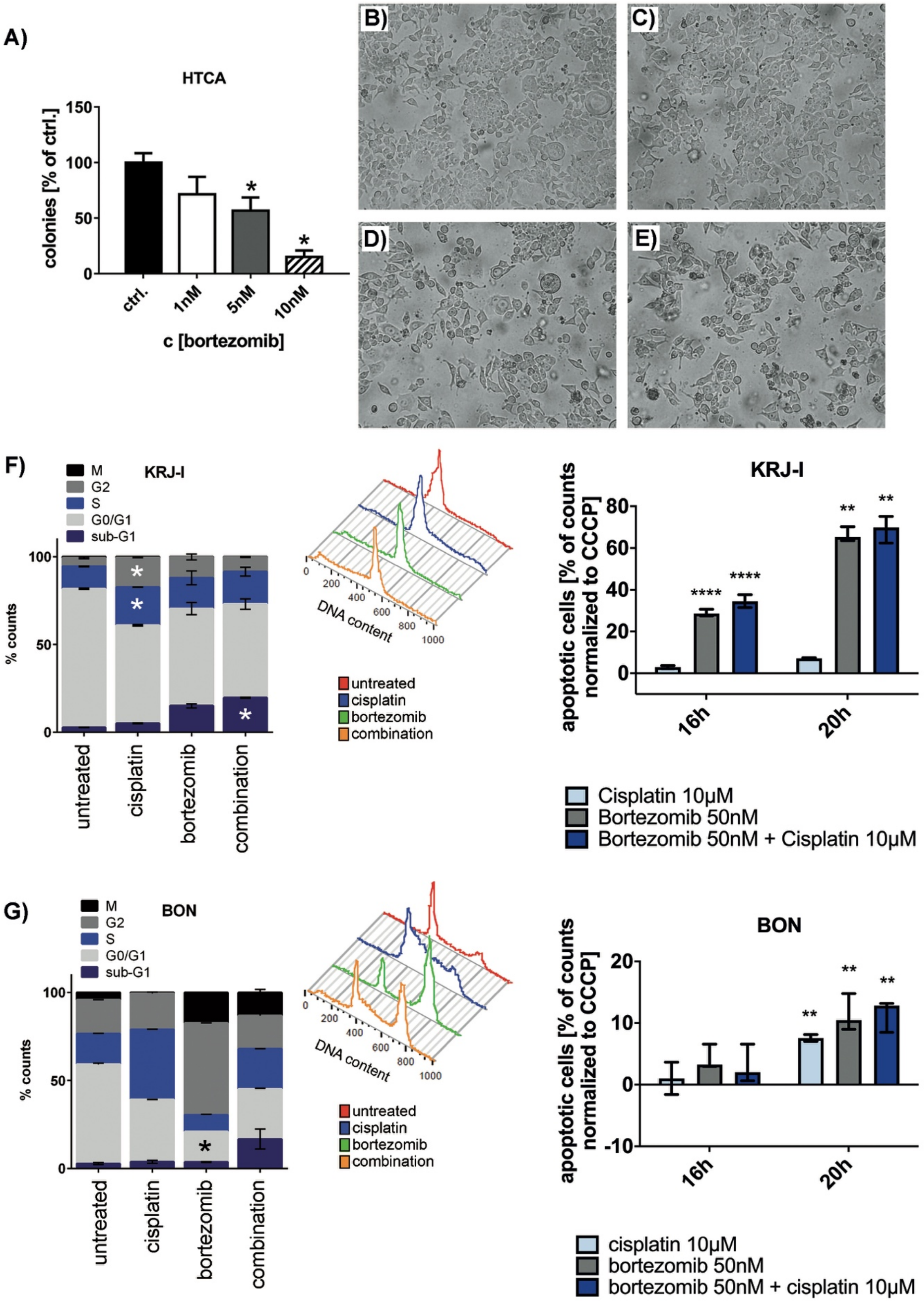
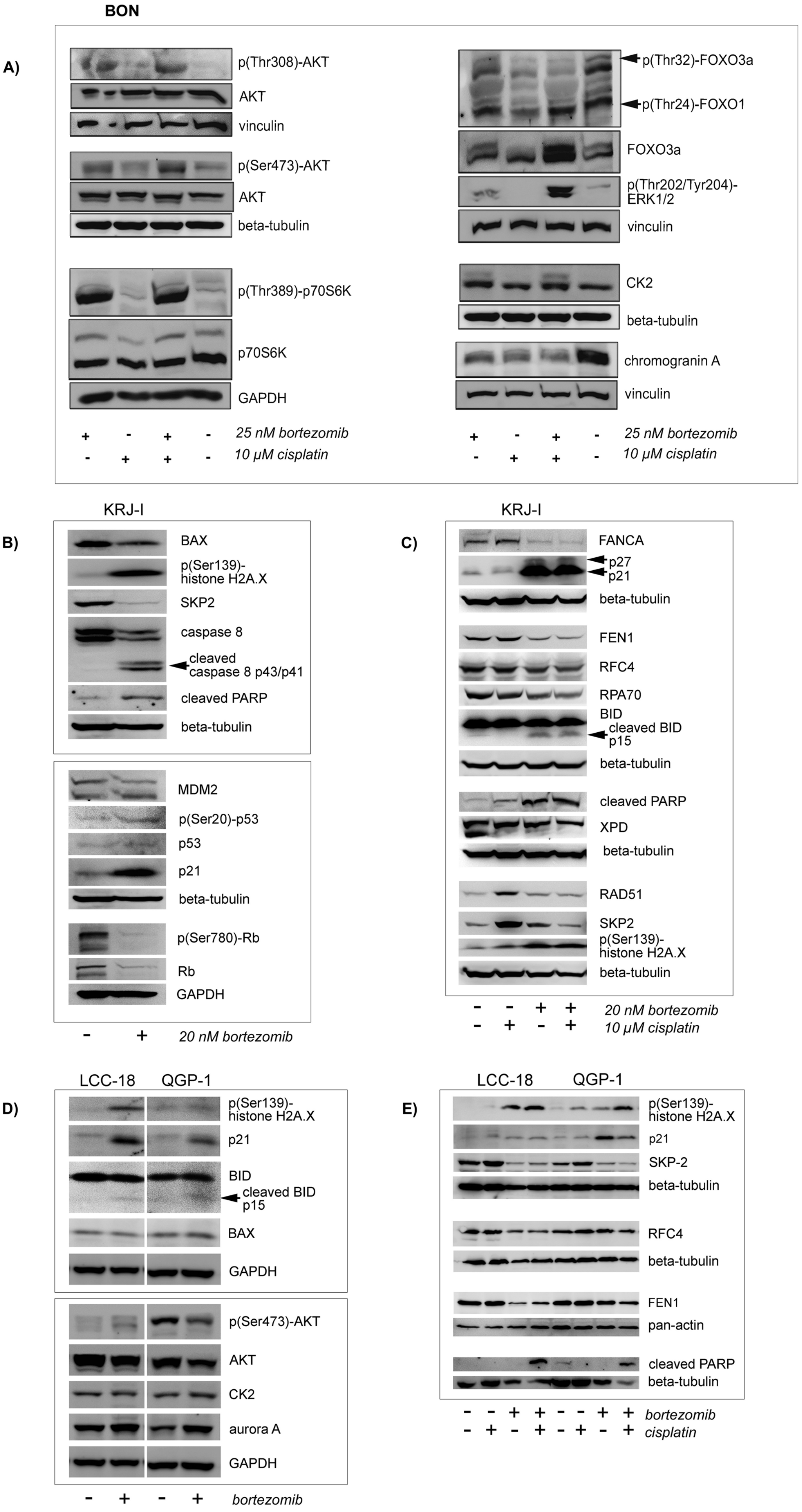
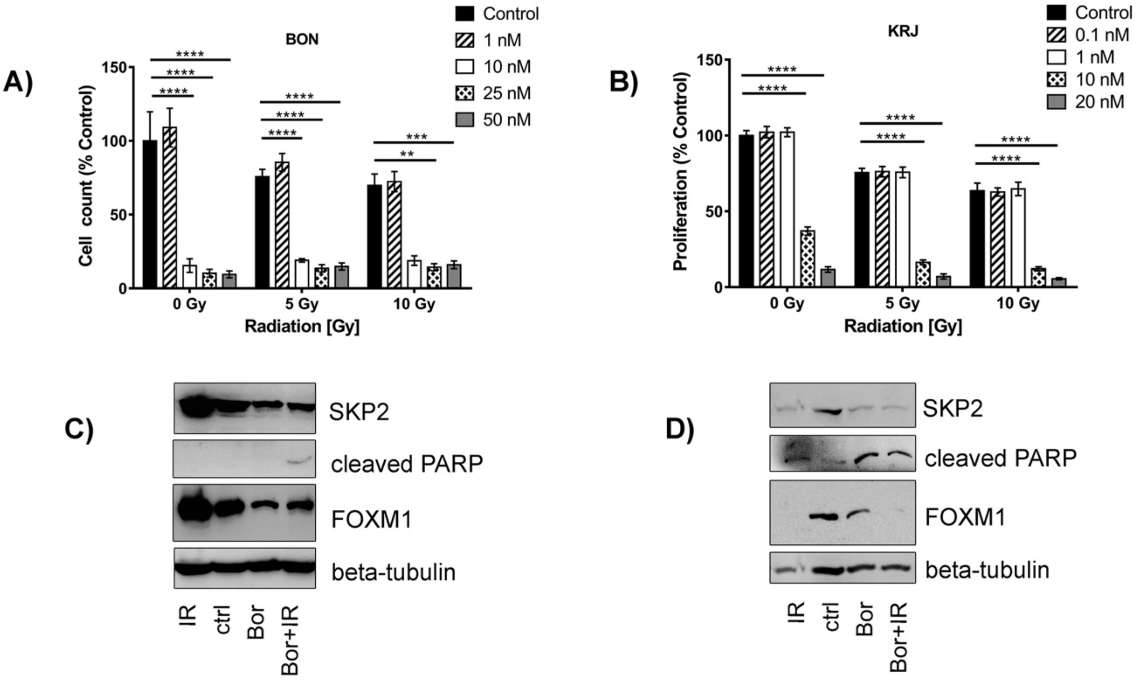
SUPPLEMENTARY FIGURES:



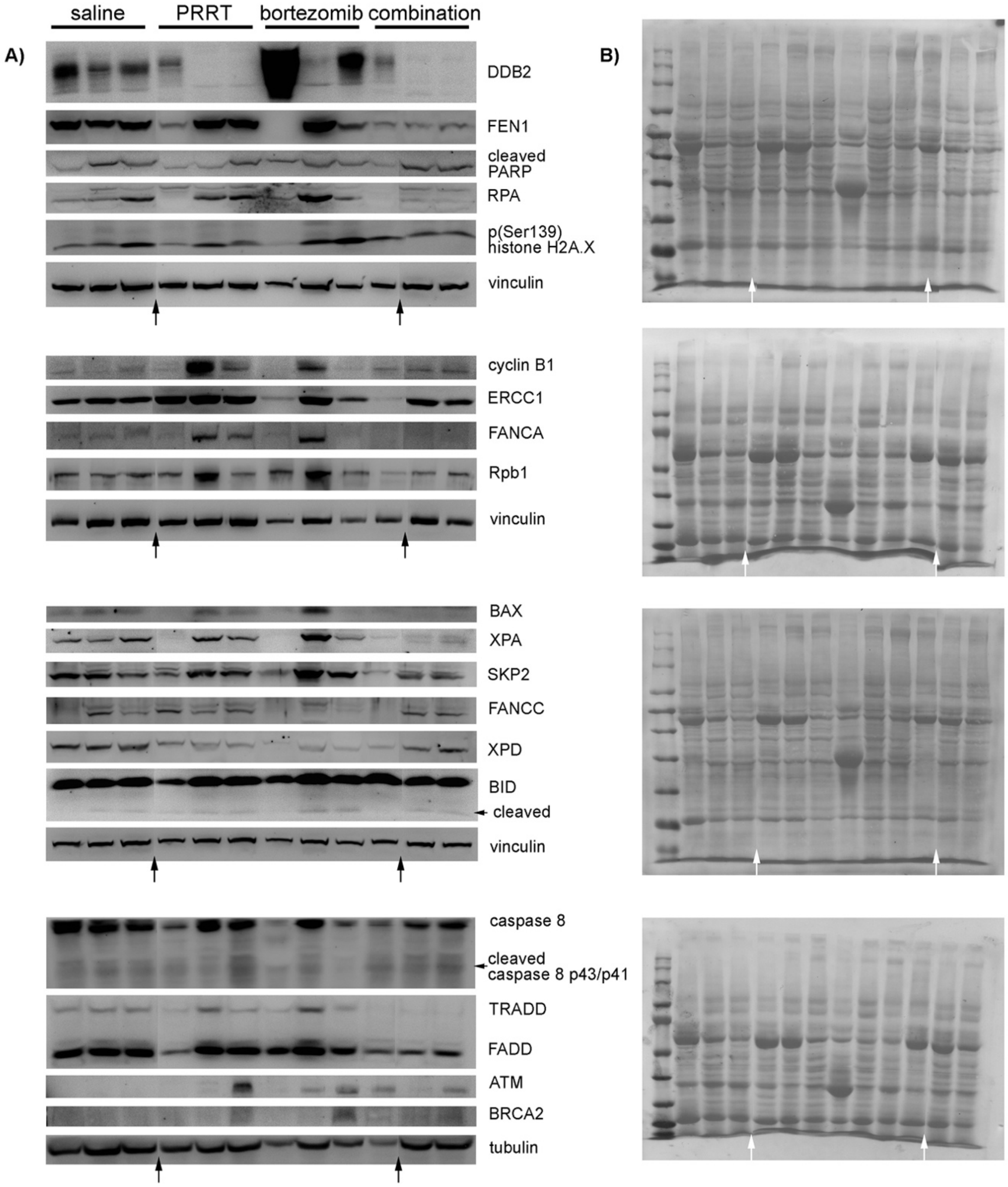
Suppl. Figure 1: Anti-tumor effect of bortezomib in BON cells involves induction of cell cycle arrest and apoptosis: A) Human tumor colony assay (HTCA) demonstrated a reduced clonogenic potential of BON cells 9 days after bortezomib treatment (representative data of three independent experiments with n=3). Captions: *$p<0.05$ (Kruskal-Wallis test with Dunn's multiple comparisons testing). Whereas **B)** control and **C)** cisplatin (10 µM) treated cells retained the characteristic morphology of BON cells in 2D culture, cells treated with **D)** bortezomib (25 nM) or **E)** bortezomib (25 nM) and cisplatin (10 µM) exhibited strong morphological changes and occurrence of anoikis as early as 24 h after treatment start. We therefore chose a short incubation time and a low dose (compared to the calculated IC50) for the following experiments. **F+G)** GEP-NEN cells were treated with 50 nM bortezomib, 10 µM cisplatin or both *versus* saline for 24 h and analyzed by phospho-histone H3 / propidium iodide flow cytometry. In KRJ-I cells cisplatin induced cell cycle arrest in S- and G2-phase. Bortezomib induced G2 arrest and a higher percentage of dead cells, indicated by an increased sub-G1 phase. The combinatory treatment showed a significant rise in the sub-G1 cell population ($p=0.0429$; Kruskal-Wallis test with Dunn’s multiple comparisons test). KRJ-I cells were analyzed after 16 h and 20 h of analogous treatment by JC-1 staining of depolarized mitochondrial membranes as flow cytometry marker for early apoptosis induction. A strong apoptosis induction (p-values calculated *versus* saline controls) was shown after bortezomib and combinatory treatment (ANOVA with Dunnett’s multiple comparisons test). BON cells exhibited an increased S-phase after cisplatin and G2/M arrest after bortezomib treatment along with a reduced G1 population. The combinatory treatment showed a marginally enhanced induction of cell death resulting in a sub-G1 peak (Kruskal-Wallis test with Dunn’s multiple comparisons test). This induced cell death was in part verified as apoptosis and reached significance (*versus* saline) for bortezomib monotherapy and combination after 20 h (ANOVA with Dunnett’s multiple comparisons test). Representative data of n=3 independent experiments; Captions: *$p<0.05$; **$p<0.01$; ***$p<0.001$; ****$p<0.0001$.


