

**Molecular Cell, Volume 74**

## **Supplemental Information**

### **MDC1 Interacts with TOPBP1 to Maintain**

### **Chromosomal Stability during Mitosis**

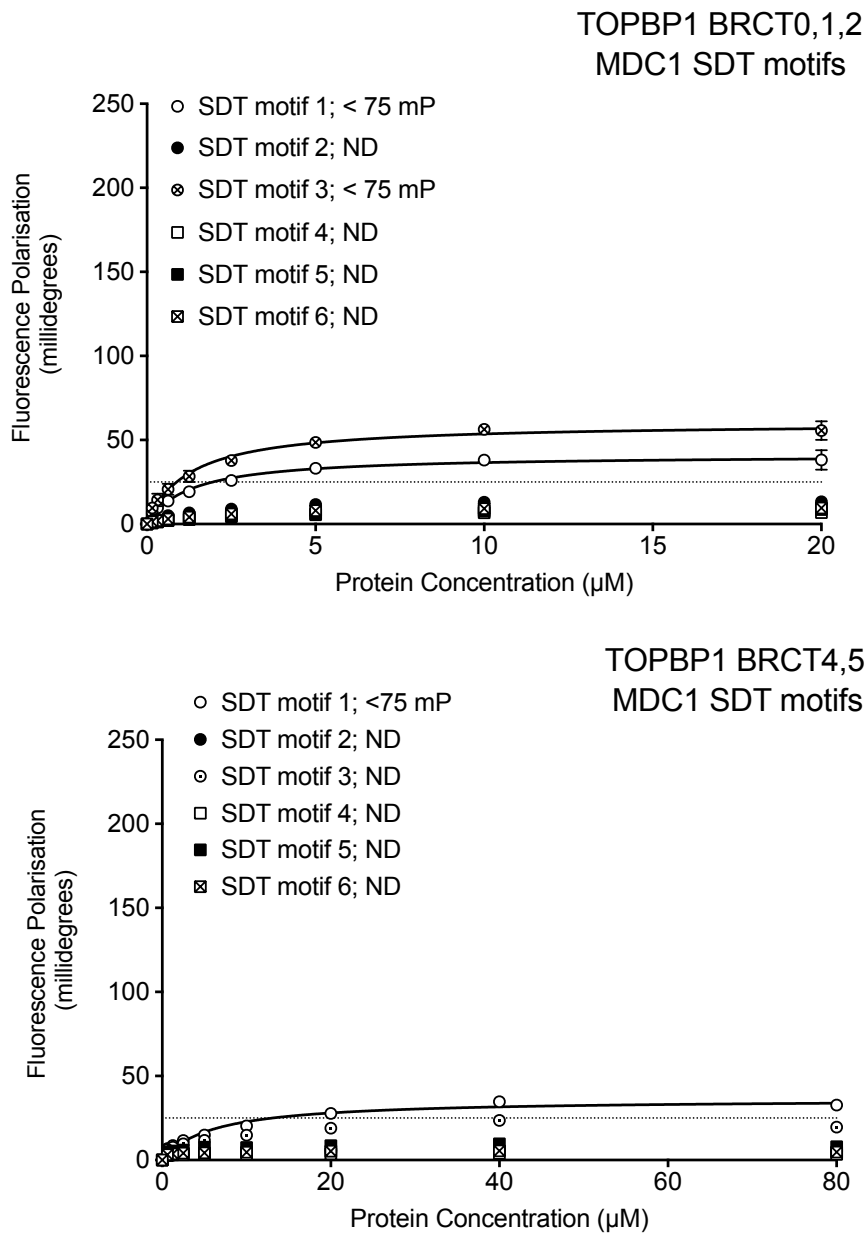
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**A**

hsMDC1	L	L	A	E	<b>D</b>	<b>S</b>	E	E	E	V	
mmMDC1	V	L	L	A	A	<b>D</b>	<b>S</b>	E	E	E	G
xlMDC1	S	V	L	A	M	<b>D</b>	<b>S</b>	G	D	E	E
drMDC1	I	T	L	V	P	<b>E</b>	<b>S</b>	D	S	D	G

