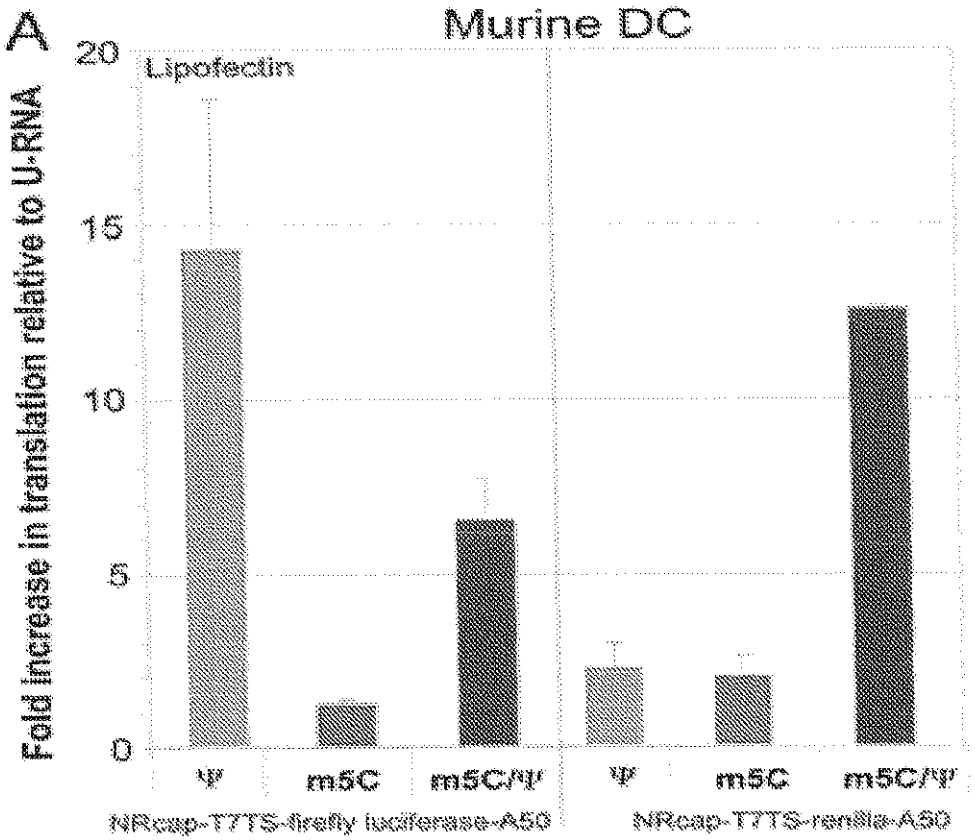

A
Murine DC
Lipofectin
Fold increase in translation relative to U-RNA
20
15
10
5
0
Ψ
m5C
m5C/Ψ
Ψ
m5C
m5C/Ψ
NRcap-T7TS-firefly luciferase-A50
NRcap-T7TS-renilla-A50

FIG. 21

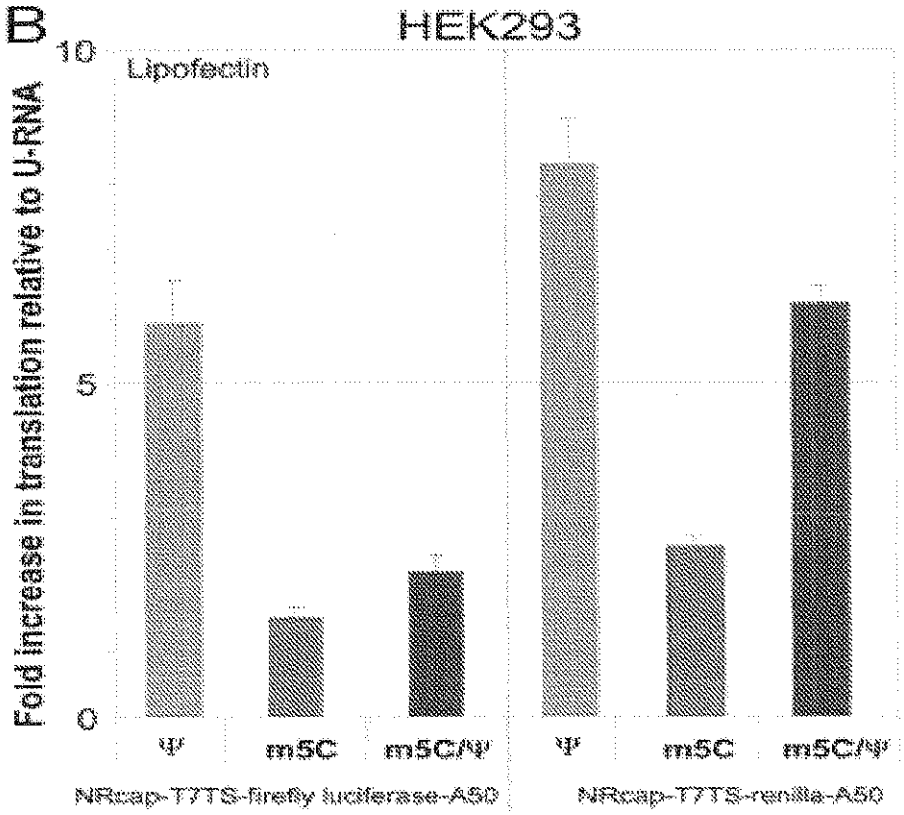

B
HEK293
Lipofectin
Fold increase in translation relative to U-RNA
10
5
0
Ψ
m5C
m5C/Ψ
Ψ
m5C
m5C/Ψ
NRcap-T7TS-firefly luciferase-A50
NRcap-T7TS-renilla-A50

