Fig. 1

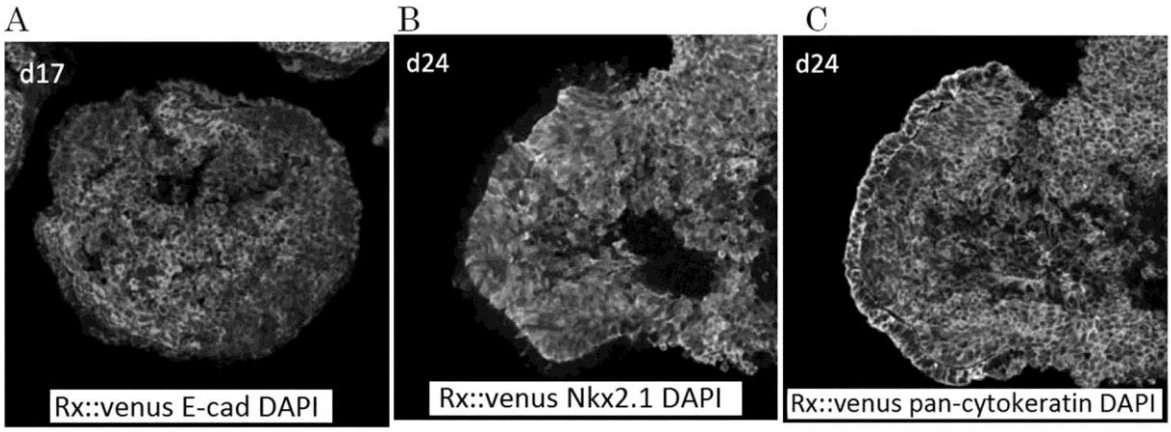

A
d17
Rx::venus E-cad DAPI
B
d24
Rx::venus Nkx2.1 DAPI
C
d24
Rx::venus pan-cytokeratin DAPI

