

Supplementary Table 1: Primer sequences used for (i) RT-PCR analyses of the mRNA expression of candidate genes and (ii) genomic PCR to analyze *rac1* knock-out.

Gene	Primer forward	Primer reverse
Ccne1	AGCCCTGGGATGATAATTCA	GCTCTGGGTGGTCTGATT
Cdkn1a	ACCTGAATAGCACTTTGGAAA	TCTGAGCAATGTCAAGAGTC
Collagene1	CACCCTCAAGAGCCTGAGTC	AGACGGCTGAGTAGGGAACA
Ctgf	CAAAGCAGCTGCAAATACCA	GGCCAAATGTGTCTTCCAGT
Cxcr4	ATACCTGACTTCATCTTTGCC	TGGAGTGTGACAGCTTAGA
Elk1	AGCCTGAGGTGTCTGTAA	GTGTTGGGAAGCACTGAG
Fancc	GCTTGTTGGAATCCTCTCAT	CCACGAGTTAAGTCCTGAC
Fen1	GGAACGATACTGAAAGAACGG	CGGCGAAGAGGAATGTTT
Fos	AACTTCGACCATGATGTTCT	GCACTAGAGACGGACAGA
Gapdh	TCTCCTGCGACTTCAACA	TCTCTTGCTCAGTGTCTT
Hmox1	CCAGAGTCCCTCACAGAT	CCCAAGAGAAGAGAGCCA
Hspa1b	AGACGCTGACAGCTACTC	CTCGCTTCTGGAAGGCT
Icam1	TGCTCAGGTATCCATCCAT	GGAAACGAATACACGGTGAT
Il6	AGTTGCCTTCTTGGGACTGA	CAGAATTGCCATTGCACAAC
Jun	AACTTTCCTGACCCAGAG	GCGAACTGGTATGAGTATAG
MMP1	GCCACCTTCTTCTTGTGTA	TAGTATGATTTCAAGTAGTGCTCTG
Mdr1	ACCATGGAGGAAATCACAGC	TGGTGGCATCATCCAAGATA
Mrp1	AGGCTACTACCCAGCATT	CAGTCTCTCCACTGCCACAA
MxCre	CATGTGTCTTGGTGGGCTGA	CGCATAACCAGTGAAACAGC
Rac1 cDNA	AACCTGCCTGCTCATCAGTT	CTTGAGTCCTCGCTGTGTGA
Rac1 DNA	1:ATTTTGTGCCAAGGACAGTG 2:GAAGGAGAAGAAGCTGACTC	CAGCCACAGGCAATGACAGA
Rad51	CAGCGATGTCCTAGATAATGTAG	TTACCACTGCGACACCAA
RhoB	CAGCATCAGCCATCACTTC	CTAGGCTCGCTAACTGCA
Tgf β	TGCGCTTGACAGAGATTAATA	AGCCCTGTATTCCGTCTCCT
Timp2	CAAAGCAGTGAGCGAGAA	CATCTTGCCATCTCCTTCTG
Top2 β	TGGGTGAACAATGCTACAAA	TGTATGTATCAGGACGAAGGA
Wee1	GTAGTCTCTATTCATGGACACA	GTTGCTTTCAGTAATTGTAATTCTT
Wrm	TGATTGCTCCTTCTGTCT	ACTGCGACTCTGCTTCTT
Xpc	GCGAAAGAACGGGAAAGA	AAGCGAATTGGAATGATGGA
Xrcc3	GGAGGAAGTCTGAGTTGGT	CTCTTAACCGCAGCAGTAAT
α Sma	GGACGTACAACCTGGTATTGTGC	CGGCAGTAGTCACGAAGGAAT
β Actin	GCATTGCTGACAGGATGCAG	CCTGCTTGCTGATCCACATC

Supplementary Table 2: Semi-customized PCR array used for qRT-PCR-based analysis of the mRNA expression of 94 genes involved in DNA repair, stress response and cell death. For internal control, mRNA expression of GAPDH and beta-actin were used. The genes are listed in alphabetical order.