FIG. 21

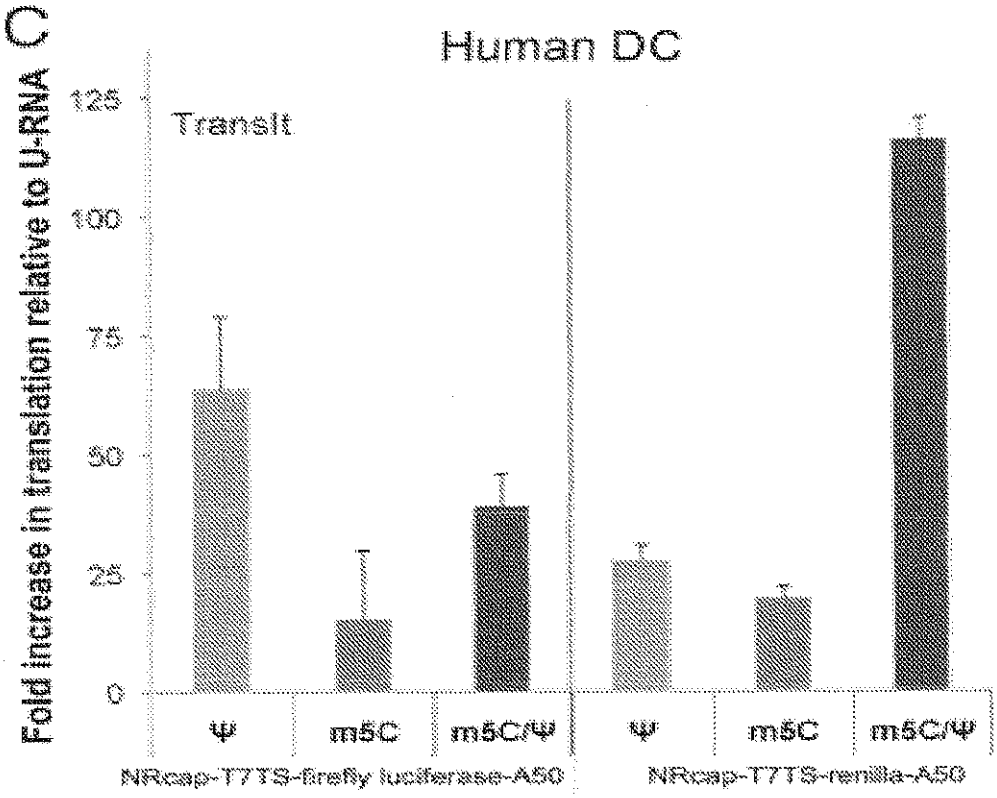

C
Human DC
Transit
Fold increase in translation relative to U-RNA
125
100
75
50
25
0
Ψ
m5C
m5C/Ψ
Ψ
m5C
m5C/Ψ
NRcap-T7TS-firefly luciferase-A50
NRcap-T7TS-renilla-A50