Fig. 2

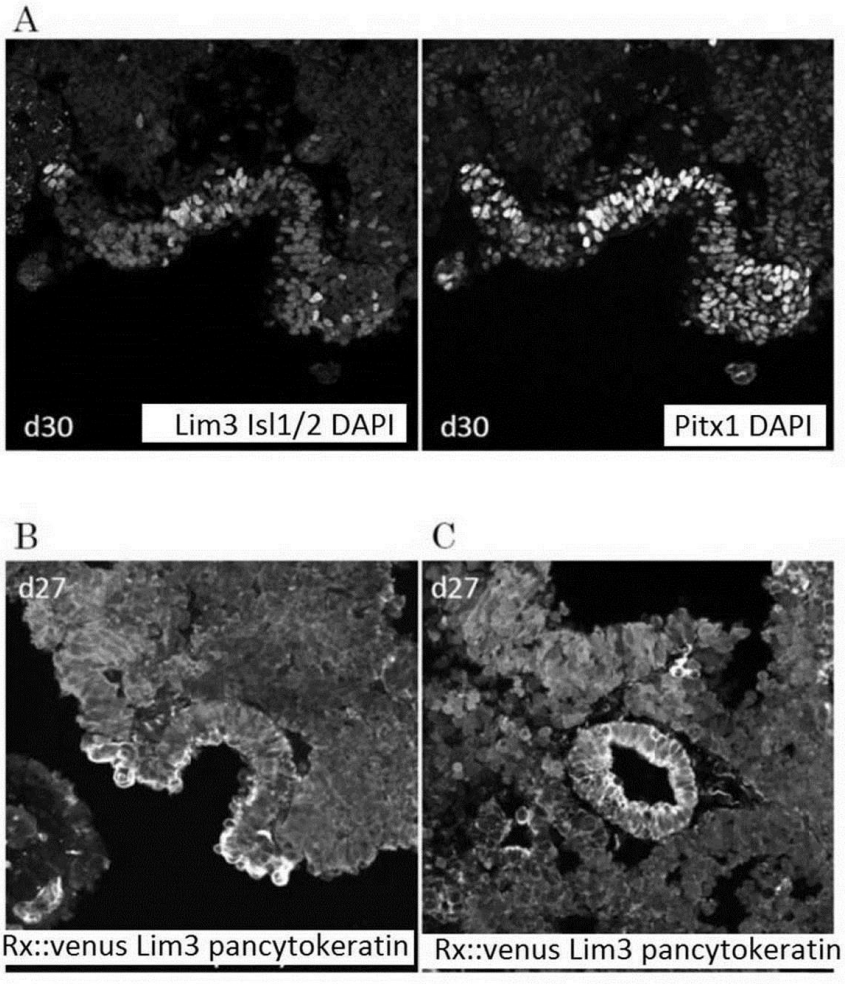
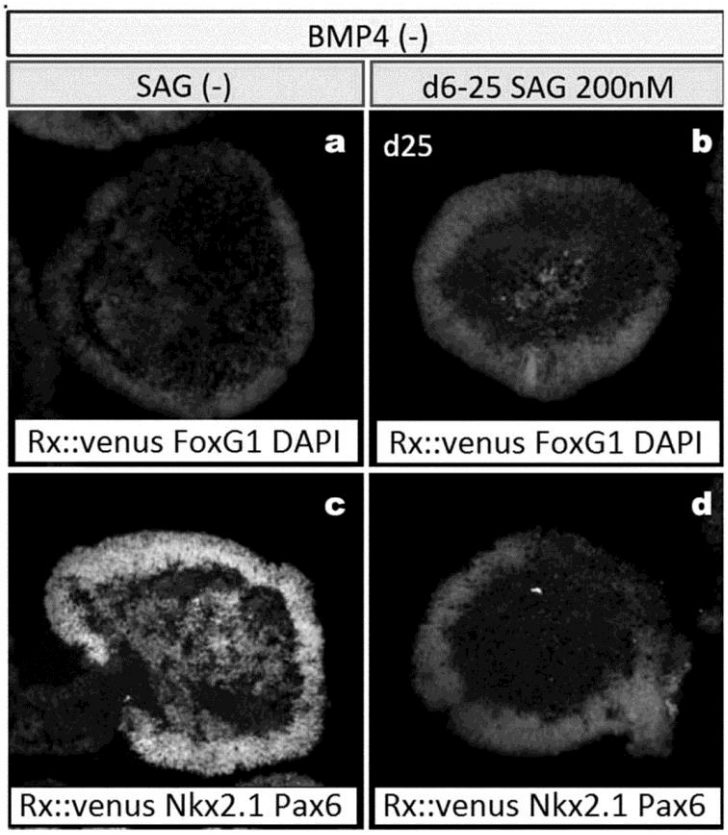
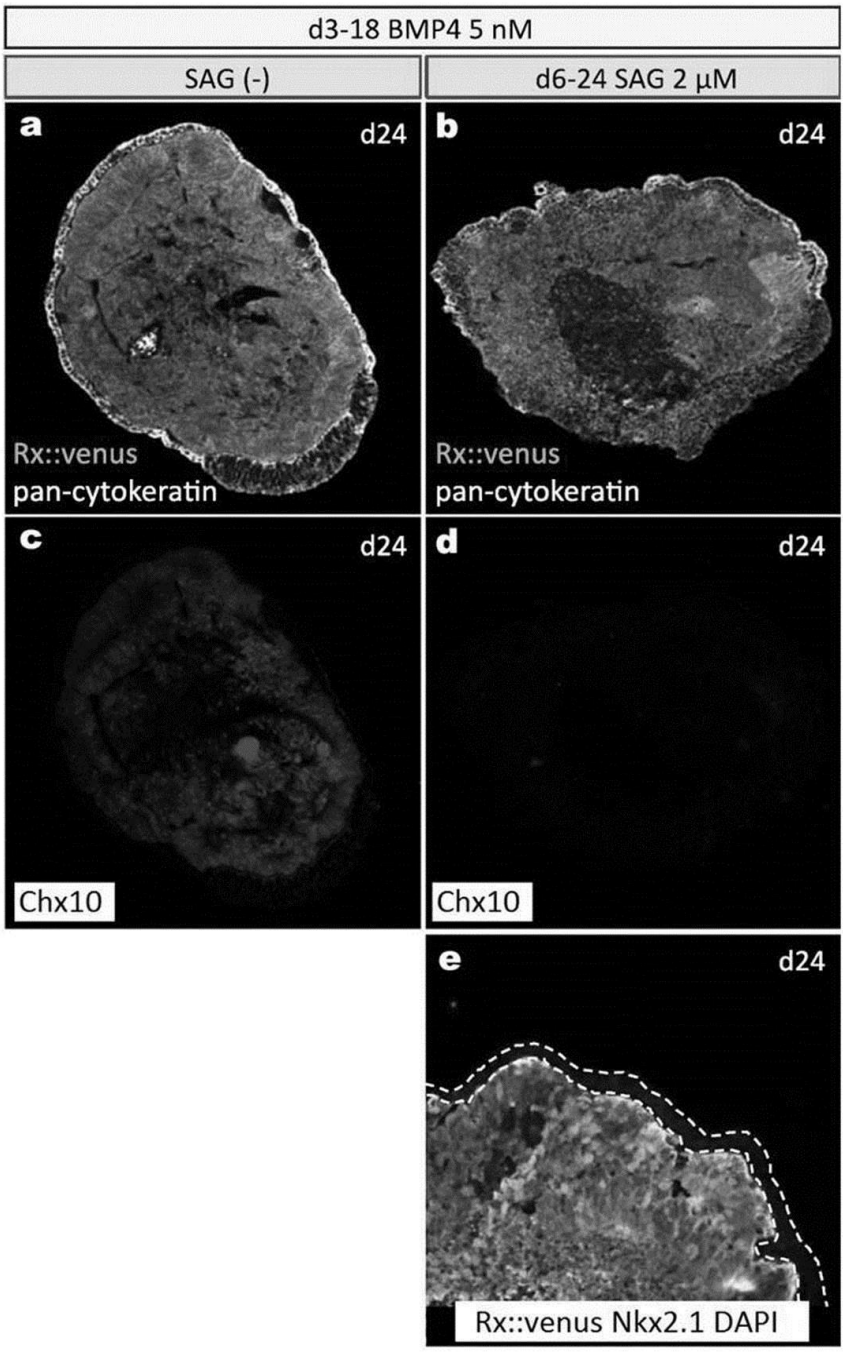

A
d30
Lim3 Isl1/2 DAPI
d30
Pitx1 DAPI
B
d27
Rx::venus Lim3 pancytokeratin
C
d27
Rx::venus Lim3 pancytokeratin

