Figure S1

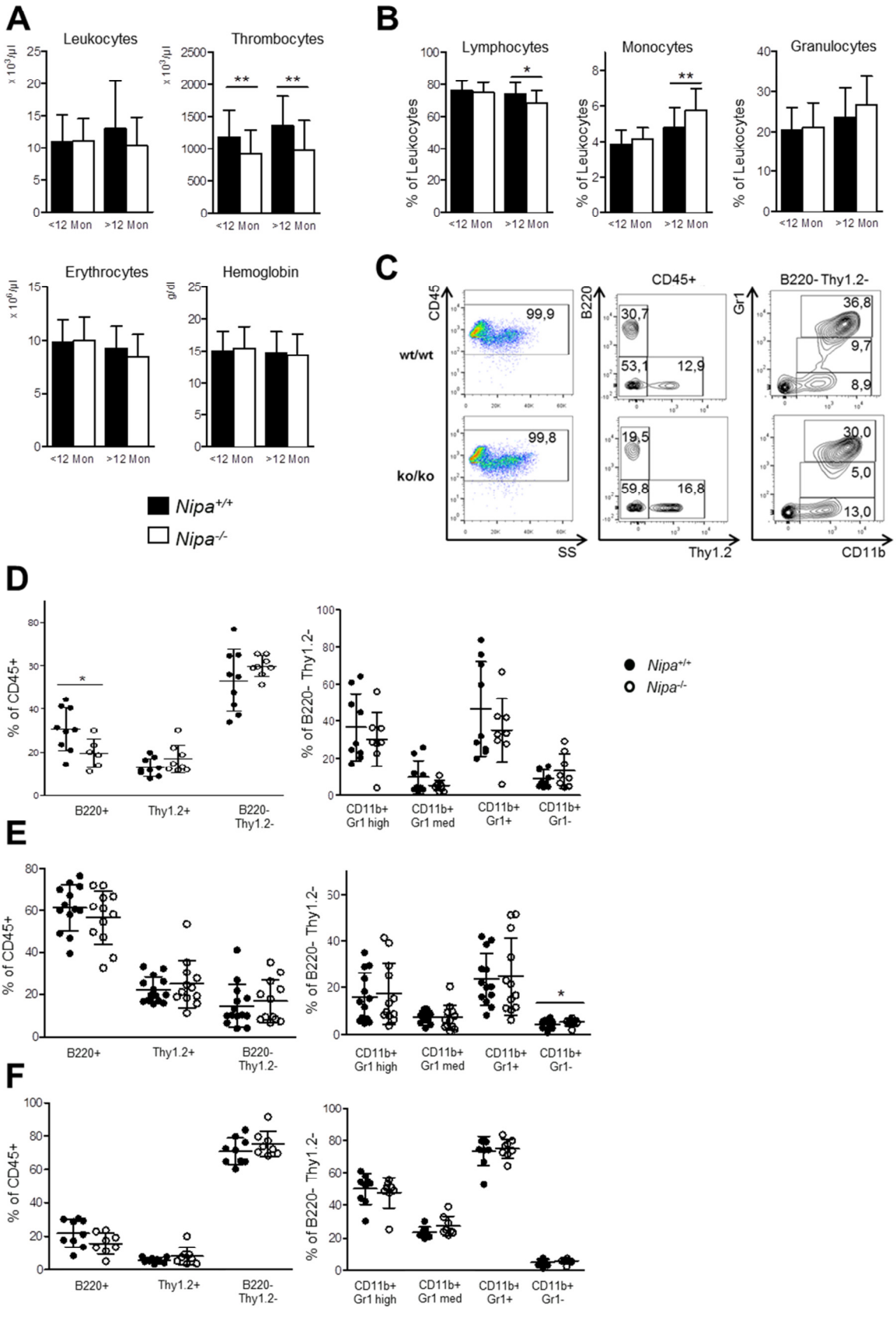
A
Leukocytes
Thrombocytes
Erythrocytes
Hemoglobin
<12 Mon
>12 Mon
B
Lymphocytes
Monocytes
Granulocytes
% of Leukocytes
C
CD45
SS
wt/wt
ko/ko
99,9
99,8
B220
Thy1.2
CD45+
30,7
53,1
12,9
19,5
59,8
16,8
Gr1
CD11b
B220- Thy1.2-
36,8
9,7
8,9
30,0
5,0
13,0
Nipa+/+
Nipa-/-
D
% of CD45+
B220+
Thy1.2+
B220- Thy1.2-
% of B220- Thy1.2-
CD11b+ Gr1 high
CD11b+ Gr1 med
CD11b+ Gr1+
CD11b+ Gr1-
E
F

Fig. S1, related to Fig. 1:

A) Blood counts of *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice younger and older than 12 months. n(*Nipa*$^{+/+}$)=32, n(*Nipa*$^{-/-}$)=30.

B) Percentages of lymphocytes, monocytes and granulocytes within leukocytes of *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice younger and older than 12 months. n(*Nipa*$^{+/+}$)=32, n(*Nipa*$^{-/-}$)=30.

C) Representative flow cytometry gating strategy of hematopoietic lineages in PB of 17-27-month-old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice.

D) Hematopoietic lineages determined by flow cytometry in PB of 17-27 months old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice. n(*Nipa*$^{+/+}$)≥6, n(*Nipa*$^{-/-}$)≥5.

E) Hematopoietic lineages determined by flow cytometry in spleen cells of 17-27 months old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice. n(*Nipa*$^{+/+}$)=12, n(*Nipa*$^{-/-}$)=13.

F) Hematopoietic lineages determined by flow cytometry in BMCs of 17-27 months old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice. n(*Nipa*$^{+/+}$)=9, n(*Nipa*$^{-/-}$)≥7.

A p-value less than 0.05 was considered significant. *p<0.05; **p<0.01. An unpaired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean ±SD.