FIG. 22

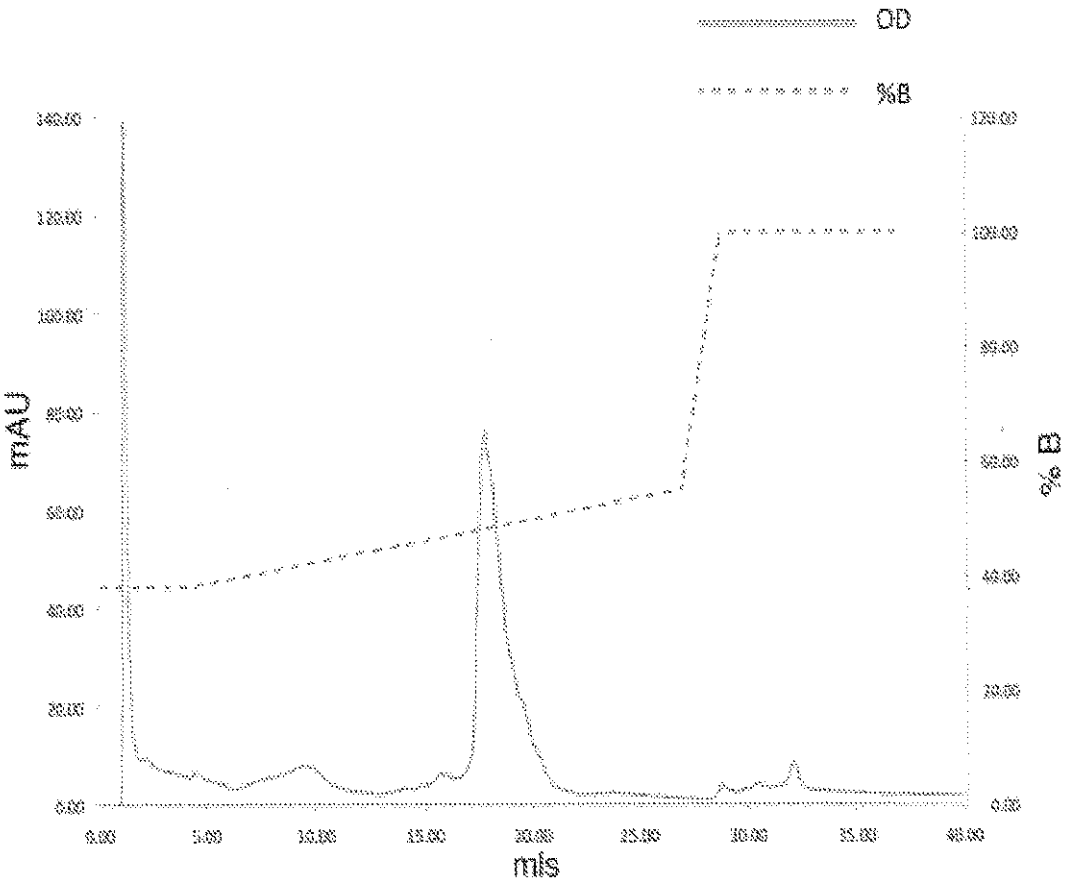


FIG. 23

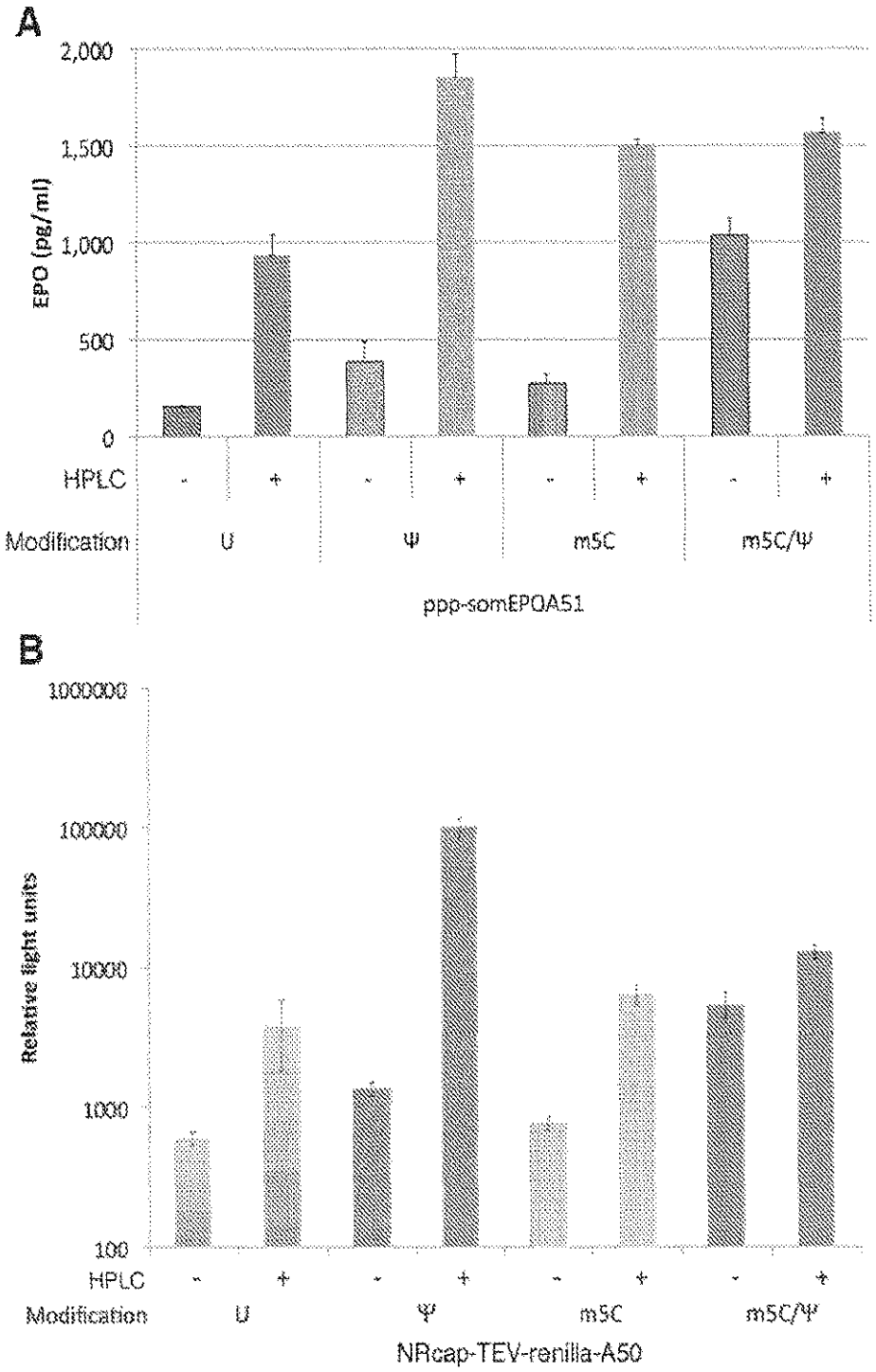

A
2,000
1,500
1,000
500
0
EPO (pg/ml)
HPLC
- + - + - + - +
Modification
U
Ψ
m5C
m5C/Ψ
ppp-somEPOA51
B
1000000
100000
10000
1000
100
Relative light units
HPLC
- + - + - + - +
Modification
U
Ψ
m5C
m5C/Ψ
NRcap-TEV-renilla-A50

FIG. 24

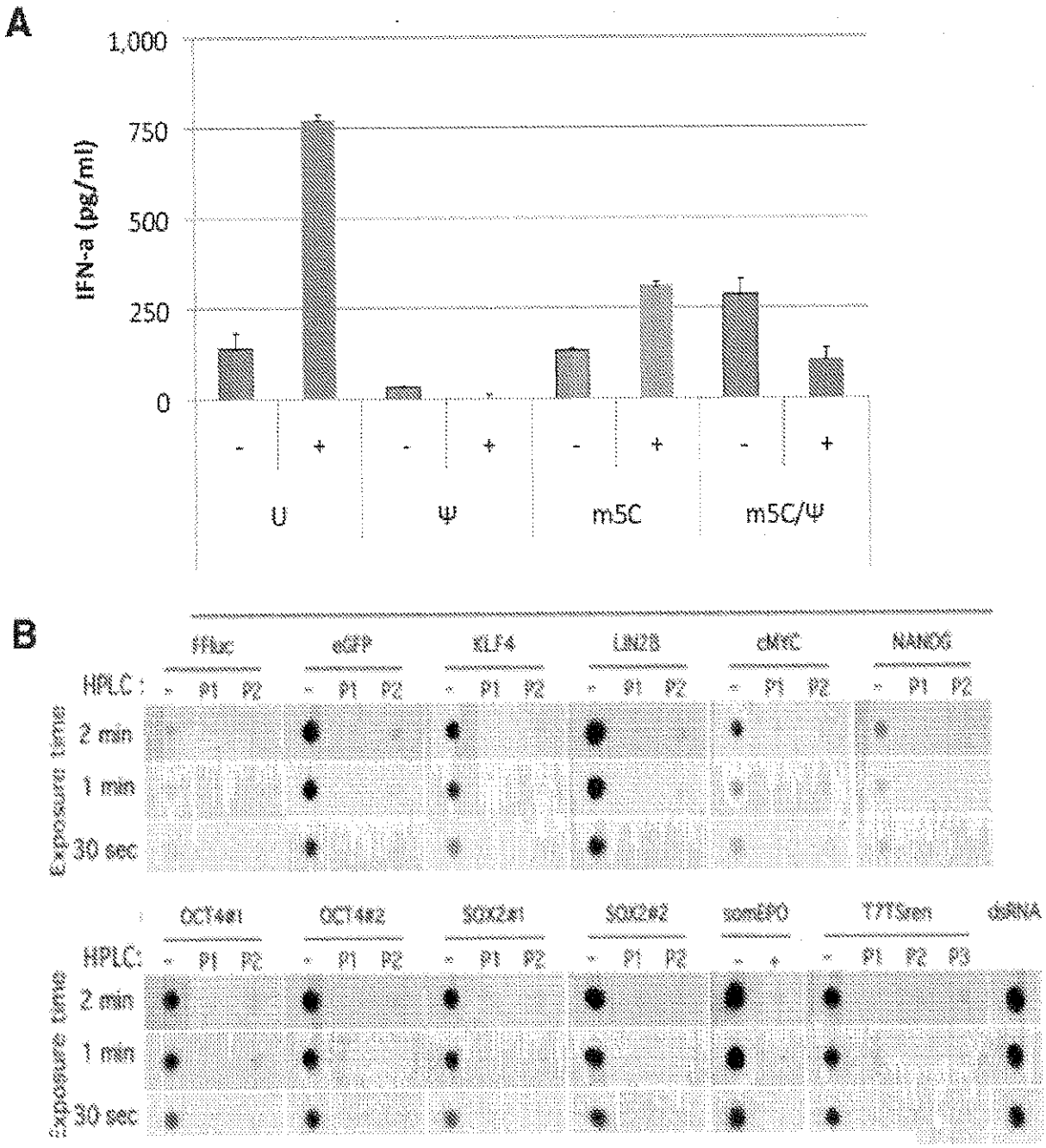

A
1,000
750
500
250
0
IFN-α (pg/ml)
-
+
-
+
-
+
-
+
U
Ψ
m5C
m5C/Ψ
B
FFLuc
eGFP
KLF4
LIN28
cMYC
NANOG
HPLC:
-
P1
P2
2 min
1 min
30 sec
exposure time
OCT4#1
OCT4#2
SOX2#1
SOX2#2
semEPO
T7TSeen
dsRNA
-
+
P3

FIG. 24

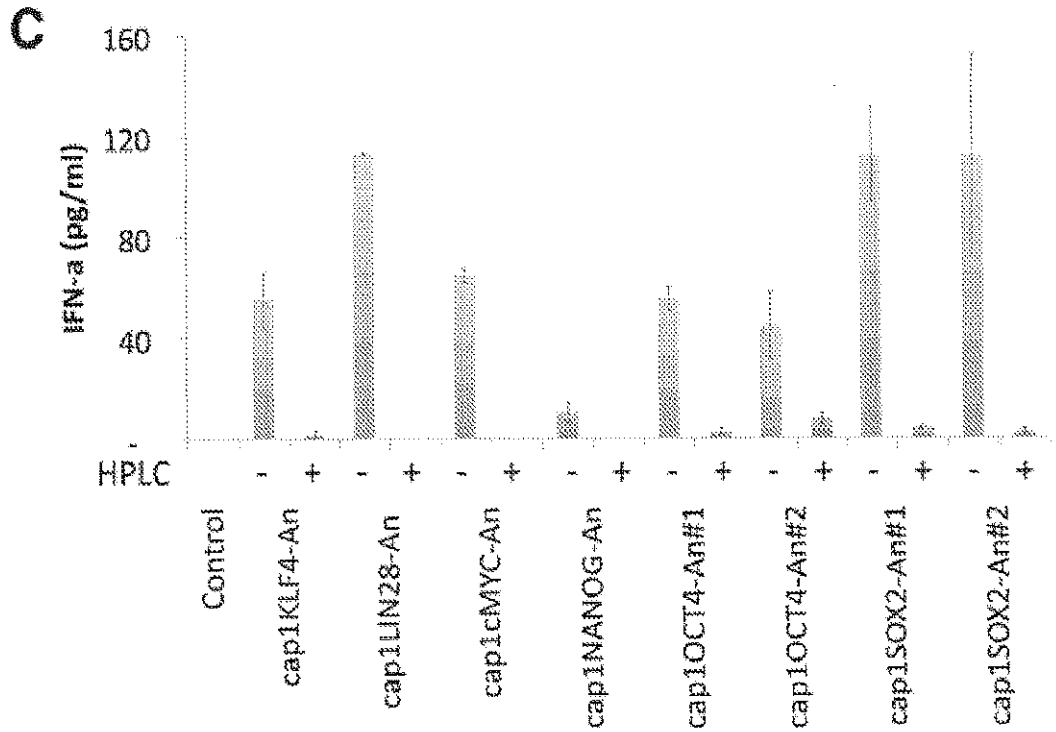

C
160
120
80
40
-
IFN-a (pg/ml)
HPLC
- + - + - + - + - + - + - + - + - +
Control
cap1KLF4-An
cap1LIN28-An
cap1cMYC-An
cap1NANOG-An
cap1OCT4-An#1
cap1OCT4-An#2
cap1SOX2-An#1
cap1SOX2-An#2