Fig. 3


BMP4 (-)
SAG (-)
d6-25 SAG 200nM
a
d25
b
Rx::venus FoxG1 DAPI
Rx::venus FoxG1 DAPI
c
d
Rx::venus Nkx2.1 Pax6
Rx::venus Nkx2.1 Pax6

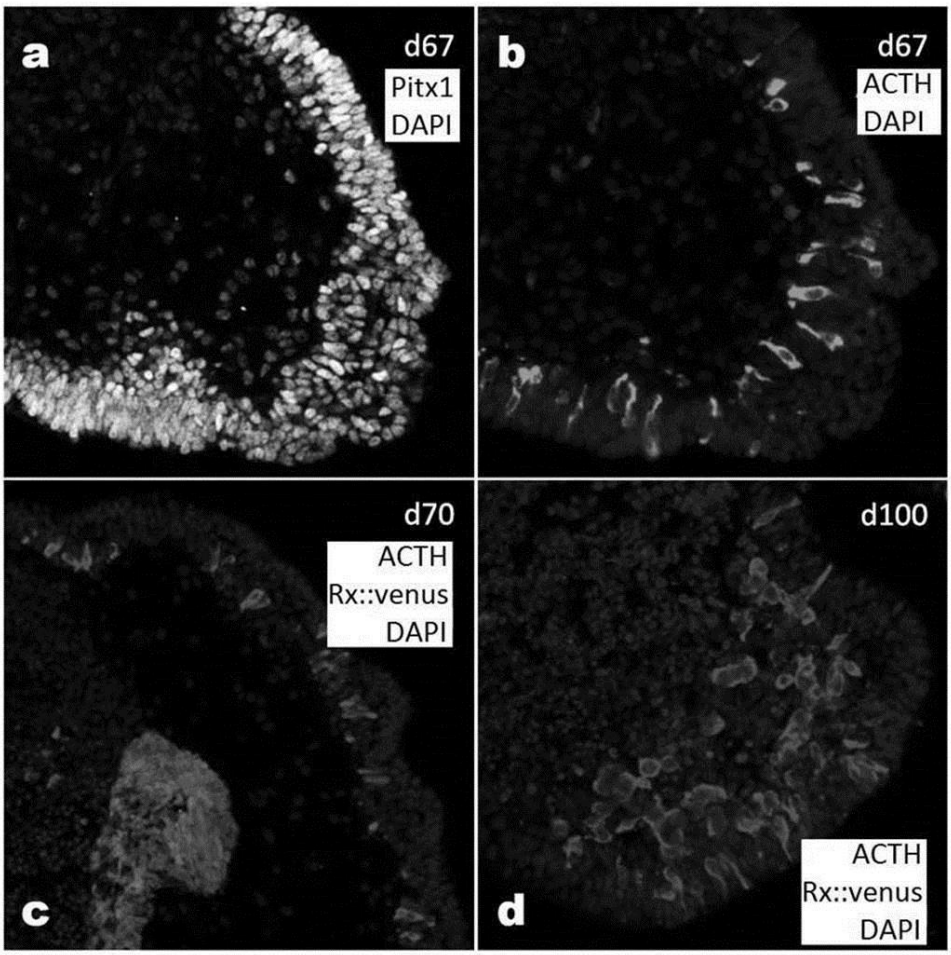
5

Fig. 4


d3-18 BMP4 5 nM
SAG (-)
d6-24 SAG 2 µM
a
d24
Rx::venus
pan-cytokeratin
b
d24
Rx::venus
pan-cytokeratin
c
d24
Chx10
d
d24
Chx10
e
d24
Rx::venus Nkx2.1 DAPI

