Table S1

Wt fibroblasts	*Fanca*$^{-/-}$ fibroblasts	*Fanca*$^{-/-}$ iPSC
40, XY [18] (P2)	40, XY [18] (P2) 4 cells contained a total of 3 chromatid breaks, 2 chromatid gaps, 1 chromosome gap and 2 marker chromosomes	40, XY [15] / 39, X, -Y [2] (P4)
40, XX [16] (P2)	40, XX [11] (P2)	40, XY [15] / 41, XYY [3](P5)
40, XX [20] (P3)	40, XY [16] (P2) 5 cells contained breakage, with a total of 13 chromatid breaks, 5 chromatid gaps, 3 double minutes, and 1 marker chromosome	40, XY [16] / 39, X, -Y [3] (P6)
40, XY [20] (P3) 2 cells exhibited a chromosome break	40, XY [20] (P3) Chromosome breaks in 6 cells, 1 cell contained an acentric chromosome fragment	39, X [20] (P6)
		39, X [18] / 39, X, add(3) [2] (P7)

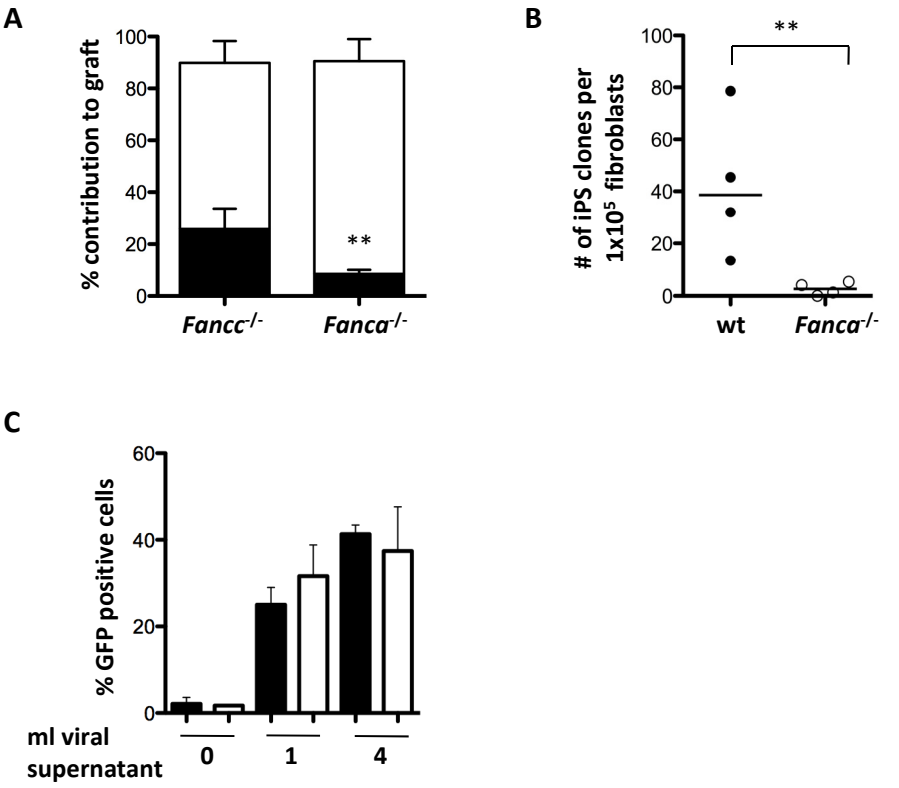
Table S2

Sample #	iPSC clone (passage #)	CHG result
1	WT 1 + GFP (6)	Chromosome 1: 49 kb gain Start: 173444942 End: 173493944 Chromosome 14: 205 KB gain Start: 69877295 End: 70082914
2	WT 2 + GFP (6)	No significant aberration
3	*Fanca*$^{-/-}$ + GFP (5)	Chromsome 4: 152089 KB loss Start: 3463864 End: 1.56E+08 Chromsome 14: 115837 KB loss Start: 8670652 End: 1.25E+08 Chromosome 17: 90580 KB loss Start: 3119246 End: 93699798
4	*Fanca*$^{-/-}$ + GFP (4)	No significant aberration
5	*Fanca*$^{-/-}$ + GFP (4)	No significant aberration
6	*Fanca*$^{-/-}$ + FANCA (4)	Chromosome 2: 3474 KB loss Start: 39924441 End: 43399236 Chromosome 19: 3599 KB loss Start: 20414325 End: 24013487
7	*Fanca*$^{-/-}$ + FANCA (4)	No significant aberration
8	*Fanca*$^{-/-}$ + FANCA (4)	No significant aberration