FIG. 25

KLF4 mRNA cds (SEQ ID NO:12)

5′AUGAGGCAGCCACCUGGCGAGUCUGACAUGGCUGUCAGCGACGCGCUGCUCCCAUCUUUCUC
CACGUUCGCGUCUGGCCCGGCGGGAAGGGAGAAGACACUGCGUCAAGCAGGUGCCCCGAAUAAC
CGCUGGCGGGAGGAGCUCUCCCACAUGAAGCGACUUCCCCCAGUGCUUCCCGGCCGCCCCUAUG
ACCUGGCGGCGGCGACCGUGGCCACAGACCUGGAGAGCGGCGGAGCCGGUGCGGCUUGCGGCGG
UAGCAACCUGGCGCCCCUACCUCGGAGAGAGACCGAGGAGUUCAACGAUCUCCUGGACCUGGAC
UUUAUUCUCUCCAAUUCGCUGACCCAUCCUCCGGAGUCAGUGGCCGCCACCGUGUCCUCGUCAG
CGUCAGCCUCCUCUUCGUCGUCGCCGUCGAGCAGCGGCCCUGCCAGCGCGCCCUCCACCUGCAG
CUUCACCUAUCCGAUCCGGGCCGGGAACGACCCGGGCGUGGCGCCGGGCGGCACGGGCGGAGGC
CUCCUCUAUGGCAGGGAGUCCGCUCCCCCUCCGACGGCUCCCUUCAACCUGGCGGACAUCAACG
ACGUGAGCCCCUCGGGCGGCUUCGUGGCCGAGCUCCUGCGGCCAGAAUUGGACCCGGUGUACAU
UCCGCCGCAGCAGCCGCAGCCGCCAGGUGGCGGGCUGAUGGGCAAGUUCGUGCUGAAGGCGUCG
CUGAGCGCCCCUGGCAGCGAGUACGGCAGCCCGUCGGUCAUCAGCGUCAGCAAAGGCAGCCCUG
ACGGCAGCCACCCGGUGGUGGUGGCGCCCUACAACGGCGGGCCGCCGCGCACGUGCCCCAAGAU
CAAGCAGGAGGCGGUCUCUUCGUGCACCCACUUGGGCGCUGGACCCCCUCUCAGCAAUGGCCAC
CGGCCGGCUGCACACGACUUCCCCCUGGGGCGGCAGCUCCCCAGCAGGACUACCCCGACCCUGG
GUCUUGAGGAAGUGCUGAGCAGCAGGGACUGUCACCCUGCCCUGCCGCUUCCUCCCGGCUUCCA
UCCCCACCCGGGGCCCAAUUACCCAUCCUUCCUGCCCGAUCAGAUGCAGCCGCAAGUCCCGCCG
CUCCAUUACCAAGAGCUCAUGCCACCCGGUUCCUGCAUGCCAGAGGAGCCCAAGCCAAAGAGGG
GAAGACGAUCGUGGCCCCGGAAAAGGACCGCCACCCACACUUGUGAUUACGCGGGCUGCGGCAA
AACCUACACAAAGAGUUCCCAUCUCAAGGCACACCUGCGAACCCACACAGGUGAGAAACCUUAC
CACUGUGACUGGGACGGCUGUGGAUGGAAAUUCGCCCGCUCAGAUGAACUGACCAGGCACUACC
GUAAACACACGGGGCACCGCCCGUUCCAGUGCCAAAAAUGCGACCGAGCAUUUUCCAGGUCGGA
CCACCUCGCCUUACACAUGAAGAGGCAUUUUUAA-3′

LIN28 mRNA cds (SEQ ID NO:13)

5′AUGGGCUCCGUGUCCAACCAGCAGUUUGCAGGUGGCUGCGCCAAGGCGGCAGAAGAGGCGCC
CGAGGAGGCGCCGGAGGACGCGGCCCGGGCGGCGGACGAGCCUCAGCUGCUGCACGGUGCGGGC
AUCUGUAAGUGGUUCAACGUGCGCAUGGGGUUCGGCUUCCUGUCCAUGACCGCCCGCGCCGGGG
UCGCGCUCGACCCCCCAGUGGAUGUCUUUGUGCACCAGAGUAAGCUGCACAUGGAAGGGUUCCG
GAGCUUGAAGGAGGGUGAGGCAGUGGAGUUCACCUUUAAGAAGUCAGCCAAGGGUCUGGAAUCC
AUCCGUGUCACCGGACCUGGUGGAGUAUUCUGUAUUGGGAGUGAGAGGCGGCCAAAAGGAAAGA
GCAUGCAGAAGCGCAGAUCAAAAGGAGACAGGUGCUACAACUGUGGAGGUCUAGAUCAUCAUGC
CAAGGAAUGCAAGCUGCCACCCCAGCCCAAGAAGUGCCACUUCUGCCAGAGCAUCAGCCAUAUG
GUAGCCUCAUGUCCGCUGA-3′

FIG. 26

cMYC mRNA cds (SEQ ID NO:14)