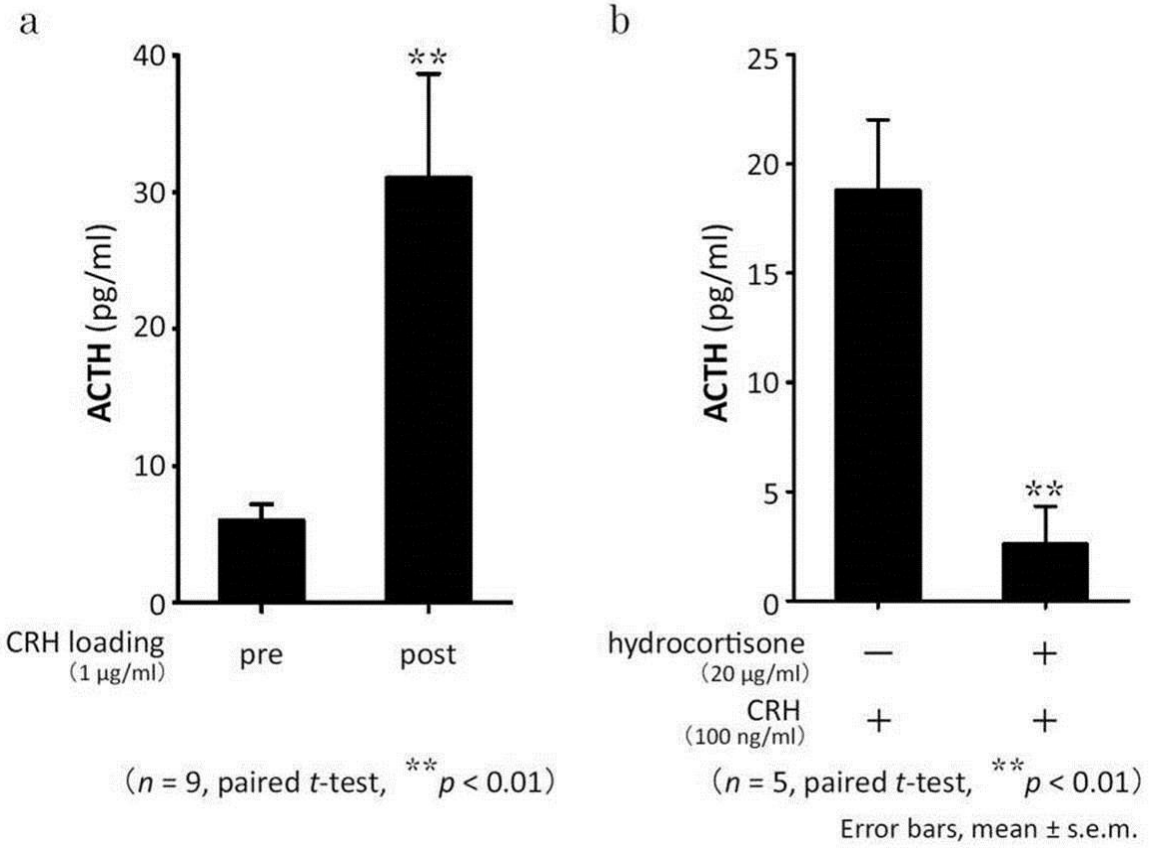
5

Fig. 5


a
d67
Pitx1
DAPI
b
d67
ACTH
DAPI
c
d70
ACTH
Rx::venus
DAPI
d
d100
ACTH
Rx::venus
DAPI

5

Fig. 6


a
40
30
20
10
0
ACTH (pg/ml)
**
CRH loading
(1 μg/ml)
pre
post
(n = 9, paired t-test, **p < 0.01)
b
25
20
15
10
5
0
ACTH (pg/ml)
**
hydrocortisone
(20 μg/ml)
—
+
CRH
(100 ng/ml)
+
+
(n = 5, paired t-test, **p < 0.01)
Error bars, mean ± s.e.m.