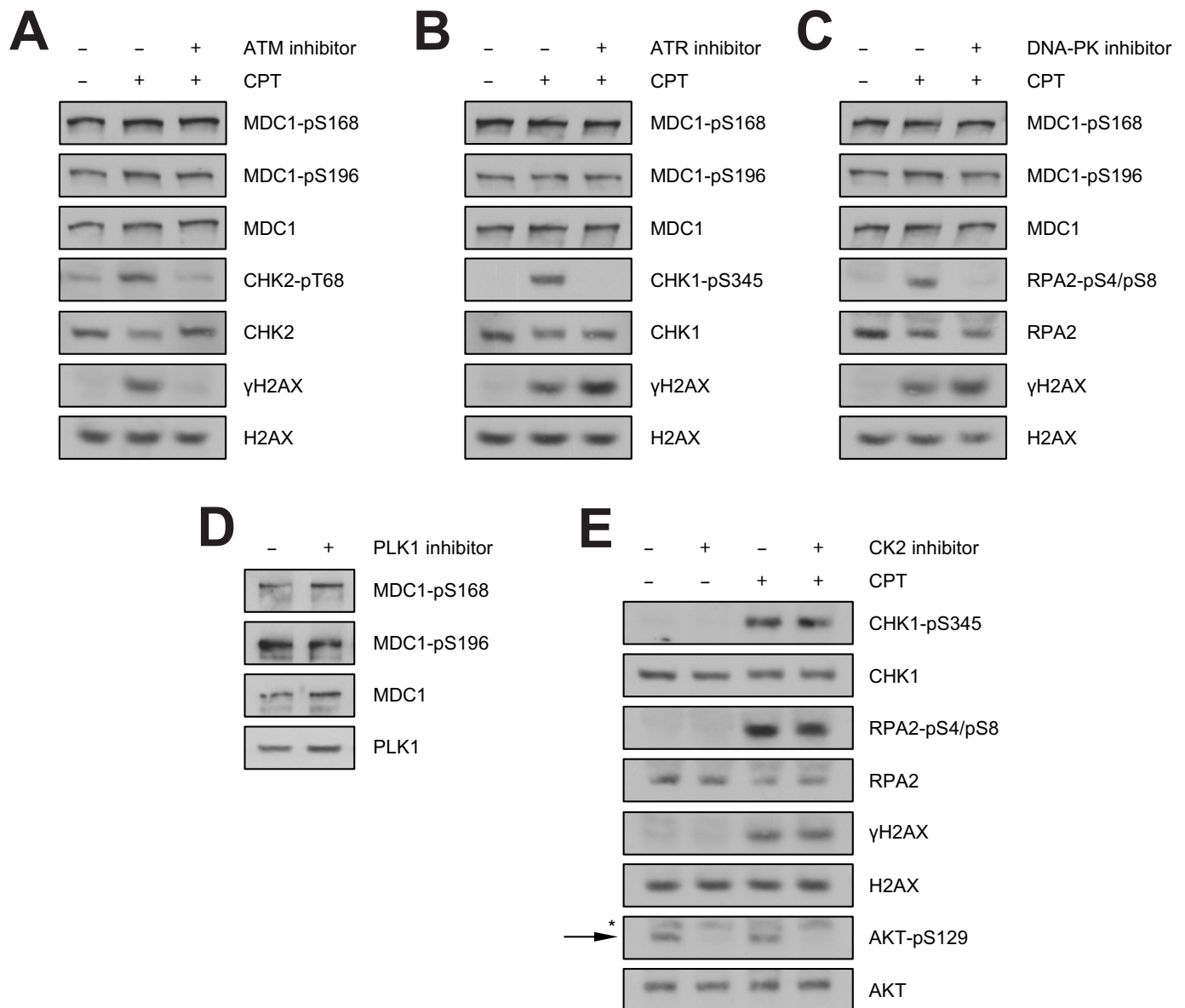
  

hsRAD9	P	V	L	A	E	<b>D</b>	<b>S</b>	E	G	E	G
mmRAD9	P	V	L	A	E	<b>D</b>	<b>S</b>	D	G	E	G
xlRAD9	E	L	L	A	E	<b>D</b>	<b>S</b>	D	G	E	E
drRAD9	E	V	L	A	S	<b>D</b>	<b>S</b>	E	D	E	N

**B****Figure S1** (related to Figure 2).

(A) Sequence alignment showing the evolutionary conservation and similarity of the TOPBP1 BRCT1-binding motifs in MDC1 (centred around S168 in humans) and RAD9 (centred around S387 in humans). hs = Homo sapiens, mm = Mus musculus, xl = Xenopus laevis, dr = Danio rerio. Key phosphorylated serines are highlighted in bold.

(B) Fluorescence polarization with indicated recombinant TOPBP1 BRCT domains and the 6 SDT motifs found in human MDC1 synthesized as phosphopeptides. ND = not determined.



**Figure S2** (related to Figure 3).

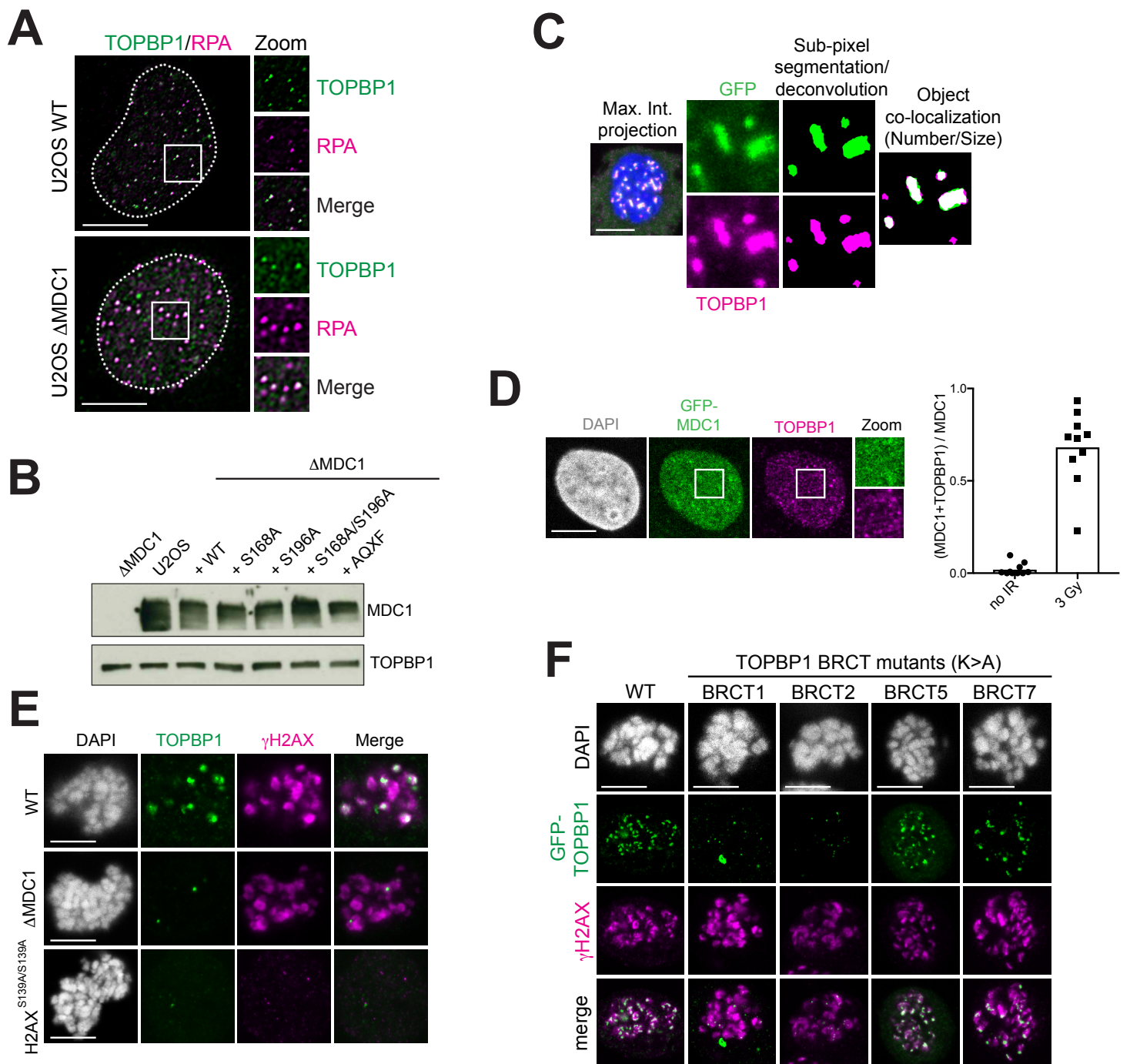
(A) U2OS cells treated as indicated with 10  $\mu$ M ATM inhibitor AZD0156 and/or 1  $\mu$ M camptothecin (CPT) were harvested for western blotting with the indicated antibodies. CHK2-pT68 and  $\gamma$ H2AX are positive controls for AZD0156 activity as they are ATM-dependent after CPT treatment.

(B) U2OS cells treated as indicated with 1  $\mu$ M ATR inhibitor AZD6738 and/or 1  $\mu$ M CPT were harvested for western blotting with the indicated antibodies. CHK1-pS345 is a positive control for AZD6738 activity as its levels are ATR-dependent.

(C) U2OS cells treated as indicated with 3  $\mu$ M DNA-PK inhibitor NU7441 and/or 1  $\mu$ M CPT were harvested for western blotting with the indicated antibodies. RPA2-pS4/pS8 is a positive control for NU7441 activity as it is DNA-PK-dependent after CPT treatment.

(D) U2OS cells treated as indicated with 100 nM PLK1 inhibitor BI 2536 or DMSO vehicle control were harvested for western blotting with the indicated antibodies.

(E) U2OS cells treated as indicated with 10  $\mu$ M CK2 inhibitor CX-4945 and/or 1  $\mu$ M camptothecin (CPT) were harvested for western blotting with the indicated antibodies. CHK1, RPA and H2AX phosphorylation in response to CPT are dependent on ATR, DNA-PK and ATM, respectively; AKT-pS129 is a positive control for CX-4945 activity as AKT is a known CK2 substrate.