5AUGGAUUUUUUUCGGGUAGUGGAAAACCAGCAGCCUCCCGCGACGAUGCCCCUCAACGUUAGC
UUCACCAACAGGAACUAUGACCUCGACUACGACUCGGUGCAGCCGUAUUUCUACUGCGACGAGG
AGGAGAACUUCUACCAGCAGCAGCAGCAGAGCGAGCUGCAGCCCCCGGCGCCCAGCGAGGAUAU
CUGGAAGAAAUUCGAGCUGCUGCCCACCCCGCCCCUGUCCCCUAGCCGCCGCUCCGGGCUCUGC
UCGCCCUCCUACGUUGCGGUCACACCCUUCUCCCUUCGGGGAGACAACGACGGCGGUGGCGGGA
GCUUCUCCACGGCCGACCAGCUGGAGAUGGUGACCGAGCUGCUGGGAGGAGACAUGGUGAACCA
GAGUUUCAUCUGCGACCCGGACGACGAGACCUUCAUCAAAAACAUCAUCAUCCAGGACUGUAUG
UGGAGCGGCUUCUCGGCCGCCGCCAAGCUCGUCUCAGAGAAGCUGGCCUCCUACCAGGCUGCGC
GCAAAGACAGCGGCAGCCCGAACCCCGCCCGCGGCCACAGCGUCUGCUCCACCUCCAGCUUGUA
CCUGCAGGAUCUGAGCGCCGCCGCCUCAGAGUGCAUCGACCCCUCGGUGGUCUUCCCCUACCCU
CUCAACGACAGCAGCUCGCCCAAGUCCUGCGCCUCGCAAGACUCCAGCGCCUUCUCUCCGUCCU
CGGAUUCUCUGCUCUCCUCGACGGAGUCCUCCCCGCAGGGCAGCCCCGAGCCCCUGGUGCUCCA
UGAGGAGACACCGCCCACCACCAGCAGCGACUCUGAGGAGGAACAAGAAGAUGAGGAAGAAAUC
GAUGUUGUUUCUGUGGAAAAGAGGCAGGCUCCUGGCAAAAGGUCAGAGUCUGGAUCACCUUCUG
CUGGAGGCCACAGCAAACCUCCUCACAGCCCACUGGUCCUCAAGAGGUGCCACGUCUCCACACA
UCAGCACAACUACGCAGCGCCUCCCUCCACUCGGAAGGACUAUCCUGCUGCCAAGAGGGUCAAG
UUGGACAGUGUCAGAGUCCUGAGACAGAUCAGCAACAACCGAAAAUGCACCAGCCCCAGGUCCU
CGGACACCGAGGAGAAUGUCAAGAGGCGAACACACAACGUCUUGGAGCGCCAGAGGAGGAACGA
GCUAAAACGGAGCUUUUUUGCCCUGCGUGACCAGAUCCCGGAGUUGGAAAACAAUGAAAAGGCC
CCCAAGGUAGUUAUCCUUAAAAAAGCCACAGCAUACAUCCUGUCCGUCCAAGCAGAGGAGCAAA
AGCUCAUUUCUGAAGAGGACUUGUUGCGGAAACGACGAGAACAGUUGAAACACAAACUUGAACA
GCUACGGAACUCUUGUGCGUAA-3′

NANOG mRNA cds (SEQ ID NO:15)

5′-
AUGAGUGUGGAUCCAGCUUGUCCCCAAAGCUUGCCUUGCUUUGAAGCAUCCGACUGUAAAGAAU
CUUCACCUAUGCCUGUGAUUUGUGGGCCUGAAGAAAACUAUCCAUCCUUGCAAAUGUCUUCUGC
UGAGAUGCCUCACACAGAGACUGUCUCUCCUCUUCCUUCCUCCAUGGAUCUGCUUAUUCAGGAC
AGCCCUGAUUCUUCCACCAGUCCCAAAGGCAAACAACCCACUUCUGCAGAGAAUAGUGUCGCAA
AAAAGGAAGACAAGGUCCCGGUCAAGAAACAGAAGACCAGAACUGUGUUCUCUUCCACCCAGCU
GUGUGUACUCAAUGAUAGAUUUCAGAGACAGAAAUACCUCAGCCUCCAGCAGAUGCAAGAACUC
UCCAACAUCCUGAACCUCAGCUACAAACAGGUGAAGACCUGGUUCCAGAACCAGAGAAUGAAAU
CUAAGAGGUGGCAGAAAAACAACUGGCCGAAGAAUAGCAAUGGUGUGACGCAGAAGGCCUCAGC
ACCUACCUACCCCAGCCUCUACUCUUCCUACCACCAGGGAUGCCUGGUGAACCCGACUGGGAAC
CUUCCAAUGUGGAGCAACCAGACCUGGAACAAUUCAACCUGGAGCAACCAGACCCAGAACAUCC
AGUCCUGGAGCAACCACUCCUGGAACACUCAGACCUGGUGCACCCAAUCCUGGAACAAUCAGGC
CUGGAACAGUCCCUUCUAUAACUGUGGAGAGGAAUCUCUGCAGUCCUGCAUGCACUUCCAGCCA
AAUUCUCCUGCCAGUGACUUGGAGGCUGCCUUGGAAGCUGCUGGGGAAGGCCUUAAUGUAAUAC
AGCAGACCACUAGGUAUUUUAGUACUCCACAAACCAUGGAUUUAUUCCUAAACUACUCCAUGAA
CAUGCAACCUGAAGACGUGUGA-3′

FIG. 27

OCT4 mRNA cds (SEQ ID NO:16)

5′-

AUGGCGGGACACCUGGCUUCAGAUUUUGCCUUCUCGCCCCCUCCAGGUGGUGGAGGUGAUGGGC
CAGGGGGGCCGGAGCCGGGCUGGGUUGAUCCUCGGACCUGGCUAAGCUUCCAAGGCCCUCCUGG
AGGGCCAGGAAUCGGGCCGGGGGUUGGGCCAGGCUCUGAGGUGUGGGGGAUUCCCCCAUGCCCC
CCGCCGUAUGAGUUCUGUGGGGGGAUGGCGUACUGUGGGCCCCAGGUUGGAGUGGGGCUAGUGC
CCCAAGGCGGCUUGGAGACCUCUCAGCCUGAGGGCGAAGCAGGAGUCGGGGUGGAGAGCAACUC
CGAUGGGGCCUCCCCGGAGCCCUGCACCGUCACCCCUGGUGCCGUGAAGCUGGAGAAGGAGAAG
CUGGAGCAAAACCCGGAGGAGUCCCAGGACAUCAAAGCUCUGCAGAAAGAACUCGAGCAAUUUG
CCAAGCUCCUGAAGCAGAAGAGGAUCACCCUGGGAUAUACACAGGCCGAUGUGGGGCUCACCCU
GGGGGUUCUAUUUGGGAAGGUAUUCAGCCAAACGACCAUCUGCCGCUUUGAGGCUCUGCAGCUU
AGCUUCAAGAACAUGUGUAAGCUGCGGCCCUUGCUGCAGAAGUGGGUGGAGGAAGCUGACAACA
AUGAAAAUCUUCAGGAGAUAUGCAAAGCAGAAACCCUCGUGCAGGCCCGAAAGAGAAAGCGAAC
CAGUAUCGAGAACCGAGUGAGAGGCAACCUGGAGAAUUUGUUCCUGCAGUGCCCGAAACCCACA
CUGCAGCAGAUCAGCCACAUCGCCCAGCAGCUUGGGCUCGAGAAGGAUGUGGUCCGAGUGUGGU
UCUGUAACCGGCGCCAGAAGGGCAAGCGAUCAAGCAGCGACUAUGCACAACGAGAGGAUUUUGA
GGCUGCUGGGUCUCCUUUCUCAGGGGGACCAGUGUCCUUUCCUCUGGCCCCAGGGCCCCAUUUU
GGUACCCCAGGCUAUGGGAGCCCUCACUUCACUGCACUGUACUCCUCGGUCCCUUUCCCUGAGG
GGGAAGCCUUUCCCCCUGUCUCUGUCACCACUCUGGGCUCUCCCAUGCAUUCAAACUGA-3′

SOX2 mRNA cds (SEQ ID NO:17)

