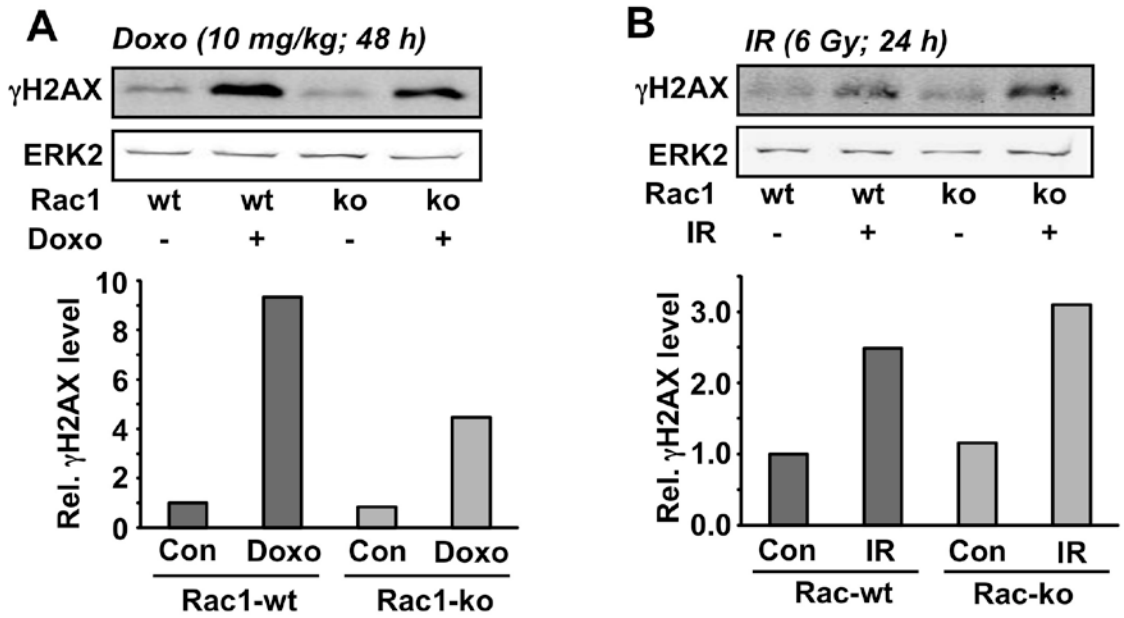
Supplementary Figure S1, Bopp et al



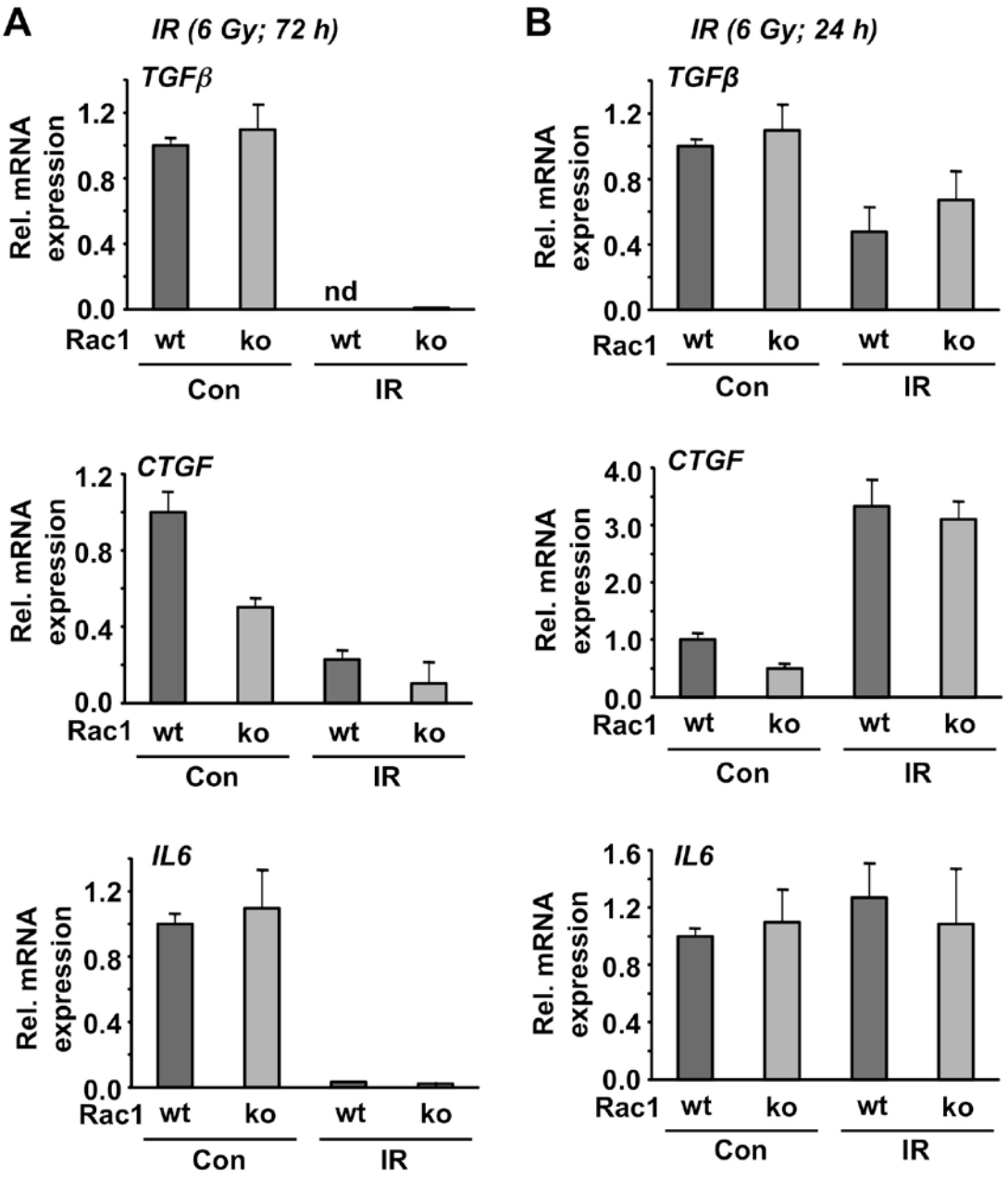
Supplementary Figure S1: Influence of *rac1* knock-out on hepatic DNA damage induction following treatment with doxorubicin

$Rac1^{flox/flox/Mx1\text{-}Cre+}$ mice were left untreated or were treated with poly(I:C) (3 x 0.5 mg) every other day in order to induce Cre-mediated hepatic knock-out of *rac1*. Three weeks later animals were exposed to a single dose of doxorubicin (A) or were irradiated (B). Rac1-wt, mice harbouring wild-type *rac1*; Rac1-ko, mice with recombinational knock-out of the hepatic *rac1* gene. Data shown were obtained from the analysis of a representative animal.

A: Animals were treated with 10 mg/kg BW and experiment was terminated 48 h later. Protein level of γH2AX was analyzed in whole liver extracts by Western blot analysis.

B: Mice were irradiated with 6 Gy. 24 h later, the level of γH2AX was analyzed in total liver extracts by Western blot analysis.