**Figure S3** (related to Figure 4 and 5).

(A) Immunofluorescence experiment of irradiated (3 Gy) WT U2OS cells and  $\Delta$ MDC1 cells. Cells were stained with TOPBP1 and RPA2 antibodies 3 hr after IR and images were deconvoluted for better assessment of protein co-localization.

(B) Western blot of extracts derived from  $\Delta$ MDC1 cell line stably transfected with GFP-tagged MDC1 WT and mutants.

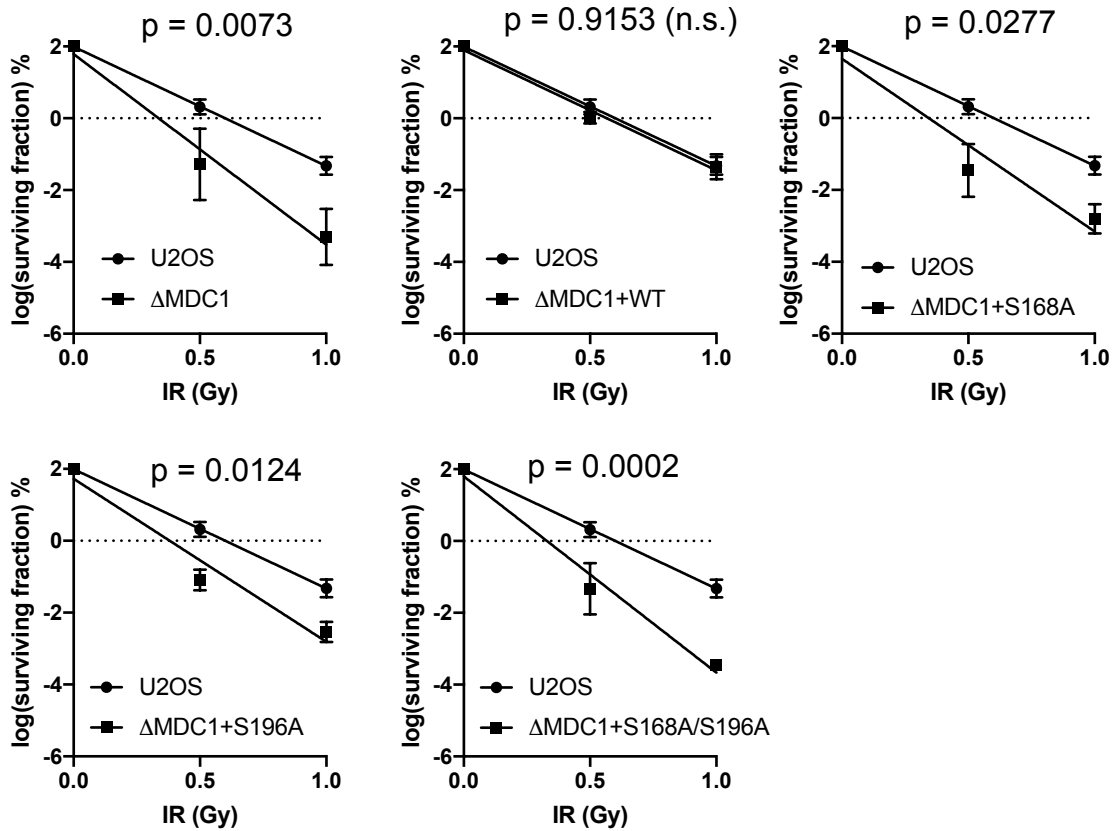
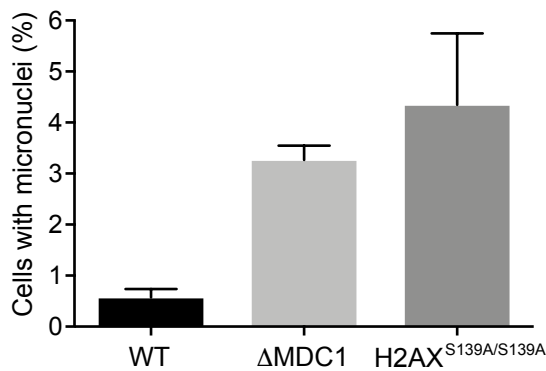
(C) Sub-pixel segmentation/deconvolution by SQUASSH. See Star Methods for details.

(D) Left: Confocal microscopy of untreated GFP-MDC1-WT expressing U2OS cells, stained with TOPBP1 antibodies. Right: SQUASSH analysis of untreated and IR treated GFP-MDC1 expressing U2OS cells. Each data point represents one cell ( $n=10$ ), bars represent the mean.

(E) Confocal microscopy of RPE-1 WT,  $\Delta$ MDC1 and H2AX<sup>S139A/S139A</sup> cells, arrested in mitosis by nocodazole, treated with 0.5 Gy of IR, 1 hr after release from the nocodazole block (100 ng/ml).

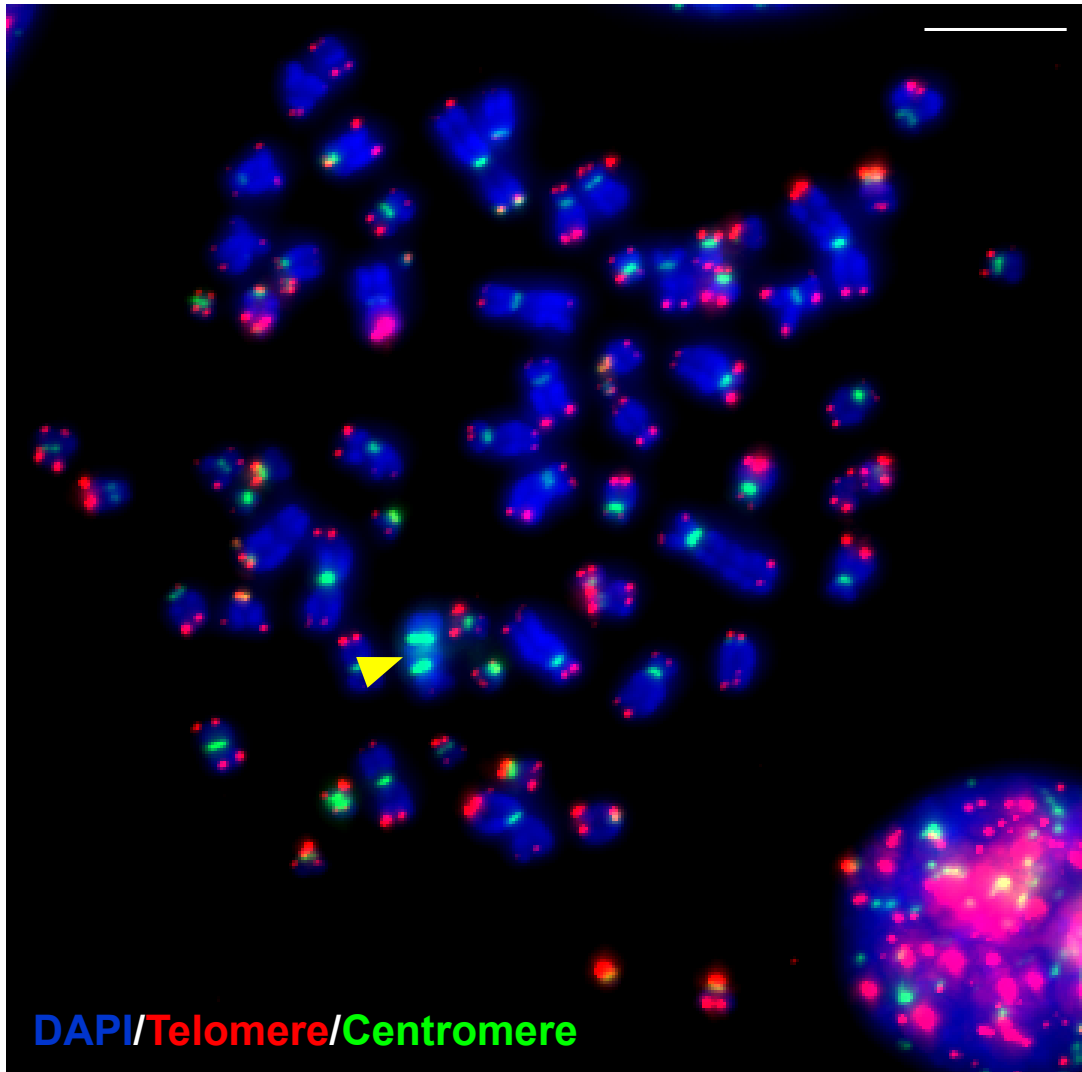
(F) Confocal microscopy of 293T cells transfected with GFP-TOPBP1 WT and BRCT mutants BRCT1 (K155A), BRCT2 (K250A), BRCT5 (K704A) or BRCT7 (K1317A), arrested with 100 ng/ml nocodazole, 1 hr after treatment with 0.5 Gy of IR.