Figure S2

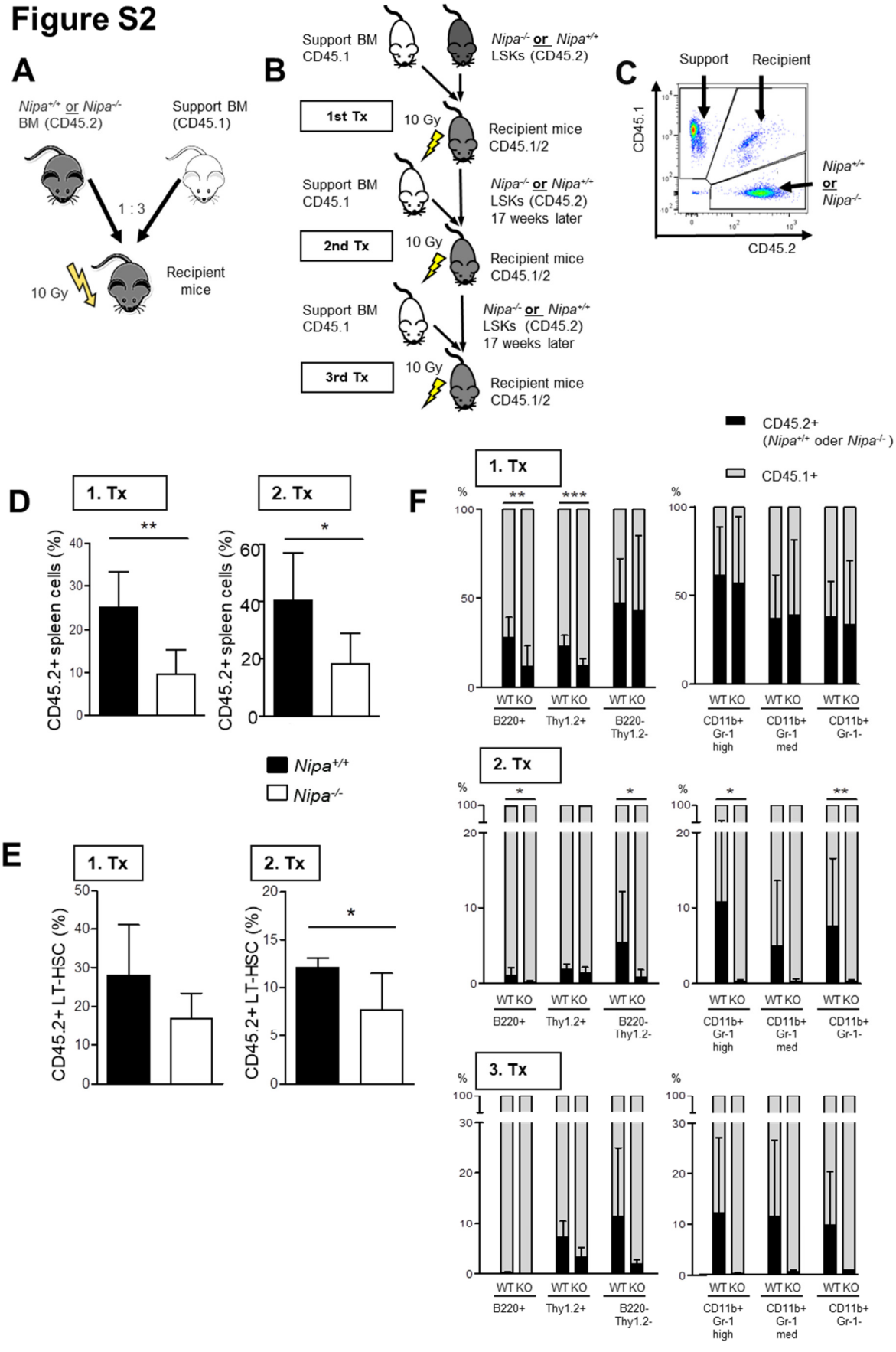
A
Nipa+/+ or Nipa-/- BM (CD45.2)
Support BM (CD45.1)
1 : 3
10 Gy
Recipient mice
B
Support BM CD45.1
Nipa-/- or Nipa+/+ LSKs (CD45.2)
1st Tx
10 Gy
Recipient mice CD45.1/2
Support BM CD45.1
Nipa-/- or Nipa+/+ LSKs (CD45.2) 17 weeks later
2nd Tx
10 Gy
Recipient mice CD45.1/2
Support BM CD45.1
Nipa-/- or Nipa+/+ LSKs (CD45.2) 17 weeks later
3rd Tx
10 Gy
Recipient mice CD45.1/2
C
Support
Recipient
CD45.1
CD45.2
Nipa+/+ or Nipa-/-
D
1. Tx
2. Tx
CD45.2+ spleen cells (%)
Nipa+/+
Nipa-/-
E
1. Tx
2. Tx
CD45.2+ LT-HSC (%)
F
CD45.2+ (Nipa+/+ oder Nipa-/-)
CD45.1+
1. Tx
2. Tx
3. Tx
WT KO
B220+
Thy1.2+
B220- Thy1.2-
CD11b+ Gr-1 high
CD11b+ Gr-1 med
CD11b+ Gr-1-

Fig. S2, related to Fig. 2:

A) Scheme of competitive BM Tx assay. CD45.2^{+} *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ BMCs were mixed with CD45.1^{+} wt BMCs (test:support = 1:3) and transplanted into lethally irradiated CD45.2 positive recipient mice.

B) Scheme of serial LSK Tx assay. Briefly, 2000 CD45.2^{+} *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ LSKs were mixed with 300000 CD45.1^{+} wt BMCs and transplanted into lethally irradiated CD45.1/CD45.2 double positive recipient mice. LSKs were isolated after 17 weeks for the second and after another 17 weeks for the third serial Tx.

C) Representative flow cytometry profile of PB chimerism of transplanted recipient mice of serial LSK Tx.

D) Percentage of donor-derived spleen cells analyzed by flow cytometry at the end of the first and second serial LSK Tx assay. 1st Tx: n(*Nipa*$^{+/+}$)=6, n(*Nipa*$^{-/-}$)=6. 2nd Tx: n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=5.

E) Percentage of donor-derived LT-HSCs analyzed by flow cytometry at the end of first and second serial LSK Tx assay. 1st Tx: n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=2. 2nd Tx: n(*Nipa*$^{+/+}$)=7, n(*Nipa*$^{-/-}$)=9.

F) Relative compositions of B- (B220+), T- (Thy1.2+), myeloid (B220-/Thy1.2-) cell (left) and immature (CD11b+/Gr-1^{intermediate}) and mature (CD11b+/Gr-1^{high}) granulocyte as well as monocyte (CD11b+/Gr-1-) (right) chimerism in PB cells of recipient mice at the end of serial LSK Tx analyzed by flow cytometry. 1st Tx: n(*Nipa*$^{+/+}$)=8, n(*Nipa*$^{-/-}$)=8. 2nd Tx: n(*Nipa*$^{+/+}$)=8, n(*Nipa*$^{-/-}$)=12. 3rd Tx: n(*Nipa*$^{+/+}$)=5, n(*Nipa*$^{-/-}$)=2.

A p-value less than 0.05 was considered significant. *p<0.05; **p<0.01; ***p<0.001. An unpaired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S3