BON
A)
p(Thr308)-AKT
AKT
vinculin
p(Ser473)-AKT
AKT
beta-tubulin
p(Thr389)-p70S6K
p70S6K
GAPDH
+ - + -
25 nM bortezomib
- + + -
10 μM cisplatin
p(Thr32)-FOXO3a
p(Thr24)-FOXO1
FOXO3a
p(Thr202/Tyr204)-ERK1/2
vinculin
CK2
beta-tubulin
chromogranin A
vinculin
+ - + -
25 nM bortezomib
- + + -
10 μM cisplatin
KRJ-I
B)
BAX
p(Ser139)-histone H2A.X
SKP2
caspase 8
cleaved caspase 8 p43/p41
cleaved PARP
beta-tubulin
MDM2
p(Ser20)-p53
p53
p21
beta-tubulin
p(Ser780)-Rb
Rb
GAPDH
- +
20 nM bortezomib
KRJ-I
C)
FANCA
p27
p21
beta-tubulin
FEN1
RFC4
RPA70
BID
cleaved BID p15
beta-tubulin
cleaved PARP
XPD
beta-tubulin
RAD51
SKP2
p(Ser139)-histone H2A.X
beta-tubulin
- - + +
20 nM bortezomib
- + - +
10 μM cisplatin
LCC-18
QGP-1
D)
p(Ser139)-histone H2A.X
p21
BID
cleaved BID p15
BAX
GAPDH
p(Ser473)-AKT
AKT
CK2
aurora A
GAPDH
- + - +
bortezomib
LCC-18
QGP-1
E)
p(Ser139)-histone H2A.X
p21
SKP-2
beta-tubulin
RFC4
beta-tubulin
FEN1
pan-actin
cleaved PARP
beta-tubulin
- - + + - - + +
bortezomib
- + - + - + - +
cisplatin

Suppl. Figure 2: Western blot analyses of bortezomib-induced effects in four different GEP-NEN cell lines: Cell lines were treated for 48 h with respective doses of bortezomib alone (BON: 25 nM, KRJ-I: 20 nM, LCC-18: 500 nM, QGP-1: 5 µM) or combined with cisplatin (10 µM). **A)** Combined treatment induced cellular ER stress indicated by CK2-alpha upregulation and PI3K pathway activation. **B)** Validation of BON cell-obtained data in three other NEN cell lines: cell cycle, apoptosis and DNA-damage associated protein expression upon bortezomib treatment of KRJ-I cells and **C)** after combined treatment. **D)** Cell cycle, apoptosis and DNA-damage associated protein expression upon bortezomib treatment of QGP-1 and LCC-18 cells and **F)** protein expression after combined treatment.

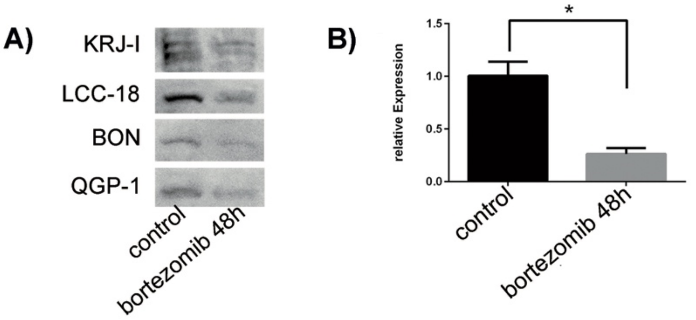


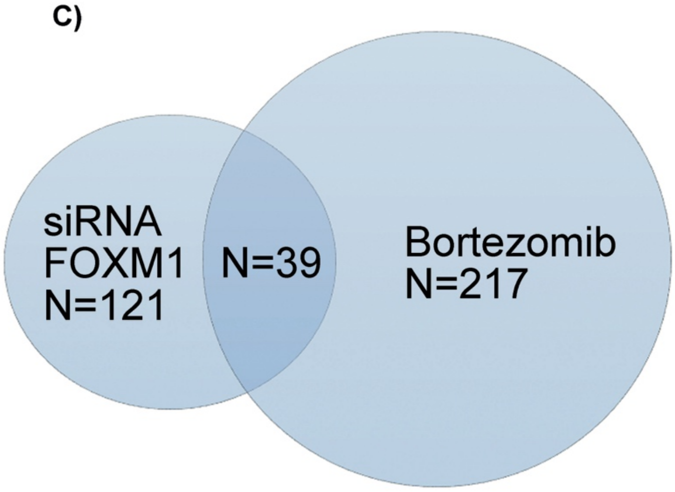
Suppl. Figure 3: Radiosensitizing effect of bortezomib: KRJ-I and BON cells were irradiated with 0, 5 or 10 Gy using a caesium-137 source and treated with increasing concentrations of bortezomib for 48 h. Metabolic activity was measured by AlamarBlues to estimate cell count. **A+B)** Addition of bortezomib induced enhanced anti-proliferative effects (*p*<0.0001) in both cell lines (ANOVA; Holm-Sidak's test for multiple testing), which were quantitated as synergistic in doses of bortezomib <20 nM in KRJ-I using the method of Chou and Talalay. **C+D)** Analysis of cells following radiation (IR), bortezomib (Bor), control (ctrl.) and combined (Bor+IR) treatment. Cells were treated with 10 Gy radiation and 5 nM bortezomib for 48 h. Respective controls were no radiation or PBS. Western Blot demonstrated the downregulation of FOXM1 and SKP2, as well as induction of apoptosis (indicated by PARP cleavage) after combination of bortezomib and radiation. Captions: **p*<0.05; ***p*<0.01; ****p*<0.001; *****p*<0.0001.



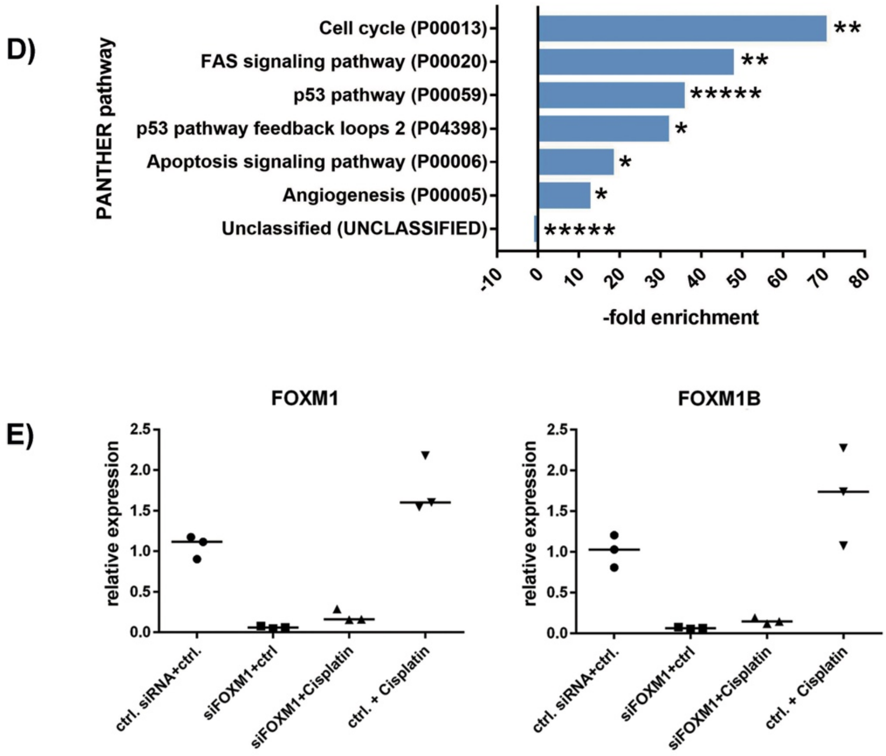
Suppl. Figure 4: **Western blot raw data of chicken CAM xenografted tumors treated with saline, PRRT, bortezomib and combined therapy.** Eggs were treated with ~20 MBq 177-Lu-DOTATOC (PRRT) i.v. with and without 25 nM bortezomib. Tumor plaques were explanted 6 days after treatment. Three independent experiments of >4 experiments are shown. Gel 1-4 were loaded with identical samples and re-probed with the specified antibodies. **A)** Western blot raw data of protein expression in chicken CAM xenografted tumors: three samples per treatment group. **B)** Protein load after western blotting was determined by ponceau S staining to evaluate total protein for normalization purposes.

Arrows indicate positions where one lane was excluded from the analyses due to poor total protein abundance of the (predominantly necrotic) tissue lysate.



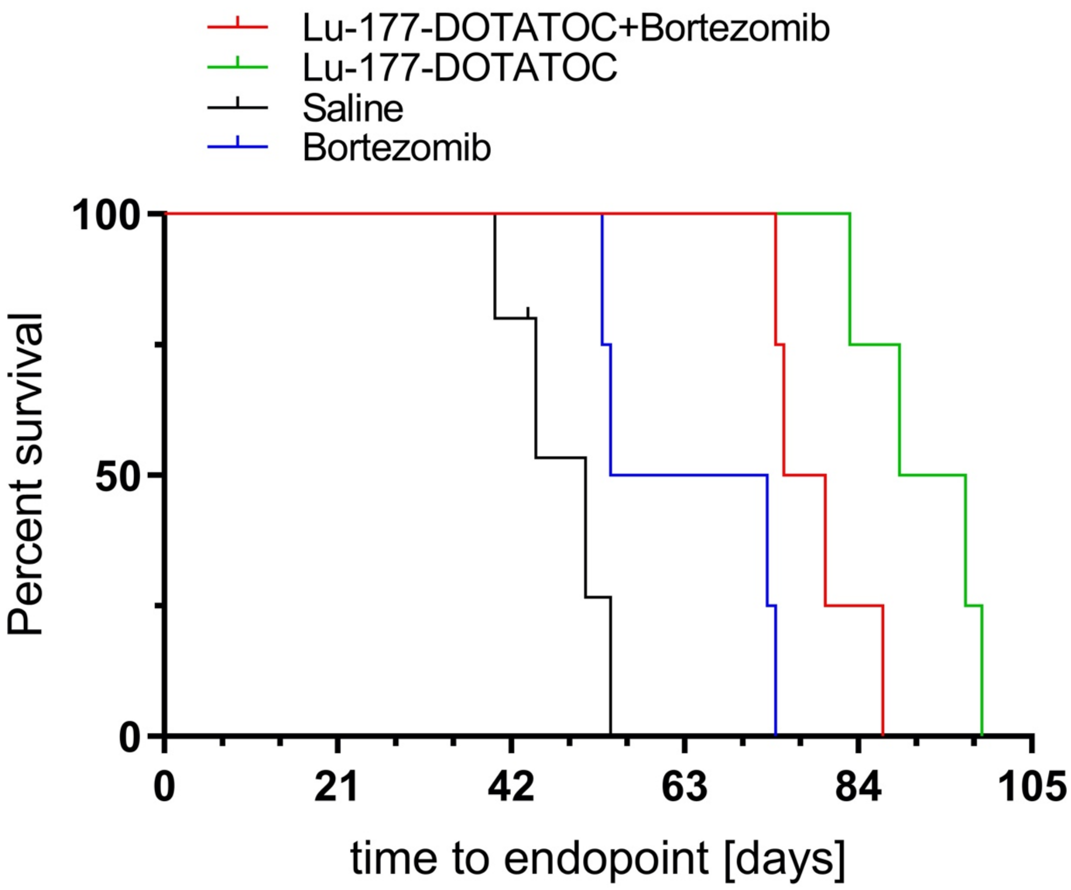


negatively regulated genes	positively regulated genes
AKT1	*CASP7*
CCNA2	*CASP8*
CCNB1	*DUSP5*
CCNE1	*FLNA*
CCNE2	*FOSL1*
CDK6	*GADD45B*
CDKN2C	*HSPA1A*
CXXC4	*HSPB1*
DLL1	*IL6R*
DNMT3A	*MET*
ETS2	*SHC1*
GNG4	*SHC4*
H3F3A	*SPP1*
HDAC2	
HIST1H3B	
HIST1H3G	
ID2	
POLR2D	
PTTG2	
RAD21	
RET	
RPS27A	
SHC3	
SYK	
TBL1XR1	
WHSC1	

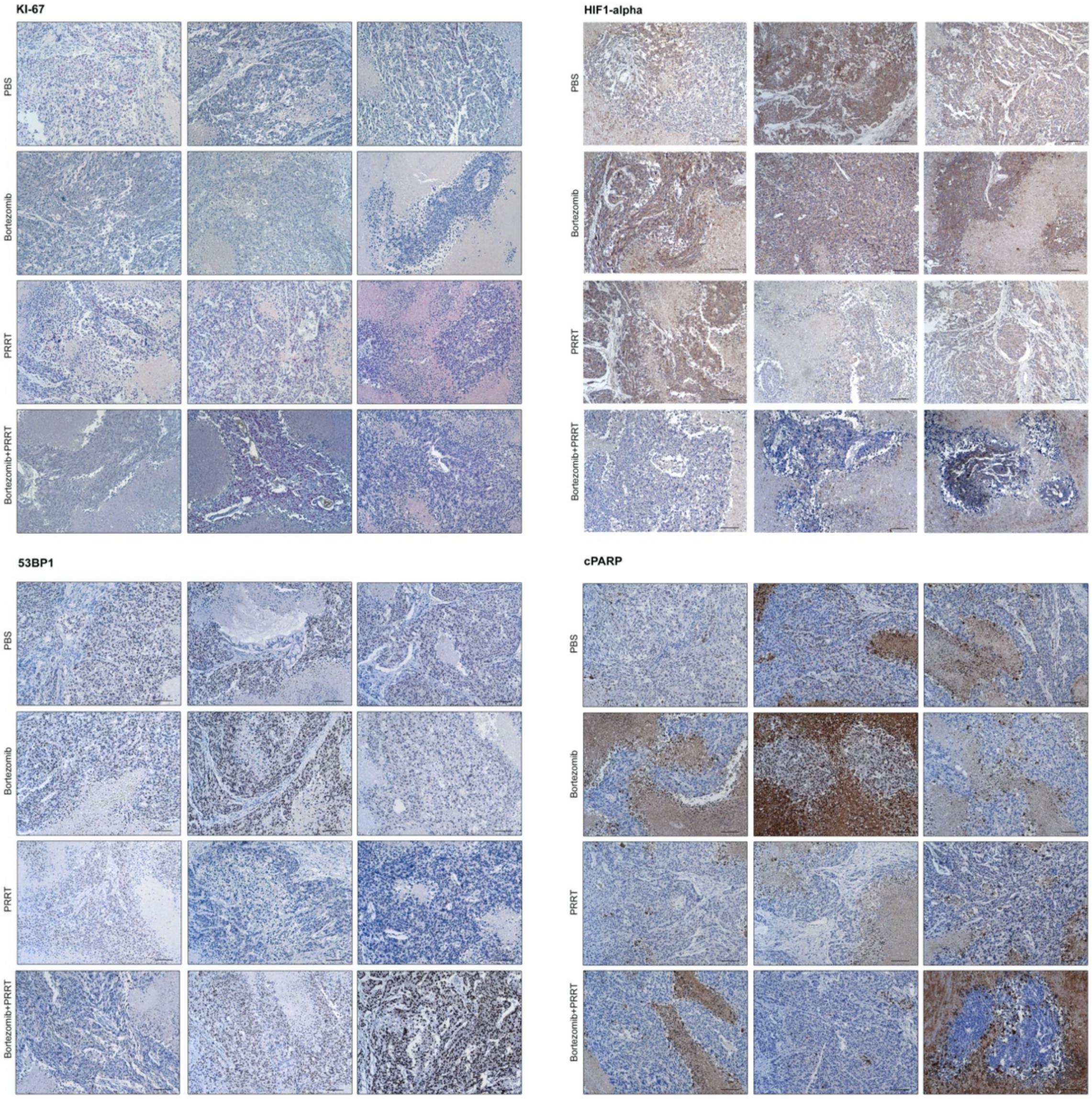


Suppl. Figure 5: Role of FOXM1 upon bortezomib treatment: Cell lines were treated with their effective doses of bortezomib (KRJ-I: 20 nM, LCC-18: 500 nM, BON: 25 nM, QGP-1: 5 µM) for 48 h in vitro. **A)** Western blot detection of FOXM1 show a reduced protein abundance after bortezomib treatment *versus* control. **B)** BON cells have further been analyzed by qPCR, demonstrating that also the FOXM1 mRNA was reduced under bortezomib treatment. This indicates a transcriptional regulation of FOXM1 by bortezomib rather than contribution of posttranscriptional mechanisms (Mann-Whitney test, p=0.0238). Captions: *p<0.05. **C)** BON cells were transfected with 40 nM *FOMX1* siRNA *versus* negative control siRNA for 72 h. Knockdown efficacy was determined by qPCR (refer to e). Alternatively, BON cells were treated with 25 nM bortezomib *versus* control for 24 h. Triplicates for every group were analyzed using the nCounter® array and differentially expressed genes (filtered by fold-change ≥1.5) were identified. The expression of 39 genes was altered in the same direction by both *FOXM1* knockdown and bortezomib. **D)** According to the PANTHER overrepresentation analysis, genes of cell cycle proteins and several apoptosis-associated pathways were overrepresented within these 39 analogously affected genes. **E)** RT-qPCR based determination of knockdown efficacy against *FOXM1* and the *FOXM1* isoform *B*. Median data of three independent experiments is shown. Each point itself represents the median of five technical replicates that are not shown in detail.