Table S3

Clone #	Normal donor iPSC	FANC-A + *FANCA* iPSC
1	46 XY [20]	46 XY [20]
2	46, XY [20]	46 XY [18]
3	46 XY [20]	46 XY [20]

Figure S1


A
% contribution to graft
100
80
60
40
20
0
**
Fancc-/-
Fanca-/-
B
# of iPS clones per 1x10^5 fibroblasts
**
wt
Fanca-/-
C
% GFP positive cells
60
40
20
0
ml viral supernatant
0
1
4

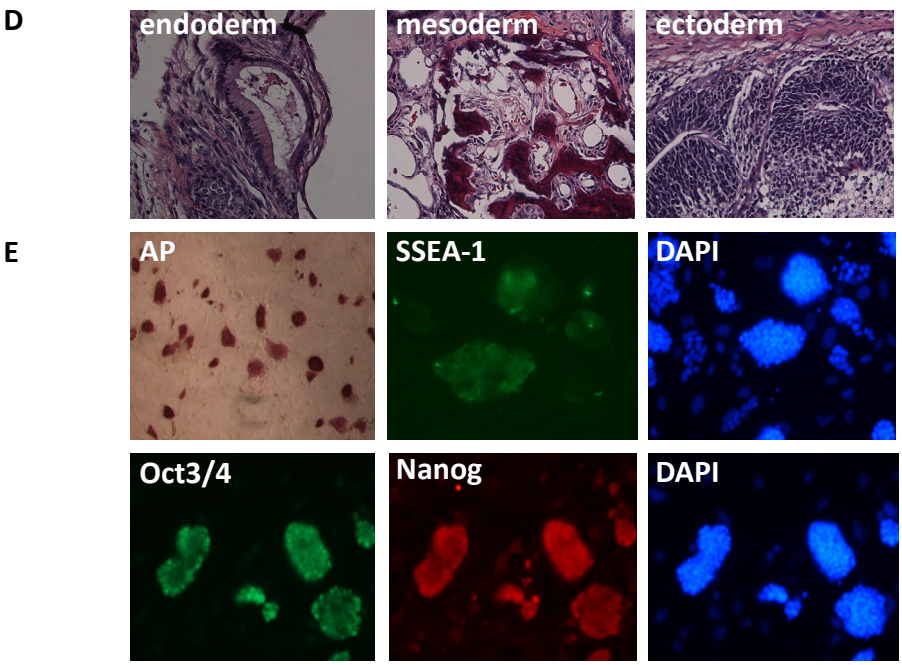
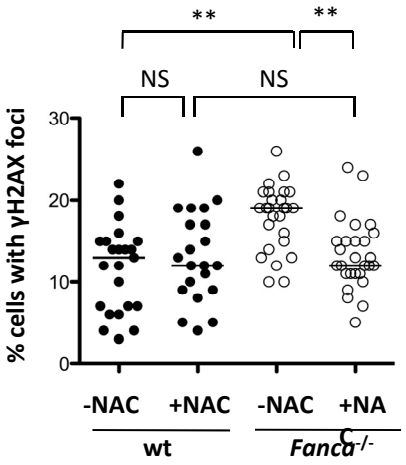

D
endoderm
mesoderm
ectoderm
E
AP
SSEA-1
DAPI
Oct3/4
Nanog
DAPI

Figure S2

A


**
**
NS
NS
% cells with γH2AX foci
30
20
10
0
-NAC
+NAC
-NAC
+NAC
wt
Fanca-/-

B

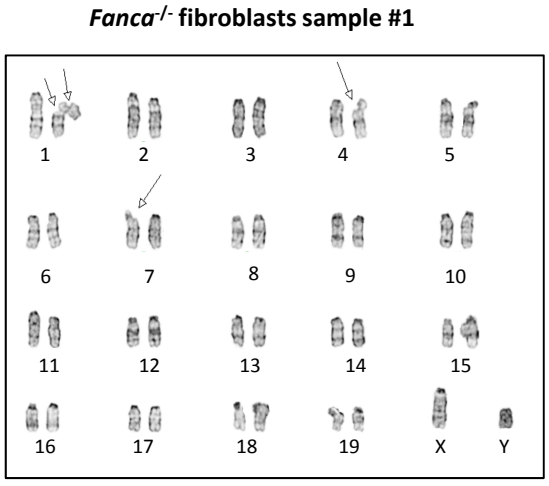
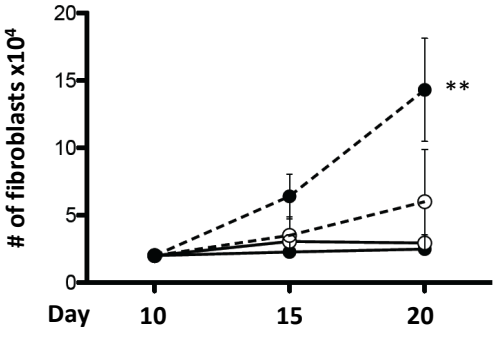
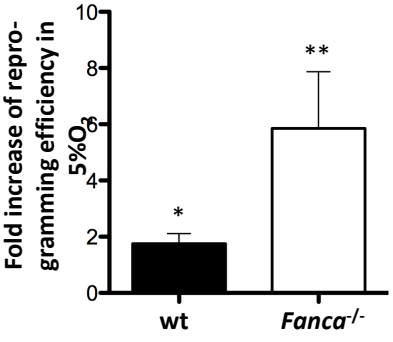