All scale bars represent 10  $\mu$ m.

**A****B****Figure S4** (related to Figure 6)

(A) Statistical evaluation of clonogenic survival analysis of U2OS cells,  $\Delta$ MDC1 cells and MDC1 complemented cell lines by linear regression. Each engineered cell line was compared to the parental U2OS cell line. Note that due to multiple comparisons,  $\alpha=0.05$  should be interpreted as familywise error rate.

(B) Quantification of micronuclei formation in untreated RPE-1 cell lines (bars represent mean  $\pm$  SD,  $n=3$ ; at least 1000 cells analyzed per condition).

**A****B**

	U2OS	$\Delta$ MDC1		
		-	+WT	+S196A
Experiment #1	44.3%	80.5%	49.2%	91.3%
Experiment #2	48.7%	76.5%	41.5%	88.0%

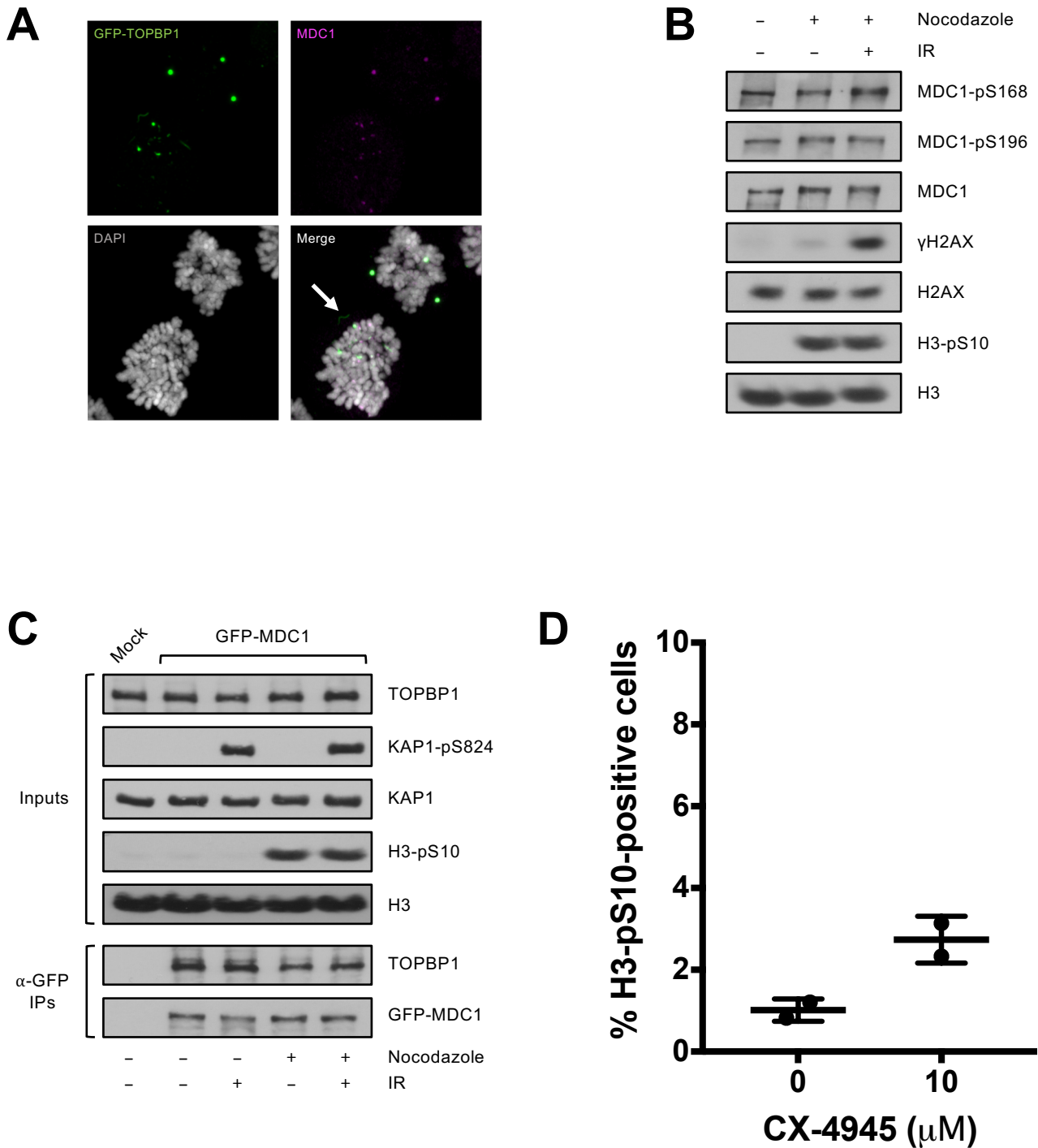
Metaphases with >0 dicentric chromosomes

**Figure S5** (related to Figure 7)

(A) Example of metaphase spread derived from U2OS,  $\Delta$ MDC1 cells and  $\Delta$ MDC1 cells stably transfected with TOPBP1 binding mutants, hybridized with a telomere Cy3-labeled PNA probe and centromere Cy5-labeled PNA probe. A dicentric chromosome is highlighted by an arrowhead.

