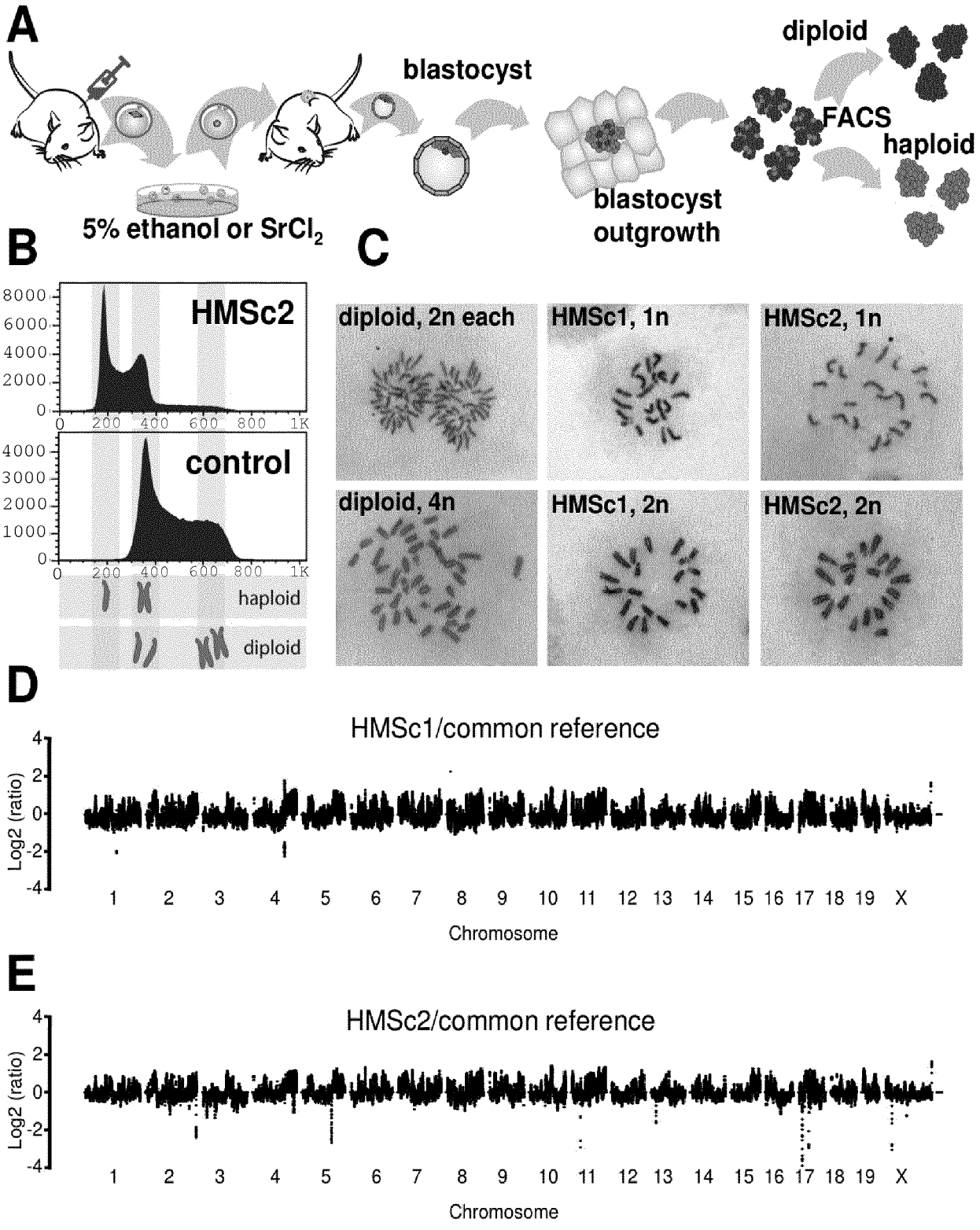

A
blastocyst
diploid
FACS
haploid
5% ethanol or SrCl2
blastocyst outgrowth
B
HMSc2
control
haploid
diploid
C
diploid, 2n each
HMSc1, 1n
HMSc2, 1n
diploid, 4n
HMSc1, 2n
HMSc2, 2n
D
HMSc1/common reference
Log2 (ratio)
Chromosome
E
HMSc2/common reference
Log2 (ratio)
Chromosome

**Figure 1**

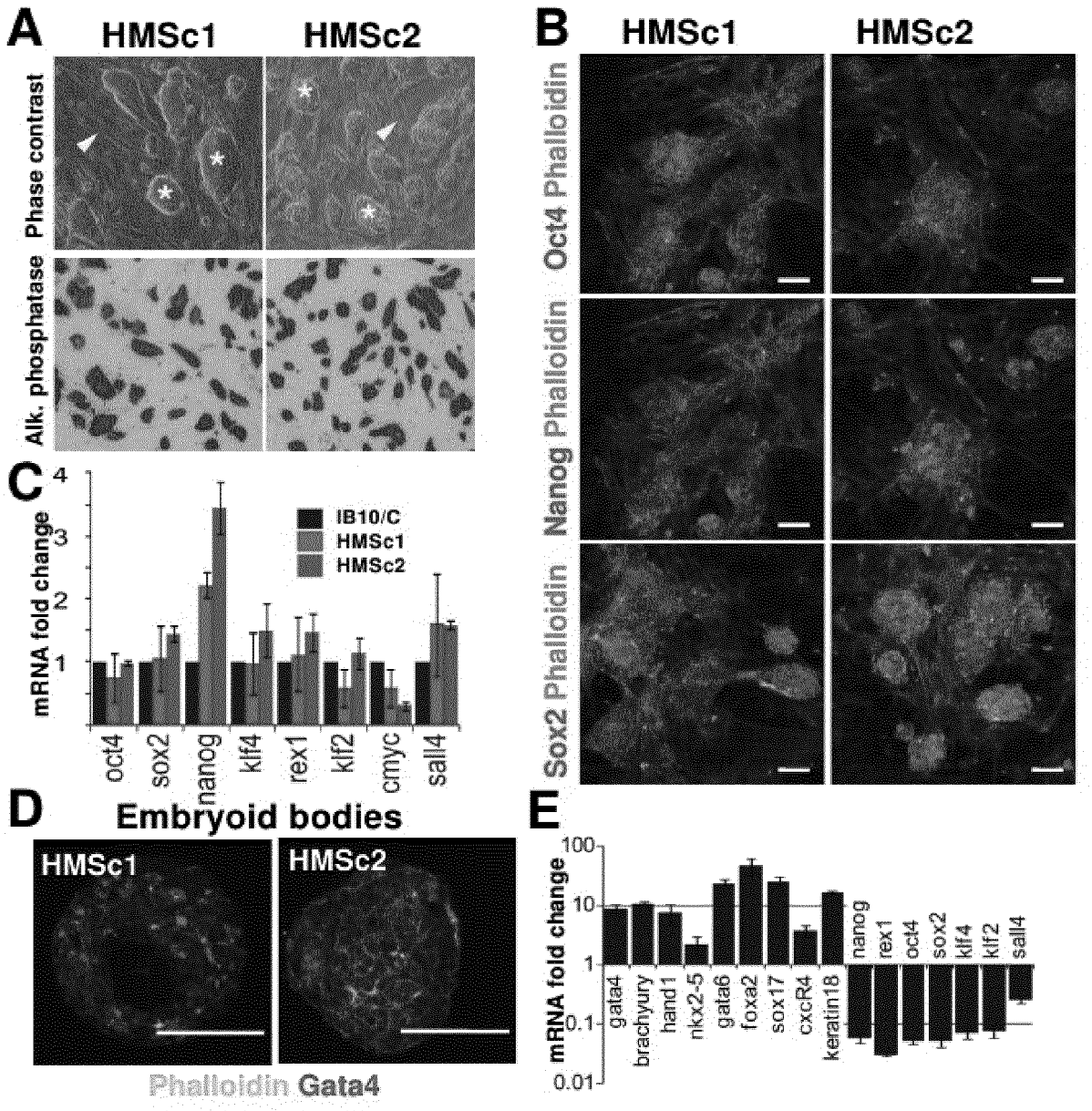

A
HMSc1
HMSc2
Phase contrast
Alk. phosphatase
B
HMSc1
HMSc2
Oct4 Phalloidin
Nanog Phalloidin
Sox2 Phalloidin
C
mRNA fold change
IB10/C
HMSc1
HMSc2
oct4
sox2
nanog
klf4
rex1
klf2
cmyc
sall4
D
Embryoid bodies
HMSc1
HMSc2
Phalloidin Gata4
E
mRNA fold change
gata4
brachyury
hand1
nkx2-5
gata6
foxa2
sox17
cxcR4
keratin18
nanog
rex1
oct4
sox2
klf4
klf2
sall4