5

Fig. 7

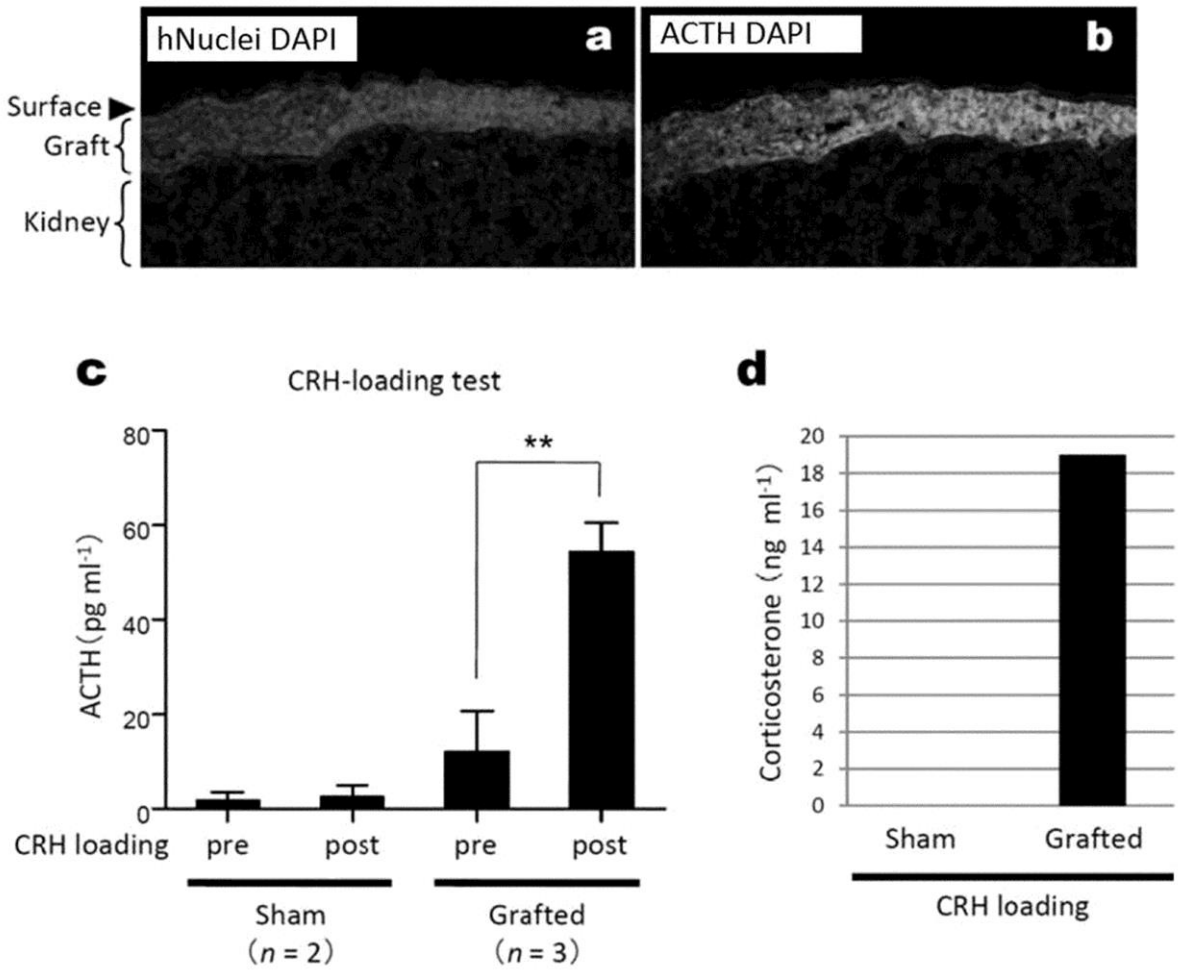

hNuclei DAPI
a
ACTH DAPI
b
Surface
Graft
Kidney
c
CRH-loading test
**
ACTH (pg ml-1)
80
60
40
20
0
CRH loading
pre
post
pre
post
Sham
(n = 2)
Grafted
(n = 3)
d
Corticosterone (ng ml-1)
20
18
16
14
12
10
8
6
4
2
0
Sham
Grafted
CRH loading

Fig. 8

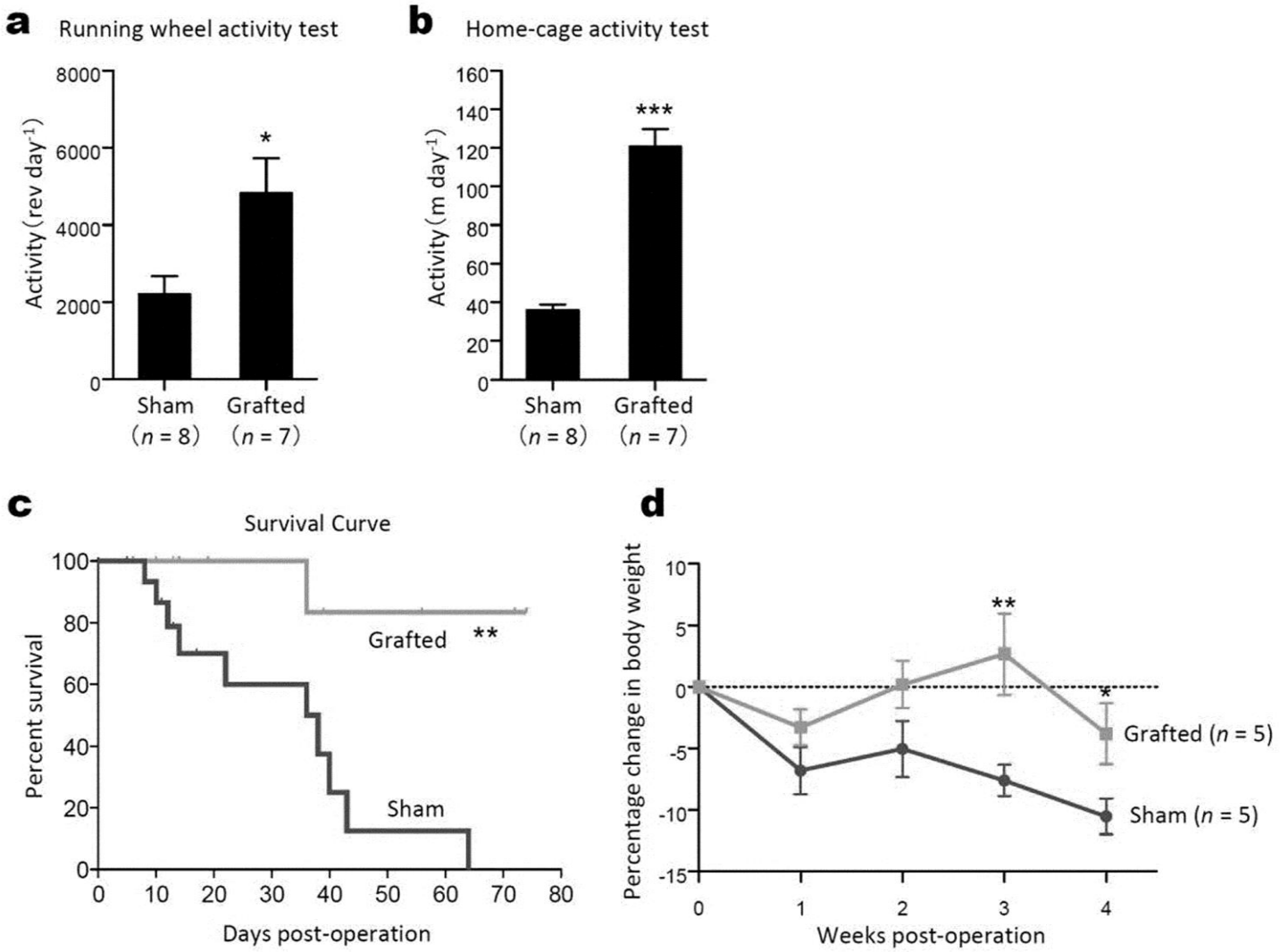

a
Running wheel activity test
Activity (rev day-1)
8000
6000
4000
2000
0
*
Sham
(n = 8)
Grafted
(n = 7)
b
Home-cage activity test
Activity (m day-1)
160
140
120
100
80
60
40
20
0
***
Sham
(n = 8)
Grafted
(n = 7)
c
Survival Curve
Percent survival
100
80
60
40
20
0
Grafted
**
Sham
0
10
20
30
40
50
60
70
80
Days post-operation
d
Percentage change in body weight
10
5
0
-5
-10
-15
**
*
Grafted (n = 5)
Sham (n = 5)
0
1
2
3
4
Weeks post-operation