(B) Quantification of the frequency of dicentric chromosomes in metaphase spreads of U2OS cells,  $\Delta$ MDC1 cells and  $\Delta$ MDC1 cells stably transfected with WT MDC1 and the S196A TOPBP1 binding mutant (two independent experiments).

Scale bar represents 10  $\mu$ m.



**Figure S6** (related to Figure 7 and Discussion).

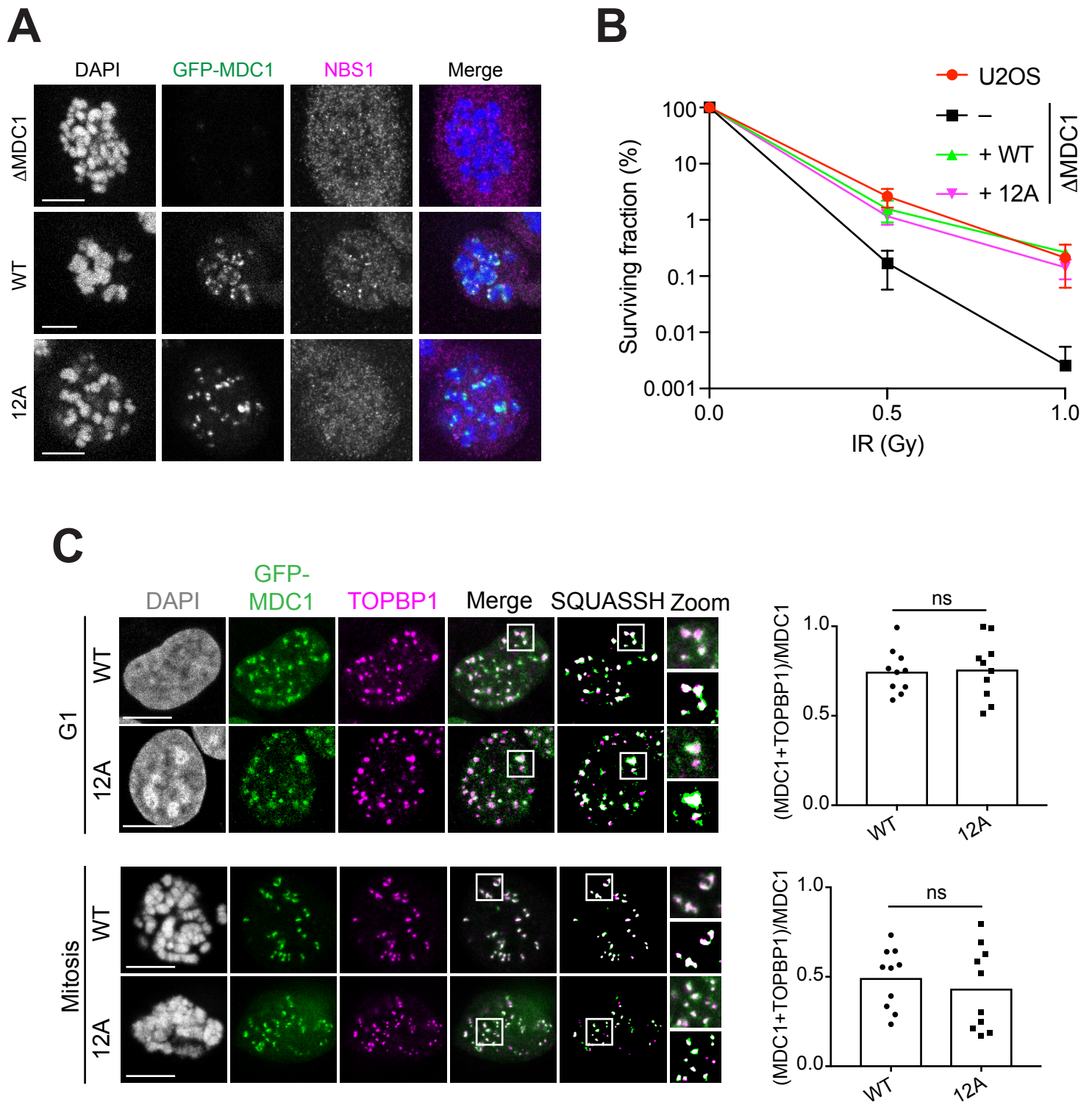
(A) Maximum intensity projections of Airyscan images of unirradiated U2OS cells expressing GFP-TOPBP1. Arrow indicates example of a TOPBP1 filament that does not colocalize with condensed chromatin or MDC1.

(B) Western blot of lysates from U2OS cells treated with 40 ng/ml nocodazole and/or 10 Gy IR as indicated.

(C) GFP-pulldowns from 293FT cells either mock-transfected or transfected with GFP-MDC1 plasmid, and treated with 40 ng/ml nocodazole and/or 10 Gy IR as indicated.

(D) Graph of flow cytometry analyses demonstrating the effect of the CK2 inhibitor CX-4945 on the mitotic index of U2OS cells.





**Figure S7** (related to Discussion).

(A) Confocal microscopy of  $\Delta$ MDC1 cells and  $\Delta$ MDC1 cells stably transfected with WT MDC1 and 12A mutant, arrested with 100 ng/ml nocodazole, 1 hr after treatment with 0.5 Gy of IR.

(B) Clonogenic survival assay of mitotic U2OS,  $\Delta$ MDC1 and  $\Delta$ MDC1 cells stably transfected with GFP-MDC1 WT and 12A mutant (mean of 3 independent experiments, error bars:  $\pm$  SD).

(C) Confocal microscopy of irradiated  $\Delta$ MDC1 U2OS cells expressing GFP-tagged MDC1 WT and 12A mutant. Upper panel: interphase cells, 3 hr after 3 Gy; lower panel: cells arrested in mitosis by 100 ng/ml nocodazole, 1 hr after 0.5 Gy. Quantification of GFP-MDC1 and TOPBP1 co-localization by SQUASSH object number co-localization (bars represent mean;  $n=10$ , unpaired t-test,  $\alpha=0.05$ ).

Scale bars represent 10  $\mu$ m.