**Figure 2**

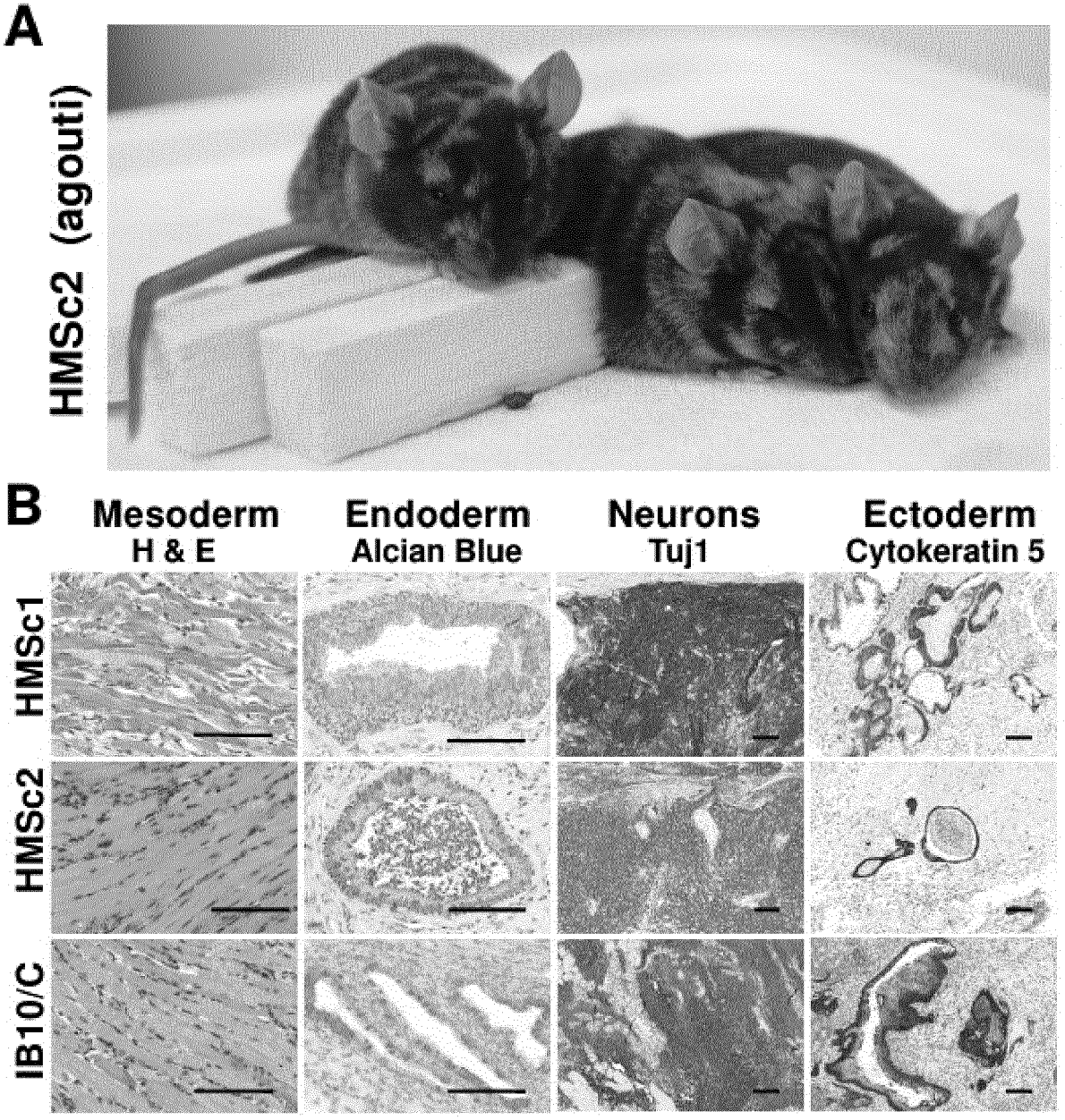

A
HMSc2 (agouti)
B
Mesoderm
H & E
Endoderm
Alcian Blue
Neurons
Tuj1
Ectoderm
Cytokeratin 5
HMSc1
HMSc2
IB10/C

Figure 3

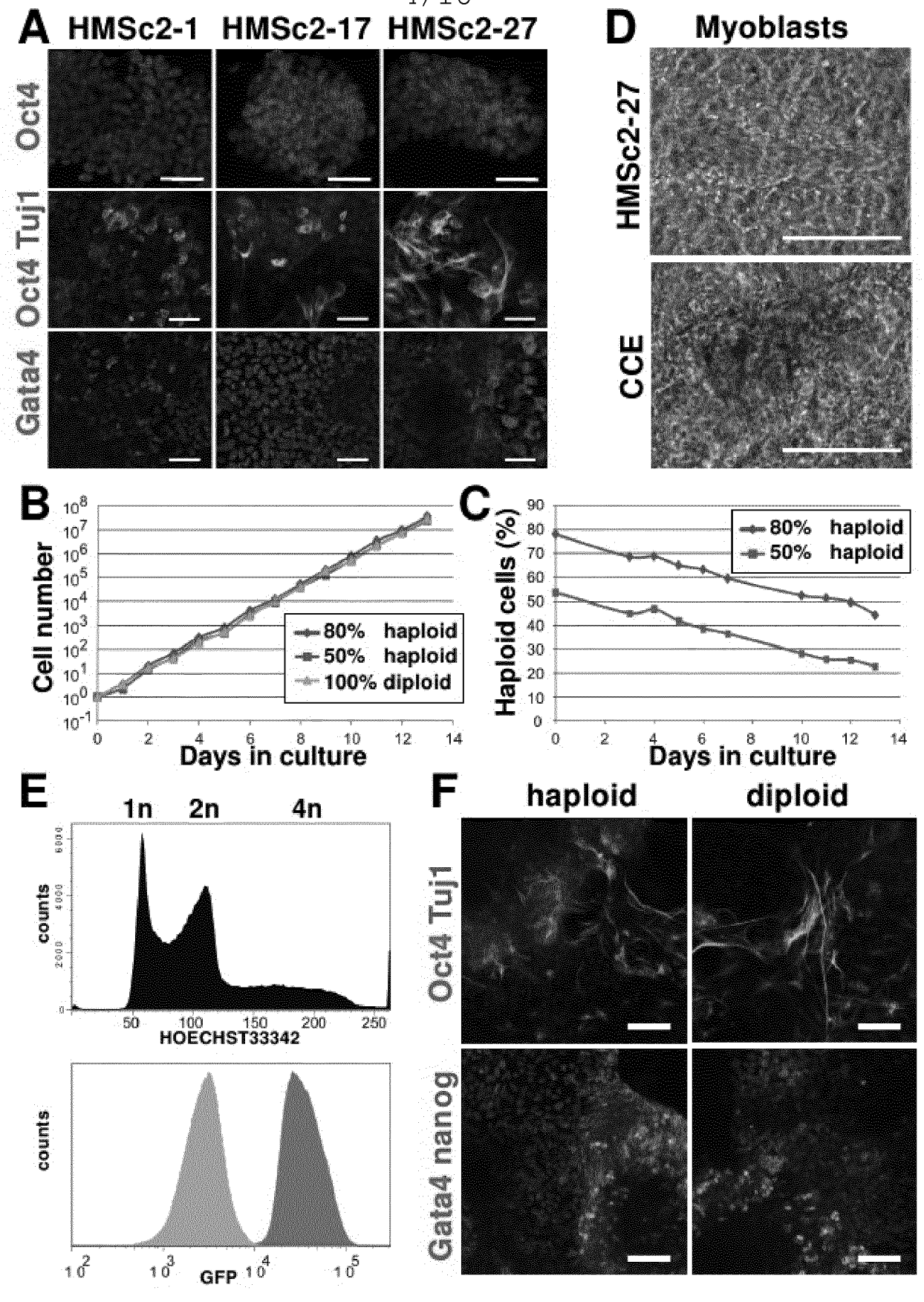

A
HMSc2-1
HMSc2-17
HMSc2-27
Oct4
Oct4 Tuj1
Gata4
D
Myoblasts
HMSc2-27
CCE
B
Cell number
Days in culture
80% haploid
50% haploid
100% diploid
C
Haploid cells (%)
Days in culture
80% haploid
50% haploid
E
1n
2n
4n
counts
HOECHST33342
counts
GFP
F
haploid
diploid
Oct4 Tuj1
Gata4 nanog