Fig. 9

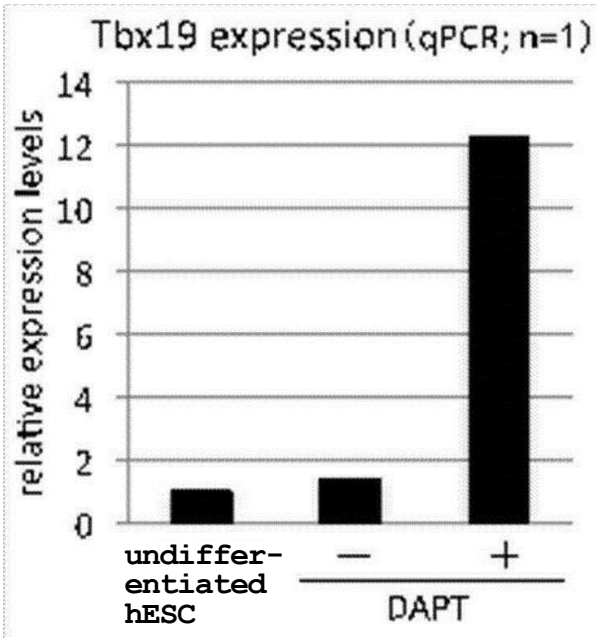

Tbx19 expression (qPCR; n=1)
relative expression levels
14
12
10
8
6
4
2
0
undiffer-
entiated
hESC
—
+
DAPT