Gene	NCBI Reference sequence	Primer sequences (5'-3')
<i>Actb</i> Actin, beta	NM_007393	GCATTGCTGACAGGATGCAG CCTGCTTGCTGATCCACATC
<i>Akt1</i> Thymoma viral proto-oncogene 1	NM_009652	AGAAGAGACTCTGAGCATCA AAGGTGCCATCGTTCTTG
<i>Apex1</i> Apurinic/aprimidinic endonuclease 1	NM_009687	AGAAATTGACCTCCGTAACC CGCCAACCAACATTCTTAGA
<i>Arhgdia</i> Rho GDP dissociation inhibitor (GDI) alpha	NM_133796	CCCTACCTACCCCAAACC TGGACAACCCTGACAGTG
<i>Atf2</i> Activating transcription factor 2	NM_009715	TATCGTTCGTCCAGCATCA TACTTGAGGTTGGTGAAGGTA
<i>Atg3</i> Autophagy-related 3 (yeast)	NM_026402	ACCACCTCCTATGTGTTCA TGTGTAGTCATATTCTATTGTTGGA
<i>Atg7</i> Autophagy-related 7 (yeast)	NM_028835	GCACAACACCAACACACT CGAAGGTCAGGAGCAGAA
<i>Atm</i> Ataxia telangiectasia mutated homolog (human)	NM_007499	ACCAGAGGATGCTGTTCA ATCATTAAGTCTATGTTGAGTCCAA
<i>Bax</i> Bcl2-associated X protein	NM_007527	CTGGACACTGGACTTCCT GCCACAAAGATGGTCACT
<i>Bcl2</i> B-cell leukemia/lymphoma 2	NM_009741	GTGTGGTTGCCTTATGTAT GTATATCCGCTACAAGTTACA
<i>Becn1</i> Beclin 1, autophagy related	NM_019584	GATGGGAACTCTGGAGGT

<i>Bid</i>	BH3 interacting domain death agonist	NM_007544	GGCTGTGGTAAGTAATGGA CACCATGTACCTTTGTCCTATC ACCTCTCCTAATGCTGTTCT
<i>Birc3</i>	Baculoviral IAP repeat-containing 3	NM_007464	GCTGACACCTTTGAGTTGA GCAGAAGCACTTGACCTT
<i>Brca1</i>	Breast cancer 1	NM_009764	TTGTGAGCGTTTGAATGA ACCTGGCTTAGTTACTGT
<i>Brca2</i>	Breast cancer 2	NM_009765	TAACGCCTGCTGACTCTC TGCCAGATGAATCTCCTAACA
<i>Casp2</i>	Caspase 2	NM_007610	TACTGCTCACAACCCTCTC GGACCATCACCATTATCTAAGG
<i>Ccna1</i>	Cyclin A1	NM_007628	GAGGGCATCATATTTGAGGAT CTTGGGTCTGTGTCTTACTTC
<i>Ccnb1</i>	Cyclin B1	NM_172301	GGTCACTAGGAACACGAAA TTTGGTAGGGCTTTAAACAGT
<i>Ccne1</i>	Cyclin E1	NM_007633	AGCCCTGGGATGATAATTCA GCTCTGGGTGGTCTGATT
<i>Cd44</i>	CD44 antigen	NM_009851	ACACCTACCTTCCTACTG TTGTGGACTGTGAATTACC
<i>Cdc25a</i>	Cell division cycle 25 homolog A (S. pombe)	NM_007658	TCAAATGAAAGTGAATCAGGAAAT CTTCATATTCTCGCCATCCA
<i>Cdc25b</i>	Cell division cycle 25 homolog B (S. pombe)	NM_023117	CACATCCCTCTCCTCACT GAAGCCATCAGACTCAAACCT
<i>Cdkn1a</i>	Cyclin-dependent kinase inhibitor 1A (p21)	NM_007669	ACCTGAATAGCACTTTGGAAA TCTGAGCAATGTCAAGAGTC
<i>Cdkn1b</i>	Cyclin-dependent kinase inhibitor 1B (p27)	NM_009875	CCCTCCAGTACACTTGAT