Figure 4

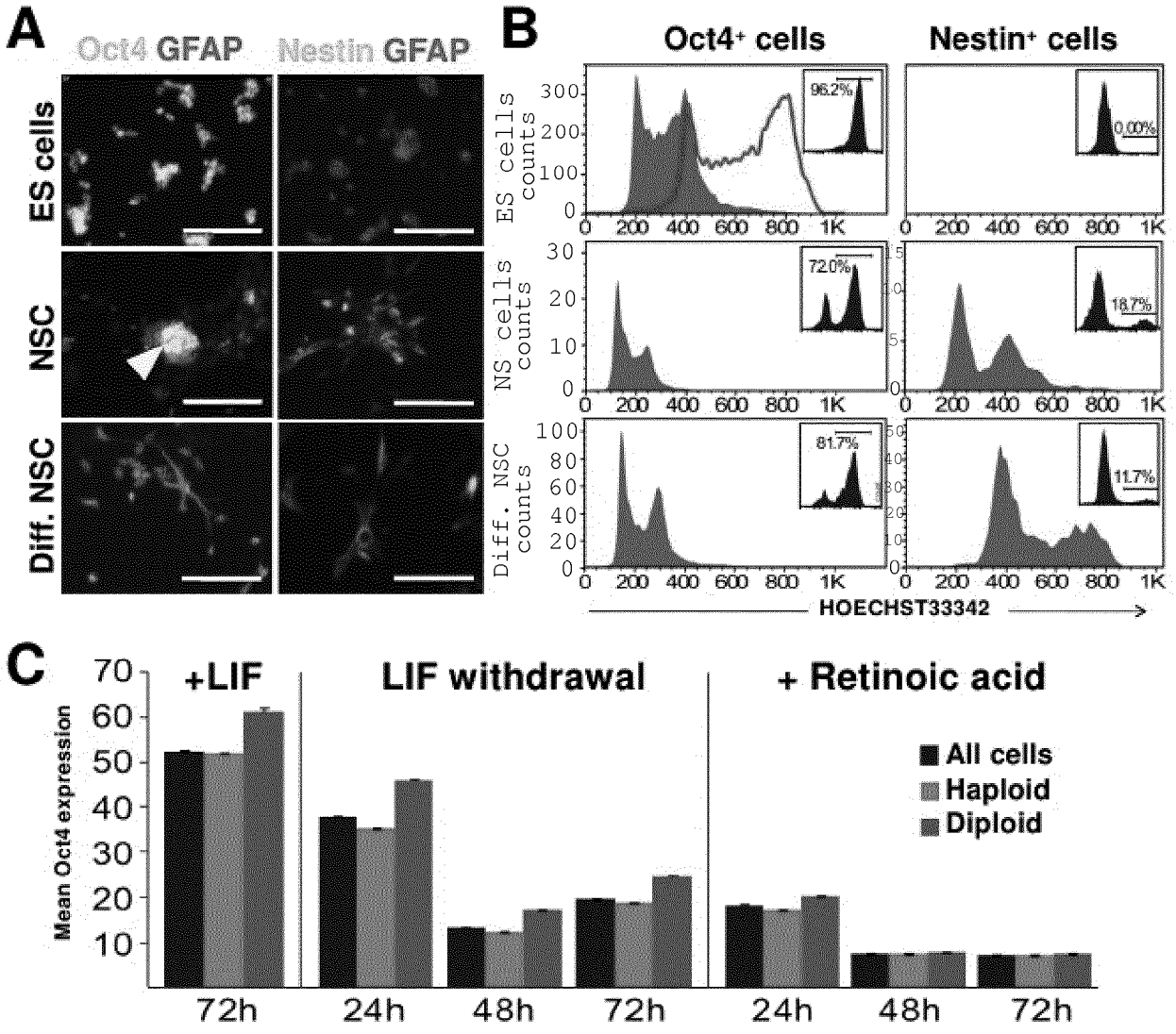

A
Oct4 GFAP
Nestin GFAP
ES cells
NSC
Diff. NSC
B
Oct4+ cells
Nestin+ cells
ES cells counts
NS cells counts
Diff. NSC counts
96.2%
0.00%
72.0%
18.7%
81.7%
11.7%
HOECHST33342
C
+LIF
LIF withdrawal
+ Retinoic acid
Mean Oct4 expression
All cells
Haploid
Diploid
72h
24h
48h
72h
24h
48h
72h

Figure 5

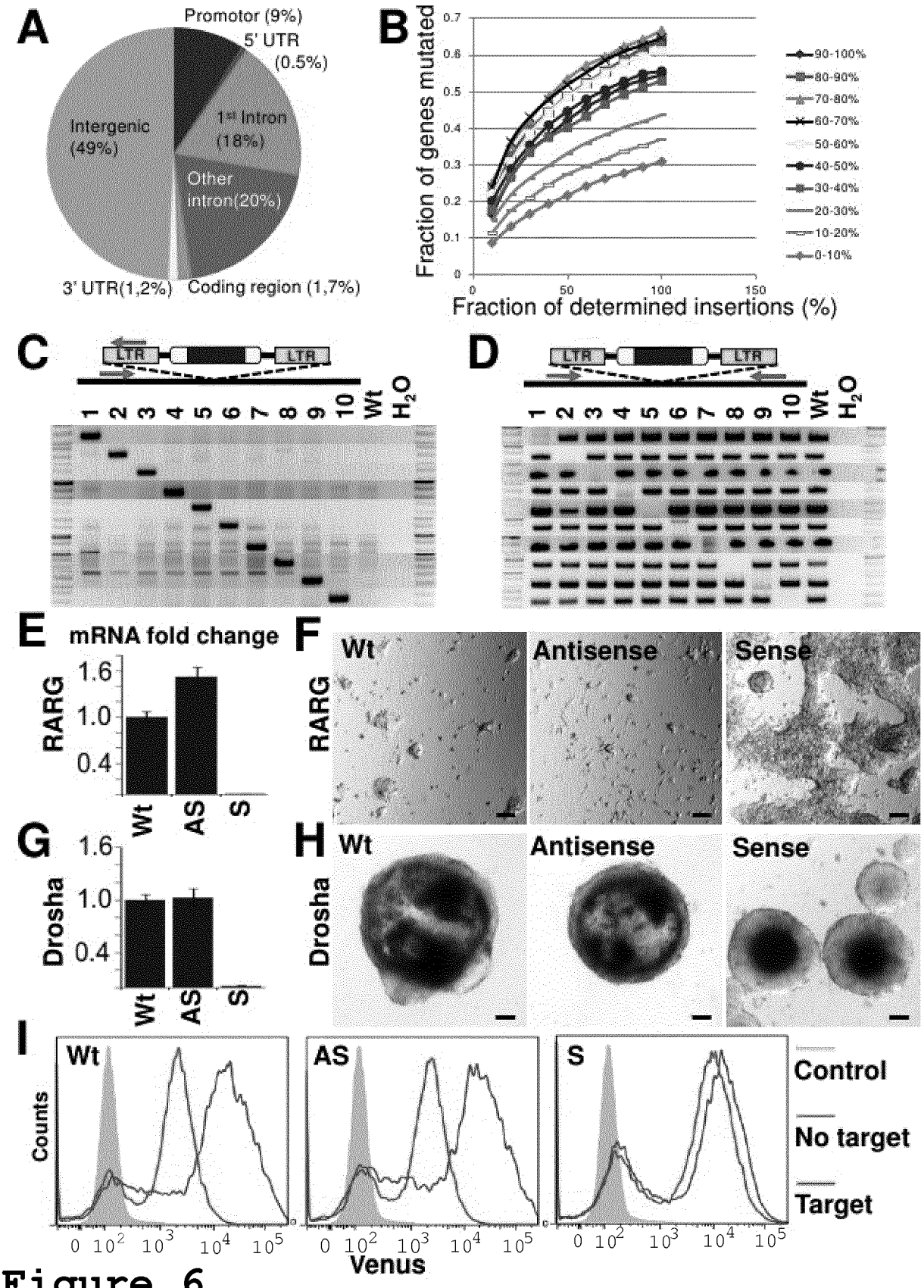
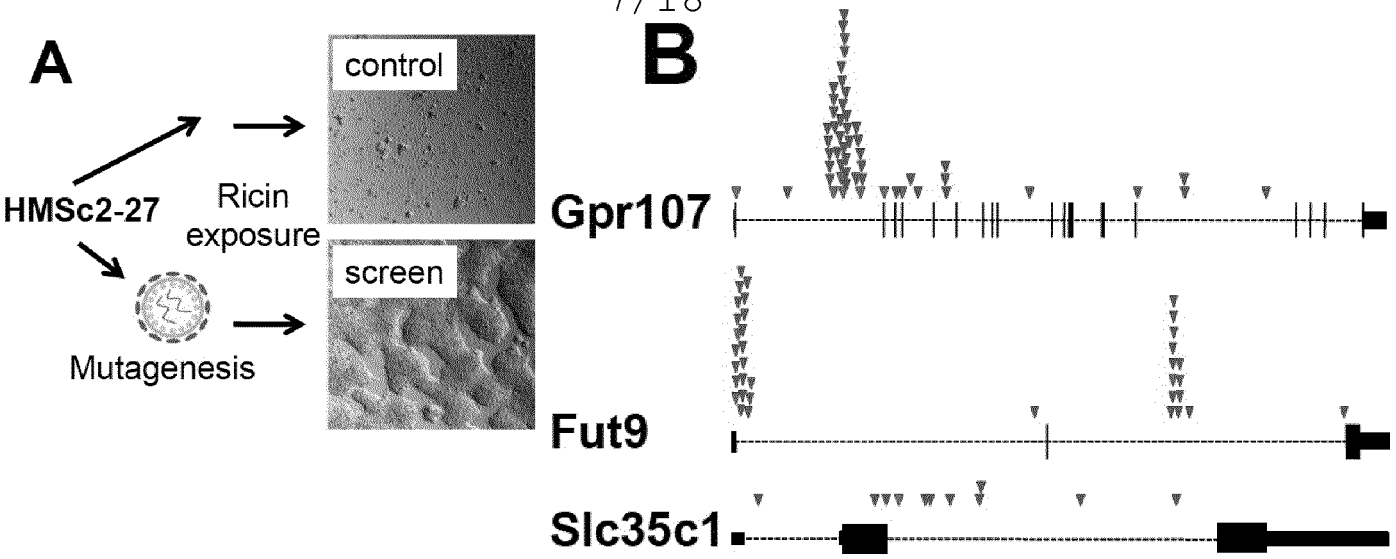

A
Promotor (9%)
5' UTR (0.5%)
1st Intron (18%)
Other intron(20%)
Coding region (1,7%)
3' UTR(1,2%)
Intergenic (49%)
B
Fraction of genes mutated
Fraction of determined insertions (%)
90-100%
80-90%
70-80%
60-70%
50-60%
40-50%
30-40%
20-30%
10-20%
0-10%
C
LTR
LTR
1 2 3 4 5 6 7 8 9 10 Wt H2O
D
LTR
LTR
1 2 3 4 5 6 7 8 9 10 Wt H2O
E
mRNA fold change
RARG
1.6
1.0
0.4
Wt AS S
F
RARG
Wt
Antisense
Sense
G
Drosha
1.6
1.0
0.4
Wt AS S
H
Drosha
Wt
Antisense
Sense
I
Wt
AS
S
Counts
0 10^2 10^3 10^4 10^5
Venus
Control
No target
Target

Figure 6




C

| Gene | Indep. disrupt. | p-value (direction) | Glycosyl. Fucosyl. | Glyco-protein | Golgi |
|---|---|---|---|---|---|
| **Gpr107** | 49 | 1.13E-10 | | X | |
| **Fut9** | 33 | 3.95E-06 | X | X | X |
| **Tcf7l1** | 19 | 0.000189 | | | |
| **Slc35c1** | 10 | 0.000199 | X | | X |
| **Fgfr2** | 8 | 0.001114 | | X | |
| **Galnt2** | 8 | 0.696341 | X | X | X |
| **Mid1** | 8 | 0.88577 | | | |
| **B4galt1** | 7 | 0.994061 | X | X | X |
| **B4galnt3** | 6 | 0.012157 | X | | X |
| **Plcd3** | 4 | 0.022826 | | | |
| **Ror2** | 4 | 0.042857 | | | |
| **Samd4b** | 4 | 0.042857 | | | |
| **Gcnt2** | 4 | 0.042857 | X | X | X |
| **Ggta1** | 4 | 0.080468 | X | X | X |