Captions: *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001; *****p<0.00001. Corresponding gene expression raw data can be found in suppl. tables 2 and 4.



Suppl. Figure 6: Kaplan-Maier survival analysis of cumulative time to endpoint (volume=1400 mm^3). Since mice were euthanized at a defined end point and did not die spontaneously, the survival was defined as time to endpoint. The time to endpoint was significantly increased in the Lu-177-DOTATOC and the combined treatment group *versus* saline according to a Log-rank (Mantel-Cox) test (p=0.0079). Combination therapy increased the median time to endpoint from 63.5 days in the bortezomib to 77.5 days in the combined group (p=0.0169). However, Lu-177-DOTATOC demonstrated the longest median time to endpoint with 93 days, indicating a significant prolongation (p=0.026)



Suppl. Figure 7: Raw data of immunohistochemically stained mouse xenograft tumor specimens: Mouse xenograft tumors were explanted, paraffin embedded and specimens of the tumor rim area were stained against the proliferation marker anti-Ki-67, the hypoxia marker HIF1-alpha, the DNA damage marker anti-53BP1 and the apoptosis marker cleaved PARP. Captions: cPARP=cleaved Poly- (ADP-ribose)- polymerase. 3/4 specimens are shown. Light microscopy: original x100 magnification, scale bar indicates 100 µm.

SUPPLEMENTARY TABLES:

Suppl. table 1: differentially expressed genes after 24 h of 10 µM cisplatin treatment of BON cells incl. pathway allocations.

Gene symbol	**Log2 fold change**	**Upper confidence limit**	**Lower confidence limit**	***p*-value**	**FDR**	**pathway**
ABL1	-0,1557	-0,2562	-0,0553	1,89E-02	6,26E-01	RAS, CC
ALK	-1,1623	-1,9890	-0,3356	2,83E-02	7,88E-01	
ALKBH2	0,3965	0,1160	0,6770	2,77E-02	7,86E-01	DNARepair
ALKBH3	-0,1642	-0,2905	-0,0379	3,82E-02	9,37E-01	DNARepair
ARID1A	-0,4049	-0,6050	-0,2048	5,42E-03	3,13E-01	ChromMod
ARNT2	-0,4080	-0,5429	-0,2732	5,82E-04	7,35E-02	TXmisReg
ATRX	-0,3186	-0,4877	-0,1495	7,73E-03	3,61E-01	
BID	0,4140	0,1932	0,6348	7,91E-03	3,65E-01	Apop
BMP4	0,3652	0,2423	0,4880	6,46E-04	7,60E-02	HH, TGFB
BMP7	-0,4353	-0,6170	-0,2536	2,22E-03	1,75E-01	TGFB
BMP8A	0,6066	0,3084	0,9048	5,28E-03	3,10E-01	TGFB
BMPR1B	-0,3590	-0,4757	-0,2423	5,27E-04	7,26E-02	TGFB
BNIP3	0,1887	0,0750	0,3025	1,40E-02	5,20E-01	ChromMod
BRCA1	0,4938	0,2614	0,7262	4,22E-03	2,72E-01	DNARepair, PI3K
BRCA2	0,2619	0,0776	0,4462	2,71E-02	7,77E-01	DNARepair
BRIP1	0,2572	0,0721	0,4423	2,96E-02	7,96E-01	DNARepair
C19orf40	0,4330	0,1356	0,7304	2,46E-02	7,35E-01	DNARepair
CACNA1C	-0,9017	-1,4513	-0,3521	1,47E-02	5,29E-01	MAPK
CACNA1H	-0,6506	-0,8638	-0,4373	5,53E-04	7,26E-02	MAPK
CACNA2D1	-0,5224	-0,6725	-0,3722	2,49E-04	4,72E-02	MAPK
CACNA2D2	-0,5838	-0,8792	-0,2883	6,11E-03	3,35E-01	MAPK
CACNB2	-0,4375	-0,7676	-0,1073	3,56E-02	8,99E-01	MAPK
CARD11	-1,4065	-1,8095	-1,0035	2,44E-04	4,72E-02	
CASP7	0,1719	0,0488	0,2950	2,91E-02	7,93E-01	Apop
CASP9	0,4542	0,0855	0,8229	4,65E-02	1,00E+00	PI3K, Apop
CBL	-0,4682	-0,8480	-0,0883	4,64E-02	1,00E+00	STAT
CCNA2	0,2112	0,0670	0,3554	2,40E-02	7,35E-01	CC
CCNB1	-0,2276	-0,3697	-0,0855	1,64E-02	5,70E-01	CC
CCNE1	0,5971	0,3730	0,8213	1,22E-03	1,16E-01	PI3K, CC
CCNE2	0,7290	0,5643	0,8937	5,42E-05	1,95E-02	PI3K, CC
CDC25A	0,6863	0,4798	0,8928	3,30E-04	5,79E-02	CC
CDC25B	0,1945	0,0839	0,3052	1,07E-02	4,42E-01	MAPK, CC
CDC25C	-0,5170	-0,7974	-0,2366	8,58E-03	3,77E-01	CC
CDC6	0,4345	0,2735	0,5954	1,13E-03	1,11E-01	CC
CDC7	0,1784	0,0371	0,3196	4,26E-02	1,00E+00	CC
CDH1	-0,2515	-0,3834	-0,1195	7,32E-03	3,55E-01	
CDKN1A	1,2748	1,0970	1,4527	2,19E-06	2,49E-03	TXmisReg, PI3K, CC
CEBPA	0,8934	0,2456	1,5413	3,05E-02	8,13E-01	TXmisReg
CHEK1	0,2561	0,1214	0,3907	7,38E-03	3,55E-01	CC
COL27A1	-0,9882	-1,2013	-0,7751	4,00E-05	1,95E-02	PI3K

CREB3L4	-0,3792	-0,6751	-0,0833	4,03E-02	9,62E-01	PI3K
CUL1	0,1332	0,0254	0,2410	4,59E-02	1,00E+00	Wnt, TGFB, CC
CXXC4	-0,8076	-1,3992	-0,2160	3,17E-02	8,35E-01	Wnt
DDB2	0,2720	0,2053	0,3387	9,18E-05	2,61E-02	DNARepair
DDIT3	-0,3751	-0,5862	-0,1639	1,02E-02	4,32E-01	TXmisReg, MAPK
DKK1	-0,4734	-0,7443	-0,2025	1,11E-02	4,49E-01	Wnt
DKK4	0,6348	0,2654	1,0042	1,19E-02	4,69E-01	Wnt
DLL1	-0,3344	-0,5661	-0,1028	2,54E-02	7,46E-01	Notch
DLL3	-0,3865	-0,5692	-0,2039	4,31E-03	2,72E-01	Notch
DLL4	-0,4829	-0,7430	-0,2228	8,30E-03	3,77E-01	Notch
DUSP5	-0,4323	-0,6160	-0,2485	2,45E-03	1,82E-01	MAPK
DUSP6	-0,4258	-0,6763	-0,1753	1,26E-02	4,82E-01	TXmisReg, MAPK
EFNA5	-0,5419	-0,7946	-0,2892	4,02E-03	2,69E-01	PI3K, RAS
EGFR	-0,2313	-0,4166	-0,0459	4,44E-02	1,00E+00	MAPK, PI3K, RAS
EPOR	-0,5802	-0,8952	-0,2653	8,62E-03	3,77E-01	STAT, PI3K
ETV1	-0,4662	-0,6115	-0,3208	4,10E-04	6,60E-02	TXmisReg
EZH2	0,2823	0,0812	0,4833	2,84E-02	7,88E-01	
FANCA	0,2219	0,0789	0,3649	1,88E-02	6,26E-01	DNARepair
FANCB	0,2866	0,0681	0,5050	3,70E-02	9,20E-01	DNARepair
FANCF	-0,3887	-0,6550	-0,1223	2,43E-02	7,35E-01	DNARepair
FAS	0,8078	0,2996	1,3161	1,69E-02	5,78E-01	MAPK, Apop
FEN1	0,4841	0,2756	0,6926	2,63E-03	1,91E-01	DNARepair
FGF11	-0,4957	-0,6860	-0,3055	1,39E-03	1,25E-01	MAPK, PI3K, RAS
FGF12	-0,4392	-0,6094	-0,2690	1,47E-03	1,28E-01	MAPK, PI3K, RAS
FGF14	-0,7653	-0,8350	-0,6955	1,19E-07	4,05E-04	MAPK, PI3K, RAS
FGFR1	-0,2498	-0,4015	-0,0980	1,45E-02	5,27E-01	MAPK, PI3K, RAS
FGFR3	0,5514	0,3679	0,7350	6,07E-04	7,39E-02	MAPK, PI3K, RAS
FLNC	-0,8631	-1,5720	-0,1542	4,84E-02	1,00E+00	MAPK
FUBP1	-0,3625	-0,5684	-0,1567	1,07E-02	4,42E-01	
FUT8	-0,5141	-0,9000	-0,1282	3,49E-02	8,88E-01	TXmisReg
GADD45G	-0,8854	-1,0810	-0,6898	4,68E-05	1,95E-02	MAPK, CC
GNAQ	-0,2308	-0,3508	-0,1107	7,02E-03	3,52E-01	
GNG12	-0,5537	-0,7125	-0,3949	2,45E-04	4,72E-02	MAPK, PI3K, RAS
GSK3B	-0,2320	-0,3239	-0,1401	1,66E-03	1,35E-01	Wnt, HH, PI3K, CC
HDAC10	-0,6103	-0,9132	-0,3074	5,54E-03	3,15E-01	ChromMod
HDAC4	-0,7292	-1,1514	-0,3070	1,17E-02	4,65E-01	ChromMod
HDAC6	-0,3654	-0,6195	-0,1114	2,58E-02	7,46E-01	ChromMod
HELLS	0,2754	0,0629	0,4879	3,87E-02	9,37E-01	ChromMod
HGF	-0,5717	-0,9692	-0,1743	2,58E-02	7,46E-01	PI3K, RAS
HIST1H3G	-0,4718	-0,7970	-0,1465	2,49E-02	7,40E-01	TXmisReg
HIST1H3H	-0,9513	-1,2992	-0,6034	1,05E-03	1,06E-01	TXmisReg

HMGA2	-0,4619	-0,7449	-0,1789	1,51E-02	5,31E-01	TXmisReg
HNF1A	-0,8291	-1,4885	-0,1696	4,32E-02	1,00E+00	
HSP90B1	-0,4192	-0,5282	-0,3101	1,34E-04	3,51E-02	PI3K
HSPA2	-0,2078	-0,3682	-0,0474	3,87E-02	9,37E-01	MAPK
ID2	-0,3185	-0,5249	-0,1121	1,93E-02	6,31E-01	TXmisReg, TGFB
IGF1R	-0,4040	-0,6126	-0,1954	6,75E-03	3,45E-01	TXmisReg, PI3K, RAS
INHBB	-0,3738	-0,5988	-0,1488	1,39E-02	5,20E-01	TGFB
JAG1	-0,2598	-0,3915	-0,1280	6,18E-03	3,35E-01	Notch
KDM5C	-0,2776	-0,4454	-0,1097	1,42E-02	5,22E-01	
KMT2C	-0,2337	-0,4080	-0,0594	3,40E-02	8,79E-01	
LAMA5	-0,5816	-0,9717	-0,1915	2,23E-02	7,04E-01	PI3K
LAMC2	-0,2888	-0,4843	-0,0933	2,32E-02	7,18E-01	PI3K
LAT	-1,0356	-1,5789	-0,4924	7,30E-03	3,55E-01	RAS
LEPR	-0,8405	-1,1676	-0,5134	1,50E-03	1,28E-01	STAT
LFNG	-0,8445	-1,0766	-0,6124	1,88E-04	4,59E-02	Notch
LIFR	-0,6193	-0,9782	-0,2604	1,17E-02	4,65E-01	STAT
LTBP1	-0,5514	-0,8218	-0,2810	5,21E-03	3,10E-01	TGFB
MAD2L2	0,3689	0,2913	0,4464	3,40E-05	1,95E-02	DNARepair, CC
MAP2K6	-0,4078	-0,5531	-0,2626	9,04E-04	9,64E-02	MAPK
MAPK8	-0,2056	-0,2678	-0,1435	3,39E-04	5,79E-02	Wnt, MAPK, RAS
MAPT	-1,0542	-1,4114	-0,6969	6,75E-04	7,67E-02	MAPK
MDC1	-0,3587	-0,6216	-0,0958	3,18E-02	8,35E-01	DNARepair
MET	0,1854	0,0828	0,2880	9,44E-03	4,08E-01	TXmisReg, PI3K, RAS
MLLT3	-0,2374	-0,3279	-0,1469	1,34E-03	1,23E-01	TXmisReg
MLLT4	-0,4147	-0,6688	-0,1607	1,51E-02	5,31E-01	RAS
MSH2	0,2387	0,1319	0,3455	3,23E-03	2,20E-01	
MYB	0,2744	0,0799	0,4688	2,79E-02	7,86E-01	PI3K
NASP	0,3552	0,1246	0,5859	1,94E-02	6,31E-01	ChromMod
NFKBIA	0,3243	0,1885	0,4602	2,26E-03	1,75E-01	Apop
NKD1	-0,5607	-0,7819	-0,3394	1,62E-03	1,35E-01	Wnt
NOTCH1	1,0325	0,3372	1,7277	2,26E-02	7,09E-01	Notch
NOTCH2	-0,5027	-0,8327	-0,1728	2,03E-02	6,54E-01	Notch
NRAS	-0,2296	-0,3678	-0,0915	1,39E-02	5,20E-01	MAPK, PI3K, RAS
NSD1	-0,3992	-0,7025	-0,0959	3,65E-02	9,15E-01	ChromMod
NUMBL	0,4564	0,2150	0,6978	7,59E-03	3,60E-01	Notch
PBX1	-0,6909	-0,9148	-0,4669	5,18E-04	7,26E-02	TXmisReg
PDGFD	-0,4389	-0,5964	-0,2813	9,46E-04	9,78E-02	PI3K, RAS
PIK3R1	-0,2889	-0,4750	-0,1028	1,88E-02	6,26E-01	STAT, PI3K, RAS, Apop
PLA2G4C	-0,3983	-0,7170	-0,0796	4,41E-02	1,00E+00	MAPK, RAS
PLCB1	-1,3180	-1,4962	-1,1399	1,77E-06	2,49E-03	Wnt
PLCG2	-0,6667	-0,9626	-0,3708	3,09E-03	2,15E-01	RAS
POLD4	-0,3172	-0,4546	-0,1797	2,72E-03	1,94E-01	DNARepair
POLE2	0,4328	0,1126	0,7529	3,30E-02	8,59E-01	DNARepair
POLR2D	0,2532	0,1106	0,3957	1,03E-02	4,32E-01	DNARepair
PRKAR1B	-0,2775	-0,4082	-0,1468	4,24E-03	2,72E-01	Apop