5′-

AUGUACAACAUGAUGGAGACGGAGCUGAAGCCGCCGGGCCCGCAGCAAACUUCGGGGGGCGGCG
GCGGCAACUCCACCGCGGCGGCGGCCGGCGGCAACCAGAAAAACAGCCCGGACCGCGUCAAGCG
GCCCAUGAAUGCCUUCAUGGUGUGGUCCCGCGGGCAGCGGCGCAAGAUGGCCCAGGAGAACCCC
AAGAUGCACAACUCGGAGAUCAGCAAGCGCCUGGGCGCCGAGUGGAAACUUUUGUCGGAGACGG
AGAAGCGGCCGUUCAUCGACGAGGCUAAGCGGCUGCGAGCGCUGCACAUGAAGGAGCACCCGGA
UUAUAAAUACCGGCCCCGGCGGAAAACCAAGACGCUCAUGAAGAAGGAUAAGUACACGCUGCCC
GGCGGGCUGCUGGCCCCCGGCGGCAAUAGCAUGGCGAGCGGGGUCGGGGUGGGCGCCGGCCUGG
GCGCGGGCGUGAACCAGCGCAUGGACAGUUACGCGCACAUGAACGGCUGGAGCAACGGCAGCUA
CAGCAUGAUGCAGGACCAGCUGGGCUACCCGCAGCACCCGGGCCUCAAUGCGCACGGCGCAGCG
CAGAUGCAGCCCAUGCACCGCUACGACGUGAGCGCCCUGCAGUACAACUCCAUGACCAGCUCGC
AGACCUACAUGAACGGCUCGCCCACCUACAGCAUGUCCUACUCGCAGCAGGGCACCCCUGGCAU
GGCUCUUGGCUCCAUGGGUUCGGUGGUCAAGUCCGAGGCCAGCUCCAGCCCCCCUGUGGUUACC
UCUUCCUCCCACUCCAGGGCGCCCUGCCAGGCCGGGGACCUCCGGGACAUGAUCAGCAUGUAUC
UCCCCGGCGCCGAGGUGCCGGAACCCGCCGCCCCCAGCAGACUUCACAUGUCCCAGCACUACCA
GAGCGGCCCGGUGCCCGGCACGGCCAUUAACGGCACACUGCCCCUCUCACACAUGUGA-3′

FIG. 28

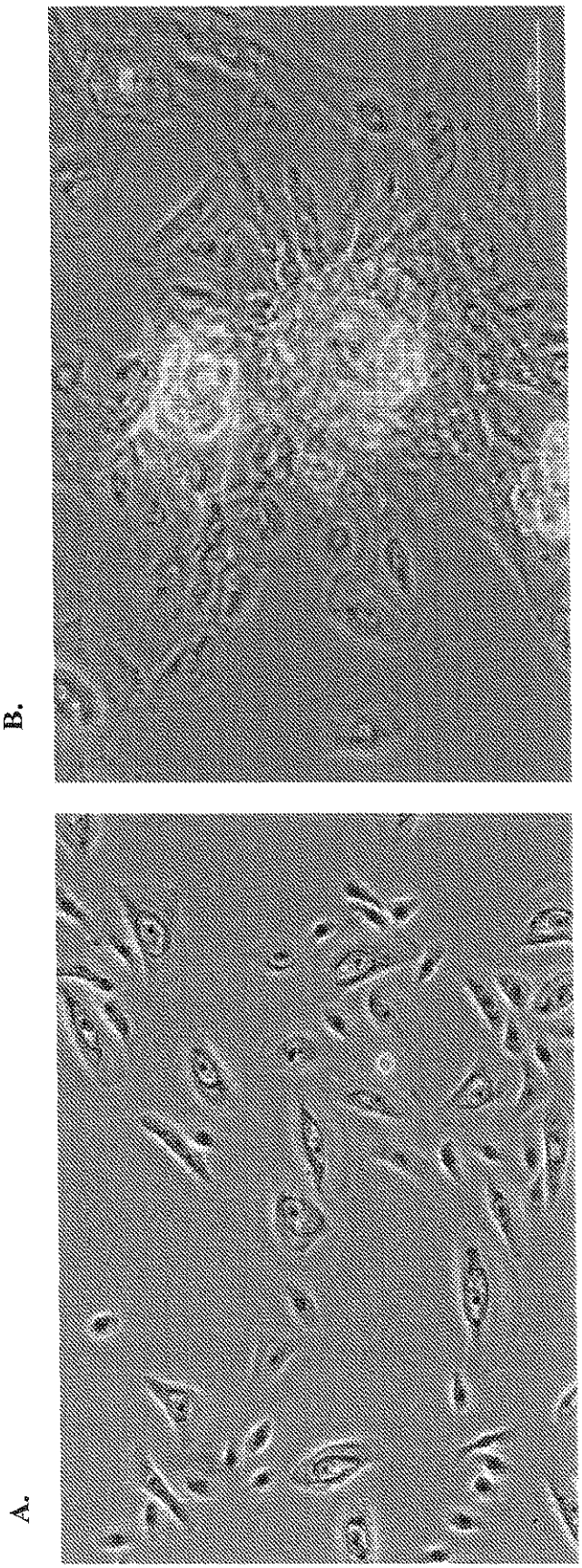


FIG. 28

C.