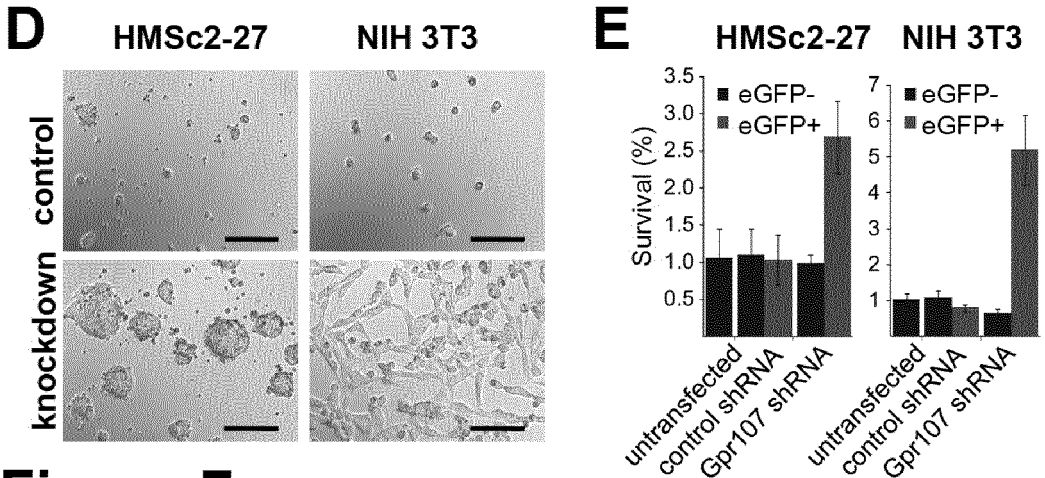



Figure 7

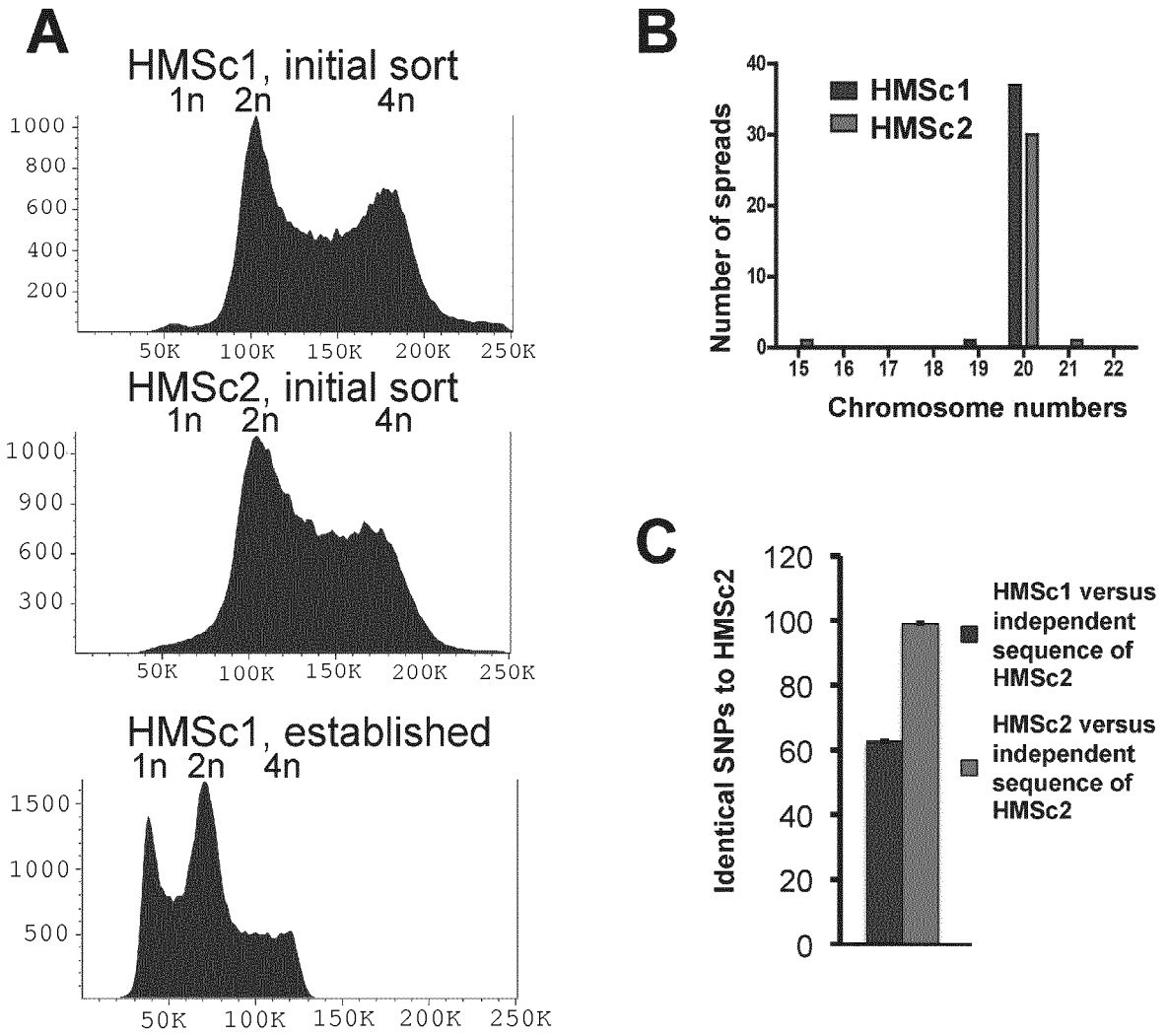

A
HMSc1, initial sort
1n 2n 4n
1000
800
600
400
200
50K 100K 150K 200K 250K
HMSc2, initial sort
1n 2n 4n
1000
900
600
300
50K 100K 150K 200K 250K
HMSc1, established
1n 2n 4n
1500
1000
500
50K 100K 150K 200K 250K
B
HMSc1
HMSc2
Number of spreads
40
30
20
10
0
15 16 17 18 19 20 21 22
Chromosome numbers
C
Identical SNPs to HMSc2
120
100
80
60
40
20
0
HMSc1 versus independent sequence of HMSc2
HMSc2 versus independent sequence of HMSc2

**Figure 8**

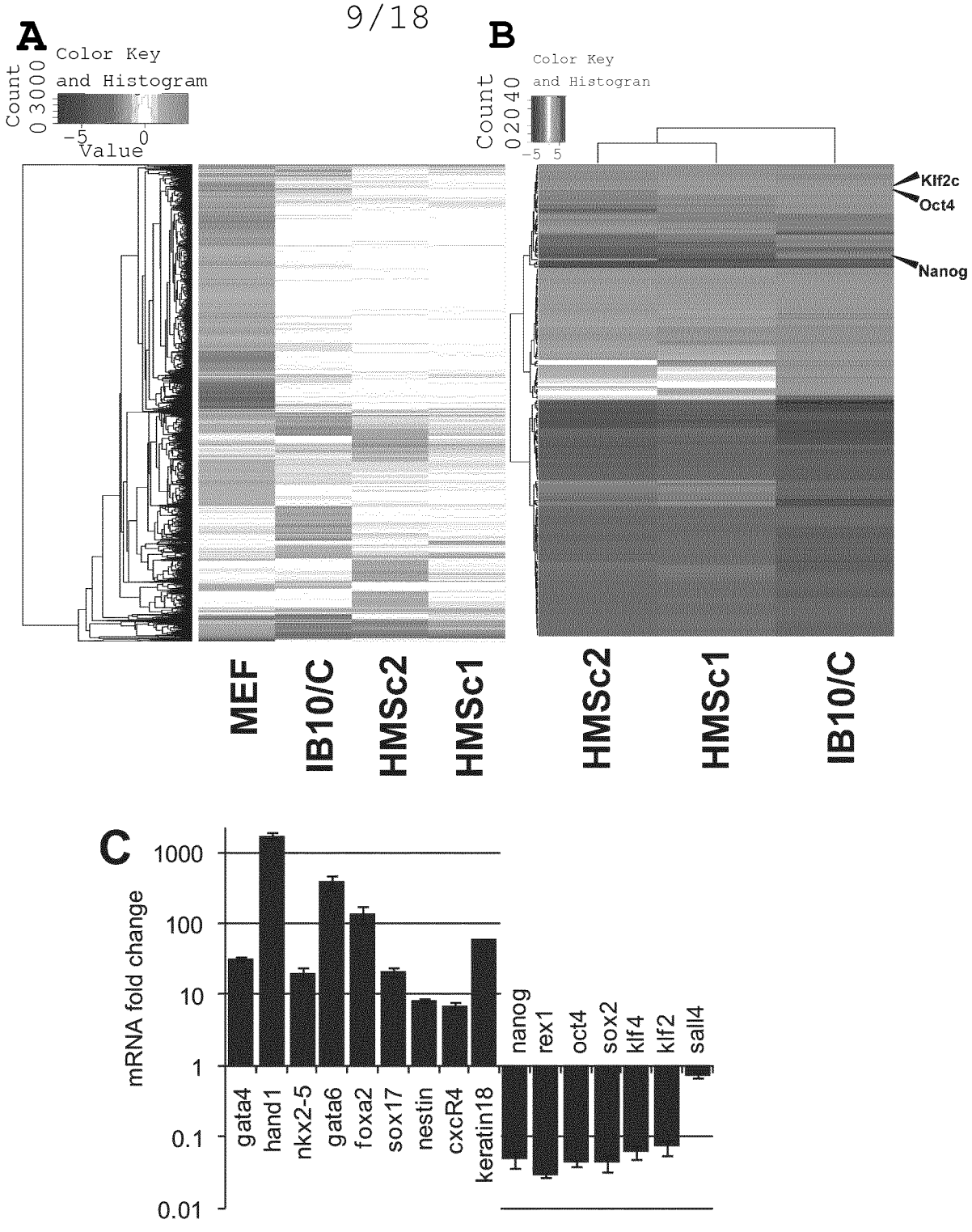

A
Color Key
and Histogram
Count
0 3000
−5 0
Value
B
Color Key
and Histogran
Count
0 20 40
−5 5
Klf2c
Oct4
Nanog
MEF
IB10/C
HMSc2
HMSc1
HMSc2
HMSc1
IB10/C
C
mRNA fold change
1000
100
10
1
0.1
0.01
gata4
hand1
nkx2-5
gata6
foxa2
sox17
nestin
cxcR4
keratin18
nanog
rex1
oct4
sox2
klf4
klf2
sall4