Fanca-/- fibroblasts sample #1
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
X
Y

Figure S3

A



B



C

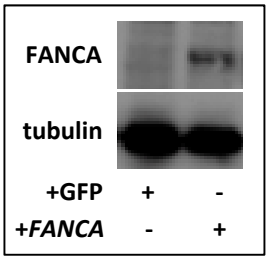
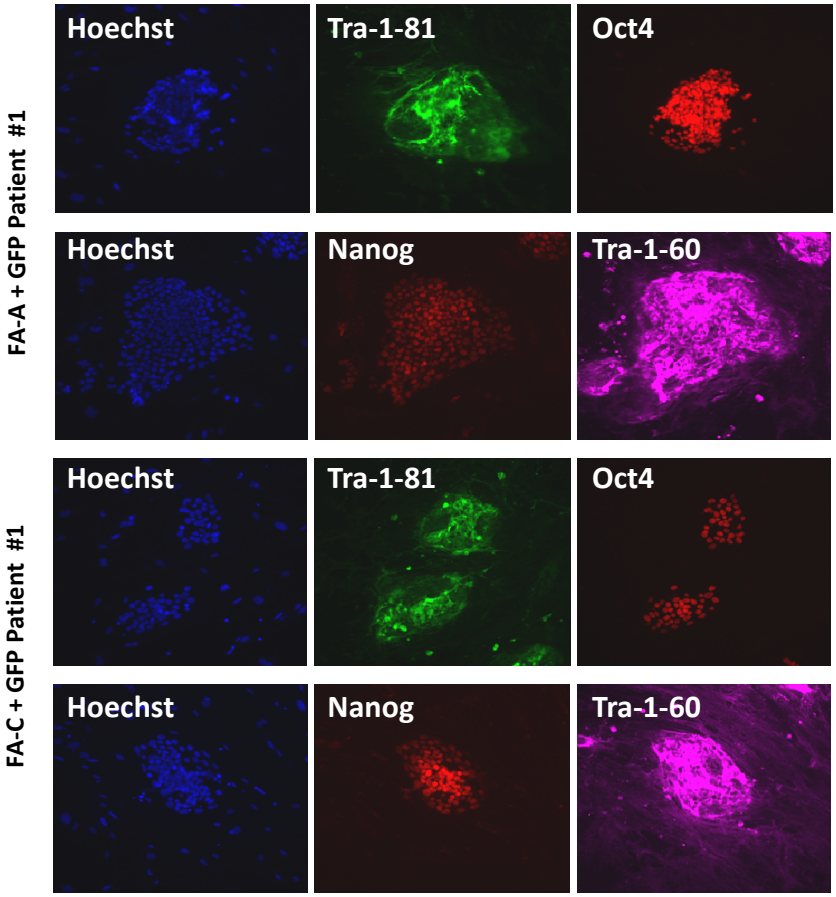