Fig. 10

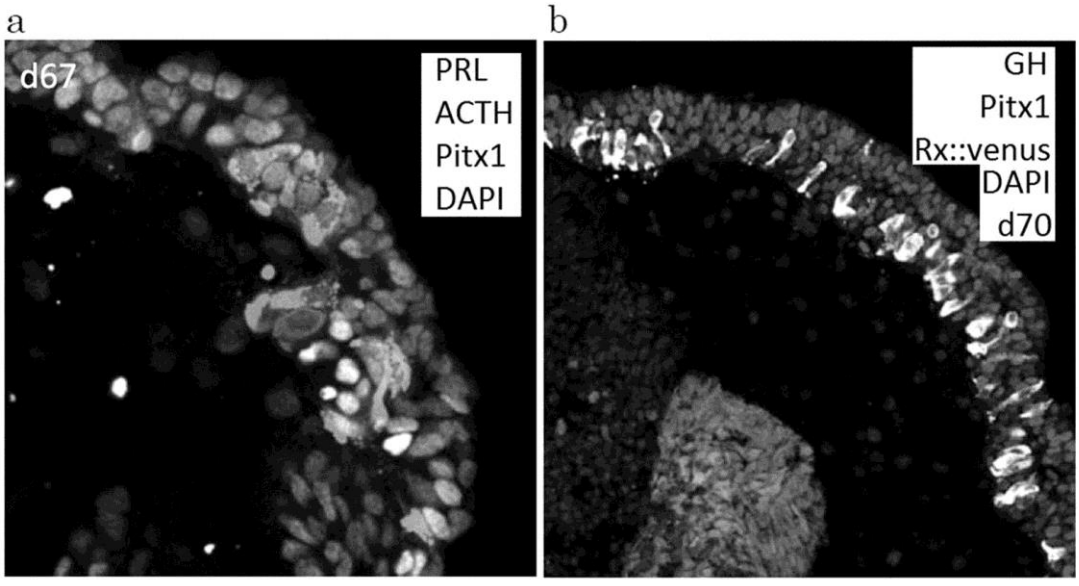

a
d67
PRL
ACTH
Pitx1
DAPI
b
GH
Pitx1
Rx::venus
DAPI
d70

Fig. 11

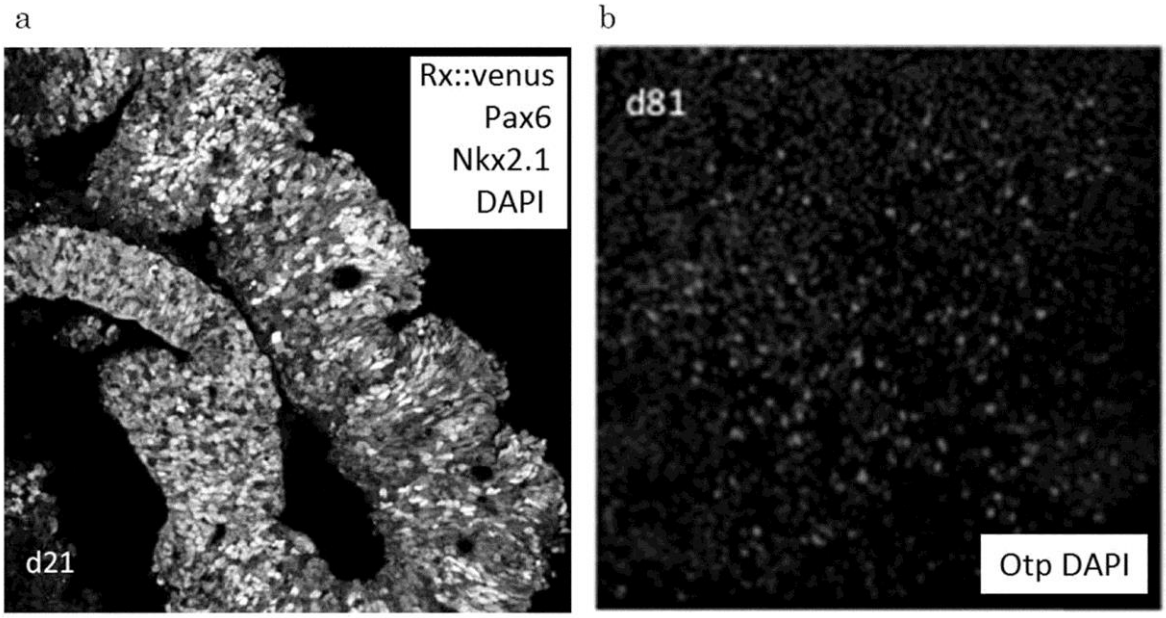

a
b
Rx::venus
Pax6
Nkx2.1
DAPI
d21
d81
Otp DAPI

Fig. 12

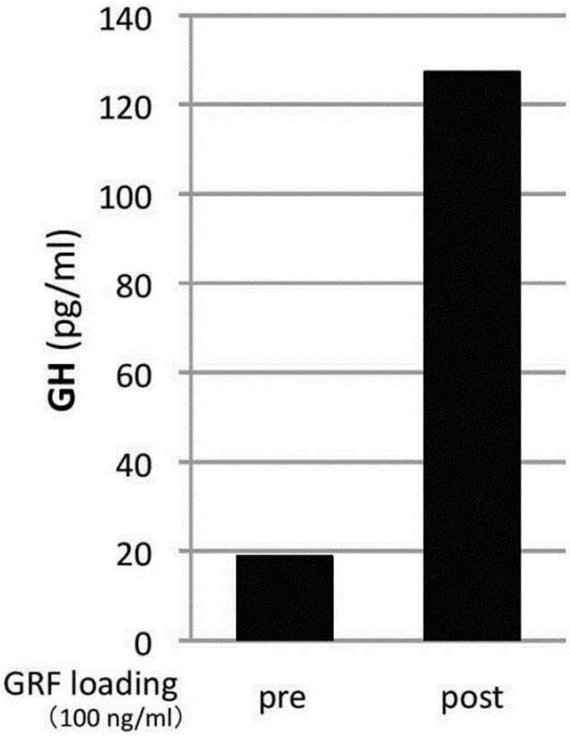
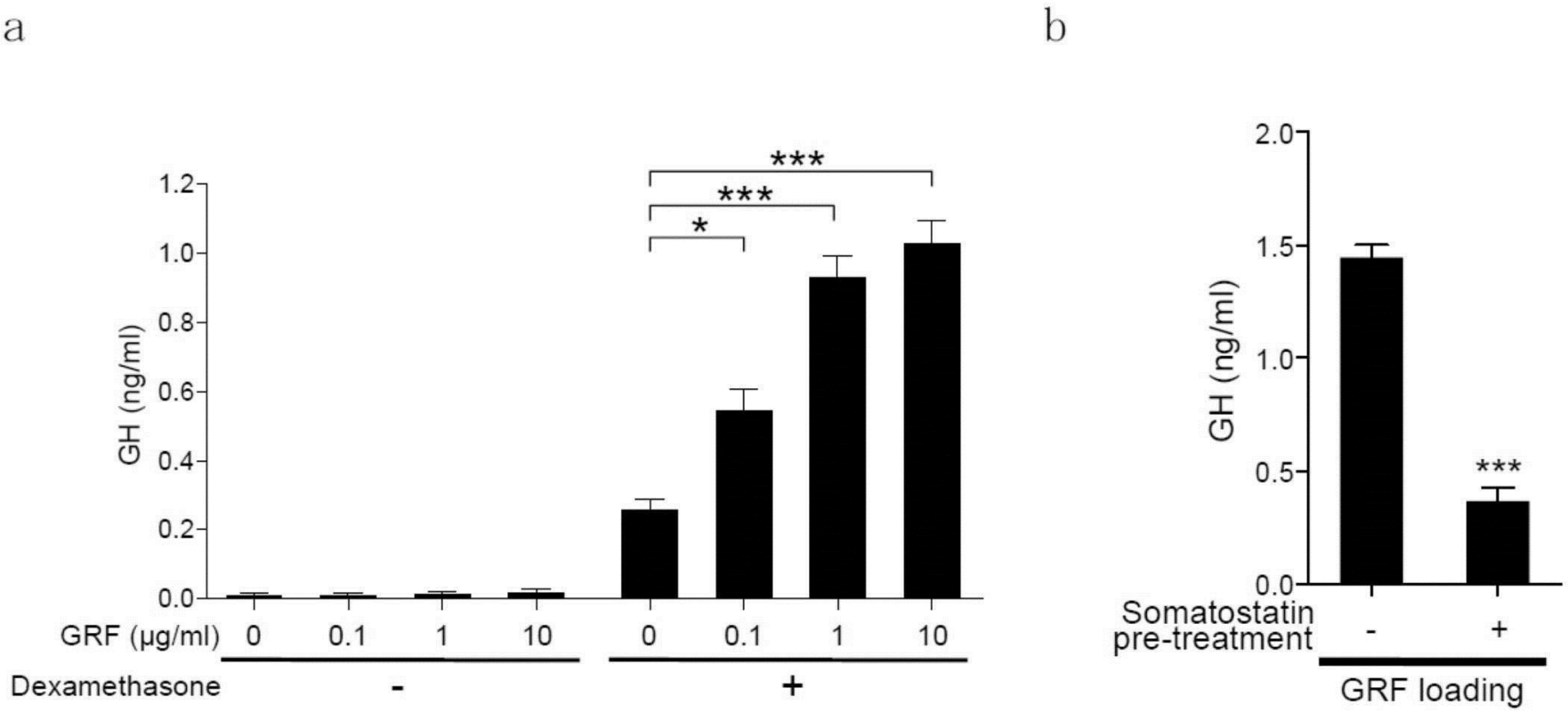