<i>Chek1</i>	Checkpoint kinase 1 homolog (S. pombe)	NM_007691	TAAACAACAAAACCGAACAAA TGAACGCTTACTGAACAAGAT CCACAGGACCAAACATCAA
<i>Chek2</i>	CHK2 checkpoint homolog (S. pombe)	NM_016681	TGAGAAGGACGGACAAGT TCTACATAGTGAAAGTGCGATTT
<i>Cxcr4</i>	Chemokine (C-X-C motif) receptor 4	NM_009911	ATACCTGACTTCATCTTTGCC TGGAGTGTGACAGCTTAGA
<i>Cyp1a1</i>	Cytochrome P450, family 1, subfamily a, polypeptide 1	NM_009992	CCTCCGTTACCTGCCTAA GTCCTGACAATGCTCAATGA
<i>Cyp1b1</i>	Cytochrome P450, family 1, subfamily b, polypeptide 1	NM_009994	GACGATGCGGAGTTCCTA GCTGAAGTTGCGGTTGAG
<i>Ddb2</i>	Damage specific DNA binding protein 2	NM_028119	AGGCAACATTCTCAGAGT CATTCCGGAGGTTCCAAAG
<i>Ddit3</i>	DNA-damage inducible transcript 3	NM_007837	GTCAGTTATCTTGAGCCTAA GTGTGGTGGTGTATGAAG
<i>Elk1</i>	ELK1, member of ETS oncogene family	NM_007922	AGCCTGAGGTGTCTGTAA GTGTTGGGAAGCACTGAG
<i>Ercc1</i>	Excision repair cross-complementing rodent repair deficiency, complementation group 1	NM_007948	AAACAGGAGCAAAGTCTAAT GGATGTAGTCTGGATGGA
<i>Fancc</i>	Fanconi anemia, complementation group C	NM_007985	GCTTGTTGGAATCCTCTCAT CCACGAGTTAAGTCCTGAC
<i>Fas</i>	Fas (TNF receptor superfamily member 6)	NM_007987	AGAACCTCCAGTCGTGAA ATCTATCTTGCCCTCCTTGA
<i>Fasl</i>	Fas ligand (TNF superfamily, member 6)	NM_010177	CTGGAATGGGAAGACACATAT TGGTCAGCACTGGTAAGA
<i>Fen1</i>	Flap structure specific endonuclease 1	NM_007999	GGAACGATACTGAAAGAACGG