PRKCG	-0,6555	-0,9898	-0,3212	6,35E-03	3,38E-01	Wnt, MAPK, RAS
RAD21	-0,1477	-0,2213	-0,0740	5,68E-03	3,18E-01	CC
RAD51	0,4556	0,3065	0,6048	5,50E-04	7,26E-02	DNARepair
RASGRF2	-0,4793	-0,8553	-0,1034	4,11E-02	9,73E-01	MAPK, RAS
RFC3	0,4220	0,3281	0,5160	4,91E-05	1,95E-02	DNARepair
RFC4	0,0951	0,0172	0,1730	4,80E-02	1,00E+00	DNARepair
SHC2	-0,4916	-0,8278	-0,1554	2,41E-02	7,35E-01	RAS
SKP2	-0,2696	-0,3311	-0,2082	5,71E-05	1,95E-02	CC
SMC3	0,1585	0,0449	0,2720	2,91E-02	7,93E-01	CC
SOS2	-0,4143	-0,5617	-0,2670	8,96E-04	9,64E-02	MAPK, STAT, PI3K, RAS
SPOP	-0,7133	-1,2651	-0,1614	3,90E-02	9,38E-01	
SPRY1	-0,3783	-0,5642	-0,1923	5,28E-03	3,10E-01	STAT
SPRY2	-0,6930	-0,9862	-0,3998	2,39E-03	1,81E-01	STAT
SPRY4	-0,8303	-0,9832	-0,6774	1,42E-05	1,21E-02	STAT
SUV39H2	0,3127	0,0784	0,5471	3,46E-02	8,88E-01	ChromMod
TGFB3	-0,6653	-0,8196	-0,5110	6,41E-05	1,99E-02	TGFB, MAPK, CC
TIAM1	-0,5262	-0,8355	-0,2169	1,25E-02	4,82E-01	RAS
TLX1	0,3876	0,1095	0,6658	2,93E-02	7,93E-01	TXmisReg
TNFSF10	-0,4301	-0,6624	-0,1977	8,42E-03	3,77E-01	Apop
TNR	-1,2474	-1,6056	-0,8892	2,47E-04	4,72E-02	PI3K
TSC1	-0,3084	-0,5014	-0,1154	1,66E-02	5,71E-01	PI3K
UBE2T	0,3179	0,0740	0,5618	3,78E-02	9,35E-01	DNARepair
WHSC1	-0,1499	-0,2231	-0,0766	5,12E-03	3,10E-01	TXmisReg
WHSC1L1	-0,0795	-0,1319	-0,0270	2,09E-02	6,65E-01	ChromMod
WNT3	0,7061	0,3416	1,0707	6,75E-03	3,45E-01	Wnt, HH
WNT7A	-0,8165	-1,4859	-0,1472	4,81E-02	1,00E+00	Wnt, HH
XRCC4	-0,7366	-0,9677	-0,5055	4,26E-04	6,60E-02	DNARepair
ZBTB16	-0,4513	-0,6844	-0,2181	6,77E-03	3,45E-01	TXmisReg

Suppl. table 2: differentially expressed genes after 24 h of 25 nM bortezomib treatment of BON cells incl. pathway allocations; transcripts with FDR>0.05 were excluded.

Gene symbol	Log2 fold change	Upper confidence limit	Lower confidence limit	*p*-value	FDR	pathway
ABL1	0,3366	0,2243	0,4489	6,15E-04	1,42E-02	RAS, CC
AKT1	-0,6591	-0,8659	-0,4524	4,24E-04	1,07E-02	MAPK, STAT, PI3K, RAS, Apop
AKT2	-0,6014	-0,8642	-0,3386	2,85E-03	4,61E-02	MAPK, STAT, PI3K, RAS, Apop
ALKBH3	0,5896	0,4484	0,7308	7,88E-05	2,93E-03	DNARepair
AMER1	-0,7898	-1,0707	-0,5089	8,97E-04	1,84E-02	
ARID1A	-0,5421	-0,7658	-0,3183	2,09E-03	3,52E-02	ChromMod
ARNT2	-0,8587	-1,0095	-0,7080	1,03E-05	5,96E-04	TXmisReg
ATR	-0,8217	-1,1364	-0,5070	1,37E-03	2,54E-02	CC
B2M	-0,9285	-1,0701	-0,7870	3,99E-06	2,83E-04	
BAIAP3	-1,3912	-1,5774	-1,2051	1,65E-06	1,64E-04	TXmisReg
BAX	-0,6289	-0,7962	-0,4616	1,53E-04	4,76E-03	Apop
BCL2	-1,2656	-1,6325	-0,8987	2,62E-04	7,52E-03	PI3K, Apop
BCOR	-1,3179	-1,5292	-1,1065	5,62E-06	3,49E-04	
BID	0,6998	0,4530	0,9467	8,54E-04	1,78E-02	Apop
BMP6	1,4292	0,8547	2,0036	1,80E-03	3,09E-02	TGFB
BMP7	-1,5367	-1,7399	-1,3335	1,52E-06	1,64E-04	TGFB
BMPR1B	-0,4257	-0,5562	-0,2952	3,69E-04	9,69E-03	TGFB
BNIP3	0,7793	0,6521	0,9065	6,32E-06	3,73E-04	ChromMod
BRCA2	-0,5108	-0,7168	-0,3047	1,84E-03	3,13E-02	DNARepair
BRIP1	-0,6544	-0,8613	-0,4474	4,47E-04	1,10E-02	DNARepair
CACNA2D1	-1,1894	-1,3573	-1,0215	2,37E-06	2,08E-04	MAPK
CACNB2	-1,0934	-1,4625	-0,7242	6,60E-04	1,49E-02	MAPK
CAPN2	1,1210	1,0385	1,2035	2,70E-08	1,74E-05	Apop
CASP3	-0,6546	-0,8157	-0,4935	9,38E-05	3,30E-03	MAPK, Apop
CASP7	0,6847	0,5471	0,8224	2,53E-05	1,16E-03	Apop
CASP8	0,5109	0,3014	0,7204	2,01E-03	3,42E-02	Apop
CCNA2	-1,2025	-1,3637	-1,0413	1,67E-06	1,64E-04	CC
CCNB1	-0,4559	-0,6148	-0,2971	7,95E-04	1,72E-02	CC
CCND1	-1,8714	-2,1630	-1,5799	4,63E-06	3,10E-04	Wnt, STAT, PI3K, CC
CCNE1	-2,1695	-2,4202	-1,9189	6,05E-07	9,50E-05	PI3K, CC
CCNE2	-1,6783	-1,8624	-1,4941	4,25E-07	8,06E-05	PI3K, CC
CDC14A	-0,8511	-1,0427	-0,6595	5,30E-05	2,10E-03	CC
CDC25A	-0,8937	-1,1246	-0,6628	1,28E-04	4,11E-03	CC
CDC25B	-0,8173	-0,9410	-0,6936	3,81E-06	2,82E-04	MAPK, CC
CDC6	-0,5857	-0,7656	-0,4058	3,74E-04	9,75E-03	CC
CDC7	-1,2969	-1,4549	-1,1390	8,70E-07	1,23E-04	CC
CDH1	-0,4427	-0,5903	-0,2951	6,12E-04	1,42E-02	
CDK4	-0,8264	-0,9800	-0,6728	1,51E-05	7,67E-04	PI3K, CC
CDK6	-0,5940	-0,8092	-0,3787	1,00E-03	2,00E-02	PI3K, CC

CDKN1A	1,2400	1,0411	1,4388	5,62E-06	3,49E-04	TXmisReg, PI3K, CC
CDKN2D	-0,7955	-1,0911	-0,4998	1,16E-03	2,23E-02	CC
CEBPA	2,2668	1,5425	2,9911	4,75E-04	1,17E-02	TXmisReg
CHEK2	-0,7792	-0,9532	-0,6052	5,02E-05	2,01E-03	CC
CHUK	-0,4777	-0,6444	-0,3110	8,03E-04	1,72E-02	MAPK, PI3K, RAS, Apop
CREB3L1	-0,8368	-1,0037	-0,6700	2,39E-05	1,12E-03	PI3K
CUL1	0,2741	0,1535	0,3946	2,95E-03	4,72E-02	Wnt, TGFB, CC
CXXC4	-1,5557	-2,2171	-0,8943	2,46E-03	4,03E-02	Wnt
CYLD	0,7492	0,5581	0,9403	1,18E-04	3,98E-03	
DDB2	-0,7378	-0,8124	-0,6632	2,42E-07	6,35E-05	DNARepair
DDIT3	1,5447	1,3087	1,7808	4,07E-06	2,83E-04	TXmisReg, MAPK
DLL1	-2,1333	-2,3923	-1,8743	8,51E-07	1,23E-04	Notch
DLL3	-1,7651	-1,9693	-1,5608	6,12E-07	9,50E-05	Notch
DLL4	-1,8699	-2,1607	-1,5791	4,57E-06	3,10E-04	Notch
DNMT1	-0,4372	-0,5895	-0,2849	7,94E-04	1,72E-02	
DNMT3A	-0,4498	-0,6234	-0,2763	1,43E-03	2,62E-02	
DUSP4	-0,8571	-1,0377	-0,6764	3,44E-05	1,45E-03	MAPK
DUSP5	0,6059	0,4005	0,8114	6,77E-04	1,51E-02	MAPK
DUSP6	-2,1433	-2,4234	-1,8632	1,41E-06	1,60E-04	TXmisReg, MAPK
E2F1	-1,4315	-1,5713	-1,2916	1,91E-07	5,93E-05	CC
E2F5	-1,7917	-1,9837	-1,5998	3,61E-07	7,71E-05	TGFB, CC
EFNA5	-0,7824	-1,0649	-0,4998	9,79E-04	1,98E-02	PI3K, RAS
ENDOG	-1,8438	-2,1961	-1,4914	1,81E-05	8,95E-04	Apop
EPOR	-1,0915	-1,4436	-0,7393	5,03E-04	1,21E-02	STAT, PI3K
ERCC2	-0,5733	-0,8260	-0,3205	2,99E-03	4,74E-02	DNARepair
ETS2	-1,6853	-1,8216	-1,5490	5,19E-08	1,97E-05	RAS
ETV1	-1,7784	-1,9410	-1,6159	1,21E-07	4,12E-05	TXmisReg
ETV4	-0,7773	-1,0095	-0,5452	3,15E-04	8,46E-03	TXmisReg
FANCA	-0,8619	-1,0218	-0,7021	1,48E-05	7,67E-04	DNARepair
FANCC	-0,6863	-0,8866	-0,4860	2,73E-04	7,71E-03	DNARepair
FANCL	-0,8263	-1,1568	-0,4957	1,75E-03	3,05E-02	DNARepair
FBXW7	-0,6781	-0,9783	-0,3779	3,05E-03	4,80E-02	
FEN1	-1,0517	-1,2848	-0,8186	4,78E-05	1,94E-03	DNARepair
FGF11	-0,5135	-0,7263	-0,3008	2,13E-03	3,56E-02	MAPK, PI3K, RAS
FGF14	-1,5055	-1,5835	-1,4275	2,34E-09	2,67E-06	MAPK, PI3K, RAS
FGF9	0,9364	0,6966	1,1762	1,21E-04	4,00E-03	MAPK, PI3K, RAS
FGFR3	-0,8419	-1,0471	-0,6367	8,82E-05	3,13E-03	MAPK, PI3K, RAS
FLNA	1,2589	1,1022	1,4157	1,01E-06	1,23E-04	MAPK
FLNC	1,7934	1,0008	2,5860	3,03E-03	4,78E-02	MAPK
FN1	0,4402	0,2757	0,6046	1,19E-03	2,27E-02	PI3K
FOSL1	2,4229	2,1215	2,7242	1,00E-06	1,23E-04	Wnt
FZD10	-0,9869	-1,2775	-0,6962	2,89E-04	8,02E-03	Wnt

FZD3	-0,6598	-0,9402	-0,3795	2,44E-03	4,03E-02	Wnt
GADD45B	0,9785	0,6142	1,3429	1,17E-03	2,24E-02	MAPK, CC
GATA2	-1,2123	-1,7156	-0,7090	2,15E-03	3,59E-02	
GNG12	-1,1866	-1,3642	-1,0091	3,52E-06	2,73E-04	MAPK, PI3K, RAS
GNG4	-1,1454	-1,4793	-0,8114	2,72E-04	7,71E-03	PI3K, RAS
GRB2	0,6103	0,4898	0,7309	2,25E-05	1,10E-03	MAPK, STAT, PI3K, RAS
H2AFX	-0,8751	-1,1496	-0,6006	4,25E-04	1,07E-02	DNARepair
H3F3A	-1,3733	-1,6261	-1,1206	1,41E-05	7,44E-04	TXmisReg
H3F3C	-0,9595	-1,1560	-0,7631	2,85E-05	1,30E-03	TXmisReg
HDAC1	-0,7388	-0,8912	-0,5863	3,00E-05	1,33E-03	Notch, ChromMod, TXmisReg, CC
HDAC2	-0,5119	-0,7021	-0,3216	1,16E-03	2,23E-02	Notch, ChromMod, TXmisReg, CC
HELLS	-0,8021	-1,0397	-0,5645	3,00E-04	8,18E-03	ChromMod
HES1	-2,3624	-2,6929	-2,0319	2,23E-06	2,01E-04	Notch
HHEX	0,7536	0,5615	0,9457	1,17E-04	3,98E-03	TXmisReg
HIST1H3B	-1,2289	-1,6789	-0,7788	1,06E-03	2,10E-02	TXmisReg
HIST1H3G	-1,6737	-2,0373	-1,3101	4,20E-05	1,73E-03	TXmisReg
HIST1H3H	-0,9114	-1,3004	-0,5224	2,51E-03	4,09E-02	TXmisReg
HMGA2	-3,0097	-3,3262	-2,6933	3,17E-07	7,71E-05	TXmisReg
HOXA10	-0,8548	-1,1332	-0,5764	5,32E-04	1,27E-02	TXmisReg
HRAS	-0,7561	-1,0229	-0,4893	8,55E-04	1,78E-02	MAPK, PI3K, RAS
HSP90B1	0,6654	0,5434	0,7873	1,37E-05	7,43E-04	PI3K
HSPA1A	6,2823	5,5134	7,0513	8,99E-07	1,23E-04	MAPK
HSPA2	-0,4965	-0,6758	-0,3171	9,81E-04	1,98E-02	MAPK
HSPB1	2,5675	1,9314	3,2036	9,78E-05	3,41E-03	MAPK
ID1	-3,6501	-4,0387	-3,2614	3,46E-07	7,71E-05	TGFB
ID2	-3,0798	-3,3106	-2,8491	3,05E-08	1,74E-05	TXmisReg, TGFB
ID4	-1,6233	-1,8406	-1,4061	1,65E-06	1,64E-04	TGFB
IDH2	-1,7407	-1,9404	-1,5409	5,79E-07	9,50E-05	
IGFBP3	0,6462	0,3946	0,8979	1,51E-03	2,72E-02	TXmisReg
IKBKG	0,7964	0,5923	1,0005	1,21E-04	4,00E-03	MAPK, PI3K, RAS, Apop
IL12A	1,1282	0,6822	1,5742	1,64E-03	2,90E-02	STAT
IL12RB2	-0,6300	-0,8500	-0,4099	8,07E-04	1,72E-02	STAT
IL1R2	-0,8068	-1,1608	-0,4529	2,91E-03	4,68E-02	TXmisReg, MAPK
IL20RB	1,2389	0,6929	1,7850	2,98E-03	4,74E-02	STAT
IL6R	0,7019	0,4670	0,9368	6,26E-04	1,42E-02	STAT, PI3K
INHBB	-1,7327	-1,9843	-1,4811	2,87E-06	2,34E-04	TGFB
IRS1	-0,8036	-1,0853	-0,5220	8,22E-04	1,74E-02	PI3K
ITGA3	-0,5896	-0,7512	-0,4280	1,85E-04	5,63E-03	PI3K
ITGB8	-2,0583	-2,4307	-1,6858	1,26E-05	7,05E-04	PI3K
JAG2	-1,0978	-1,3808	-0,8148	1,26E-04	4,09E-03	Notch
KITLG	-0,6441	-0,8968	-0,3913	1,57E-03	2,81E-02	PI3K, RAS