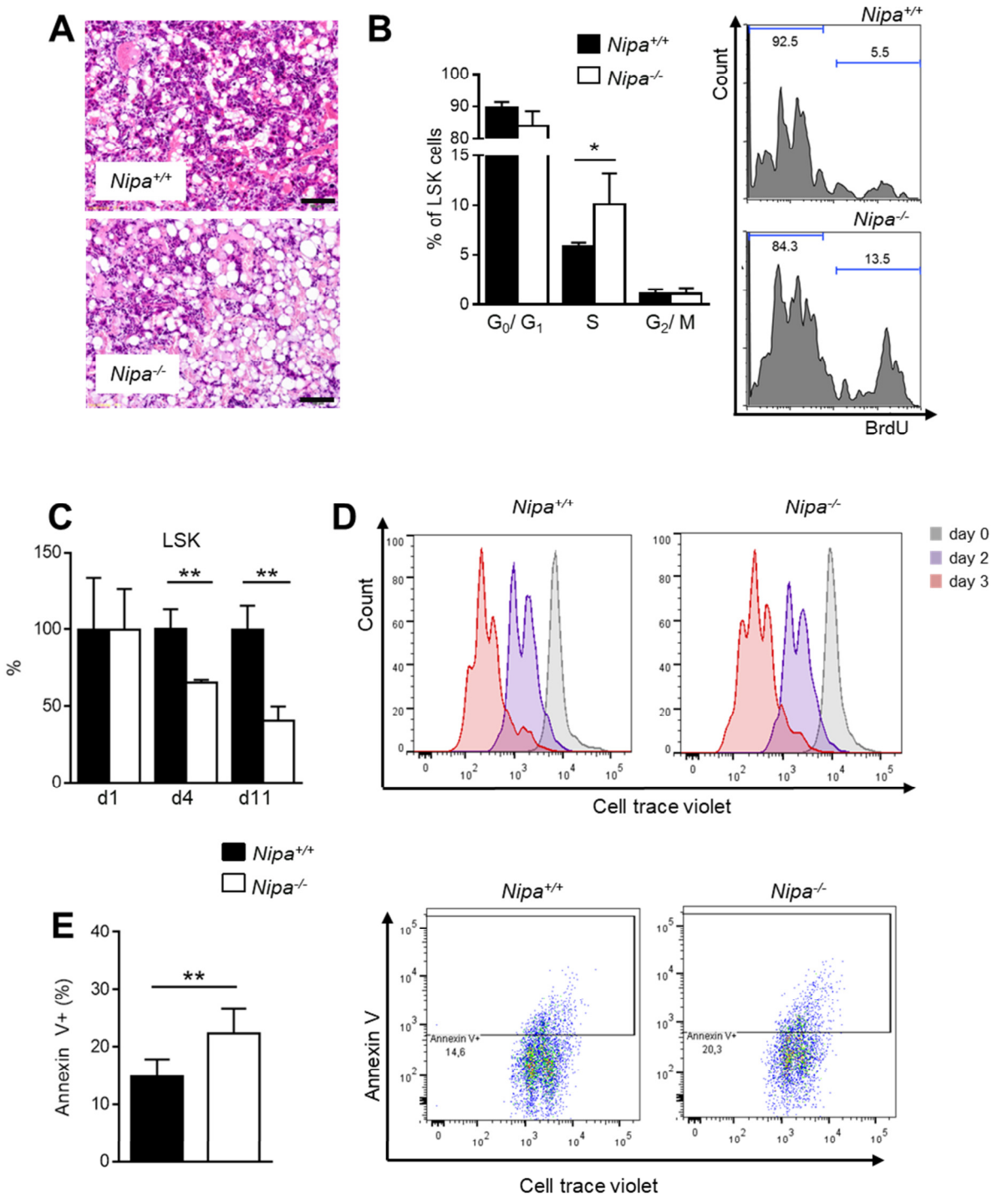

Fig. S3, related to Fig. 2:

A) Representative H&E staining of BM sections of 8 months old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice after 5-FU treatment day -10 and -3. 10x magnification. Scale bar represents 100 µm.

B) Cell cycle analysis of *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ LSKs after 5-FU activation day -5, measured by labeling with BrdU and PI. Representative flow cytometry profile on the right. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=4.

C) Absolut number of LSK cells harvested from *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice after 5-FU administration (i.p.) at indicated time points (days). Wildtype LSKs are set to 100%. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=4.

D) Representative flow cytometry profile of LSK cells isolated from *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice 24 hours after 5-FU administration (i.p.) and labeling with cell trace violet. Analysis was done at day 0, 2 and 3 of *ex vivo* culture. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=4.

E) Percentages of apoptotic cells (Annexin V+) within the LSK population isolated from *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice after 5-FU administration (i.p., day -1) and culture *ex vivo* for 4 days. Representative flow cytometrie profile on the right. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=4.

A p-value less than 0.05 was considered significant. *p<0.05. An unpaired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S4

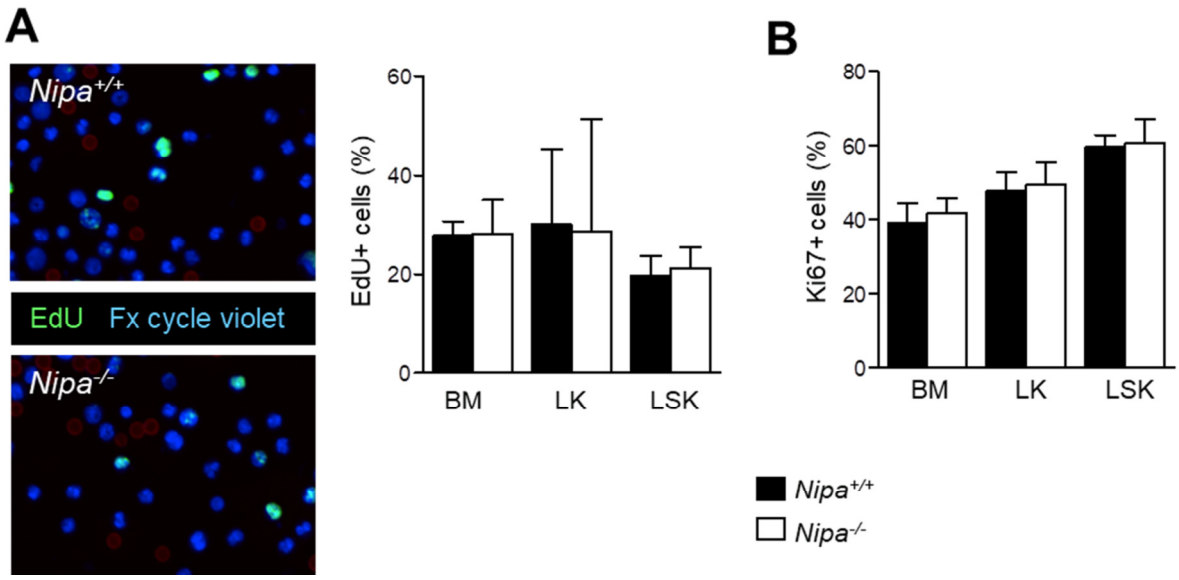

Fig S4, related to Fig. 2:

A) Cell cycle image cytometry analysis of EdU/ FxCycleViolet staining of BMCs, LK and LSK cells of 21-27 month old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice. Representative ScanR microscopy (left) and quantitative analysis of EdU+ cells (right). n(*Nipa*$^{+/+}$)=8, n(*Nipa*$^{-/-}$)=5.

B) Image cytometry analysis of Ki67 staining of BMCs, LK and LSK cells of 21-27 month old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice. n(*Nipa*$^{+/+}$)=8, n(*Nipa*$^{-/-}$)=5.

A p-value less than 0.05 was considered significant. An unpaired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S5