<i>Fos</i>	FBJ osteosarcoma oncogene	NM_010234	CGGCGAAGAGGAATGTTC AACTTCGACCATGATGTTCT GCACTAGAGACGGACAGA
<i>Gadd45a</i>	Growth arrest and DNA-damage-inducible 45 alpha	NM_007836	GTCGCTACATGGATCAGTG GTGACTGCTTGAGTAACTACA
<i>Gapdh</i>	Glyceraldehyde-3-phosphate dehydrogenase	NM_008084	TCTCCTGCGACTTCAACA TCTCTTGCTCAGTGTCTT
<i>Gpx1</i>	Glutathione peroxidase 1	NM_008160	TTGGTGATTACTGGCTGC TGATATTCAGCACTTTATTCTTAGTAG
<i>Gstm1</i>	Glutathione S-transferase, mu 1	NM_010358	ACACAGCCTTCATTCTCC AATTCTAGGAAGCGTGAGTT
<i>Hif1a</i>	Hypoxia inducible factor 1, alpha subunit	NM_010431	GAGGAGCGCCTAGGAACC CGGAGAAAGAGACAAGTCCA
<i>Hmox1</i>	Heme oxygenase (decycling) 1	NM_010442	CCAGAGTCCCTCACAGAT CCCAAGAGAAGAGAGCCA
<i>Hsp90aa1</i>	Heat shock protein 90, alpha (cytosolic), class A member 1	NM_010480	CGGAGGCTTCTGGAAGA CATCGTGGCTGAATGAACA
<i>Hspa1b</i>	Heat shock protein 1B (Hsp70)	NM_010478	AGACGCTGACAGCTACTC CTCGCTTCTGGAAGGCT
<i>Hus1</i>	Hus1 homolog (S. pombe)	NM_008316	TGGAAGGAGTCTCTGAAGAA AGGGAAAGTGTGGTTAGTCA
<i>Icam1</i>	Intercellular adhesion molecule 1	NM_010493	TGCTCAGGTATCCATCCAT GGAAACGAATACACGGTGAT
<i>Il12a</i>	Interleukin 12a	NM_008351	GGAACACACAAGAACGAGAG CGCCATTATGATTCAGAGACT
<i>Itgb1</i>	Integrin beta 1 (fibronectin receptor beta)	NM_010578	GCCAGCCAAGTGACATAG

<i>Jun</i>	Jun oncogene	NM_010591	ACTTCTGTGGTTCTCCTGAT AACTTTCCTGACCCAGAG GCGAACTGGTATGAGTATAG
<i>Lamp1</i>	Lysosomal-associated membrane protein 1	NM_010684	AAGTGGAGAACAAGAACAGAG TCAGTGAATGGTTGGAGATG
<i>Lig1</i>	Ligase I, DNA, ATP-dependent	NM_010715	ATTTCTGGGTTTTCGCTCTC ACCACTTGATTCTCTCTCTT
<i>Lig4</i>	Ligase IV, DNA, ATP-dependent	NM_176953	GTGTCCTGATGCTTAGTTGT CTCCTTGAAGTGCCTGATT
<i>Mdm2</i>	Transformed mouse 3T3 cell double minute 2	NM_010786	AAGGTGGGAGTGATCTGAA TCTGTGTTCTCTTCTGTCTCA
<i>Mgmt</i>	O-6-methylguanine-DNA methyltransferase	NM_008598	GCTGCTGAAGTTGTGAA TCTCATTGCTCCTCCTACTG
<i>Mmp13</i>	Matrix metalloproteinase 13; collagenase 1; Mmp1	NM_008607	GCCACCTTCTTCTTGTGA TAGTATGATTTCAAGTAGTGCTCTG
<i>Mmp3</i>	Matrix metalloproteinase 3	NM_010809	GCTGTGGGAAAGTCAATGA GCCATAGTAGTTTTCTAGGTATT
<i>Mmp7</i>	Matrix metalloproteinase 7	NM_010810	GAACAGGCTCAGAATTATCTTAGA CCACTACGATCCGAGGTAA
<i>Mpg</i>	N-methylpurine-DNA glycosylase	NM_010822	CTGTATGTGTACCTCATCTATGG CAGAGTTCACGGTCCTTG
<i>Mre11a</i>	Meiotic recombination 11 homolog A (<i>S. cerevisiae</i>)	NM_018736	TACGGCTTAGGCTCCATT ATGCTTACTCCTGTTCTGATG
<i>Msh2</i>	MutS homolog 2 (<i>E. coli</i>)	NM_008628	GTCTAAGGAGAATGAGTGGTATC CCATAACGCCAACGGAAG
<i>Nos2</i>	Nitric oxide synthase 2, inducible	NM_010927	GCTGTTAGAGACACTTCTGAG