KMT2C	0,5618	0,3669	0,7567	7,74E-04	1,70E-02	
KRAS	0,3098	0,2481	0,3714	2,36E-05	1,12E-03	MAPK, PI3K, RAS
LAMB3	1,1657	1,0156	1,3158	1,27E-06	1,50E-04	PI3K
LFNG	-3,2693	-3,5288	-3,0098	4,55E-08	1,97E-05	Notch
LIF	-1,3323	-1,6544	-1,0102	8,37E-05	3,05E-03	STAT
LIG4	-0,8566	-1,1094	-0,6037	2,93E-04	8,07E-03	DNARepair
MAD2L2	-0,3714	-0,4581	-0,2846	6,71E-05	2,59E-03	DNARepair, CC
MAP2K1	0,5927	0,5132	0,6721	1,68E-06	1,64E-04	MAPK, PI3K, RAS
MAP2K2	0,6737	0,4485	0,8988	6,21E-04	1,42E-02	MAPK, PI3K, RAS
MAP2K6	-0,9997	-1,1621	-0,8373	6,13E-06	3,73E-04	MAPK
MAP3K14	1,1246	0,7391	1,5101	7,22E-04	1,60E-02	MAPK, Apop
MAP3K5	-1,0524	-1,3704	-0,7344	3,38E-04	9,02E-03	MAPK
MAPK3	-0,6705	-0,8603	-0,4807	2,26E-04	6,71E-03	TGFB, MAPK, PI3K, RAS
MAPK8	-0,4408	-0,5103	-0,3713	5,01E-06	3,29E-04	Wnt, MAPK, RAS
MAPT	0,9231	0,5237	1,3225	2,70E-03	4,39E-02	MAPK
MCM4	-0,6520	-0,8921	-0,4120	1,10E-03	2,14E-02	CC
MCM5	-0,7211	-0,9718	-0,4704	7,85E-04	1,72E-02	CC
MCM7	-0,5832	-0,8082	-0,3581	1,43E-03	2,62E-02	CC
MECOM	-1,3960	-1,7220	-1,0699	6,71E-05	2,59E-03	MAPK
MET	1,0025	0,8878	1,1171	5,66E-07	9,50E-05	TXmisReg, PI3K, RAS
MLF1	-0,5015	-0,6301	-0,3729	1,22E-04	4,00E-03	TXmisReg
MLLT3	-0,6653	-0,7665	-0,5641	3,94E-06	2,83E-04	TXmisReg
MSH2	-0,3092	-0,4285	-0,1898	1,44E-03	2,62E-02	
MYB	-2,7014	-2,9188	-2,4840	5,01E-08	1,97E-05	PI3K
MYC	-0,9651	-1,1465	-0,7838	1,62E-05	8,12E-04	Wnt, TXmisReg, TGFB, MAPK, STAT, PI3K, CC
NFKB1	-1,2252	-1,5769	-0,8735	2,47E-04	7,20E-03	TXmisReg, MAPK, PI3K, RAS, Apop
NFKBIA	-0,4176	-0,5695	-0,2658	1,02E-03	2,02E-02	Apop
NKD1	-0,6500	-0,8973	-0,4026	1,32E-03	2,48E-02	Wnt
NOTCH1	2,3585	1,5812	3,1358	5,72E-04	1,35E-02	Notch
NOTCH3	1,3095	0,9004	1,7187	4,15E-04	1,06E-02	Notch
NPM2	-1,0013	-1,4249	-0,5777	2,39E-03	3,96E-02	ChromMod
NTHL1	-0,7357	-1,0301	-0,4412	1,76E-03	3,05E-02	DNARepair
NUMBL	1,4653	1,1954	1,7351	1,42E-05	7,44E-04	Notch
PBRM1	-0,5134	-0,7137	-0,3131	1,52E-03	2,74E-02	
PBX1	-0,8061	-1,0565	-0,5558	4,00E-04	1,03E-02	TXmisReg
PBX3	-0,7303	-0,9050	-0,5556	7,82E-05	2,93E-03	TXmisReg
PDGFD	-0,7036	-0,8798	-0,5275	1,05E-04	3,60E-03	PI3K, RAS
PGF	2,1554	1,7744	2,5365	1,08E-05	6,14E-04	PI3K, RAS

PIK3CB	-0,6277	-0,8776	-0,3779	1,70E-03	2,99E-02	STAT, PI3K, RAS, Apop
PIK3R1	-0,6156	-0,8236	-0,4075	6,65E-04	1,49E-02	STAT, PI3K, RAS, Apop
PIK3R3	-0,4713	-0,6442	-0,2984	1,07E-03	2,10E-02	STAT, PI3K, RAS, Apop
PLA2G4C	1,1272	0,7709	1,4836	4,45E-04	1,10E-02	MAPK, RAS
POLD4	-0,5233	-0,6770	-0,3696	2,84E-04	7,95E-03	DNARepair
POLE2	-0,8989	-1,2568	-0,5409	1,71E-03	2,99E-02	DNARepair
POLR2D	-0,7733	-0,9327	-0,6140	2,97E-05	1,33E-03	DNARepair
POLR2H	-1,0265	-1,2751	-0,7778	8,48E-05	3,05E-03	DNARepair
PPP2CB	0,6087	0,4438	0,7736	1,72E-04	5,28E-03	TGFB, PI3K
PPP2R2C	1,7855	1,4991	2,0719	5,63E-06	3,49E-04	PI3K
PPP3CB	-0,8778	-1,2076	-0,5480	1,23E-03	2,33E-02	Wnt, MAPK, Apop
PRKACA	-0,8361	-0,9573	-0,7149	2,84E-06	2,34E-04	Wnt, HH, MAPK, RAS, Apop
PRKAR1B	-0,6250	-0,7711	-0,4788	6,76E-05	2,59E-03	Apop
PRKAR2A	-0,5185	-0,6814	-0,3557	4,28E-04	1,07E-02	Apop
PRKCG	-0,9894	-1,3631	-0,6156	1,27E-03	2,39E-02	Wnt, MAPK, RAS
PTCH1	-1,5642	-1,9771	-1,1513	1,46E-04	4,58E-03	HH
PTTG2	-0,8886	-1,2041	-0,5730	8,88E-04	1,84E-02	CC
RAD21	-0,5044	-0,5867	-0,4220	6,34E-06	3,73E-04	CC
RBX1	-0,4333	-0,5762	-0,2904	5,75E-04	1,35E-02	Wnt, TGFB, CC
RET	-2,3199	-2,6334	-2,0064	1,77E-06	1,67E-04	
RFC3	-0,3268	-0,4318	-0,2218	4,91E-04	1,20E-02	DNARepair
RFC4	-0,7051	-0,7921	-0,6180	9,57E-07	1,23E-04	DNARepair
RPS27A	-0,3945	-0,5260	-0,2630	6,11E-04	1,42E-02	DNARepair
RXRG	-0,8353	-1,1354	-0,5351	9,52E-04	1,95E-02	TXmisReg
SETBP1	-0,6859	-0,9268	-0,4450	8,32E-04	1,75E-02	
SFN	0,7006	0,4280	0,9733	1,50E-03	2,72E-02	CC
SHC1	0,6532	0,5177	0,7887	3,10E-05	1,34E-03	RAS
SHC3	-0,9839	-1,2595	-0,7082	2,12E-04	6,36E-03	RAS
SHC4	1,8139	1,0644	2,5633	2,10E-03	3,53E-02	RAS
SKP1	0,3852	0,2758	0,4947	2,31E-04	6,80E-03	Wnt, TGFB, CC
SKP2	-1,7866	-1,8553	-1,7180	2,92E-10	9,96E-07	CC
SMARCA4	-0,5060	-0,6525	-0,3595	2,60E-04	7,52E-03	
SMC1A	-0,6373	-0,8812	-0,3935	1,37E-03	2,54E-02	CC
SMC3	-0,5299	-0,6568	-0,4029	7,91E-05	2,93E-03	CC
SOS1	0,2741	0,1924	0,3558	3,12E-04	8,44E-03	MAPK, STAT, PI3K, RAS
SOX9	-1,1863	-1,4995	-0,8731	1,46E-04	4,58E-03	
SPP1	3,6997	3,5318	3,8676	9,32E-10	1,59E-06	PI3K
SPRY1	-1,9010	-2,1089	-1,6931	4,16E-07	8,06E-05	STAT
SPRY2	-2,2614	-2,5893	-1,9336	2,84E-06	2,34E-04	STAT
SPRY4	-1,7156	-1,8865	-1,5446	2,19E-07	6,23E-05	STAT
STMN1	-0,8861	-1,0082	-0,7640	2,01E-06	1,86E-04	MAPK
SUV39H2	-0,9394	-1,2014	-0,6774	2,06E-04	6,23E-03	ChromMod

SYK	-0,9234	-1,0631	-0,7838	3,78E-06	2,82E-04	PI3K
TBL1XR1	-0,8011	-0,9949	-0,6073	8,41E-05	3,05E-03	Wnt
TFDP1	-1,1946	-1,3691	-1,0202	2,98E-06	2,37E-04	TGFB, CC
TGFB3	-2,9226	-3,0951	-2,7501	5,81E-09	4,96E-06	TGFB, MAPK, CC
TGFBR2	-1,2031	-1,4429	-0,9633	2,39E-05	1,12E-03	TXmisReg, TGFB, MAPK
THEM4	-1,0476	-1,3652	-0,7299	3,46E-04	9,15E-03	PI3K
TIAM1	-0,8622	-1,2080	-0,5164	1,78E-03	3,07E-02	RAS
TSPAN7	-0,5830	-0,8127	-0,3533	1,61E-03	2,86E-02	TXmisReg
UBB	0,9993	0,7894	1,2092	3,37E-05	1,44E-03	DNARepair
WEE1	-0,9888	-1,1700	-0,8076	1,37E-05	7,43E-04	CC
WHSC1	-0,3151	-0,3970	-0,2332	1,33E-04	4,23E-03	TXmisReg
WNT4	-1,9228	-2,3387	-1,5069	4,08E-05	1,70E-03	Wnt, HH
XPA	-0,6332	-0,8370	-0,4293	4,97E-04	1,20E-02	DNARepair
ZBTB16	-1,2574	-1,5180	-0,9967	3,09E-05	1,34E-03	TXmisReg
ZIC2	-1,6596	-2,2613	-1,0579	1,00E-03	2,00E-02	HH

Suppl. table 3: differentially expressed genes after 24 h of 10 µM cisplatin plus 25 nM bortezomib treatment of BON cells incl. pathway allocations; transcripts with FDR>0.05 were excluded.

Gene symbol	Log2 fold change	Upper confidence limit	Lower confidence limit	*p*-value	FDR	pathway
AKT1	-0,9807	-1,1656	-0,7958	1,66E-05	5,04E-04	MAPK, STAT, PI3K, RAS, Apop
AKT2	-1,0736	-1,3087	-0,8385	4,42E-05	1,10E-03	MAPK, STAT, PI3K, RAS, Apop
ALKBH2	0,6423	0,3618	0,9229	2,84E-03	3,68E-02	DNARepair
ALKBH3	0,3576	0,2313	0,4839	8,60E-04	1,29E-02	DNARepair
AMER1	-0,8477	-1,0989	-0,5964	3,01E-04	5,24E-03	
ARID1A	-1,0200	-1,2201	-0,8199	2,15E-05	6,22E-04	ChromMod
ARID1B	-1,3941	-1,6962	-1,0920	4,13E-05	1,04E-03	
ARID2	-0,5133	-0,7274	-0,2991	2,22E-03	3,00E-02	
ARNT2	-1,7084	-1,8432	-1,5735	4,38E-08	1,07E-05	TXmisReg
ATR	-0,9776	-1,2591	-0,6961	2,51E-04	4,64E-03	CC
ATRX	-0,6803	-0,8495	-0,5112	1,00E-04	2,06E-03	
B2M	-0,9631	-1,0896	-0,8365	1,46E-06	7,80E-05	
BAIAP3	-1,3572	-1,5237	-1,1907	9,14E-07	6,24E-05	TXmisReg
BAX	-0,7434	-0,8931	-0,5938	2,55E-05	7,01E-04	Apop
BCL2	-1,3639	-1,6921	-1,0357	8,12E-05	1,73E-03	PI3K, Apop
BCL2L1	-0,7880	-1,1406	-0,4354	3,23E-03	4,09E-02	TXmisReg, STAT, PI3K, RAS, Apop
BCOR	-1,2635	-1,4526	-1,0745	3,52E-06	1,56E-04	
BID	0,8028	0,5820	1,0236	1,89E-04	3,59E-03	Apop
BMP7	-2,0759	-2,2576	-1,8942	8,97E-08	1,61E-05	TGFB
BMPR1B	-0,9132	-1,0299	-0,7965	1,21E-06	6,95E-05	TGFB
BNIP3	0,9796	0,8659	1,0934	6,28E-07	4,87E-05	ChromMod
BRCA2	-1,0197	-1,2040	-0,8354	1,25E-05	4,03E-04	DNARepair
CACNA1C	-1,7950	-2,3446	-1,2454	3,67E-04	6,26E-03	MAPK
CACNA1D	-1,3292	-1,7231	-0,9353	3,00E-04	5,24E-03	MAPK
CACNA1H	-1,5805	-1,7937	-1,3672	1,75E-06	8,77E-05	MAPK
CACNA2D1	-2,0198	-2,1699	-1,8696	2,89E-08	8,97E-06	MAPK
CACNA2D2	-1,3458	-1,6413	-1,0504	4,49E-05	1,10E-03	MAPK
CACNB2	-1,0392	-1,3693	-0,7090	4,59E-04	7,53E-03	MAPK
CAPN2	0,7980	0,7242	0,8718	1,31E-07	2,13E-05	Apop
CASP3	-0,3290	-0,4731	-0,1849	2,88E-03	3,73E-02	MAPK, Apop
CASP7	0,7982	0,6751	0,9213	4,32E-06	1,80E-04	Apop
CASP8	0,6028	0,4154	0,7902	4,02E-04	6,78E-03	Apop
CBLC	-1,2965	-1,6672	-0,9259	2,41E-04	4,46E-03	STAT
CCNA2	-1,1654	-1,3096	-1,0212	9,68E-07	6,35E-05	CC
CCNB1	-0,8035	-0,9456	-0,6614	1,08E-05	3,65E-04	CC
CCND1	-2,5093	-2,7701	-2,2485	2,93E-07	3,29E-05	Wnt, STAT, PI3K, CC