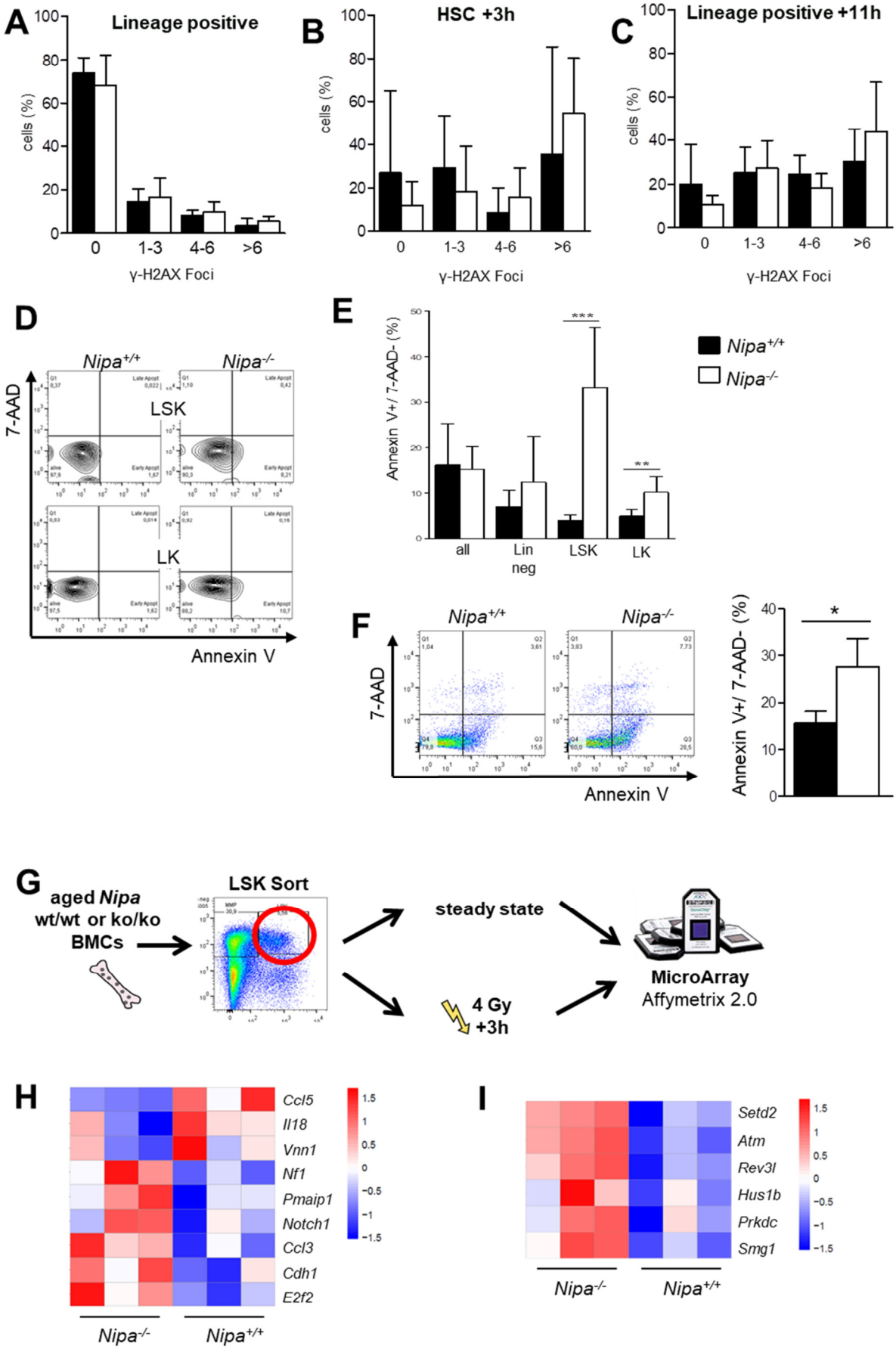
A
Lineage positive
cells (%)
γ-H2AX Foci
B
HSC +3h
C
Lineage positive +11h
D
Nipa+/+
Nipa-/-
LSK
LK
7-AAD
Annexin V
E
Annexin V+/ 7-AAD- (%)
all
Lin neg
LSK
LK
F
G
aged Nipa wt/wt or ko/ko BMCs
LSK Sort
steady state
4 Gy +3h
MicroArray
Affymetrix 2.0
H
Ccl5
Il18
Vnn1
Nf1
Pmaip1
Notch1
Ccl3
Cdh1
E2f2
I
Setd2
Atm
Rev3l
Hus1b
Prkdc
Smg1

Fig. S5, related to Fig. 3:

A) Immunofluorescence for γ-H2AX foci in aged (11-18 months) *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ lineage positive cells. n(*Nipa*$^{+/+}$)=326, n(*Nipa*$^{-/-}$)=358.

B) Immunofluorescence for γ-H2AX foci in 8 months old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ HSCs 3 hours after 4 Gy IR. n(*Nipa*$^{+/+}$)=105, n(*Nipa*$^{-/-}$)=280.

C) Immunofluorescence for γ-H2AX foci in 8 months old *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ lineage positive cells 11 hours after 4 Gy IR. n(*Nipa*$^{+/+}$)=228, n(*Nipa*$^{-/-}$)=218.

D) Representative flow cytometry profiles for Annexin V/ 7-AAD staining of LSKs and LKs from *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice older than 20 months.

E) Percentages of early apoptotic cells (Annexin V+/7-AAD-) within hematopoietic subpopulations in aged (>20 months) *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ hematopoietic cells isolated from spleen. n(*Nipa*$^{+/+}$)=8, n(*Nipa*$^{-/-}$)=8.

F) Percentages of early apoptotic cells within donor-derived *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ BMCs of recipient mice at the end of 2nd serial LSK Tx. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=4.

G) Scheme of microarray experimental strategy.

H) Heat map of expression levels of apoptosis related genes between aged (>20 months) 4 Gy irradiated *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ HSCs analyzed by microarray. Color scale represents row Z-score mRNA intensity values.

I) Heat map of expression levels of DNA damage repair related genes between aged (>20 months) untreated *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ HSCs analyzed by microarray. Color scale represents row Z-score mRNA intensity values.

A p-value less than 0.05 was considered significant. *p<0.05; **p<0.01; ***p<0.001. An unpaired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S6

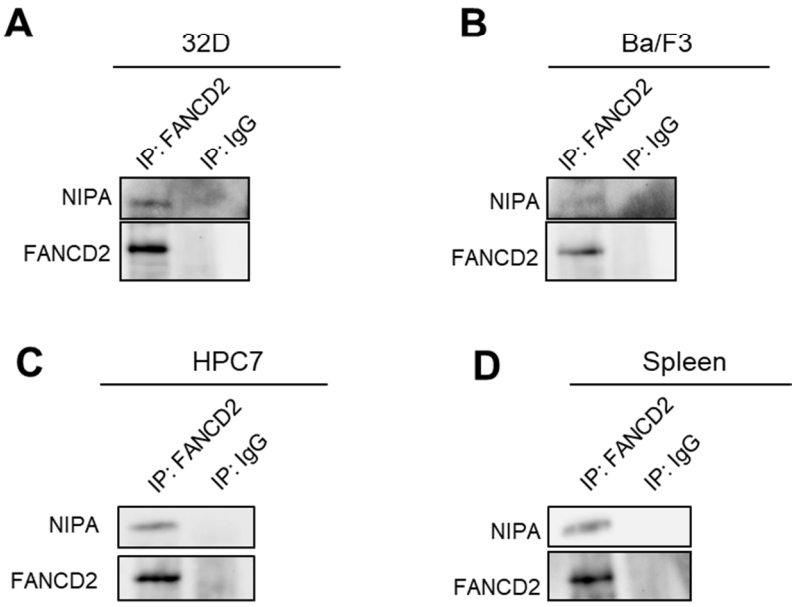

Fig S6, related to Fig. 4:

A) FANCD2-Co-Immunoprecipitation of untreated 32D cells with endogenous levels of NIPA.

B) FANCD2-Co-Immunoprecipitation of untreated Baf3 cells with endogenous levels of NIPA.

C) FANCD2-Co-Immunoprecipitation of untreated HPC7 cells with endogenous levels of NIPA.

D) FANCD2-Co-Immunoprecipitation of untreated *Nipa*$^{+/+}$ spleen cells with endogenous levels of NIPA.

Figure S7

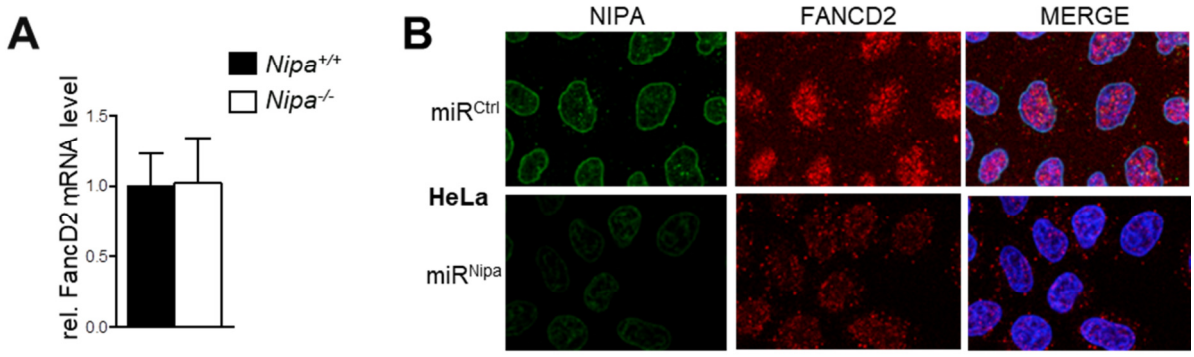

Fig S7, related to Fig. 4:

A) Expression level of *FancD2* in *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs analyzed by real-time PCR. Results were normalized to GAPDH. Data of 3 independent experiments. n(*Nipa*$^{+/+}$)=8, n(*Nipa*$^{-/-}$)=8.