**Table S1** (related to Figure 1)  
Raw LC-MS/MS data

Protein IDs	Protein names	Gene names	Fasta headers	LFQ intensity, median centred				log pMDC1/MDC1, replicate 1	log pMDC1/MDC1, replicate 2	# of unique peptides
				MDC1, replicate 1	MDC1, replicate 2	pMDC1, replicate 1	pMDC1, replicate 2			
Q13083;Q13085-4;Q1	Acetyl-CoA carboxylase 1;Biotin carboxylase	ACACA	sp Q13085	1357.8	350.8	299.3	1045.5	-2.2	1.6	88
Q92547;H0Y817	DNA topoisomerase 2-binding protein 1	TOPBP1	sp Q92547	0.2	0.1	72.3	1172.8	8.4	13.1	48
P35527;CON_P3552	Keratin, type I cytoskeletal 9	KRT9	sp P35527	1900.9	5294.7	4583.4	2967.6	1.3	-0.35	42
P04264;CON_P0426	Keratin, type II cytoskeletal 1	KRT1	sp P04264	3055.0	13788.1	11573.7	5399.7	1.9	-1.4	41
P15924;P15924-3;P1	Desmoplakin	DSP	sp P15924	1.8	55.7	36.7	13.9	4.3	-2.0	39
Q96RQ3;E9PHF7;F5G1	Methylcrotonoyl-CoA carboxylase subunit alpha, mitr	MCCC1	sp Q96RQ3	274.9	44.0	42.5	134.0	-2.7	1.6	23
O00763;O00763-3;O0	Acetyl-CoA carboxylase 2;Biotin carboxylase	ACACB	sp O00763	19.7	3.1	2.8	12.1	-2.8	2.0	19
Q00839-2;Q00839;Q5	Heterogeneous nuclear ribonucleoprotein U	HNRNPU	sp Q00839	124.1	11.8	29.9	135.6	-2.1	3.5	17
Q02413;Q02413-2	Desmoglein-1	DSG1	sp Q02413	1.8	39.9	30.7	8.4	4.1	-2.3	17
P12883;P13533;P128	Myosin-6	MYH7;MYH	sp P12883	26.9	1.2	0.9	24.6	-4.9	4.3	16
P11498;E9P568;P114	Pyruvate carboxylase, mitochondrial	PC	sp P11498	21.2	3.5	2.8	11.5	-2.9	1.7	15
A0A0C4DG89;Q7L014	Probable ATP-dependent RNA helicase DDX46	DDX46	tr A0A0C4	60.1	0.0	2.3	31.8	-4.7	#DIV/0!	14
P14923;C9JTX4;C9J82	Junction plakoglobin	JUP	sp P14923	2.3	18.5	20.3	2.0	3.2	-3.2	13
P04406;P04406-2;E7I	Glyceraldehyde-3-phosphate dehydrogenase	GAPDH	sp P04406	5.3	2.1	8.5	5.8	0.7	1.5	11
P07355;P07355-2;H0	Annexin A2;Annexin;Putative annexin A2-like protein	ANXA2;AN	sp P07355	1.3	14.2	6.4	6.2	2.3	-1.2	11
Q08188	Protein-glutamine gamma-glutamyltransferase E;Prot	TGM3	sp Q08188	1.1	5.8	15.7	3.7	3.9	-0.6	10
Q5JPS3;P07437;Q5ST	Tubulin beta chain;Tubulin beta-4B chain;Tubulin bet	TUBB;TUBB	tr Q5JPS3	20.2	3.7	10.3	19.2	-1.0	2.4	10
Q9HCC0;Q9HCC0-2;Df	Methylcrotonoyl-CoA carboxylase beta chain, mitoch	MCCC2	sp Q9HCC0	21.5	1.6	1.8	8.5	-3.6	2.4	10
A0A0J9YU3;A0A0J9Y9	Poly(U)-binding-splicing factor PUF60	PUF60	tr A0A0J9	9.1	2.6	3.1	12.0	-1.6	2.2	9
F5H5D3;Q9BQE3;P68	Tubulin alpha-1C chain;Tubulin alpha-1B chain;Tubul	TUBA1C;TU	tr F5H5D3	8.7	8.1	6.3	10.1	-0.5	0.3	9
P11142;E9PKE3;P111	Heat shock cognate 71 kDa protein	HSPA8	sp P11142	8.0	4.0	5.3	10.7	-0.6	1.4	9
P22735;P22735-2;H0	Protein-glutamine gamma-glutamyltransferase K	TGM1	sp P22735	0.0	12.8	4.0	0.0	#DIV/0!	#NUM!	9
P29508;P29508-2;H0	Serpin B3;Serpin B4	SERP1NB3;S	sp P29508	0.0	2.1	1.9	0.0	#DIV/0!	#NUM!	9
Q13867;K7E5E8;J3K5E	Bleomycin hydrolase	BLMH	sp Q13867	0.3	5.5	10.1	5.3	-1.0	1.9	9
Q5VTE0;P68104;A0A0	Putative elongation factor 1-alpha-like 3;Elongation fa	EEF1A1P5;I	sp Q5VTE0	44.4	19.4	32.3	71.6	-0.5	1.9	9
F6VRR5;Q9B77;F8W	Polymerase delta-interacting protein 3	POLDIP3	tr F6VRR5	10.3	3.5	3.1	13.2	-1.7	1.9	8
H0YH81;P06576;F8W	ATP synthase subunit beta;ATP synthase subunit beta	ATP5B	tr H0YH81	0.0	14.7	7.8	0.0	#DIV/0!	#NUM!	8
P04083;Q5T3N1;Q5T3	Annexin A1;Annexin	ANXA1	sp P04083	0.0	0.2	0.1	0.2	#DIV/0!	0.5	8
P25311;C9JEV0;H7BZ	Zinc-alpha-2-glycoprotein	AZGP1	sp P25311	259.3	835.1	1251.8	272.4	2.3	1.4	8
P38646;D6RUI2;H0Y8	Stress-70 protein, mitochondrial	HSPA9	sp P38646	12.9	1.4	3.7	15.2	-1.8	3.4	8
Q08554-2;Q08554	Desmocollin-1	DSC1	sp Q08554	6.1	61.8	37.8	18.1	2.6	-1.8	8
Q86V81;E9PB61	THO complex subunit 4	ALYREF	sp Q86V81	93.7	26.1	32.5	79.6	-1.5	1.6	8
P04040	Catalase	CAT	sp P04040	0.0	16.2	5.6	2.4	#DIV/0!	-2.8	7
P05089;P05089-2;P0	Arginase-1	ARG1	sp P05089	1.9	7.8	6.7	12.7	1.8	0.7	7
P31944	Caspase-14;Caspase-14 subunit p17, mature form;Cas	CASP14	sp P31944	0.9	8.1	2.4	5.0	1.3	-0.7	7
Q8TA86;C9J6V2	Retinitis pigmentosa 9 protein	RP9	sp Q8TA86	24.8	0.5	0.0	8.8	#NUM!	4.2	7
Q96P63;Q96P63-2	Serpin B12	SERP1NB12	sp Q96P63	0.0	10.6	11.0	0.0	#DIV/0!	#NUM!	7
H0Y4X3;Q14498-3;Q1	RNA-binding protein 39	RBM39	tr H0Y4X3	14.9	0.1	0.0	4.6	#NUM!	5.4	6
P01040;C9J0E4	Cystatin-A;Cystatin-A, N-terminally processed	CSTA	sp P01040	6.0	8.2	8.4	12.9	0.5	0.7	6
P02452	Collagen alpha-1(I) chain	COL1A1	sp P02452	11.8	0.4	247.9	0.2	4.4	-1.2	6
P06702	Protein S100-A9	S100A9	sp P06702	0.0	18.1	16.5	5.6	#DIV/0!	-1.7	6
P06733;P06733-2;K7I	Alpha-enolase;Enolase	ENO1	sp P06733	1.7	7.9	1.8	0.0	0.1	#NUM!	6
P25705-3;P25705;K7I	ATP synthase subunit alpha, mitochondrial	ATP5A1	sp P25705	0.0	6.4	4.4	0.0	#DIV/0!	0.0	6
A0A087WTA8;P08123	Collagen alpha-2(I) chain	COL1A2	tr A0A087	0.0	0.1	269.8	0.0	#DIV/0!	-2.0	5
A0A0C4DGB6;CON_P	Serum albumin	ALB	tr A0A0C4	0.8	1.7	0.5	1.2	-0.8	-0.5	5
H0Y449;P67809;C9J5	Nuclease-sensitive element-binding protein 1	YBX1	tr H0Y449	3.7	1.0	1.3	5.2	-1.5	2.4	5