CCNE1	-1,5851	-1,8093	-1,3609	2,41E-06	1,14E-04	PI3K, CC
CDC14A	-0,8155	-0,9869	-0,6441	3,38E-05	9,02E-04	CC
CDC25B	-1,1744	-1,2851	-1,0638	1,49E-07	2,31E-05	MAPK, CC
CDC25C	-0,8165	-1,0970	-0,5361	7,30E-04	1,13E-02	CC
CDC7	-1,2397	-1,3810	-1,0984	5,52E-07	4,57E-05	CC
CDH1	-0,7341	-0,8661	-0,6021	1,21E-05	4,00E-04	
CDK4	-0,7709	-0,9083	-0,6335	1,14E-05	3,81E-04	PI3K, CC
CDK6	-1,2526	-1,4451	-1,0600	4,23E-06	1,80E-04	PI3K, CC
CDKN1A	1,6324	1,4545	1,8102	4,05E-07	3,95E-05	TXmisReg, PI3K, CC
CDKN2D	-0,8283	-1,0928	-0,5639	4,72E-04	7,71E-03	CC
CEBPA	3,5734	2,9255	4,2212	1,28E-05	4,07E-04	TXmisReg
CHEK2	-0,6977	-0,8533	-0,5421	4,98E-05	1,21E-03	CC
COL27A1	-1,5967	-1,8098	-1,3836	1,62E-06	8,40E-05	PI3K
CREB3L1	-1,1121	-1,2613	-0,9629	1,68E-06	8,57E-05	PI3K
CREBBP	-0,9996	-1,4521	-0,5472	3,44E-03	4,31E-02	Notch, Wnt, ChromMod, TGFB, STAT, CC
CXXC4	-1,8885	-2,4801	-1,2969	4,21E-04	7,01E-03	Wnt
CYLD	0,9466	0,7757	1,1175	1,24E-05	4,03E-04	
DDB2	-0,4997	-0,5664	-0,4330	1,63E-06	8,40E-05	DNARepair
DDIT3	1,6567	1,4455	1,8679	1,19E-06	6,95E-05	TXmisReg, MAPK
DKK1	-0,5927	-0,8636	-0,3217	3,62E-03	4,51E-02	Wnt
DLL1	-2,1847	-2,4164	-1,9530	3,36E-07	3,59E-05	Notch
DLL3	-2,1013	-2,2840	-1,9187	8,54E-08	1,61E-05	Notch
DLL4	-2,0373	-2,2974	-1,7772	1,20E-06	6,95E-05	Notch
DNMT1	-0,6796	-0,8158	-0,5433	2,48E-05	6,94E-04	
DNMT3A	-0,6120	-0,7672	-0,4568	1,14E-04	2,28E-03	
DUSP4	-1,5784	-1,7400	-1,4169	2,64E-07	3,21E-05	MAPK
DUSP6	-2,3266	-2,5771	-2,0761	3,74E-07	3,75E-05	TXmisReg, MAPK
E2F1	-1,0131	-1,1381	-0,8880	9,54E-07	6,35E-05	CC
E2F5	-2,0717	-2,2434	-1,9000	6,15E-08	1,31E-05	TGFB, CC
EFNA3	0,9523	0,6642	1,2403	3,40E-04	5,87E-03	PI3K, RAS
EFNA5	-1,9691	-2,2218	-1,7164	1,24E-06	6,95E-05	PI3K, RAS
EGFR	-1,2340	-1,4194	-1,0487	3,62E-06	1,57E-04	MAPK, PI3K, RAS
EIF4EBP1	-0,6686	-0,8509	-0,4864	1,79E-04	3,40E-03	PI3K
ENDOG	-1,8226	-2,1377	-1,5075	9,31E-06	3,24E-04	Apop
EPOR	-1,3214	-1,6364	-1,0064	7,65E-05	1,69E-03	STAT, PI3K
ERCC2	-0,9443	-1,1704	-0,7182	7,87E-05	1,69E-03	DNARepair
ETS2	-1,6030	-1,7249	-1,4810	3,39E-08	9,64E-06	RAS
ETV1	-2,2399	-2,3852	-2,0945	1,12E-08	6,40E-06	TXmisReg
ETV4	-1,0200	-1,2276	-0,8123	2,74E-05	7,49E-04	TXmisReg
FANCA	-0,5632	-0,7062	-0,4202	1,14E-04	2,28E-03	DNARepair
FANCC	-1,0363	-1,2155	-0,8572	9,29E-06	3,24E-04	DNARepair
FANCF	-0,6172	-0,8835	-0,3509	2,66E-03	3,51E-02	DNARepair
FAS	1,1879	0,6797	1,6961	2,54E-03	3,37E-02	MAPK, Apop

FASLG	-1,3073	-1,7741	-0,8406	9,16E-04	1,37E-02	MAPK, PI3K, RAS, Apop
FBXW7	-0,9567	-1,2252	-0,6882	2,15E-04	4,03E-03	
FEN1	-0,5254	-0,7339	-0,3170	1,68E-03	2,33E-02	DNARepair
FGF11	-0,4964	-0,6867	-0,3061	1,38E-03	1,95E-02	MAPK, PI3K, RAS
FGF12	-0,9910	-1,1612	-0,8208	8,90E-06	3,20E-04	MAPK, PI3K, RAS
FGF14	-2,3022	-2,3720	-2,2325	5,54E-11	9,46E-08	MAPK, PI3K, RAS
FGF9	1,0798	0,8654	1,2943	2,33E-05	6,58E-04	MAPK, PI3K, RAS
FGFR3	-0,4816	-0,6651	-0,2980	1,34E-03	1,90E-02	MAPK, PI3K, RAS
FGFR4	-1,4136	-1,8260	-1,0011	2,73E-04	4,98E-03	MAPK, PI3K, RAS
FLNA	0,9391	0,7989	1,0794	3,48E-06	1,56E-04	MAPK
FOSL1	2,3621	2,0926	2,6317	5,57E-07	4,57E-05	Wnt
FST	0,6942	0,4412	0,9473	1,03E-03	1,51E-02	TGFB
FUT8	-1,7046	-2,0905	-1,3187	5,49E-05	1,31E-03	TXmisReg
FZD10	-0,8359	-1,0958	-0,5759	4,03E-04	6,78E-03	Wnt
GADD45A	0,4630	0,3713	0,5548	2,30E-05	6,53E-04	MAPK, CC
GADD45B	1,1070	0,7811	1,4329	2,88E-04	5,15E-03	MAPK, CC
GATA2	-1,0626	-1,5128	-0,6124	2,41E-03	3,21E-02	
GNAQ	-0,7168	-0,8369	-0,5967	7,54E-06	2,92E-04	
GNAS	-0,5071	-0,7262	-0,2879	2,68E-03	3,52E-02	
GNG12	-1,6518	-1,8106	-1,4930	1,71E-07	2,43E-05	MAPK, PI3K, RAS
GNG4	-1,7010	-1,9997	-1,4023	1,03E-05	3,52E-04	PI3K, RAS
GPC4	-1,1511	-1,4094	-0,8928	5,18E-05	1,24E-03	Wnt
GRB2	0,4380	0,3302	0,5459	9,39E-05	1,95E-03	MAPK, STAT, PI3K, RAS
GSK3B	-0,4568	-0,5487	-0,3649	2,54E-05	7,01E-04	Wnt, HH, PI3K, CC
H2AFX	-0,5660	-0,8115	-0,3204	2,74E-03	3,58E-02	DNARepair
H3F3A	-1,4337	-1,6598	-1,2077	5,02E-06	2,04E-04	TXmisReg
H3F3C	-0,8531	-1,0289	-0,6774	2,96E-05	7,96E-04	TXmisReg
HDAC1	-1,0497	-1,1860	-0,9133	1,35E-06	7,43E-05	Notch, ChromMod, TXmisReg, CC
HDAC10	-1,2320	-1,5349	-0,9291	9,32E-05	1,95E-03	ChromMod
HDAC11	-0,7660	-1,0401	-0,4918	9,29E-04	1,38E-02	ChromMod
HDAC2	-0,5455	-0,7157	-0,3753	4,11E-04	6,88E-03	Notch, ChromMod, TXmisReg, CC
HDAC4	-1,8441	-2,2662	-1,4219	5,90E-05	1,36E-03	ChromMod
HELLS	-0,5088	-0,7213	-0,2963	2,23E-03	3,01E-02	ChromMod
HES1	-2,0736	-2,3692	-1,7780	2,54E-06	1,19E-04	Notch
HHEX	1,0681	0,8962	1,2399	5,75E-06	2,28E-04	TXmisReg
HIST1H3B	-0,9909	-1,3935	-0,5883	1,91E-03	2,62E-02	TXmisReg
HIST1H3G	-1,2507	-1,5759	-0,9255	1,33E-04	2,59E-03	TXmisReg

HIST1H3H	-0,8722	-1,2202	-0,5243	1,73E-03	2,39E-02	TXmisReg
HMGA2	-3,6508	-3,9338	-3,3678	3,87E-08	1,01E-05	TXmisReg
HNF1A	-2,0197	-2,6791	-1,3602	5,41E-04	8,70E-03	
HOXA10	-1,1626	-1,4116	-0,9136	3,83E-05	9,74E-04	TXmisReg
HRAS	-1,1301	-1,3687	-0,8914	3,49E-05	9,22E-04	MAPK, PI3K, RAS
HSP90B1	0,4408	0,3317	0,5499	9,71E-05	2,01E-03	PI3K
HSPA1A	5,6833	4,9955	6,3710	8,32E-07	5,91E-05	MAPK
HSPB1	2,0536	1,4847	2,6225	1,98E-04	3,73E-03	MAPK
ID1	-3,5044	-3,8520	-3,1568	2,13E-07	2,79E-05	TGFB
ID2	-2,8198	-3,0262	-2,6134	2,60E-08	8,86E-06	TXmisReg, TGFB
ID4	-1,6000	-1,7943	-1,4057	8,53E-07	5,94E-05	TGFB
IDH1	0,5947	0,4006	0,7887	5,39E-04	8,70E-03	
IDH2	-2,0894	-2,2681	-1,9108	7,63E-08	1,53E-05	
IGF1R	-0,9114	-1,1200	-0,7028	5,89E-05	1,36E-03	TXmisReg, PI3K, RAS
IGFBP3	0,6874	0,4623	0,9125	5,50E-04	8,81E-03	TXmisReg
IKBKG	0,8559	0,6733	1,0384	3,72E-05	9,64E-04	MAPK, PI3K, RAS, Apop
IL12A	1,8824	1,4835	2,2813	3,57E-05	9,37E-04	STAT
IL12RB2	-0,8688	-1,0656	-0,6719	5,52E-05	1,31E-03	STAT
IL1R2	-0,7917	-1,1083	-0,4752	1,75E-03	2,42E-02	TXmisReg, MAPK
IL1RAP	-1,2490	-1,6894	-0,8086	8,52E-04	1,29E-02	Apop
IL20RA	-0,8809	-1,2802	-0,4817	3,46E-03	4,33E-02	STAT
IL6R	0,5510	0,3410	0,7611	1,34E-03	1,90E-02	STAT, PI3K
IL8	1,3773	1,1717	1,5829	3,47E-06	1,56E-04	TXmisReg
INHBB	-2,1667	-2,3917	-1,9417	2,91E-07	3,29E-05	TGFB
IRS1	-1,3503	-1,6022	-1,0984	1,54E-05	4,74E-04	PI3K
ITGA3	-0,8730	-1,0175	-0,7285	6,95E-06	2,73E-04	PI3K
ITGB8	-1,4632	-1,7963	-1,1300	5,69E-05	1,34E-03	PI3K
JAG2	-1,5027	-1,7558	-1,2496	7,81E-06	2,96E-04	Notch
JUN	0,9243	0,6197	1,2288	5,71E-04	9,10E-03	Wnt, MAPK
KAT2B	-1,5564	-1,9804	-1,1324	1,78E-04	3,40E-03	Notch
KRAS	0,2385	0,1833	0,2936	6,28E-05	1,43E-03	MAPK, PI3K, RAS
LAMA5	-1,0550	-1,4451	-0,6649	1,12E-03	1,63E-02	PI3K
LAMB3	1,3296	1,1954	1,4639	2,40E-07	3,03E-05	PI3K
LEPR	-0,7308	-1,0580	-0,4037	3,24E-03	4,09E-02	STAT
LFNG	-3,4769	-3,7090	-3,2448	1,37E-08	6,67E-06	Notch
LIF	-1,5129	-1,8010	-1,2248	1,77E-05	5,25E-04	STAT
LIFR	0,8740	0,5151	1,2329	2,03E-03	2,77E-02	STAT
LIG4	-0,8951	-1,1213	-0,6690	1,11E-04	2,24E-03	DNARepair
LTBP1	-1,7490	-2,0194	-1,4786	4,39E-06	1,81E-04	TGFB
MAML2	-1,6772	-2,4193	-0,9351	3,05E-03	3,88E-02	Notch
MAP2K1	0,5542	0,4831	0,6253	1,24E-06	6,95E-05	MAPK, PI3K, RAS
MAP2K6	-1,3280	-1,4733	-1,1828	4,16E-07	3,95E-05	MAPK