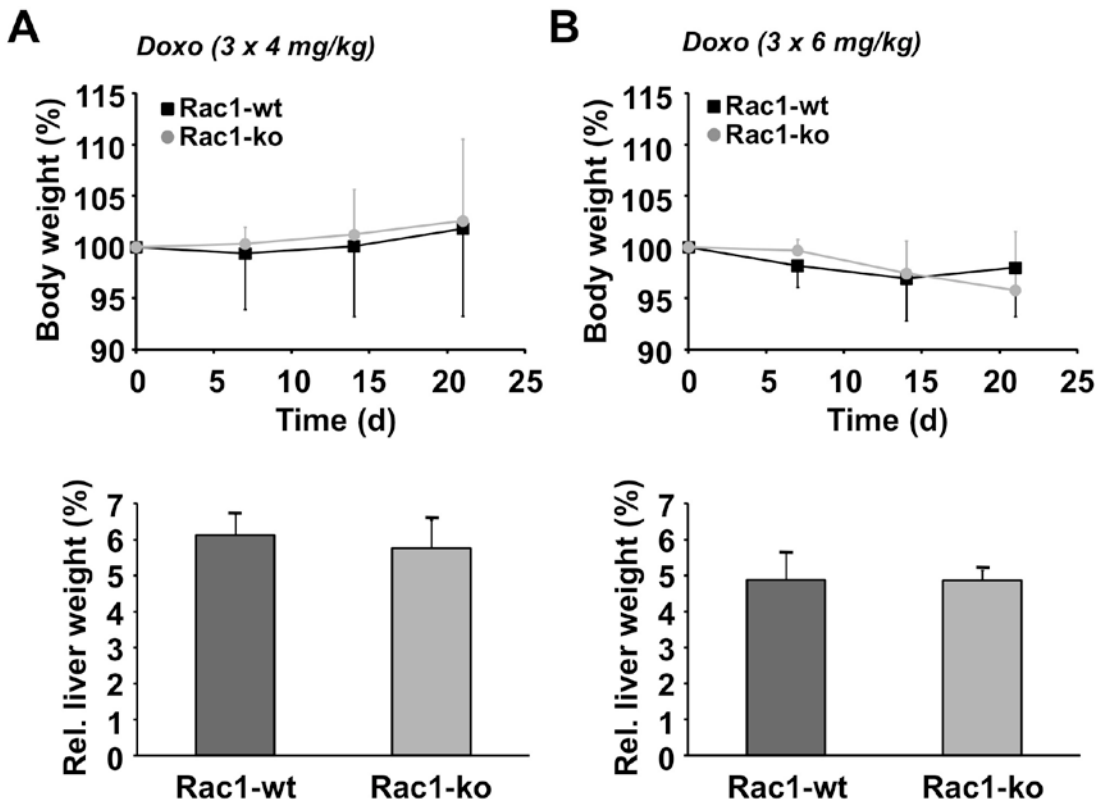
Supplementary Figure S2, Bopp et al



Supplementary Figure S2: Effect of *rac1* knock-out on ionizing radiation-induced acute pro-fibrotic and pro-inflammatory gene expression

Rac1 expressing (Rac1-wt) or *rac1* deleted (Rac1-ko) animals were irradiated with 6 Gy. After post-incubation period of 72 h (A) and 24 h (B), mRNA expression level of selected pro-fibrotic (TGFβ, CTGF) and pro-inflammatory (IL6) marker was analyzed by qRT-PCR. Relative mRNA expression of individual genes was normalized to the mRNA levels of GAPDH and β-actin and set to 1.0 in non-treated animals. Data shown are the mean ± SD from triplicate determinations using cDNA prepared from pooled RNA samples of n = 3-4 mice per group.

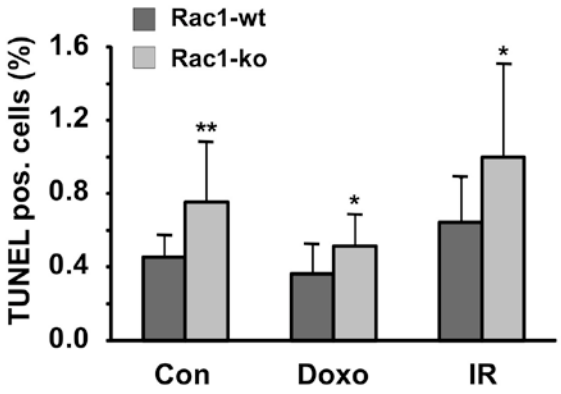
Supplementary Figure S3, Bopp et al



Supplementary Figure S3: Rac1 does not affect body and organ weight following doxorubicin treatment

Rac1 wild-type and *rac1* knock-out mice were repeatedly treated with doxorubicin (3 x 4 mg/kg (A) or 3 x 6 mg/kg (B); one application per week) as described in Methods. Body weight was analyzed up to 21 days after the first injection of doxorubicin. Liver weight was detemined at the end of the experiment. Data shown are the mean ± SD from n = 5-6 mice per group.