B) Immunofluorescence for FANCD2 in HeLa cells retrovirally transfected with pLMP miR^{Ctrl} or miR^{Nipa}.

A p-value less than 0.05 was considered significant. An unpaired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S8

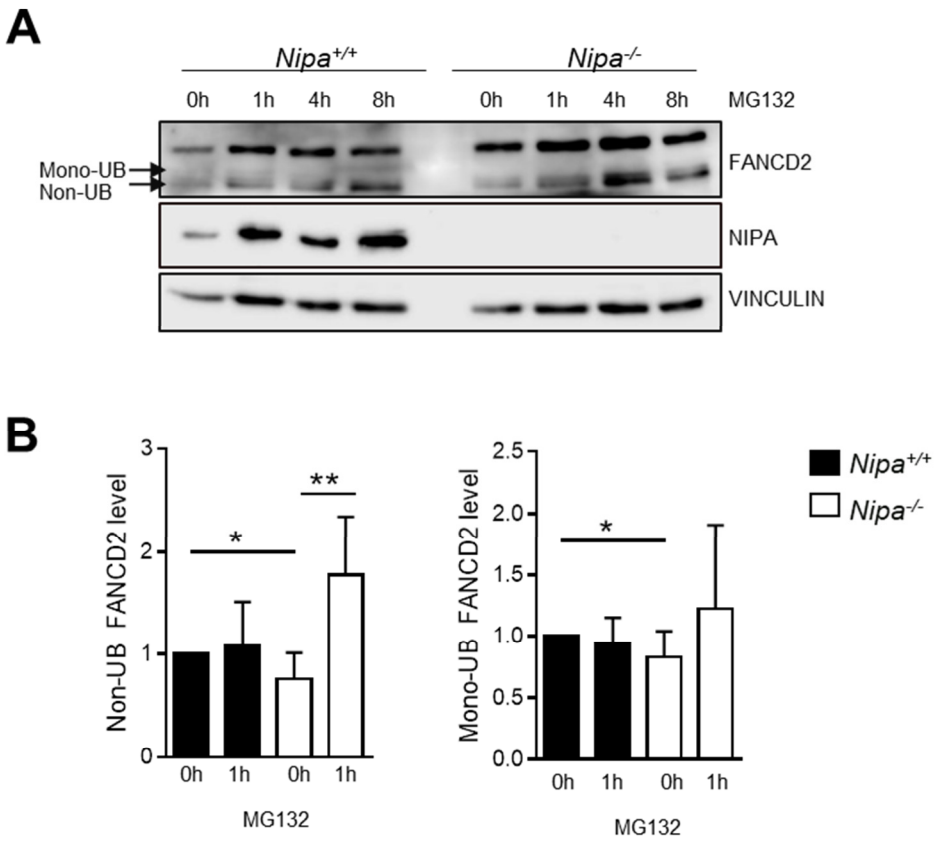

Fig S8, related to Fig. 4:

A) Representative western blot analysis of MG132 treated *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs for FANCD2, NIPA and VINCULIN.

B) Quantification of western blot analysis of non- and mono-ubiquitinated FANCD2 levels of *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs treated with MG132 for indicated time frames. n(*Nipa*$^{+/+}$)=7, n(*Nipa*$^{-/-}$)=7.

A p-value less than 0.05 was considered significant. *p<0.05; **p<0.01. A paired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S9

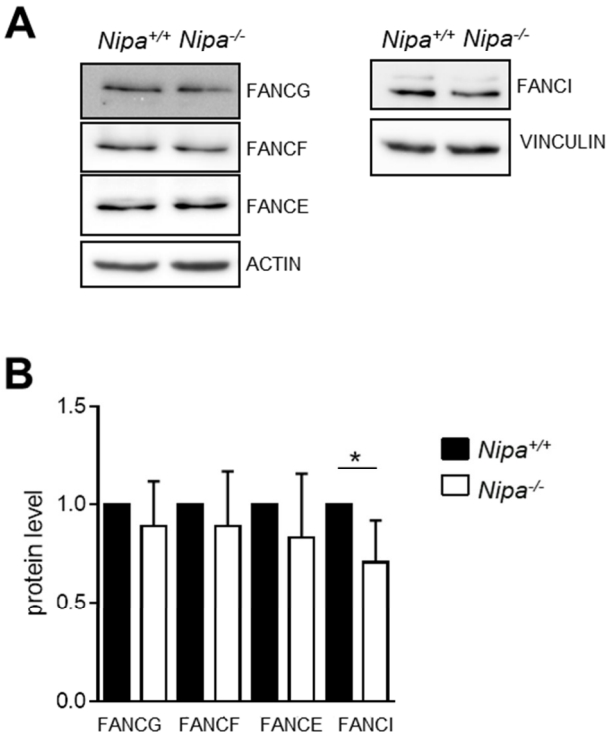

Fig S9, related to Fig. 4:

A) Representative western blot analysis of untreated *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs analysed for FANC proteins.

B) Quantification of western blot analysis of untreated *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs analysed for FANC proteins. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=4.

A p-value less than 0.05 was considered significant. *p<0.05. A paired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S10

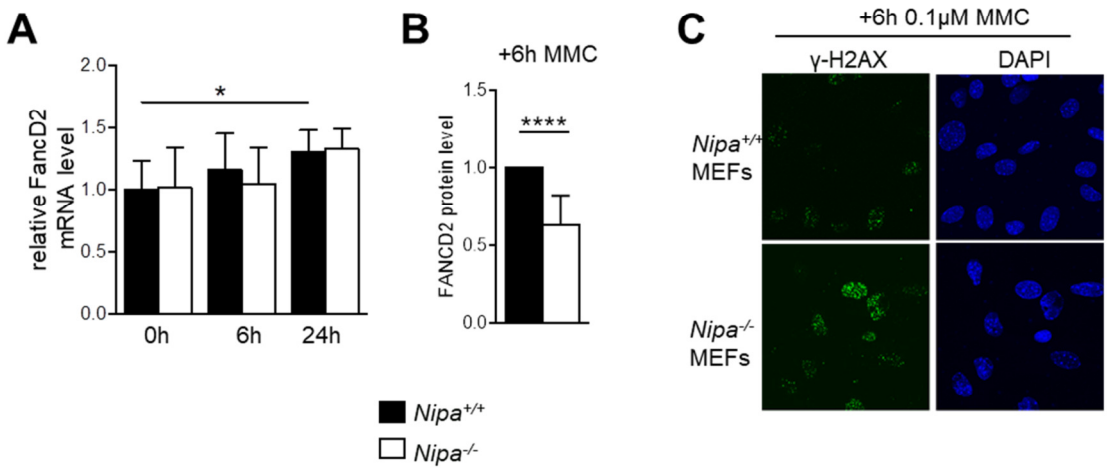

Fig. S10, related to Fig. 5:

A) Expression level of *FancD2* in untreated and MMC treated (0.5μM for 6h and 24h) *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs analyzed by real-time PCR. Results were normalized to GAPDH. Untreated and 6h: n(*Nipa*$^{+/+}$)=8, n(*Nipa*$^{-/-}$)=8. 24h: n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$) =4.

B) Quantification of relative FANCD2 protein levels of *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs). n(*Nipa*$^{+/+}$)=7, n(*Nipa*$^{-/-}$)=7.

C) Immunofluorescence for γ-H2AX foci in untreated and 6h MMC treated (0.1μM) *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs. Representative confocal microscopy images are shown.