MAP3K14	1,1213	0,7765	1,4661	3,77E-04	6,39E-03	MAPK, Apop
MAP3K5	-1,5052	-1,7896	-1,2207	1,68E-05	5,07E-04	MAPK
MAPK12	-0,8680	-1,2328	-0,5033	2,30E-03	3,08E-02	MAPK
MAPK3	-0,7089	-0,8787	-0,5392	7,87E-05	1,69E-03	TGFB, MAPK, PI3K, RAS
MAPK8	-0,3540	-0,4161	-0,2918	1,03E-05	3,52E-04	Wnt, MAPK, RAS
MAPK8IP1	-0,8032	-1,1566	-0,4498	2,96E-03	3,79E-02	MAPK
MCM7	-0,6709	-0,8722	-0,4696	3,24E-04	5,62E-03	CC
MDC1	-0,6025	-0,8654	-0,3396	2,83E-03	3,68E-02	DNARepair
MECOM	-1,8921	-2,1837	-1,6005	4,30E-06	1,80E-04	MAPK
MEN1	0,2450	0,1370	0,3531	2,99E-03	3,82E-02	TXmisReg
MET	1,0374	0,9349	1,1400	2,08E-07	2,79E-05	TXmisReg, PI3K, RAS
MFNG	-1,4404	-2,1135	-0,7672	4,07E-03	4,99E-02	Notch
MLLT3	-1,2893	-1,3798	-1,1988	1,94E-08	7,37E-06	TXmisReg
MSH2	-0,3622	-0,4689	-0,2554	2,91E-04	5,16E-03	
MTOR	-0,8275	-1,1189	-0,5362	8,45E-04	1,29E-02	PI3K
MYB	-2,8357	-3,0301	-2,6412	1,65E-08	7,03E-06	PI3K
MYC	-1,0094	-1,1716	-0,8472	5,70E-06	2,28E-04	Wnt, TXmisReg, TGFB, MAPK, STAT, PI3K, CC
MYD88	-0,9418	-1,2594	-0,6241	6,57E-04	1,03E-02	Apop
NCOR1	-0,6424	-0,8089	-0,4760	1,30E-04	2,55E-03	TXmisReg
NF1	-0,6167	-0,7958	-0,4377	2,64E-04	4,85E-03	MAPK, RAS
NFKB1	-1,3163	-1,6308	-1,0017	7,77E-05	1,69E-03	TXmisReg, MAPK, PI3K, RAS, Apop
NFKBIA	-0,3354	-0,4712	-0,1996	1,88E-03	2,58E-02	Apop
NKD1	-1,1863	-1,4075	-0,9650	1,54E-05	4,74E-04	Wnt
NOTCH1	2,3801	1,6849	3,0754	2,75E-04	4,99E-03	Notch
NOTCH3	1,0312	0,6653	1,3972	8,85E-04	1,32E-02	Notch
NPM2	-1,2374	-1,6162	-0,8585	3,67E-04	6,26E-03	ChromMod
NSD1	-0,9467	-1,2500	-0,6434	4,83E-04	7,84E-03	ChromMod
NTHL1	-1,0870	-1,3504	-0,8236	8,49E-05	1,80E-03	DNARepair
NUMBL	1,4168	1,1754	1,6582	8,44E-06	3,06E-04	Notch
PAX5	-1,5857	-1,9540	-1,2174	6,48E-05	1,46E-03	TXmisReg
PBRM1	-0,9680	-1,1472	-0,7889	1,46E-05	4,58E-04	
PBX1	-1,9491	-2,1730	-1,7251	5,83E-07	4,63E-05	TXmisReg
PBX3	-1,3129	-1,4692	-1,1567	7,42E-07	5,39E-05	TXmisReg
PDGFD	-1,4726	-1,6302	-1,3151	3,57E-07	3,70E-05	PI3K, RAS
PGF	2,8718	2,5310	3,2126	7,28E-07	5,39E-05	PI3K, RAS
PHF6	-0,4473	-0,5745	-0,3201	2,33E-04	4,35E-03	
PIK3CB	-1,2989	-1,5224	-1,0755	9,00E-06	3,20E-04	STAT, PI3K, RAS, Apop
PIK3R1	-0,9450	-1,1311	-0,7589	2,21E-05	6,33E-04	STAT, PI3K, RAS, Apop
PIK3R2	-1,2498	-1,7456	-0,7541	1,67E-03	2,33E-02	STAT, PI3K, RAS, Apop

PLA2G4C	0,7713	0,4526	1,0900	2,10E-03	2,86E-02	MAPK, RAS
PLCB1	-1,5653	-1,7435	-1,3872	5,46E-07	4,57E-05	Wnt
PLD1	-0,6821	-0,9400	-0,4241	1,28E-03	1,83E-02	RAS
POLB	0,6620	0,4044	0,9195	1,50E-03	2,12E-02	DNARepair
POLD1	-1,5369	-1,9425	-1,1312	1,46E-04	2,83E-03	DNARepair
POLD4	-0,7534	-0,8908	-0,6159	1,33E-05	4,21E-04	DNARepair
POLE2	-0,6949	-1,0151	-0,3748	3,77E-03	4,66E-02	DNARepair
POLR2D	-0,6428	-0,7854	-0,5003	4,80E-05	1,17E-03	DNARepair
POLR2H	-1,0426	-1,2650	-0,8202	3,73E-05	9,64E-04	DNARepair
PPARGC1A	-0,5283	-0,7555	-0,3010	2,62E-03	3,46E-02	ChromMod
PPP2CB	0,5768	0,4294	0,7243	1,19E-04	2,36E-03	TGFB, PI3K
PPP2R1A	-0,6376	-0,8703	-0,4050	1,04E-03	1,52E-02	TGFB, PI3K
PPP2R2C	1,0169	0,7608	1,2731	1,09E-04	2,21E-03	PI3K
PPP3CA	-1,0774	-1,2606	-0,8941	8,34E-06	3,06E-04	Wnt, MAPK, Apop
PPP3CB	-1,2543	-1,5493	-0,9593	7,02E-05	1,58E-03	Wnt, MAPK, Apop
PPP3R1	-0,3243	-0,4733	-0,1753	3,71E-03	4,61E-02	Wnt, MAPK, Apop
PRKACA	-0,9486	-1,0570	-0,8402	5,61E-07	4,57E-05	Wnt, HH, MAPK, RAS, Apop
PRKAR1B	-1,6063	-1,7371	-1,4756	5,41E-08	1,23E-05	Apop
PRKAR2A	-0,7558	-0,9015	-0,6101	1,92E-05	5,63E-04	Apop
PRKCA	-2,0576	-2,6609	-1,4543	2,81E-04	5,05E-03	Wnt, MAPK, PI3K, RAS
PRKCG	-1,1403	-1,4746	-0,8060	2,81E-04	5,05E-03	Wnt, MAPK, RAS
PRKDC	-0,8910	-1,1298	-0,6522	1,61E-04	3,10E-03	DNARepair, CC
PTCH1	-2,0426	-2,4119	-1,6733	1,25E-05	4,03E-04	HH
PTPN11	-0,2938	-0,3806	-0,2071	2,93E-04	5,16E-03	STAT, RAS
PTTG2	-1,3210	-1,6033	-1,0388	3,77E-05	9,66E-04	CC
RAD21	-0,5331	-0,6068	-0,4595	2,05E-06	1,00E-04	CC
RAD50	-0,9363	-1,1604	-0,7123	7,84E-05	1,69E-03	DNARepair
RASGRF2	-1,1361	-1,5120	-0,7601	5,86E-04	9,26E-03	MAPK, RAS
RBX1	-0,5826	-0,7104	-0,4547	4,48E-05	1,10E-03	Wnt, TGFB, CC
RET	-2,6902	-2,9706	-2,4099	2,99E-07	3,29E-05	
RFC4	-0,6918	-0,7697	-0,6139	5,08E-07	4,57E-05	DNARepair
RPS27A	-0,3558	-0,4734	-0,2382	5,82E-04	9,23E-03	DNARepair
RRAS2	0,5257	0,2885	0,7630	3,38E-03	4,26E-02	MAPK, RAS
RXRG	-0,9097	-1,1782	-0,6412	2,93E-04	5,16E-03	TXmisReg
SETBP1	-0,8834	-1,0988	-0,6679	8,85E-05	1,86E-03	
SFN	1,0323	0,7884	1,2761	7,22E-05	1,61E-03	CC
SHC1	0,5619	0,4408	0,6831	4,00E-05	1,01E-03	RAS
SHC2	-1,4755	-1,8117	-1,1393	5,72E-05	1,34E-03	RAS
SHC3	-1,6395	-1,8861	-1,3930	3,65E-06	1,57E-04	RAS
SHC4	1,7751	1,1048	2,4455	1,27E-03	1,82E-02	RAS
SKP1	0,5025	0,4046	0,6004	2,05E-05	5,99E-04	Wnt, TGFB, CC
SKP2	-2,1795	-2,2410	-2,1181	3,34E-11	9,46E-08	CC

SMAD2	-0,5609	-0,7725	-0,3492	1,26E-03	1,82E-02	TGFB, CC
SMAD3	-0,6981	-0,8310	-0,5653	1,76E-05	5,25E-04	Wnt, TGFB, CC
SMARCA4	-0,9498	-1,0808	-0,8188	2,03E-06	1,00E-04	
SMARCB1	-1,1409	-1,5543	-0,7274	9,99E-04	1,48E-02	
SMC1A	-1,0598	-1,2779	-0,8416	2,95E-05	7,96E-04	CC
SMC3	-0,4930	-0,6066	-0,3794	6,14E-05	1,41E-03	CC
SOCS1	0,9353	0,5641	1,3064	1,68E-03	2,33E-02	STAT
SOS2	-0,4277	-0,5751	-0,2803	7,45E-04	1,14E-02	MAPK, STAT, PI3K, RAS
SOX9	-1,1732	-1,4533	-0,8931	7,73E-05	1,69E-03	
SPP1	4,0253	3,8751	4,1755	2,37E-10	2,70E-07	PI3K
SPRY1	-3,1193	-3,3052	-2,9333	6,24E-09	4,25E-06	STAT
SPRY2	-2,5659	-2,8591	-2,2726	5,62E-07	4,57E-05	STAT
SPRY4	-1,6887	-1,8416	-1,5358	1,13E-07	1,93E-05	STAT
STAT3	-0,4100	-0,5904	-0,2297	2,95E-03	3,79E-02	STAT
STMN1	-0,8760	-0,9852	-0,7668	1,02E-06	6,51E-05	MAPK
SUV39H2	-0,6834	-0,9177	-0,4491	7,23E-04	1,13E-02	ChromMod
SYK	-1,0600	-1,1849	-0,9351	6,93E-07	5,26E-05	PI3K
TBL1XR1	-1,3606	-1,5339	-1,1872	1,18E-06	6,95E-05	Wnt
TCF3	-0,7300	-0,9163	-0,5436	1,19E-04	2,35E-03	TXmisReg
TFDP1	-1,2495	-1,4055	-1,0935	1,03E-06	6,51E-05	TGFB, CC
TGFB3	-3,3835	-3,5377	-3,2292	9,63E-10	8,21E-07	TGFB, MAPK, CC
TGFBR2	-1,6402	-1,8547	-1,4257	1,41E-06	7,65E-05	TXmisReg, TGFB, MAPK
THEM4	-0,9034	-1,1875	-0,6193	4,32E-04	7,15E-03	PI3K
TIAM1	-2,1979	-2,5072	-1,8886	2,33E-06	1,12E-04	RAS
TNFRSF10A	0,9001	0,6167	1,1834	4,34E-04	7,16E-03	Apop
TNFRSF10D	1,1259	0,7283	1,5236	8,60E-04	1,29E-02	Apop
TNFSF10	-0,5023	-0,7346	-0,2699	3,85E-03	4,75E-02	Apop
TNR	-2,8335	-3,1917	-2,4753	1,12E-06	6,95E-05	PI3K
TSPAN7	-0,8158	-1,0212	-0,6103	1,09E-04	2,21E-03	TXmisReg
UBB	1,1061	0,9183	1,2938	8,23E-06	3,05E-04	DNARepair
VHL	-0,6559	-0,8830	-0,4288	7,66E-04	1,17E-02	
WEE1	-0,9629	-1,1249	-0,8008	7,77E-06	2,96E-04	CC
WHSC1	-0,5012	-0,5745	-0,4280	3,00E-06	1,38E-04	TXmisReg
WNT3	1,0606	0,6961	1,4252	7,34E-04	1,13E-02	Wnt, HH
WNT4	-2,1991	-2,5711	-1,8271	8,04E-06	3,01E-04	Wnt, HH
XPA	-0,5015	-0,6839	-0,3192	1,02E-03	1,50E-02	DNARepair
XRCC4	-0,6974	-0,9286	-0,4663	5,91E-04	9,29E-03	DNARepair
ZBTB16	-2,4255	-2,6587	-2,1924	1,71E-07	2,43E-05	TXmisReg
ZIC2	-1,2859	-1,8241	-0,7477	2,25E-03	3,03E-02	HH

Suppl. table 4: differentially expressed genes after knockdown of *FOXM1* in BON cells incl. pathway allocations; transcripts with FDR>0.05 were excluded.

Gene symbol	**Log2 fold change**	**Upper confidence limit**	**Lower confidence limit**	***p*-value**	**FDR**	**pathway**
AKT1	-0,1870	-0,2257	-0,1483	3,06E-05	2,75E-03	MAPK, STAT, PI3K, RAS, Apop
ARID2	-0,4605	-0,6113	-0,3097	5,51E-04	2,17E-02	
ASXL1	-0,3863	-0,5145	-0,2581	5,95E-04	2,29E-02	
ATR	0,5032	0,3349	0,6715	6,24E-04	2,32E-02	CC
AXIN1	-0,2037	-0,2761	-0,1313	8,93E-04	2,89E-02	Wnt
B2M	1,0525	0,9082	1,1967	1,94E-06	4,84E-04	
BCL2	-0,6372	-0,7748	-0,4997	4,02E-05	3,42E-03	PI3K, Apop
BMP4	0,5543	0,4288	0,6798	5,49E-05	4,28E-03	HH, TGFB
BMPR1B	0,3593	0,2907	0,4279	1,80E-05	2,01E-03	TGFB
CACNA1D	-0,6287	-0,8218	-0,4357	3,73E-04	1,61E-02	MAPK
CACNA2D1	0,3568	0,2325	0,4811	7,94E-04	2,62E-02	MAPK
CASP7	0,7744	0,6268	0,9220	1,78E-05	2,01E-03	Apop
CASP8	0,5016	0,3878	0,6154	5,56E-05	4,28E-03	Apop
CCNA2	-0,5611	-0,6707	-0,4515	2,09E-05	2,12E-03	CC
CCNB1	-0,7504	-0,8912	-0,6096	1,60E-05	1,99E-03	CC
CCND1	0,3372	0,2691	0,4053	2,61E-05	2,56E-03	Wnt, STAT, PI3K, CC
CCND3	-0,1519	-0,1993	-0,1046	4,07E-04	1,71E-02	Wnt, STAT, PI3K, CC
CCNE1	-0,8845	-0,9924	-0,7765	8,83E-07	2,60E-04	PI3K, CC
CCNE2	-0,1980	-0,2730	-0,1231	1,28E-03	3,70E-02	PI3K, CC
CDC25C	-0,5600	-0,7595	-0,3605	9,05E-04	2,90E-02	CC
CDH1	-0,4856	-0,6326	-0,3387	3,41E-04	1,54E-02	
CDK6	-0,3873	-0,4845	-0,2900	1,07E-04	6,53E-03	PI3K, CC
CDKN1A	-0,5330	-0,7341	-0,3319	1,26E-03	3,67E-02	TXmisReg, PI3K, CC
CDKN2C	-0,2735	-0,3818	-0,1651	1,66E-03	4,50E-02	TXmisReg, CC
CREB3L1	0,4262	0,3610	0,4915	4,12E-06	7,40E-04	PI3K
CXXC4	-1,2706	-1,6266	-0,9145	2,13E-04	1,07E-02	Wnt
DDIT4	0,5235	0,3381	0,7088	8,74E-04	2,85E-02	PI3K
DKK1	0,9978	0,7670	1,2286	6,30E-05	4,53E-03	Wnt
DKK4	1,4017	0,8628	1,9407	1,40E-03	3,91E-02	Wnt
DLL1	-0,4583	-0,6042	-0,3124	4,65E-04	1,88E-02	Notch
DNMT1	0,1614	0,1076	0,2151	6,09E-04	2,32E-02	
DNMT3A	-0,2628	-0,3593	-0,1664	1,07E-03	3,22E-02	
DUSP4	0,6031	0,5377	0,6684	3,91E-07	1,58E-04	MAPK
DUSP5	0,9524	0,8758	1,0289	4,97E-08	5,35E-05	MAPK
EPHA2	1,0411	0,9433	1,1389	1,46E-07	9,44E-05	PI3K, RAS
ERBB2	0,9267	0,5891	1,2644	1,03E-03	3,11E-02	
ETS2	-0,3286	-0,4055	-0,2517	6,79E-05	4,74E-03	RAS
FGF12	-0,5017	-0,6490	-0,3545	2,83E-04	1,32E-02	MAPK, PI3K, RAS