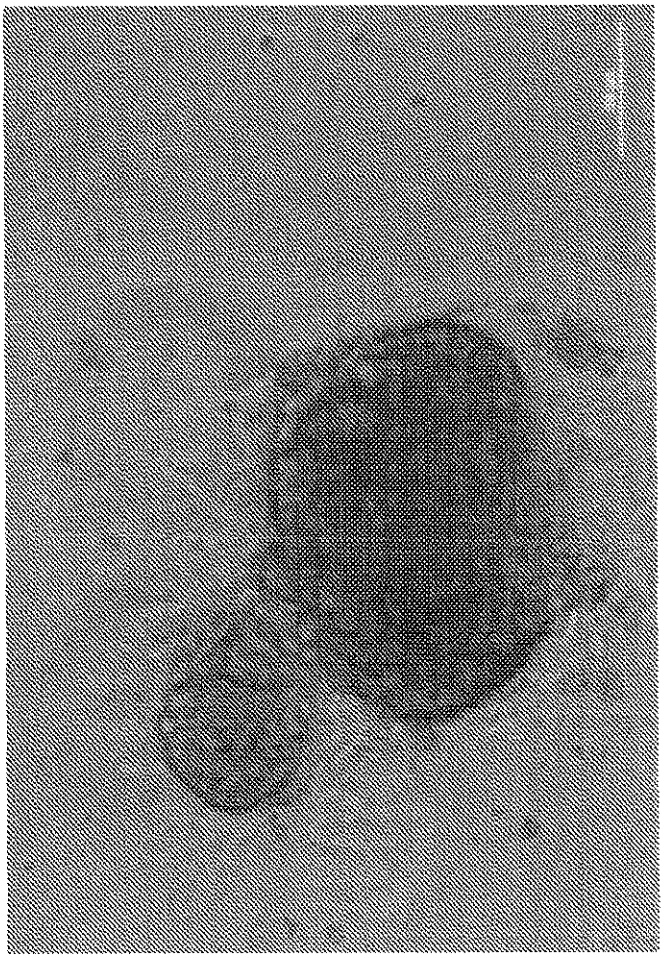


FIG. 29

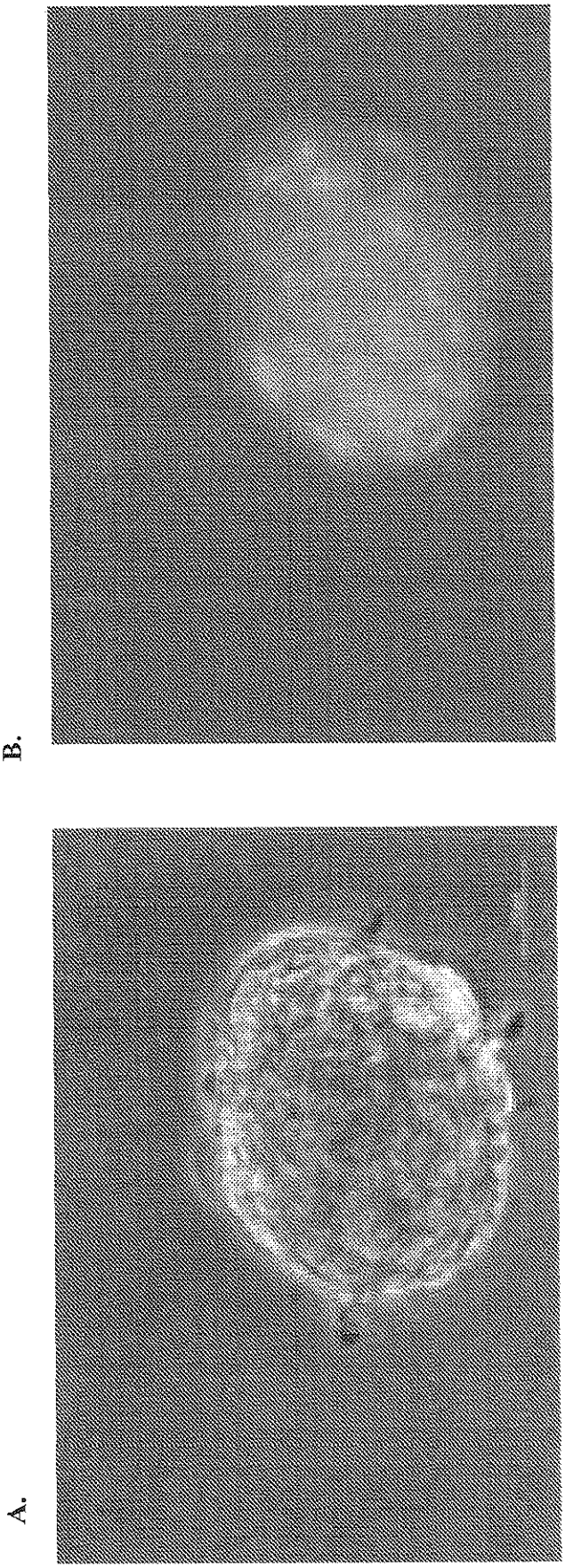


FIG. 29

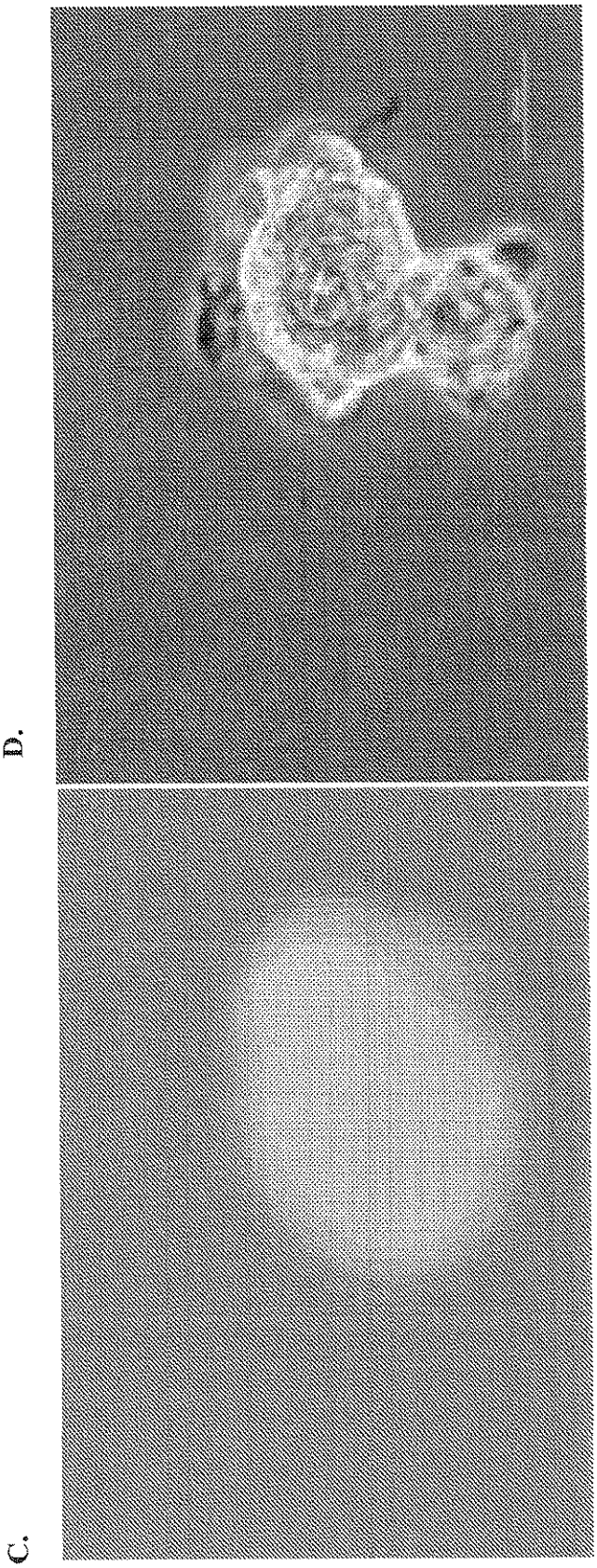


FIG. 29

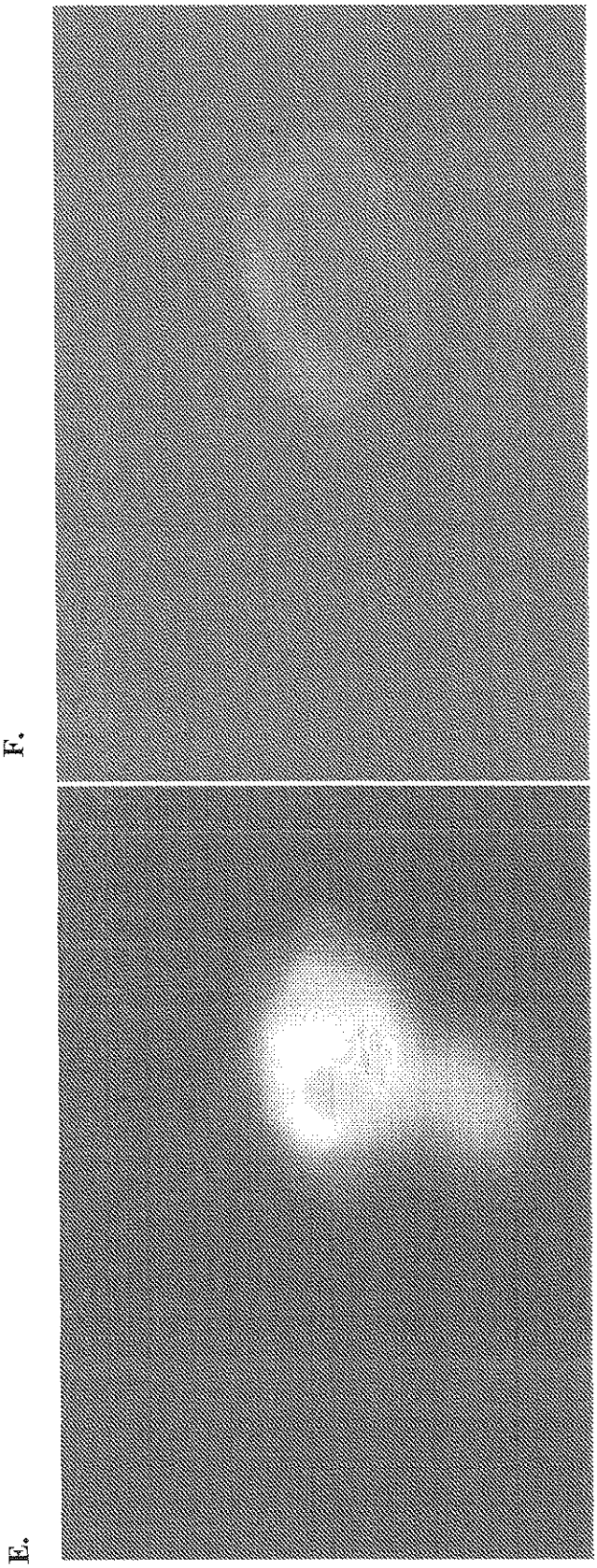


FIG. 29