<i>Nos3</i>	nitric oxide synthase 3, endothelial cell	NM_008713	CACTTTGGTAGGATTTGACTTTG GCATGGGCAACTTGAAGA AGGGTGTTCGTAGGTGATG
<i>Nox1</i>	NADPH oxidase 1	NM_172203	GGCTAAATCCCATCCAGTC CCTAAGCAGATGATATAGACGATAA
<i>Ogg1</i>	8-oxoguanine DNA-glycosylase 1	NM_010957	TGAGACTGCTGAGACAAGA GGAAGCCATGATAAGTGACA
<i>Pcna</i>	Proliferating cell nuclear antigen	NM_011045	GACTTAGATGTGGAGCAACTT GGCTAAGGTCTCGGCATA
<i>Pold1</i>	Polymerase (DNA directed), delta 1, catalytic subunit	NM_011131	CTCCATTTCTCCGCATCAC CAATGTCAGCATCCACCAT
<i>Pole</i>	Polymerase (DNA directed), epsilon	NM_011132	CGGTGGATTACTACTTCATTCA CTTCTTTGGGCACATTCTCTA
<i>Pten</i>	Phosphatase and tensin homolog	NM_008960	ATCAAGAGATCGTTAGCAGAAA TTGGCGGTGTCATAATGTC
<i>Rac1</i>	RAS-related C3 botulinum substrate 1	NM_009007	ACAAAGCCTTCTTAAAGCCTTA GCGGTCTTCTTAGCAACA
<i>Rad51</i>	RAD51 homolog (<i>S. cerevisiae</i>)	NM_011234	CAGCGATGTCCTAGATAATGTAG TTACCACTGCGACACCAA
<i>Rev1</i>	REV1 homolog (<i>S. cerevisiae</i>)	NM_019570	TCTGCGGAGGAATTGAGA ACACAGGATTGAAGTTGAGAC
<i>Rev3l</i>	REV3-like, catalytic subunit of DNA polymerase zeta RAD54 like (<i>S. cerevisiae</i>)	NM_011264	TTCTCAGATGGCATTTCAGTATC TCATTATGGCTCCGCTTTG
<i>Rhoa</i>	Ras homolog gene family, member A	NM_016802	AAGTCTGGGTGCCTCAT AATAATCGTGGTTGGCTTCTAA
<i>Rheb</i>	Ras homolog gene family, member B	NM_007483	CAGCATCAGCCATCACTTC

<i>Sele</i>	Selectin, endothelial cell	NM_011345	CTAGGCTCGCTAACTGCA TGCAGAGAAGAACGGATAGA CTGAATTGCCACCAGATGT
<i>Sod1</i>	Superoxide dismutase 1, soluble	NM_011434	ACCAGTTGTGTTGTCAGG TTTCTTAGAGTGAGGATTAATGAG
<i>Tiam1</i>	T-cell lymphoma invasion and metastasis 1	NM_009384	GGTAGAACCATTTGTGGACTG CGGTGTGGCATTAGAGAC
<i>Timp2</i>	Tissue inhibitor of metalloproteinase 2	NM_011594	CAAAGCAGTGAGCGAGAA CATCTTGCCATCTCCTTCTG
<i>Top2a</i>	Topoisomerase (DNA) II alpha	NM_011623	CTTCAGGAGCCGTCACCAT GAGCAGTATATGTTCCAGTTGT
<i>Top2b</i>	Topoisomerase (DNA) II beta	NM_009409	TGGGTGAACAATGCTACAAA TGTATGTATCAGGACGAAGGA
<i>Trex1</i>	Three prime repair exonuclease 1	NM_011637	GCTACCACTGGAACAACC TGCTATGGAAGTCTTTATTCATCA
<i>Trp53</i>	Transformation related protein 53	NM_011640	AAGTTCTGTAGCTTCAGTTCAT GGCAGTCATCCAGTCTTC
<i>Trp63</i>	Transformation related protein 63	NM_011641	AGCATCAGAAAGCAGCAA GATCTTCAGCAACATCTCGTA
<i>Trp73</i>	Transformation related protein 73	NM_011642	CTCCGCACCCTTATAACC GCTGAGCAAATTGAACTGG
<i>Txnrd1</i>	Thioredoxin reductase 1	NM_015762	CAGTTCGTCCCAACGAAAAT GCACATTGGTCTGCTCTTCA
<i>Vcam1</i>	Vascular cell adhesion molecule 1	NM_011693	ATATACTTGAAGTGTCTGTGT GACCATCTTCACAGGCATT
<i>Wee1</i>	WEE 1 homolog 1 (S. pombe)	NM_009516	GTAGTCTCTATTCATGGACACA