J3KPP4;Q95232;D6RC	Luc7-like protein 3	LUC7L3	tr J3KPP4	12.8	0.0	0.0	9.8	#NUM!	#DIV/0!	5
K7ENG2;P26368-2;P2	Splicing factor U2AF 65 kDa subunit	U2AF2	tr K7ENG2	6.0	0.4	0.3	10.8	-4.2	1.7	5
P04745;Q5T085;P199	Alpha-amylase 1;Alpha-amylase;Alpha-amylase 2B;Par	AMY1A;AM	sp P04745	0.0	0.1	0.0	0.3	#DIV/0!	4.5	5
P06732	Creatine kinase M-type;Creatine kinase M-type, N-term	CKM	sp P06732	3.0	3.1	0.0	18.1	#NUM!	2.6	5
P22626-2;P22626;A0	Heterogeneous nuclear ribonucleoproteins A2/B1	HNRNP2A8	sp P22626	2.0	0.8	0.6	0.0	-1.8	#NUM!	5
P26196;Q8I9V6	Probable ATP-dependent RNA helicase DDX6	DDX6	sp P26196	7.3	0.0	0.0	4.5	#NUM!	#DIV/0!	5
P42357-2;P42357;P4	Histidine ammonia-lyase	HAL	sp P42357	0.0	7.6	4.8	1.0	#DIV/0!	-2.9	5
P53999;D6RC37;D6R	Activated RNA polymerase II transcriptional coactivat	SUB1	sp P53999	6.1	2.4	4.1	6.5	-0.6	1.5	5
Q6UWP8;K7ESC4;Q6U	Suprabasin	SBSN	sp Q6UWP8	1.4	7.2	7.9	6.9	2.5	-0.1	5
Q96E15;Q96E15-2;A2R	Transcription elongation factor A protein-like 4	TCEAL4	sp Q96E15	5.5	2.5	1.5	6.1	-1.9	1.3	5
E7ET15;O15042-2;O1	U2 snRNP-associated SURP motif-containing protein	U2SURP	tr E7ET15	6.0	0.7	0.0	7.1	#NUM!	3.3	4
H3BP58;H3BQN4;J3KF	Fructose-bisphosphate aldolase;Fructose-bisphosphat	ALDOA	tr H3BP58	1.1	1.3	1.1	2.3	-0.1	0.8	4
H7C469;A0A1B0GW4	Cathepsin D;Cathepsin D light chain;Cathepsin D heav	CTSD	tr H7C469	0.0	1.3	1.7	1.5	#DIV/0!	0.2	4
O43809;H3BV41;H3B1	Cleavage and polyadenylation specificity factor subun	NUDT21	sp O43809	1.9	2.3	0.0	3.9	#NUM!	0.7	4
P08238;P07900;P079	Heat shock protein HSP 90-beta;Heat shock protein H:	HSP90A81;S	sp P08238	0.0	1.9	3.0	0.0	#DIV/0!	#NUM!	4
P10599;P10599-2	Thioredoxin	TXN	sp P10599	0.6	2.5	2.5	0.8	2.1	-1.7	4
P10809;C9J125;E7EXE	60 kDa heat shock protein, mitochondrial	HSPD1	sp P10809	0.5	0.7	1.0	0.4	0.9	-0.8	4
P62314;J3QLJ9;J3QLR	Small nuclear ribonucleoprotein Sm D1	SNRPD1	sp P62314	3.9	1.2	1.7	5.1	-1.2	2.1	4
Q9Y383;Q96HJ9-2;A0	Putative RNA-binding protein Luc7-like 2	LUC7L2	sp Q9Y383	29.7	0.2	0.7	45.6	-5.5	7.5	4
A0A0C4DGN4;Q96DA	Zymogen granule protein 16 homolog B	ZG16B	tr A0A0C4	0.0	0.7	1.0	1.1	#DIV/0!	0.7	3
A0A0U1RR32;A0A0U1	Histone H2A type 1-J;Histone H2A type 1-H;Histone H:	HIST1H2AJ	tr A0A0U1	1.3	1.3	1.5	3.1	0.2	1.3	3
B8Z2Q6;P06454-2;P06	Prothymosin alpha;Prothymosin alpha, N-terminally p	PTMA	tr B8Z2Q6	0.0	1.0	0.0	0.0	#DIV/0!	#NUM!	3
F5GYV5;H7BZV4;A0A0	ADP-ribosylation factor-like protein 6-interacting pro	ARL6IP4	tr F5GYV5	5.6	0.0	0.0	6.6	#NUM!	#DIV/0!	3
F8WE65;C9I557;P629	Peptidyl-prolyl cis-trans isomerase;Peptidyl-prolyl cis	PPIA	tr F8WE65	5.0	0.4	2.7	0.0	-0.9	0.6	3
H3BP7;P35637-2;P3	RNA-binding protein FUS;TATA-binding protein-associ	FUS;TAF15	tr H3BP7	2.5	1.5	1.3	1.4	-1.0	-0.1	3
H3BNT5;P14618-2;P1	Pyruvate kinase;Pyruvate kinase PKM	PKM	tr H3BNT5	1.0	1.9	1.1	1.2	0.1	-0.6	3
J3KR62;Q96QA5	Gasdermin-A	GSDMA	tr J3KR62	0.0	3.5	1.8	0.0	#DIV/0!	#NUM!	3
J3QS39;J3QTR3;F5H6	Ubiquitin-60S ribosomal protein L40;Ubiquitin;60S r	UBB;RPS27	tr J3QS39	2.0	11.7	8.5	4.3	2.1	-1.4	3
O75533;H7C341	Splicing factor 3B subunit 1	SF3B1	sp O75533	1.4	0.1	0.0	1.1	#NUM!	3.0	3
P00338;P00338-3;F5	L-lactate dehydrogenase A chain	LDHA	sp P00338	0.0	0.3	0.7	0.0	#DIV/0!	#NUM!	3
P01275	Glucagon;Glucicent;Glucicent-related polypeptide;Ox	GCG	sp P01275	0.0	1.2	1.2	0.0	#DIV/0!	#NUM!	3
P04792;F8WE04;C9J3	Heat shock protein beta-1	HSPB1	sp P04792	0.7	0.5	0.5	0.7	-0.4	0.4	3
P09874	Poly(ADP-ribose) polymerase 1	PARP1	sp P09874	1.0	0.0	1.1	0.0	0.0	#DIV/0!	3
PODN76;Q01081;Q01	Splicing factor U2AF 35 kDa subunit	U2AF1	sp PODN76	10.0	0.0	4.5	5.3	-1.1	#DIV/0!	3
P60174-4;P60174-1;P	Triosephosphate isomerase	TP1	sp P60174	0.0	0.3	0.4	0.0	#DIV/0!	#NUM!	3
P63173;J3KT73;J3QLC	60S ribosomal protein L38	RPL38	sp P63173	8.2	2.5	1.8	4.6	-2.2	0.9	3
P81605;P81605-2	Dermcidin;Survival-promoting peptide;DCD-1	DCD	sp P81605	13.2	26.2	35.5	9.0	1.4	-1.6	3
Q13835-2;Q13835	Plakophilin-1	PKP1	sp Q13835	0.0	4.1	0.0	0.0	#DIV/0!	#NUM!	3
Q15365;F8V720;F8WC	Poly(rC)-binding protein 1	PCBP1	sp Q15365	2.4	0.4	0.4	3.5	-2.5	3.2	3
Q8WVV4;Q8WVV4-1;C	Protein POF1B	POF1B	sp Q8WVV4	0.4	1.8	2.0	0.3	2.3	-2.7	3
Q9HCY8	Protein S100-A14	S100A14	sp Q9HCY8	0.0	1.2	0.0	0.0	#DIV/0!	#NUM!	3
Q9Y646;E5R835;E5R	Carboxypeptidase Q	CPQ	sp Q9Y646	14.8	0.0	0.0	12.3	#NUM!	#DIV/0!	3
A0A0A0MRM9;Q1497	Nucleolar and coiled-body phosphoprotein 1	NOLC1	tr A0A0A0	7.2	0.5	0.7	7.0	-3.4	3.8	2
A0A0D95FD2;Q8N1K5	Protein THEMIS	THEMIS	tr A0A0D9	0.0	13.6	0.3	0.0	#DIV/0!	#NUM!	2
A0A0G2J1W1;P0DMV	Heat shock 70 kDa protein 1A;Heat shock 70 kDa prot	HSPA1A;HS	tr A0A0G2	2.2	0.0	1.4	2.6	-0.7	#DIV/0!	2
A8MYV2;Q9N029-2;Q9	Putative RNA-binding protein Luc7-like 1	LUC7L1	tr A8MYV2	0.7	0.0	0.0	0.0	#NUM!	#DIV/0!	2
C9J4Z3;P61513;G5E91	60S ribosomal protein L37a	RPL37A	tr C9J4Z3	0.2	0.2	0.0	0.5	#NUM!	1.2	2
E7EQG2;P60842;Q142	Eukaryotic initiation factor 4A-I;Eukaryotic initiation	EIF4A2;EIF								