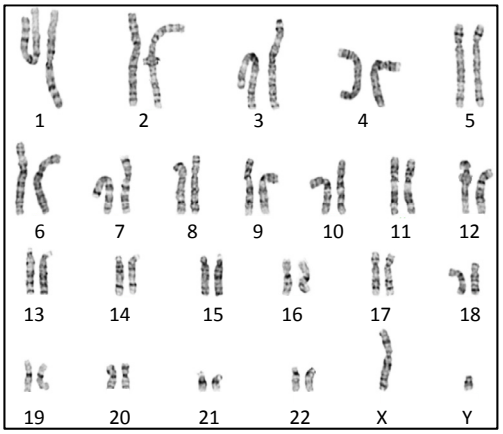
Figure S4

A



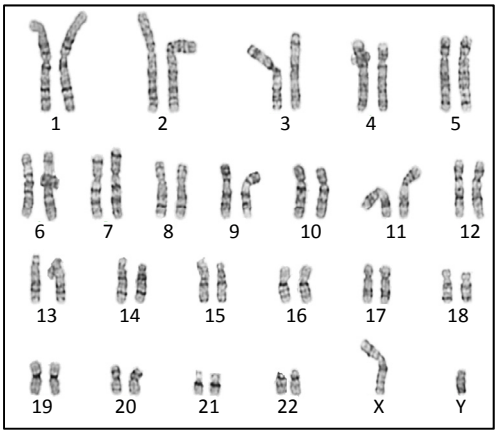
B

Normal donor iPSC clone #1



C

FA-A+ FANCA iPSC#2



Supplemental Legends

Table S1: **Summary of karyotype analyses of fibroblasts and iPSC lines**. Number of metaphases analyzed and passage number are indicated in brackets.

Table S2: Comparative genomic hybridization (CGH) of murine fibroblasts and resultant iPSC. DNA extracted from the starting fibroblast population and resultant iPSC was assessed for chromosomal imbalances using an oligo-based 44k array platform. Chromosome gains or losses observed in unique samples are denoted.

Table S3: Summary of human iPSC line karyotype analysis. The number of metaphases analyzed is noted in brackets.

Figure S1: **Engraftment, transduction efficiency and teratoma formation**. (A) Competitive repopulation of *Fancc*$^{-/-}$ and *Fanca*$^{-/-}$ low-density mononuclear bone marrow cells. 5x10^5 knock-out test cells (CD45.1) and 5x10^5 wt competitor cells (CD45.1/CD45.2) were co-injected into lethally irradiated wt BL-6 (CD45.2) recipient mice. The figure shows the mean percentage of test (solid black bars) and competitor cell (open white bars) chimerism in the graft at eight weeks post-transplantation (±SD. *Fancc*$^{-/-}$: n=36 mice; *Fanca*$^{-/-}$: n=19 mice). **P<0.01 for the comparison between *Fancc*$^{-/-}$ and *Fanca*$^{-/-}$ chimerism (Wilcoxon rank-sum test). (B) Reprogramming efficiency of 1x10^5 wt or *Fanca*$^{-/-}$ TTF reprogrammed in the absence of c-Myc (Okt3/4, Sox2, Klf4). (C) Assessment of retroviral transduction efficiency. Wt (black bars) and *Fanca*$^{-/-}$ (open bars) tail-tip fibroblasts were transduced with an eGFP-encoding retrovirus at the time of reprogramming. Percentage of GFP+ fibroblasts was determined after 48hrs by FACS analysis (n=3, ±SD). (D) Hematoxylin-eosin stains of teratomas obtained by subcutaneous injection of *Fancc*$^{-/-}$ iPS cells (4x and 20x magnification). (E) Immunofluorescence demonstrating the expression of pluriotency markers in *Fanca*$^{-/-}$ iPSC. SD: Standard deviation

Figure S2: ***Fanca*$^{-/-}$ tail-tip fibroblasts contain increased chromosome breaks**. (A) Median percentage of tail-tip fibroblasts containing ≥ 5 γH2AX four days after the infection with the reprogramming viruses. NAC: N-acetylcysteine (100 μM). (B) Example of *Fanca*$^{-/-}$ fibroblast karyogram displaying chromosome breaks prior to reprogramming. **p< 0.01, NS: not significant

Figure S3: Hypoxia enhances fibroblasts growth and reprogramming. (A) Growth rate of wt and *Fanca*$^{-/-}$ fibroblasts between days 10-20 post derivation in 21% and 5%O_2. Solid line: 21%O_2, broken line: 5%O_2, solid circle: Wt, open circle: *Fanca*$^{-/-}$ (n=9, ±SEM. **p<0.01 for comparison of cell number at 5% and 21%O_2 in wt). (B) Fold increase of iPS reprogramming efficiency in 21% or 5% O_2 (wt: n=18; *Fanca*$^{-/-}$ n=14 independent reprogramming experiments, *P<0.05, **P<0.01 for the comparison of 21% vs. 5%O_2). (C) FANCA expression as demonstrated by immunoblot in *Fanca*$^{-/-}$ iPS clones that were control transduced with eGFP or complemented with *FANCA*.

Figure S4: **Human Fanconi anemia iPSC are pluripotent**. (A) Immunofluorescence of uncomplemented patient-derived FA-A and FA-C iPSC. (B) Karyogram of a complemented patient-derived FA-A iPSC line.