A p-value less than 0.05 was considered significant. *p<0.05; ****p<0.0001. An unpaired (S10A) or paired (S10B) paired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S11

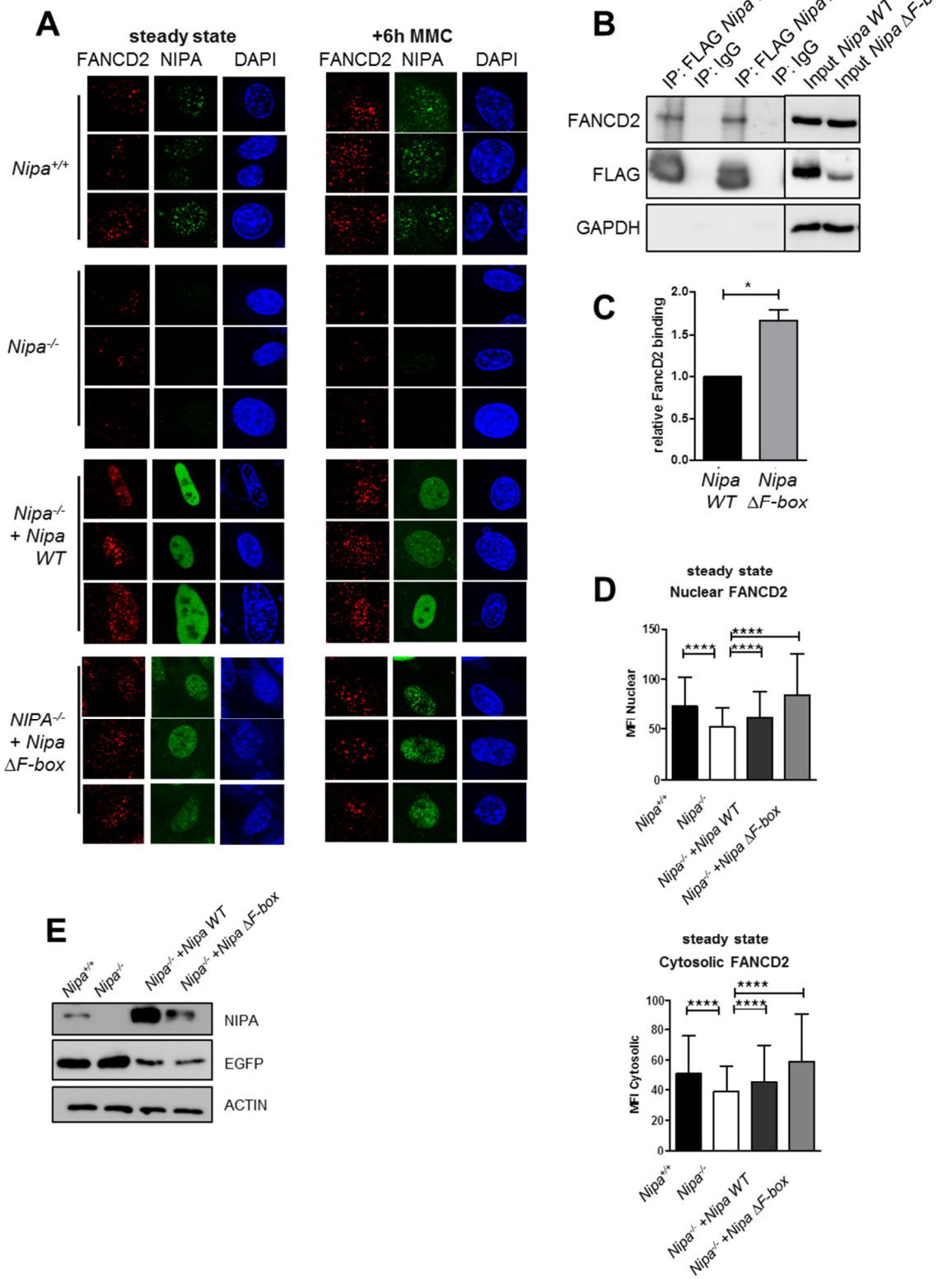
A
steady state
+6h MMC
FANCD2 NIPA DAPI
FANCD2 NIPA DAPI
Nipa+/+
Nipa-/-
Nipa-/- + Nipa WT
NIPA-/- + Nipa ΔF-box
B
IP: FLAG Nipa WT
IP: IgG
IP: FLAG Nipa ΔF-box
IP: IgG
Input Nipa WT
Input Nipa ΔF-box
FANCD2
FLAG
GAPDH
C
relative FancD2 binding
2.0
1.5
1.0
0.5
0.0
*
Nipa WT
Nipa ΔF-box
D
steady state
Nuclear FANCD2
MFi Nuclear
150
100
50
0
****
****
****
Nipa+/+
Nipa-/-
Nipa-/- +Nipa WT
Nipa-/- +Nipa ΔF-box
steady state
Cytosolic FANCD2
MFi Cytosolic
100
80
60
40
20
0
****
****
****
Nipa+/+
Nipa-/-
Nipa-/- +Nipa WT
Nipa-/- +Nipa ΔF-box
E
Nipa+/+
Nipa-/-
Nipa-/- +Nipa WT
Nipa-/- +Nipa ΔF-box
NIPA
EGFP
ACTIN

Fig S11, related to Fig. 6:

A) Immunofluorescence for FANCD2, NIPA and DAPI in untreated and 6 hour MMC (0.5µM) treated *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs retrovirally transfected with pBABE^{NipaWT} or pBABE$^{Nipa\Delta F\text{-}box}$. Additional confocal microscopy images for Figure 6A.

B) Representative Flag-Co-Immunoprecipitation of Phoenix E cells, transiently transfected with Flag-hNIPA WT or Flag-hNIPA ΔF-box.

C) Quantification of Flag-Co-Immunoprecipitation of Phoenix E cells, transiently transfected with Flag-hNIPA WT or Flag-hNIPA ΔF-box. n(Flag-hNIPA WT)=5, n(Flag-hNIPA ΔF-box)=3.

D) Average fluorescence intensity of FANCD2 staining in the nucleus and the cytosol of *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ primary MEFs (no MMC) shown in Fig. 6A, analysed by image cytometrie. Nuclear FANCD2: n(*Nipa*$^{+/+}$)=2039, n(*Nipa*$^{-/-}$)=3257, n(*Nipa*$^{-/-}$ *+Nipa WT*)=1150, n(*Nipa*$^{-/-}$ *+Nipa ΔF-box*)=262. Cytosolic FANCD2: n(*Nipa*$^{+/+}$)=1971, n(*Nipa*$^{-/-}$)=3090, n(*Nipa*$^{-/-}$ *+Nipa WT*)=1123, n(*Nipa*$^{-/-}$ *+Nipa ΔF-box*)=255.

E) *Nipa*$^{+/+}$ or *Nipa*$^{-/-}$ BMCs were retrovirally infected with pMIG^{empty}, pMIG^{NipaWT} or pMIG$^{Nipa\Delta F\text{-}box}$ and used for in vitro CFU assay. Representative western blot analysis of BMCs used for CFU assay shown.

A p-value less than 0.05 was considered significant. *p<0.05; ***p<0.001; ****p<0.0001. A paired two-tailed Student's t-test (S11C) or a nonparametric two-tailed Mann-Whitney test (S11D) was used for statistical analyses. Data are represented as mean +SD.