140
120
100
80
60
40
20
0
GH (pg/ml)
GRF loading
(100 ng/ml)
pre
post

Fig. 13


a
b
GH (ng/ml)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
***
***
*
GRF (μg/ml) 0 0.1 1 10 0 0.1 1 10
Dexamethasone - +
2.0
1.5
1.0
0.5
0.0
***
Somatostatin pre-treatment - +
GRF loading

5

10

Fig. 14

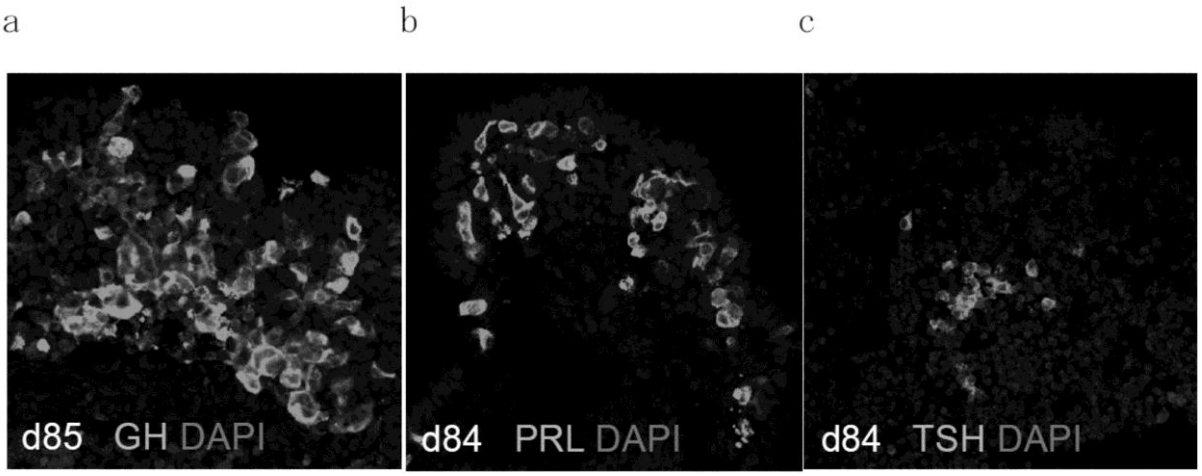
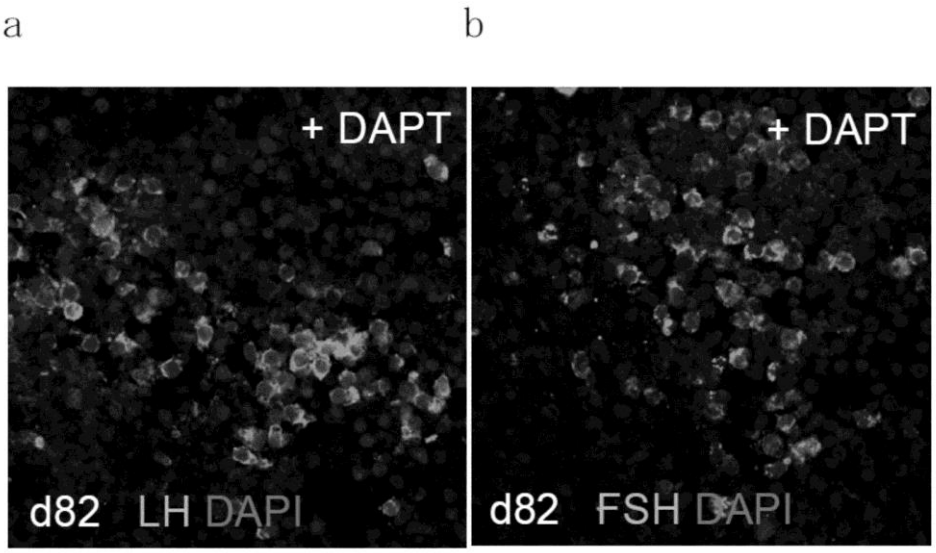

a
b
c
d85 GH DAPI
d84 PRL DAPI
d84 TSH DAPI

Fig. 15


a
b
+ DAPT
+ DAPT
d82 LH DAPI
d82 FSH DAPI