**Figure 9**

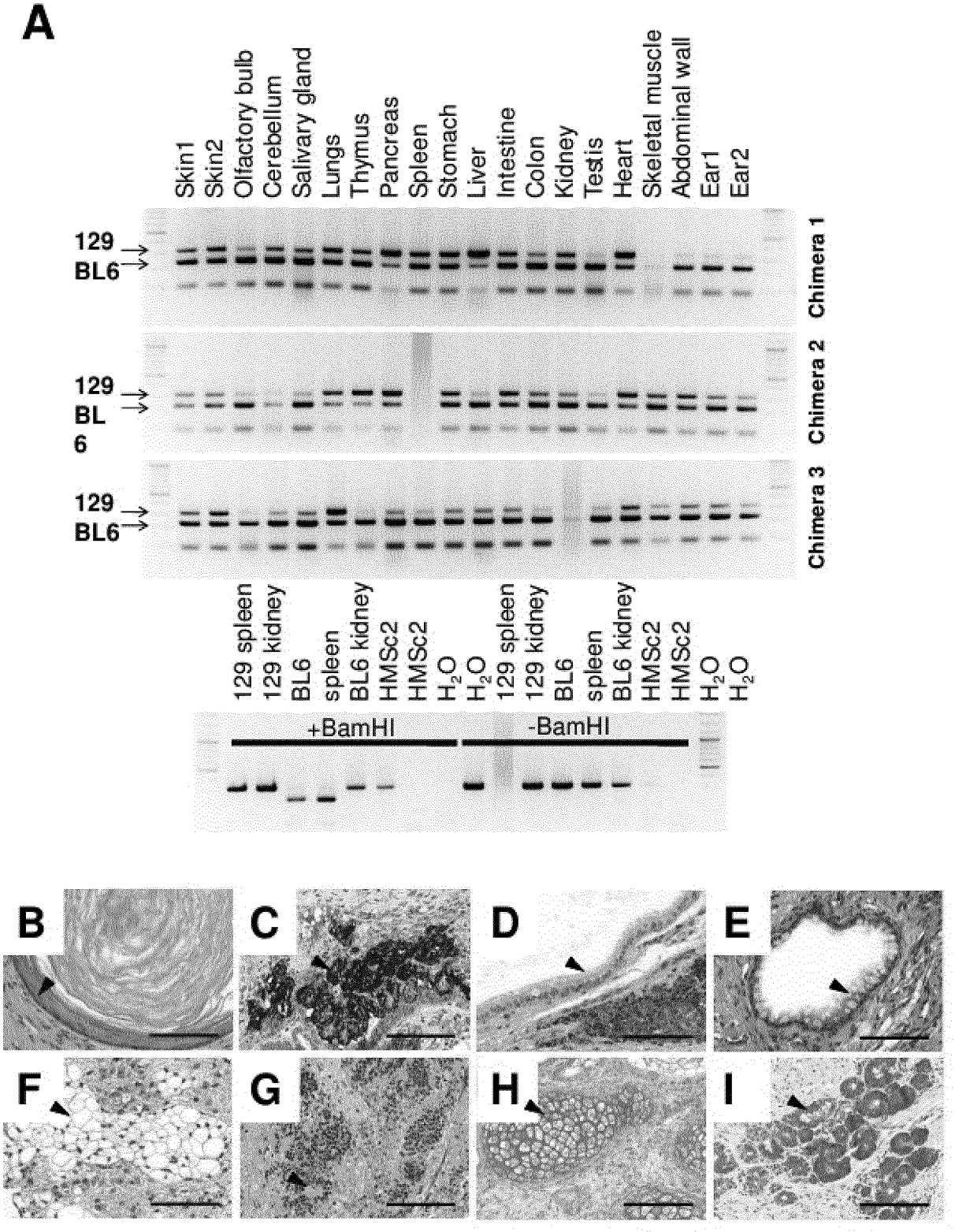

A
Skin1
Skin2
Olfactory bulb
Cerebellum
Salivary gland
Lungs
Thymus
Pancreas
Spleen
Stomach
Liver
Intestine
Colon
Kidney
Testis
Heart
Skeletal muscle
Abdominal wall
Ear1
Ear2
129
BL6
Chimera 1
129
BL
6
Chimera 2
129
BL6
Chimera 3
129 spleen
129 kidney
BL6
spleen
BL6 kidney
HMSc2
HMSc2
H2O
H2O
129 spleen
129 kidney
BL6
spleen
BL6 kidney
HMSc2
HMSc2
H2O
H2O
+BamHI
-BamHI
B
C
D
E
F
G
H
I