Figure S12

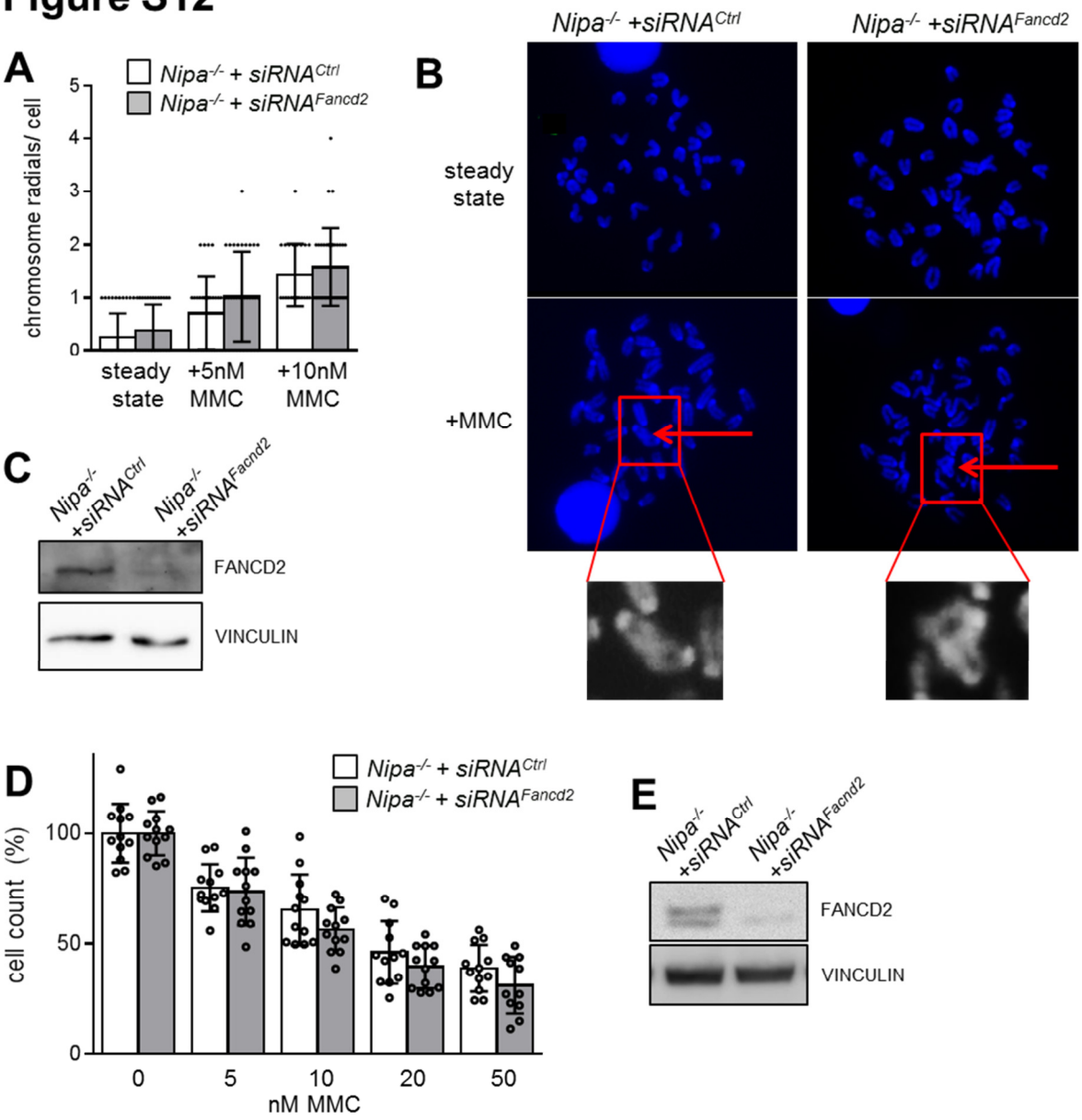

Fig S12, related to Fig. 6:

A) Quantification of chromosome radials per cell of untreated and MMC (5nM and 10 nM) treated *Nipa*$^{-/-}$ spleen cells transfected with siRNA^{Ctrl} or siRNA^{Fancd2}. no MMC: n(*Nipa*$^{-/-}$ +siRNA^{Ctrl})=34, n(*Nipa*$^{-/-}$ +siRNA^{Fancd2})=34. +MMC: n(*Nipa*$^{-/-}$ +siRNA^{Ctrl})=23, n(*Nipa*$^{-/-}$ +siRNA^{Fancd2})=34.

B) Representative images of DAPI stained metaphase spreads of untreated and MMC (5nM) treated *Nipa*$^{-/-}$ spleen cells transfected with siRNA^{Ctrl} or siRNA^{Fancd2}. Arrows indicate chromosome radials.

C) Representative western blot of spleen cells used for metaphase spreads shown in (A) and (B).

D) Cell survival assay of *Nipa*$^{-/-}$ primary MEFs transfected with siRNA^{Ctrl} or siRNA^{Fancd2} measured after 5 days of culture with indicated concentrations of MMC. Data from 3 independent test are shown. n(*Nipa*$^{-/-}$ +siRNA^{Ctrl})=12, n(*Nipa*$^{-/-}$ +siRNA^{Fancd2})=12.

E) Representative western blot of MEFs used for cell survival assay shown in (D).

A p-value less than 0.05 was considered significant. An unpaired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S13

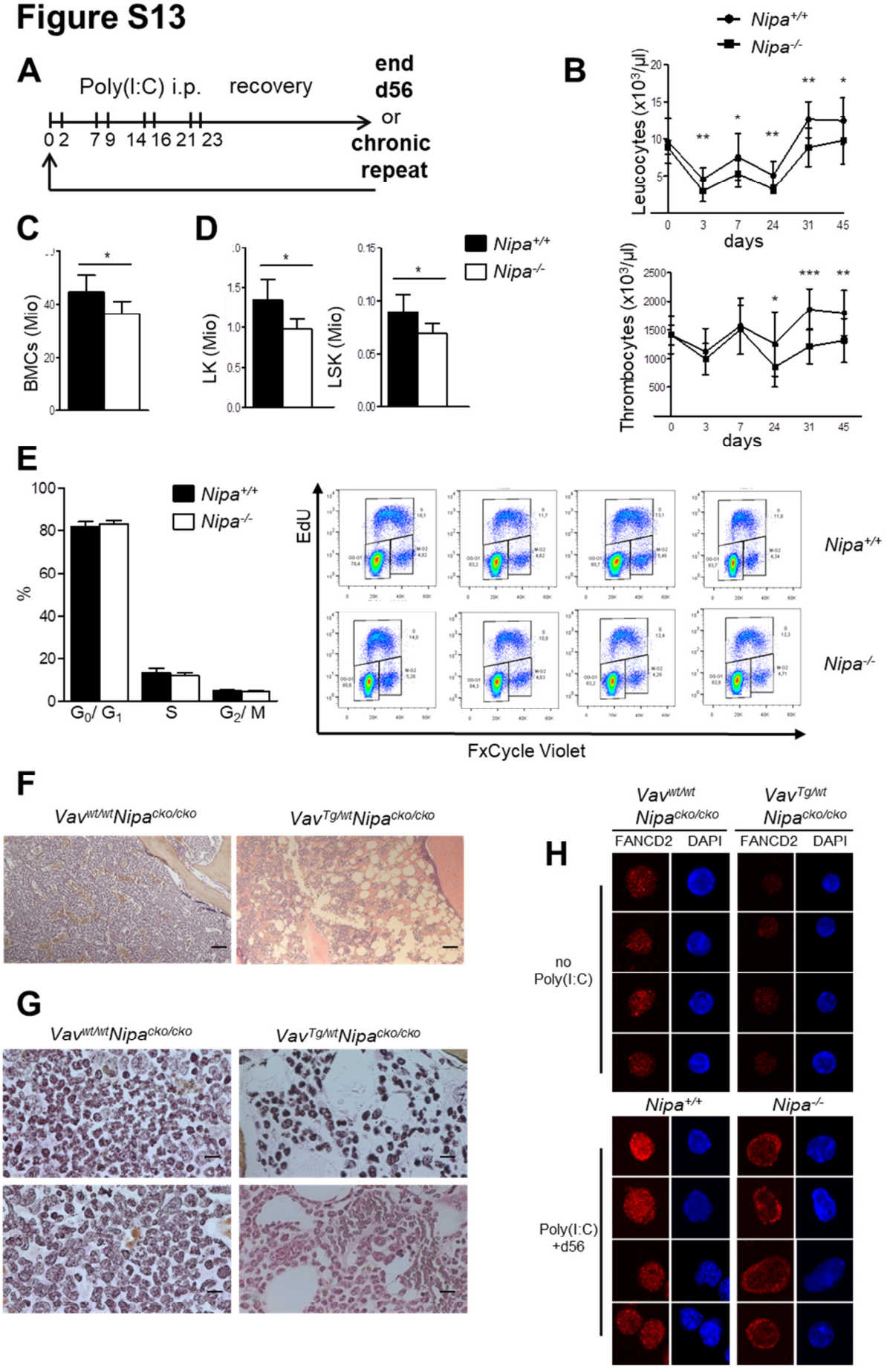
A
Poly(I:C) i.p.
recovery
0 2 7 9 14 16 21 23
end d56 or chronic repeat
B
Nipa+/+
Nipa-/-
Leucocytes (x10³/µl)
days
Thrombocytes (x10³/µl)
C
BMCs (Mio)
D
LK (Mio)
LSK (Mio)
E
%
G0/ G1
S
G2/ M
EdU
FxCycle Violet
F
Vavwt/wtNipacko/cko
VavTg/wtNipacko/cko
G
H
FANCD2
DAPI
no Poly(I:C)
Poly(I:C) +d56