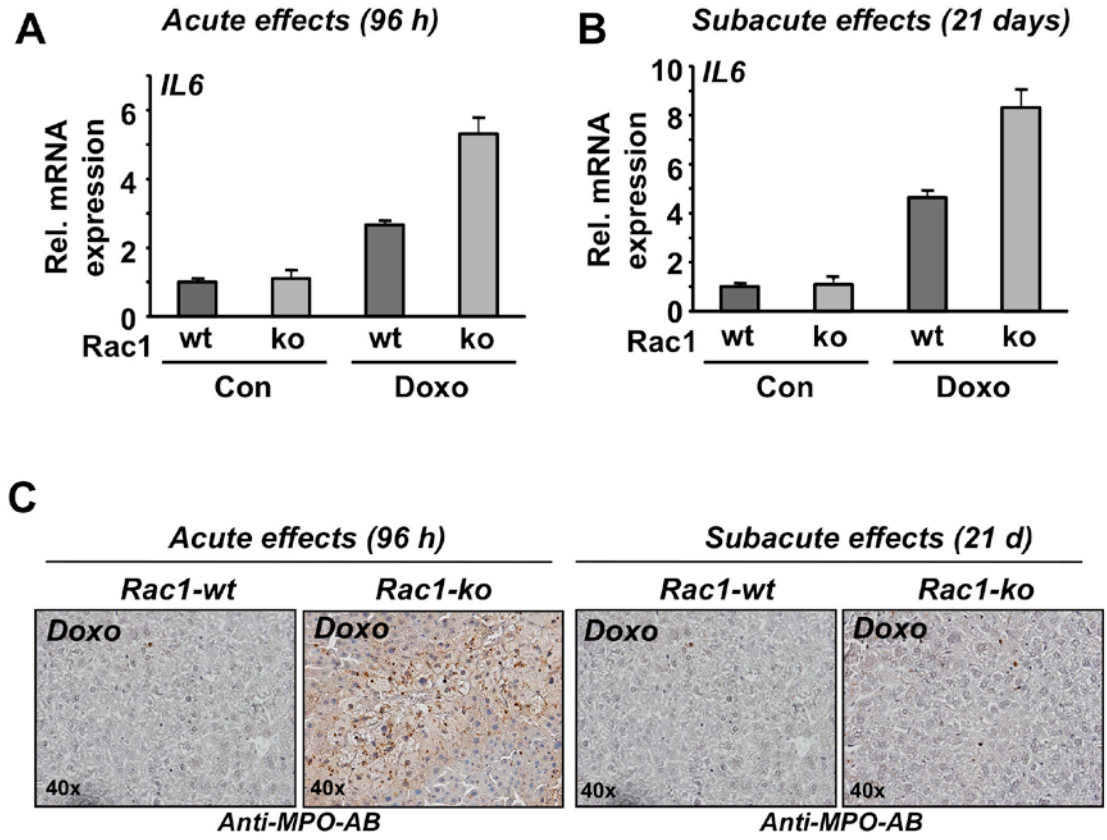
Supplementary Figure S4, Bopp et al



Supplementary Figure S4: Effect of *rac1* deletion on acute hepatotoxicity following doxorubicin and IR treatment.

$Rac1^{flox/flox/Mx1\text{-}Cre+}$ mice were left untreated or were treated with poly(I:C) (3 x 0.5 mg) every other day. Three weeks later, control mice that harbour the *rac1* gene (Rac1-wt) or mice deleted for *rac1* (Rac1-ko) were either left untreated (Con), were treated with 15 mg/kg doxorubicin (Doxo) or were irradiated with 6 Gy (IR). 96 h after doxorubicin treatment and 72 h after IR exposure, the frequency of TUNEL positive cells was analyzed in liver sections as described in Methods. Data shown are the mean ± SD from n = 3-4 mice per group. * $p<0.05$; ** $p<0.01$.

Supplementary Figure S5, Bopp et al



Supplementary Figure S5: Effect of rac1 **knock-out on doxorubicin-induced acute and subacute pro-inflammatory response.**
A,B: Rac1 expressing (Rac1-wt) or *rac1* deleted (Rac1-ko) animals were treated with a single high dose of doxorubicin (15 mg/kg) and analyzed 96 h later for acute effects (A) or were repeatedly treated with doxorubicin (3 x 6 mg/kg) (B) and sacrificed one week after the last injection to investigate subacute effects. mRNA expression level of selected marker of inflammation (IL6) was analyzed by qRT-PCR. Relative mRNA expression was normalized to the levels of GAPDH and β-actin and set to 1.0 in non-treated animals. Data shown are the mean ± SD from triplicate determinations using cDNA prepared from pooled RNA samples of n = 3-6 mice per group.
C: Mice were treated as described before. Liver sections were stained with anti-MPO antibody. Representative results are shown.