Figure 10

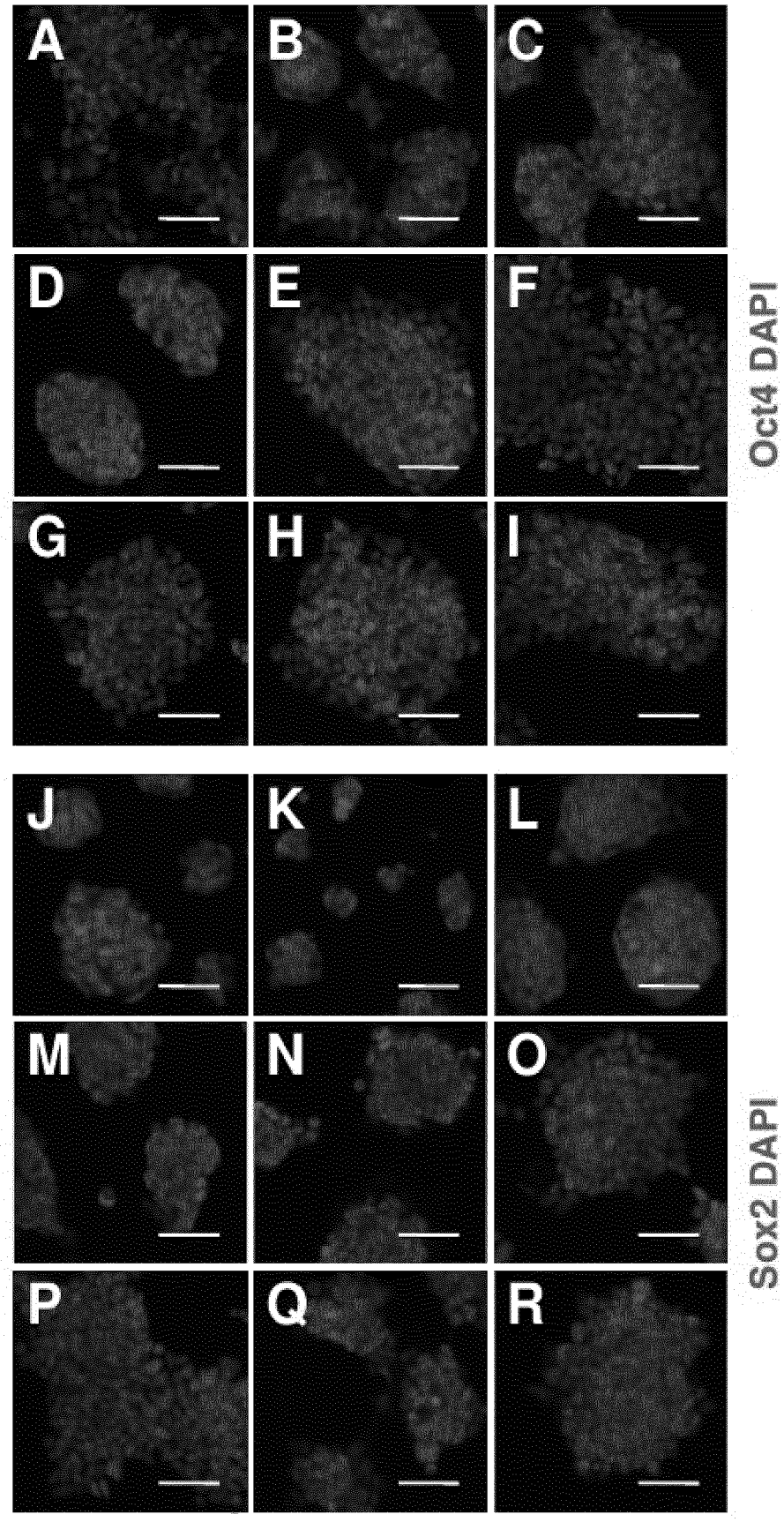



Figure 11

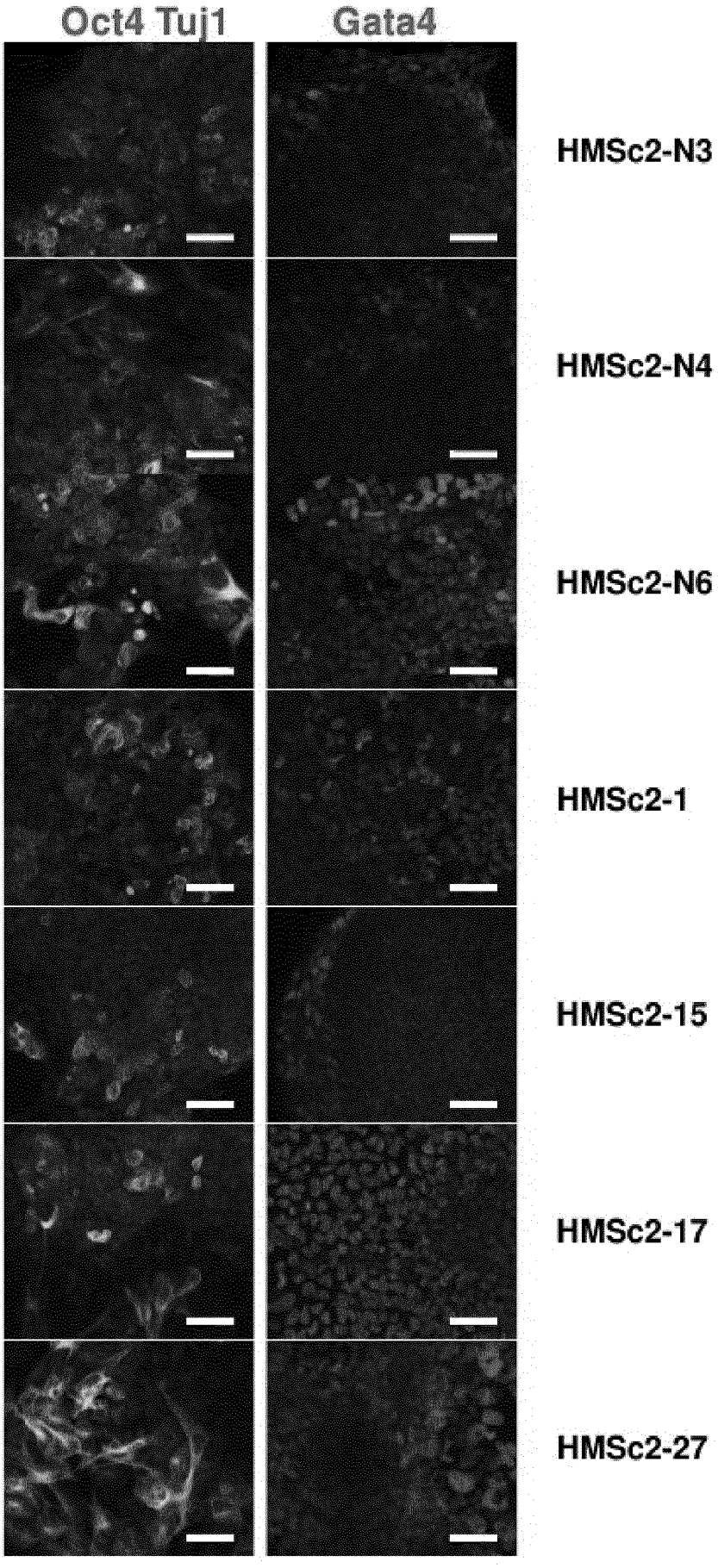

Oct4 Tuj1
Gata4
HMSc2-N3
HMSc2-N4
HMSc2-N6
HMSc2-1
HMSc2-15
HMSc2-17
HMSc2-27

Figure 12

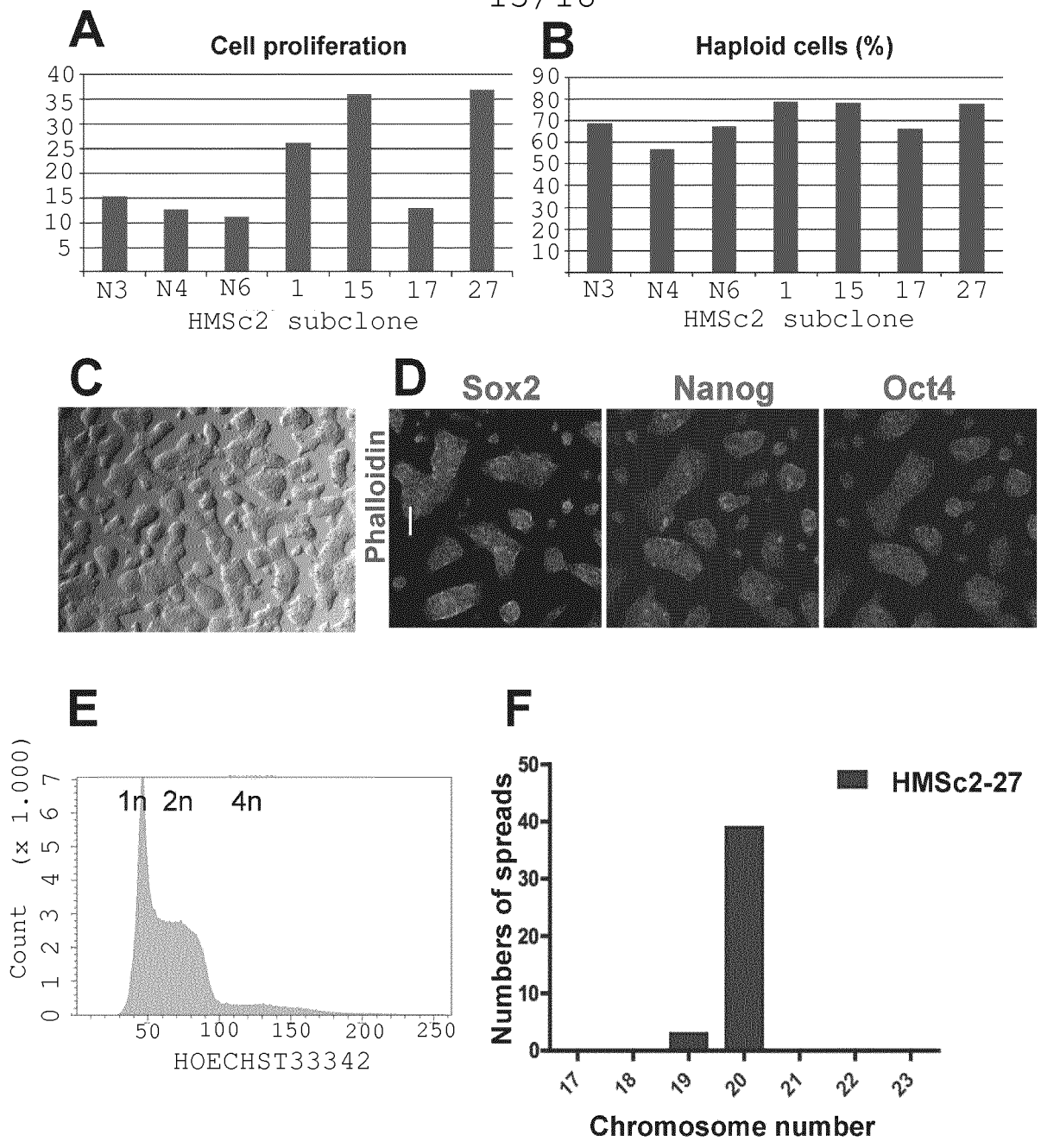
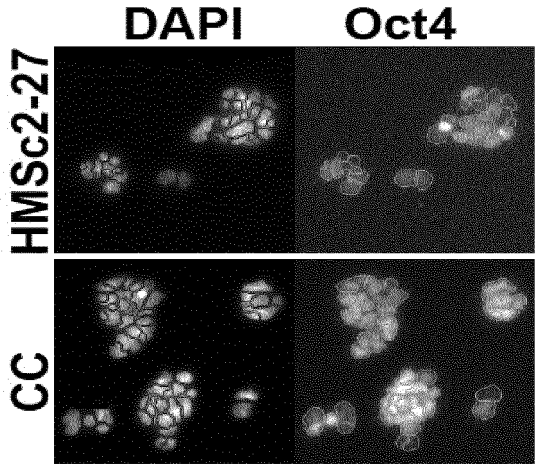

A
Cell proliferation
40
35
30
25
20
15
10
5
N3 N4 N6 1 15 17 27
HMSc2 subclone
B
Haploid cells (%)
90
80
70
60
50
40
30
20
10
N3 N4 N6 1 15 17 27
HMSc2 subclone
C
D
Sox2
Nanog
Oct4
Phalloidin
E
Count (x 1.000)
0 1 2 3 4 5 6 7
1n 2n 4n
50 100 150 200 250
HOECHST33342
F
HMSc2-27
Numbers of spreads
50
40
30
20
10
0
17 18 19 20 21 22 23
Chromosome number