Fig. S13, related to Fig. 7:

A) Scheme of short-term and chronic Poly(I:C) treatment assay. Poly(I:C) was injected i.p. into *Nipa*$^{+/+}$, *Nipa*$^{-/-}$ (short-term), *Vav*$^{wt/wt}$*Nipa*$^{cko/cko}$ and *Vav*$^{Tg/wt}$*Nipa*$^{cko/cko}$ mice (chronic) twice a week for 4 weeks, followed by 4 weeks of recovery time. Mice of short-term assay were analyzed at day 56, for chronic treatment the cycle was repeated.

B) Blood values of *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice (age 3-4 months) treated with Poly(I:C) twice a week for 4 weeks followed by 4 weeks of recovery time. n(*Nipa*$^{+/+}$)=13, n(*Nipa*$^{-/-}$)= 13.

C) BM cellularity of *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice (age 3-4 months) at day 56 after Poly(I:C) treatment. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=6.

D) Percentage of LSK and LK cells in *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ BMCs at day 56 after Poly(I:C) treatment. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=6.

E) Cell cycle flow cytometry analysis of EdU/ FxCycleViolet staining of BMCs harvested from *Nipa*$^{+/+}$ and *Nipa*$^{-/-}$ mice at day 56 after Poly(I:C) treatment. Representative flow cytometrie profiles on the right. n(*Nipa*$^{+/+}$)=4, n(*Nipa*$^{-/-}$)=5.

F) Representative H&E staining of BM sections of *Vav*$^{wt/wt}$*Nipa*$^{cko/cko}$ and *Vav*$^{Tg/wt}$*Nipa*$^{cko/cko}$ mice following regular Poly(I:C) treatment sacrificed when moribund or end of experiment. 10x magnification. Scale bar represents 100 µm.

G) Representative reticulin staining of BM sections of *Vav*$^{wt/wt}$*Nipa*$^{cko/cko}$ and *Vav*$^{Tg/wt}$*Nipa*$^{cko/cko}$ mice following regular Poly(I:C) treatment sacrificed when moribund or end of experiment. 10x magnification. Scale bar represents 100 µm.

H) LSK cells isolated of untreated or Poly(I:C) treated (day 56) mice (age 3-5 months) and stained for FANCD2 (red) and DAPI (blue). Additional confocal microscopy images for Figure 7D.

A p-value less than 0.05 was considered significant. *p<0.05; **p<0.01; ***p<0.001. An unpaired two-tailed Student's t-test was used for statistical analyses. Data are represented as mean +SD.

Figure S14

A

Patient sample	EWOG Study ID	Diagnosis	Karyotype	Germline pre-disposition	Treatment	IHC signal for NIPA
#1		IBMFS	46, XY	Fanconi anemia	Oxymetholon	physiological
#2		IBMFS	46, XY	Fanconi anemia	Wach+wait	physiological
#3		IBMFS	46, XY	Fanconi anemia	Oxymetholon	physiological
#4	D1224**	IBMFS	46, XX	Fanconi anemia	HSCT	physiological
#5		IBMFS	46, XY	Fanconi anemia	-	physiological
#6		IBMFS	46, XY	Fanconi anemia	HSCT	physiological
#7	D1143***	Secondary RCC in IBMFS	46, XY	suspected FA (syndrome; sister FA+)	HSCT	physiological
#8	D1010	Hypocellular RCC	46, XY	GATA2 mut.	HSCT	physiological
#9	D1142	Hypocellular RCC	45,XY, -7	GATA2 mut.	HSCT	physiological
#10	D1072	Hypocellular RCC	45,XX, -7	GATA2 mut.	HSCT	physiological
#11	D1127	Hypocellular RCC	45,XX, -7	SAMD9L mut.	HSCT	physiological
#12	D1160	Hypocellular RCC	46, XY	SAMD9L mut.	HSCT	physiological
#13	D1155	Normocellular RCC	46, XX	RUNX1 mut.	Wach+wait	physiological
#14	D1061	Hypocellular RCC	45,XY, -7	none identified* (syndrome suspected)	HSCT	physiological
#15	D1157	Hypocellular RCC	46, XY	none identified* (syndrome suspected)	HSCT	physiological
#16	D1080	Hypocellular RCC	46, XX	none identified*	IST (good resp)	physiological
#17	D1052	Hypocellular RCC	46, XX	none identified*	HSCT	physiological
#18	D1055	Hypocellular RCC	46, XX	none identified*	HSCT	physiological
#19	D1079	Hypocellular RCC	46, XX	none identified*	HSCT	physiological
#20	D1046	Hypocellular RCC	46, XX	none identified*	HSCT (IST unsuccessful)	physiological
#21	D1132	Hypocellular RCC (hepatitis associated)	46, XX	none identified*	HSCT	reduced
#22	D1187	Hypocellular RCC	46, XX	none identified*	HSCT	reduced
#23	D1201	Hypocellular RCC	46, XY	none identified*	Watch+wait	reduced
#24	D1048	Hypocellular RCC	46, XY	none identified*	HSCT	reduced
#25	D 995	Hypocellular RCC	46, XY	n.d.	HSCT	reduced
#26	D1205	Hypocellular RCC	46, XY	none identified*	HSCT	reduced
#27	D1193	Hypocellular RCC	46, XY	none identified*	Watch+wait	reduced
#28	D1107	Hypocellular RCC	46, XY	none identified*	HSCT	reduced
#29	D1128	Hypocellular RCC	46, XY	none identified*	Watch+wait	reduced
#30	D1030	Hypocellular RCC	46, XX	none identified*	Watch+wait	reduced
#31	D1098	Normocellular RCC	46, XX, del(20q)	none identified*	Watch+wait	reduced

Fig. S14, related to Figure 7:

A) List of patients analyzed for NIPA IHC signal. D-numbers indicate their registration number in the EWOG-MDS study. *none identified = Fanconi anemia, GATA2, SAMD9, SAMD9L, RUNX1 and TP53 mutations excluded **D1224 was included in EWOG-MDS due to secondary MDS after HSCT. At time of IHC, the diagnosis was bone marrow failure. ***D1143 is believed to suffer from FA based on his phenotype and family history (sister suffered from FA). n.d. = not described.