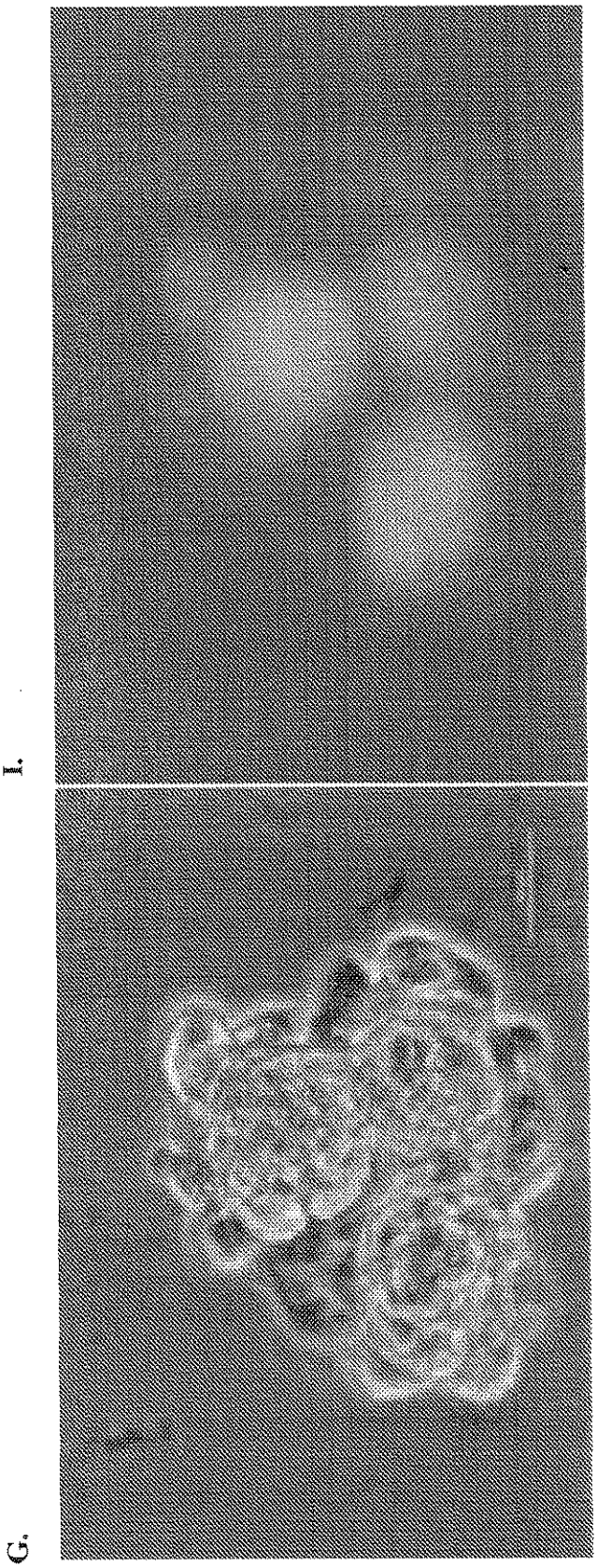
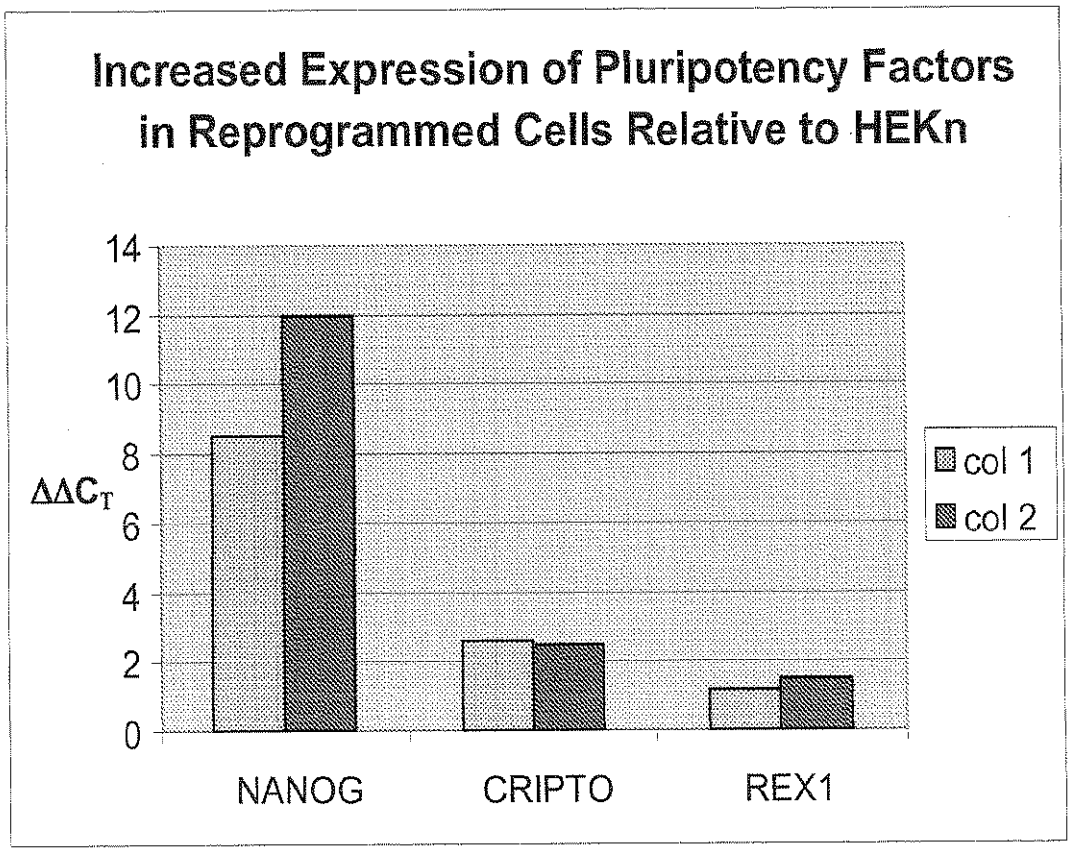


FIG. 30


Increased Expression of Pluripotency Factors in Reprogrammed Cells Relative to HEKn
14
12
10
8
6
4
2
0
ΔΔC$_T$
NANOG
CRIPTO
REX1
col 1
col 2