**Figure 13**


A
DAPI
Oct4
HMSc2-27
CC

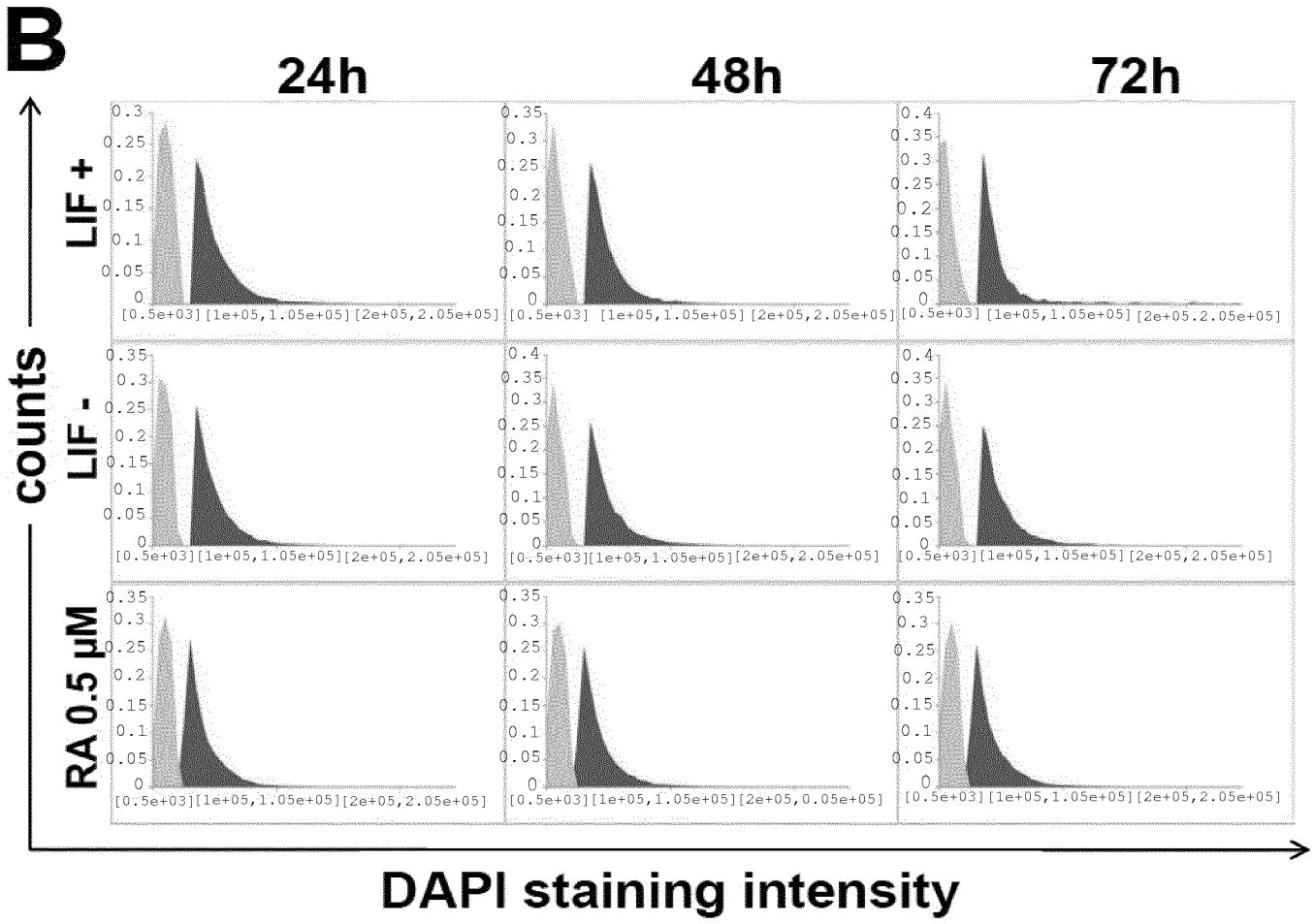
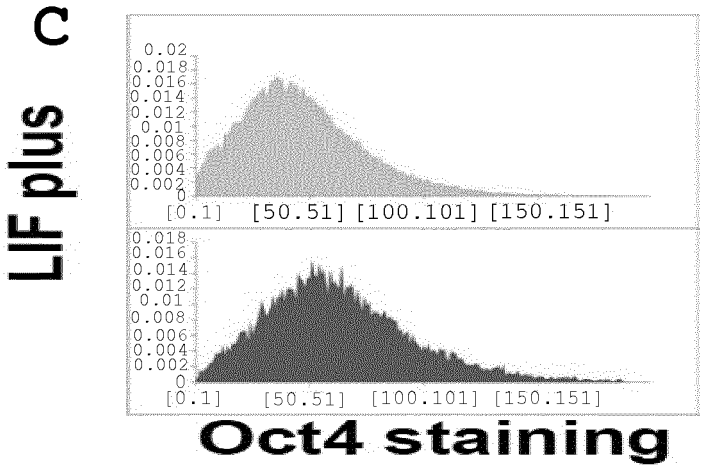
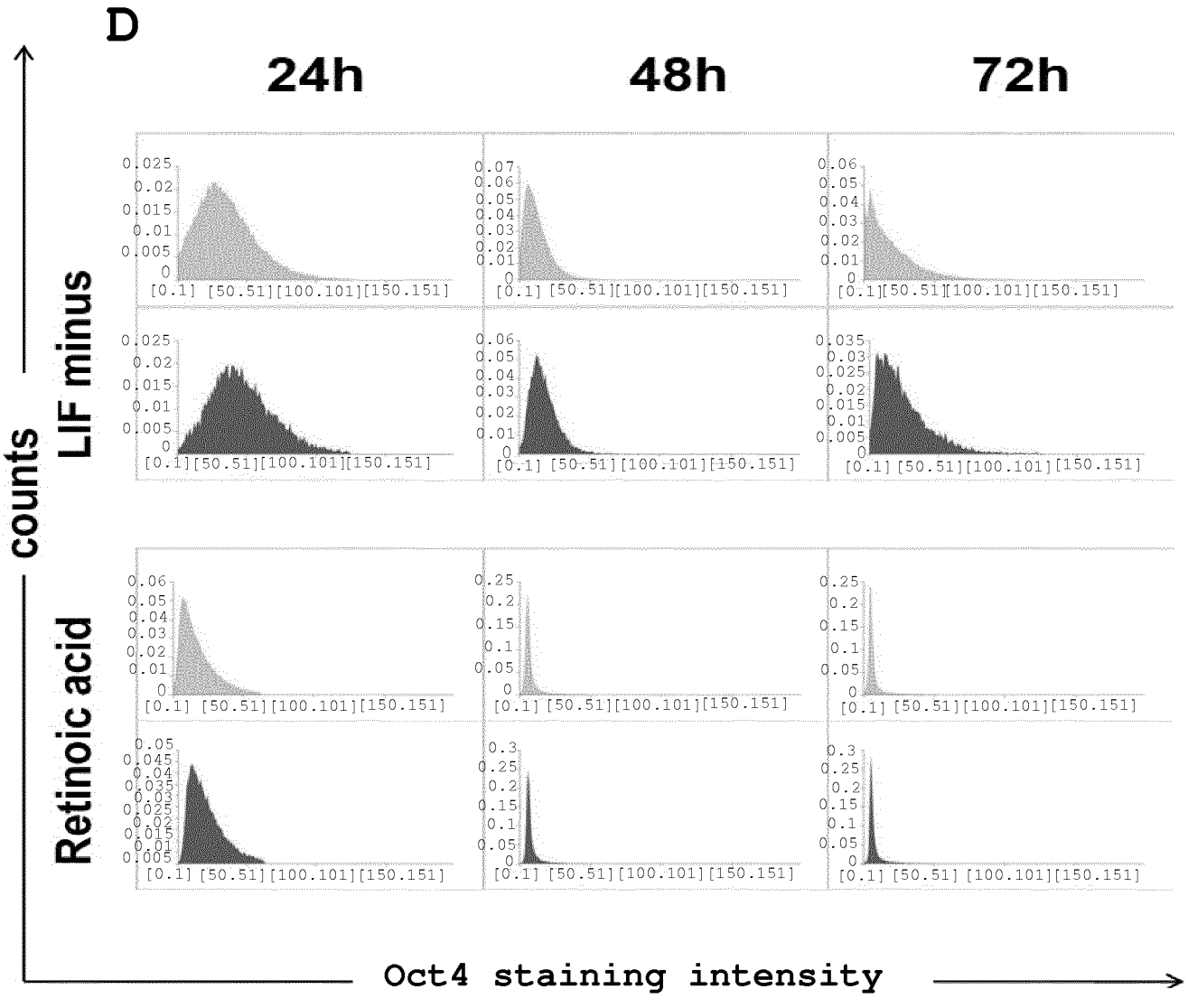