<i>Wrm</i>	Werner syndrome homolog (human)	NM_011721	GTTGCTTTCAGTAATTGTAATTCCTT TGATTGCTCCTTCCTGTCT ACTGCGACTCTGCTTCTT
<i>Wrip1</i>	Werner helicase interacting protein 1	NM_030215	GCCAATGAGATCCCTTCG AACCTTATGCTGTGCTTCTT
<i>Xpa</i>	Xeroderma pigmentosum, complementation group A	NM_011728	GACAACCACTCACCAACATA TGAACCTTGAACAGGGTCTTTA
<i>Xpc</i>	Xeroderma pigmentosum, complementation group C	NM_009531	GCGAAAGAACGGGAAAGA AAGCGAATTGGAATGATGGA
<i>Xrcc1</i>	X-ray repair complementing defective repair in Chinese hamster cells 1	NM_009532	CCAACCGTGTTTCGCATTT GCACTGTCATCCTCCTCTT
<i>Xrcc3</i>	X-ray repair complementing defective repair in Chinese hamster cells 3	NM_028875	GGAGGAAGTCTGAGTTGGT CTCTTAACCGCAGCAGTAAT
<i>Xrcc4</i>	X-ray repair complementing defective repair in Chinese hamster cells 4	NM_028012	TGCCTGGACACCATTACA CTTCTCATTTCAGCACCAAGAT

Supplementary table 3: Efficiency of Cre-mediated *rac1* knockout in several tissues. *Rac1*^{flox/flox/Mx1-Cre} mice were treated with poly(I:C) (3 x 0.5 mg) every other day. Animals were sacrificed three weeks later. DNA, mRNA and protein extracts were prepared and analysed as described in material and methods. Data shown are based on the analysis of n = 2-3 mice per group. 0: efficiency < 20%; +: efficiency 20% – 70%; ++: efficiency > 70%; n.d.: not determined.

Organ	DNA level	mRNA level	Protein level
Liver	++	++	++
Bone marrow	++	n.d.	n.d.
Blood	+	n.d.	n.d.
Lung	+	+	+
Spleen	+	+	+
Heart	+	0	+
Kidney	+	0	0
Intestine	0	0	0
Brain	0	0	0

Supplementary table 4: Serum parameters of wild-type mice as compared to mice lacking hepatic rac1 gene for different periods of time (i.e. 3 months versus 15 months). Data are shown as the mean \pm sd. * $p < 0.05$.

Time point Rac1	0 months wt (n=12)	3 months		15 months	
		wt (n=4)	ko (n=3)	wt (n=4)	ko (n=3)
Creatinine (mg/dl)	0.8	0.8	0.8	0.8	0.8
Blood urea (mg/dl)	25.0 \pm 4.9	24.0 \pm 3.3	29.3 \pm 2.3	28.0 \pm 4.0	22.6 \pm 4.6
GPT (U/l)	20.3 \pm 1.2	21.0 \pm 2.0	28.0 \pm 4.0*	20.0 \pm 0.0	20.0 \pm 0.0
GLDH (U/l)	25.3 \pm 15.9	13.3 \pm 2.9	30.3 \pm 10.2*	27.5 \pm 5.6	28.3 \pm 9.8