FGFR1	0,3585	0,2628	0,4542	1,57E-04	8,69E-03	MAPK, PI3K, RAS
FLNA	0,4967	0,4138	0,5796	7,35E-06	1,08E-03	MAPK
FOSL1	0,8222	0,6541	0,9903	2,82E-05	2,68E-03	Wnt
GADD45B	0,6718	0,4473	0,8963	6,21E-04	2,32E-02	MAPK, CC
GADD45G	-0,8258	-1,0759	-0,5756	3,44E-04	1,54E-02	MAPK, CC
GNA11	0,2854	0,2141	0,3567	1,03E-04	6,53E-03	
GNAS	-0,2327	-0,3162	-0,1492	9,46E-04	2,97E-02	
GNG4	-0,2752	-0,3552	-0,1952	2,67E-04	1,27E-02	PI3K, RAS
H3F3A	-0,3834	-0,5307	-0,2361	1,40E-03	3,91E-02	TXmisReg
H3F3C	0,2007	0,1576	0,2437	3,87E-05	3,39E-03	TXmisReg
HDAC2	-0,3492	-0,4742	-0,2242	9,31E-04	2,95E-02	Notch, ChromMod, TXmisReg, CC
HIST1H3B	-0,8900	-1,0473	-0,7328	1,07E-05	1,45E-03	TXmisReg
HIST1H3G	-0,6325	-0,8322	-0,4328	4,42E-04	1,81E-02	TXmisReg
HOXA10	0,7626	0,5902	0,9351	5,44E-05	4,28E-03	TXmisReg
HSPA1A	0,4677	0,3256	0,6099	3,51E-04	1,55E-02	MAPK
HSPB1	0,3995	0,2651	0,5339	6,46E-04	2,34E-02	MAPK
ID2	-0,4263	-0,5814	-0,2712	1,02E-03	3,11E-02	TXmisReg, TGFB
IL6R	0,3747	0,2548	0,4946	4,80E-04	1,91E-02	STAT, PI3K
IL8	1,3519	1,1337	1,5700	5,86E-06	9,10E-04	TXmisReg
IRS1	0,7333	0,4522	1,0144	1,38E-03	3,91E-02	PI3K
ITGA2	0,8082	0,6187	0,9977	6,88E-05	4,74E-03	PI3K
ITGA3	0,5313	0,3877	0,6748	1,69E-04	8,96E-03	PI3K
ITGA6	0,5878	0,4761	0,6994	1,74E-05	2,01E-03	PI3K
ITGB8	0,6457	0,4060	0,8854	1,15E-03	3,40E-02	PI3K
JAG1	0,4517	0,3417	0,5616	8,76E-05	5,78E-03	Notch
JAK1	0,4505	0,3478	0,5533	5,74E-05	4,32E-03	STAT, PI3K
JAK2	0,6858	0,4488	0,9229	7,58E-04	2,55E-02	STAT, PI3K
KITLG	0,2411	0,1594	0,3227	6,72E-04	2,36E-02	PI3K, RAS
KLF4	0,7538	0,5523	0,9554	1,59E-04	8,69E-03	
LAMA3	1,5313	1,3045	1,7581	3,29E-06	6,64E-04	PI3K
LAMC2	1,0066	0,8837	1,1294	8,83E-07	2,60E-04	PI3K
LIF	1,5118	1,2166	1,8069	2,08E-05	2,12E-03	STAT
LTBP1	0,8023	0,5500	1,0547	4,32E-04	1,79E-02	TGFB
MAP2K6	1,0272	0,9229	1,1316	2,50E-07	1,29E-04	MAPK
MAP3K5	0,4087	0,2614	0,5560	9,68E-04	3,00E-02	MAPK
MET	0,5314	0,3844	0,6784	1,96E-04	1,01E-02	TXmisReg, PI3K, RAS
MLLT3	0,8907	0,7468	1,0346	5,91E-06	9,10E-04	TXmisReg
MYC	0,5850	0,5157	0,6544	7,21E-07	2,59E-04	Wnt, TXmisReg, TGFB, MAPK, STAT, PI3K, CC
MYD88	0,8471	0,7721	0,9221	9,67E-08	7,82E-05	Apop
NBN	0,5734	0,4203	0,7265	1,57E-04	8,69E-03	DNARepair
NFKBIA	0,7915	0,5254	1,0577	6,44E-04	2,34E-02	Apop

NFKBIZ	0,6622	0,4377	0,8867	6,76E-04	2,36E-02	TXmisReg
NR4A3	0,8684	0,5222	1,2145	1,72E-03	4,59E-02	TXmisReg
PLA1A	1,4512	0,9736	1,9288	5,67E-04	2,21E-02	RAS
PLAU	1,8791	1,6161	2,1422	2,24E-06	5,16E-04	TXmisReg
PLD1	0,6417	0,4231	0,8603	6,96E-04	2,39E-02	RAS
PML	1,6182	1,5126	1,7239	1,17E-08	1,90E-05	TXmisReg
POLD4	0,4420	0,3255	0,5584	1,45E-04	8,51E-03	DNARepair
POLR2D	-0,3441	-0,4291	-0,2591	9,60E-05	6,21E-03	DNARepair
PRKAR2A	-0,5341	-0,6746	-0,3936	1,43E-04	8,51E-03	Apop
PTEN	0,1796	0,1237	0,2355	4,05E-04	1,71E-02	PI3K
PTPN11	-0,4218	-0,5278	-0,3158	1,07E-04	6,53E-03	STAT, RAS
PTTG2	-0,4419	-0,5672	-0,3165	2,30E-04	1,14E-02	CC
RAD21	-0,3560	-0,4512	-0,2608	1,58E-04	8,69E-03	CC
RASGRP1	0,6785	0,5173	0,8397	7,47E-05	5,03E-03	MAPK, RAS
RET	-0,8115	-1,1219	-0,5010	1,37E-03	3,91E-02	
RPS27A	-0,2825	-0,3809	-0,1841	7,92E-04	2,62E-02	DNARepair
RXRG	1,2438	1,0043	1,4834	1,91E-05	2,05E-03	TXmisReg
SGK2	-0,3772	-0,5250	-0,2295	1,56E-03	4,27E-02	PI3K
SHC1	0,2436	0,1689	0,3182	3,68E-04	1,61E-02	RAS
SHC3	-1,0308	-1,4028	-0,6589	9,75E-04	3,00E-02	RAS
SHC4	2,0702	1,7589	2,3816	3,65E-06	6,94E-04	RAS
SKP2	0,3097	0,2264	0,3930	1,65E-04	8,87E-03	CC
SOCS1	1,2631	1,0375	1,4887	1,16E-05	1,49E-03	STAT
SOCS3	0,6208	0,4117	0,8299	6,50E-04	2,34E-02	STAT
SOS1	-0,4488	-0,6010	-0,2966	6,78E-04	2,36E-02	MAPK, STAT, PI3K, RAS
SPP1	2,1080	1,7756	2,4404	5,02E-06	8,54E-04	PI3K
STAT1	4,2428	4,0937	4,3918	1,56E-10	5,04E-07	STAT
SYK	-0,1772	-0,2284	-0,1259	2,59E-04	1,25E-02	PI3K
TBL1XR1	-0,2651	-0,3642	-0,1660	1,19E-03	3,51E-02	Wnt
TGFB1	0,4950	0,3931	0,5969	2,95E-05	2,73E-03	TGFB, MAPK, CC
TGFBR2	0,7392	0,6379	0,8405	1,94E-06	4,84E-04	TXmisReg, TGFB, MAPK
THBS1	0,8960	0,7693	1,0226	2,40E-06	5,16E-04	TGFB, PI3K
TLX1	0,8955	0,5866	1,2044	7,50E-04	2,55E-02	TXmisReg
TNC	0,5513	0,3990	0,7037	1,95E-04	1,01E-02	PI3K
TNFAIP3	1,4017	0,8458	1,9576	1,67E-03	4,50E-02	
TNFRSF10B	0,8766	0,6836	1,0696	4,58E-05	3,80E-03	Apop
TNFRSF10D	-0,8258	-0,9705	-0,6812	1,02E-05	1,43E-03	Apop
TNFSF10	1,9171	1,7193	2,1149	2,79E-07	1,29E-04	Apop
TP53	-0,7094	-0,8720	-0,5467	5,95E-05	4,37E-03	Wnt, TXmisReg, MAPK, PI3K, Apop, CC
WEE1	0,3231	0,1986	0,4475	1,42E-03	3,92E-02	CC
WHSC1	-0,1818	-0,2341	-0,1295	2,51E-04	1,23E-02	TXmisReg
XRCC4	0,2186	0,1531	0,2841	3,21E-04	1,48E-02	DNARepair

SUPPLEMENTARY MATERIAL & METHODS:

List of antibodies used in the study

Antigen (Order Number)	obtained from	Dilution (method)
53BP1 (NB100-304)	Novus bio	1:3000 IHC
Akt (# 4685)	Cell Signaling	1:1000 WB
ATM (#2873)	Cell Signaling	1:1000 WB
Aurora A (ab1287)	Abcam	1:1000 WB
BAX (5023)	Cell Signaling	1:1000 WB
beta-Tubulin (T5201)	Sigma Aldrich	1:1000 WB
BID (#2002)	Cell Signaling	1:1000 WB
BRCA2 (sc-8326)	Santa Cruz	1:200 WB
Caspase 6 (# 9762)	Cell Signaling	1:1000 WB
Caspase 8 (# 9746)	Cell Signaling	1:1000 WB
Chromogranin A (10702)	Progen	1:50 WB
CK2 (#2656)	Cell Signaling	1:1000 WB
cleaved PARP (# 5625)	Cell Signaling	1:1000 WB
Cyclin B1 (#4138)	Cell Signaling	1:1000 WB
DDB2 (sc-25368)	Santa Cruz	1:1000 WB
ERCC1 (#3885)	Cell Signaling	1:1000 WB
FADD (556402)	BD Biosciences	1:1000 WB
FANCA (#14657)	Cell Signaling	1:1000 WB
FANCC (Sc-28216)	Santa Cruz	1:100 WB
FEN1 (sc-28355)	Santa Cruz Biotech	1:200 WB
FOXM1 (sc-502)	Santa Cruz Biotech	1:500 WB
GAPDH (GTX627408)	GeneTex	1:1000 WB
HIF1-alpha (10006421)	Cayman Chemical	1:50 IHC
Ki-67 (clone SolA15)	eBioscience	1:10000 IHC
MDM2 (SC-965)	Santa Cruz Biotech	1:500 WB
p(Ser20)-p53 (#9287)	Cell Signaling	1:200 WB
p21 (sc-397)	Santa Cruz Biotech	1:500 WB
p27 (# 2552)	Cell Signaling	1:1000 WB
p53 (#2527)	Cell Signaling	1:1000 WB
p70S6 Kinase (# 2708)	Cell Signaling	1:1000 WB
pan-actin (#4968)	Cell Signaling	1:1000 WB
Phospho-AKT (Ser473) XP® (# 4060)	Cell Signaling	1:1000 WB
Phospho-AKT (Thr308) (# 2965)	Cell Signaling	1:1000 WB
Phospho-FOXO1 (Thr24)/FOXO3a (Thr32) (# 9464)	Cell Signaling	1:1000 WB
Phospho-histone H2AX (# 9718)	Cell Signaling	1:1000 WB
Phospho-histone H3 (Ser10) XP® (# 3377)	Cell Signaling	1:1600 FACS
Phospho-p44/42 ERK1/2 (Thr202/Tyr204) (# 4370)	Cell Signaling	1:1000 WB
Phospho-p53 (Ser20) (# 9287)	Cell Signaling	1:1000 WB
Phospho-p70 S6 Kinase (Thr389) (# 9234)	Cell Signaling	1:1000 WB
Phospho-Rb (Ser780) (# 9307)	Cell Signaling	1:1000 WB
RAD51 (sc-8349)	Santa Cruz Biotech	1:200 WB
Rb (sc-50)	Santa Cruz Biotech	1:200 WB
RCF4 (sc-20996)	Santa Cruz Biotech	1:200 WB
RPA 70 (2267	Cell Signaling	1:1000 WB
Rpb1 CTD (#2629)	Cell Signaling	1:1000 WB
SKP2 (# 2652)	Cell Signaling	1:1000 WB
SSTR2 (Sc-25676)	Santa Cruz Biotech	1:50 IF

TRADD (610573)	BD Biosciences	1:1000 WB
Vinculin (# 4650)	Cell Signaling	1:1000 WB
XPA (#14607)	Cell Signaling	1:1000 WB
XPD (#11963)	Cell Signaling	1:1000 WB
β-tubulin (T5201)	Sigma Aldrich	1:1000 WB

Abbreviations: FACS: Fluorescence-activated cell sorting, IF: Immune fluorescence, IHC: Immunohistochemistry, WB: Western Blot

PET/MR imaging of mouse xenografts:

Anatomic tumor MRI scans in axial direction were acquired using a high-resolution T2-weighted 2D fast spin echo sequence (T2 FSE 2D) with the following parameters:, TR = 8700 ms; TE = 103 ms; slice thickness/gap = 1.1 mm/ 0.1 mm; matrix = 256 x 256 mm; external averages = 5 and number of excitations = 2.

To monitor glucose consumption of tumors post therapy, FDG-F18-PET imaging was performed for 30 min starting approx. 45 min post intravenous injection of 0.15 mL of FDG-F18 into mouse tail vein, corresponding to approximately 15 MBq. PET images were reconstructed as follows: (iterative image reconstruction, [ordered subset expectation maximization]; iterations, 8; subsets, 6; voxel size, 500 × 500 × 600 µm3). Acquisition protocols included a mouse whole body material map for attenuation and scatter correction during PET reconstruction. Prior to imaging, the PET/MRI system was calibrated for FDG so that local tissue concentrations in the tumor could be measured quantitatively in kBq/ml tissue.

MR imaging of *in ovo* models:

Tumor volume was determined by MR imaging prior to and after 7 days of treatment using a dedicated small animal 1 Tesla nanoScan PET/MRI (Mediso, Hungary) and a rat body coil.

First, a short localizer scan was performed to ensure the right positioning of the egg within the coil.

To monitor tumor plaque morphology and calculate the exact tumor volume, a T1 3D gradient echo (GRE) sequence was used: TR = 50 ms; TE = 2.7 ms; flip angle = 40°; slice thickness/ gap = 0.5 mm/ 0 mm; matrix = 160 x 160 mm and number of excitations = 2 and a high resolution 2D T2-w turbo-spin echo sequence (T2-TSE) was established using the following parameters: 8885/100ms (TR/TE), FOV

74 mm, matrix = 252, slice thickness = 500 µm, gap 100 µm, 4 no of average, resulting voxel size = 117x117x500 µm3. The number of axial orientated slices was adjusted to cover the whole tumor.

MR images were analyzed using the interviewFUSION software (Mediso, version 3.01.004.000). To determine total tumor volume, a volume-of-interest (VOI) was manually contoured, based on the T1w and T2w MR images.

***In ovo* SPECT/CT imaging and analyses:**

In ovo SPECT/CT measurements were performed on a nanoSPECT/CTplus (Bioscan/Mediso) using rat apertures. Lu-177-DOTATOC was injected intravenously into CAM vasculature (0.05 ml; 20 MBq/egg) and eggs were scanned 3h post injection to ensure tracer accumulation in the tumor plaque. Eggs were maintained at 37 ºC using a heated bed. For anatomical definition, a CT-scan was performed at 45 kVp, 64 mAs, 1000 ms exposure time and 360° rotation in 1° steps; image reconstruction: 150 µm cubic voxels, filtered backprojection and a Butterworth filter. Static SPECT imaging of the egg was performed (45 sec/projection, 40 min scan), reconstructed (‘Hi SPECT’, Bioscan) and analyzed (In Vivo Scope). The injected dose of radionuclide per egg (whole object activity) was determined by measuring the total activity in the syringe prior to and after injection, and all values corrected for radioactive decay. The tumor plaque activity was identified from fused SPECT/CT images by volume of interest analysis.