B
24h
48h
72h
LIF +
LIF -
RA 0.5 µM
counts
DAPI staining intensity

Figure 14

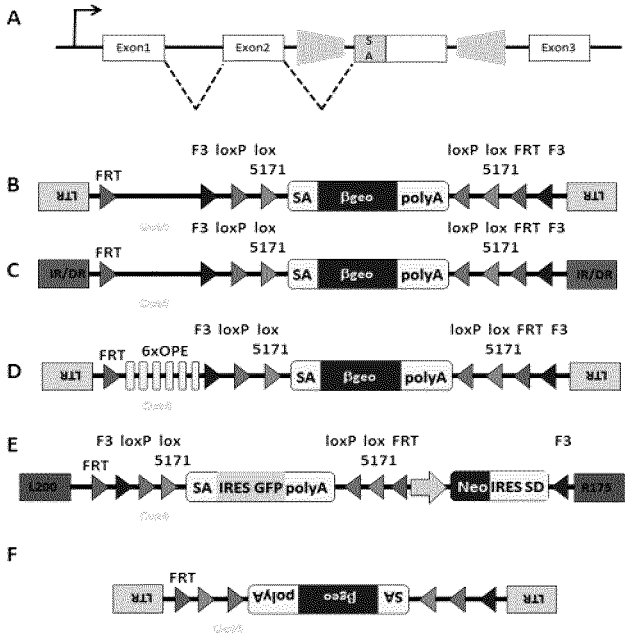

C
LIF plus
[0.1] [50.51] [100.101] [150.151]
Oct4 staining


Haploid cells
Diploid cells

Figure 14


D
24h
48h
72h
LIF minus
Retinoic acid
counts
Oct4 staining intensity

## Figure 15




## Figure 16

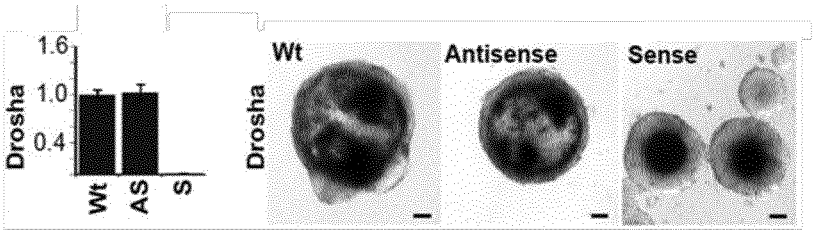


**Figure 17**

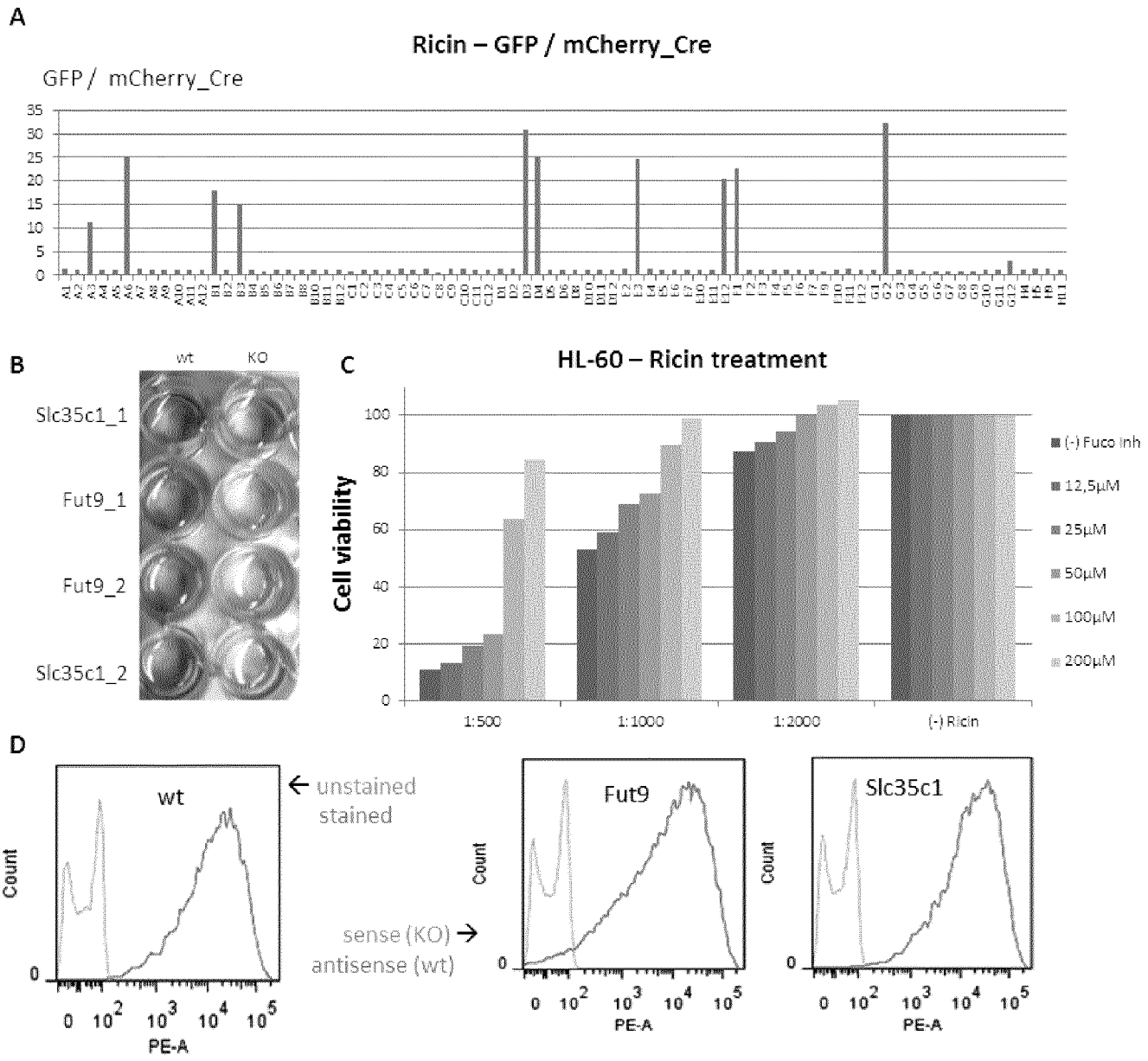
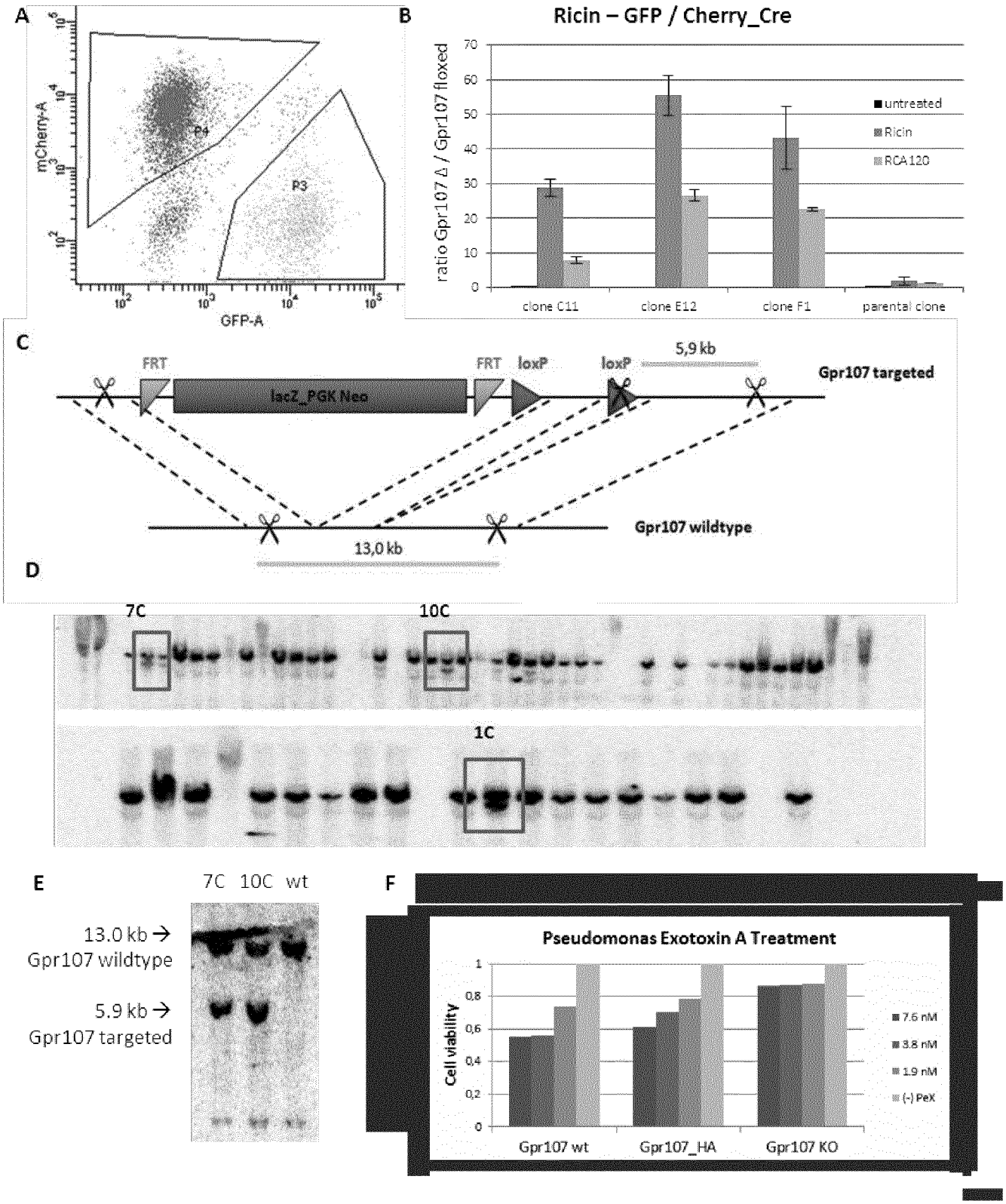

A
Ricin – GFP / mCherry_Cre
GFP / mCherry_Cre
B
wt
KO
Slc35c1_1
Fut9_1
Fut9_2
Slc35c1_2
C
HL-60 – Ricin treatment
Cell viability
(-) Fuco inh
12,5µM
25µM
50µM
100µM
200µM
1:500
1:1000
1:2000
(-) Ricin
D
wt
unstained
stained
sense (KO)
antisense (wt)
Fut9
Slc35c1
Count
PE-A

Figure 18


A
mCherry-A
GFP-A
P4
P3
B
Ricin – GFP / Cherry_Cre
ratio Gpr107 Δ / Gpr107 floxed
untreated
Ricin
RCA120
clone C11
clone E12
clone F1
parental clone
C
FRT
lacZ_PGK Neo
FRT
loxP
loxP
5,9 kb
Gpr107 targeted
Gpr107 wildtype
13,0 kb
D
7C
10C
1C
E
7C 10C wt
13.0 kb → Gpr107 wildtype
5.9 kb → Gpr107 targeted
F
Pseudomonas Exotoxin A Treatment
Cell viability
7.6 nM
3.8 nM
1.9 nM
(-) PeX
Gpr107 wt
Gpr107_HA
Gpr107 KO