E7EX29;P63104;E5RG	14-3-3 protein zeta/delta;14-3-3 protein sigma;14-3-3 YWHA2;YW tr E7EX29	0.0	0.7	0.6	0.5	#DIV/0!	-0.5	2		
E9PRD9;E9PQ75;E9PL	Vascular non-inflammatory molecule 2	VNN2	tr E9PRD9	6.7	0.0	0.4	6.2	-4.1	#DIV/0!	2
F8VW21;P05388;F8W	60S acidic ribosomal protein P0;60S acidic ribosomal RPLP0;RPL1 tr F8VW21	0.0	0.4	0.3	0.0	0.0	0.0	#DIV/0!	#NUM!	2
F8W6P5;P68871;A0A1	Hemoglobin subunit beta;LVV-hemorphin-7;Spinorpl HBB;HBD tr F8W6P5	2.9	1.6	1.0	1.7	1.7	-1.5	0.1	2	2
F8WJN3;Q16630-3;Q1	Cleavage and polyadenylation specificity factor subun CP5F6 tr F8WJN3	3.7	0.0	0.0	0.0	0.0	0.0	#NUM!	#DIV/0!	2
HOYH80;F8W6I7;P096	Heterogeneous nuclear ribonucleoprotein A1;Hetero; HNRNP1 tr HOYH80	2.9	1.8	2.1	3.3	2.0	-0.5	0.9	2	2
J3KQ96;E7EY2;Q134	Treacle protein	TCOF1	tr J3KQ96	0.7	0.0	0.0	1.1	#NUM!	#DIV/0!	2
J3QLE5;P14678-2;P63	Small nuclear ribonucleoprotein-associated proteins  SNRPN;SNRP tr J3QLE5	0.8	0.0	0.3	0.7	0.7	-1.3	#DIV/0!	2	2
J3QTJ6;Q5CZC0-2;Q5C	Fibrous sheath-interacting protein 2	FSIP2	tr J3QTJ6	0.0	1.4	0.0	0.0	0.0	#NUM!	2
K7EK07;P84243;K7E	V Histone H3;Histone H3.3;Histone H3.2 H3F3B;H3F tr K7EK07	1.0	0.0	0.0	1.2	0.0	-0.1	-0.1	#DIV/0!	2
M0R0Y6;M0QYQ7;M0I	Heterogeneous nuclear ribonucleoprotein M	HNRNPM	tr M0R0Y6	0.0	0.1	0.2	0.1	0.1	#DIV/0!	2
O43143	Pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	sp O43143	0.4	0.0	0.3	0.3	-0.4	#DIV/0!	2	2
P05109	Protein S100-A8;Protein S100-A8, N-terminally proce S100A8	sp P05109	0.0	4.5	3.6	2.2	2.2	#DIV/0!	-1.0	2
P05141;Q9HOC2	ADP/ATP translocase 2;ADP/ATP translocase 2, N-term SLC25A5	sp P05141	0.0	1.3	2.2	0.0	0.0	#DIV/0!	#NUM!	2
P06748-3;P06748-2;P	Nucleophosmin	NPM1	sp P06748	0.7	0.7	0.6	0.0	-0.1	#NUM!	2
P11021	78 kDa glucose-regulated protein	HSPA5	sp P11021	0.0	0.5	0.6	0.4	#DIV/0!	-0.3	2
P11387	DNA topoisomerase 1	TOP1	sp P11387	12.2	0.0	0.0	6.8	#NUM!	#DIV/0!	2
P12273	Pro lactin-inducible protein	PIP	sp P12273	0.0	5.7	3.1	2.0	#DIV/0!	-1.5	2
P17900;HOYB73;E5R	Ganglioside GM2 activator;Ganglioside GM2 activato; GM2A	sp P17900	0.0	0.8	0.0	0.0	0.0	#DIV/0!	#NUM!	2
P21796;C9JH7	Voltage-dependent anion-selective channel protein 1	VDAC1	sp P21796	0.0	0.7	0.0	0.0	#DIV/0!	#NUM!	2
P32119;A6NIW5;A0A1	Peroxioredoxin-2	PRDX2	sp P32119	0.9	12.0	6.9	1.5	3.0	-3.0	2
P40938-2;P40938;A0	Replication factor C subunit 3	RFC3	sp P40938	0.5	0.3	0.0	0.3	#NUM!	0.0	2
P47929	Galectin-7	LGALS7	sp P47929	0.0	1.6	0.5	0.0	#DIV/0!	-2.3	2
P84090;G3V279	Enhancer of rudimentary homolog	ERH	sp P84090	0.6	0.0	0.7	1.1	0.0	#DIV/0!	2
Q15459	Splicing factor 3A subunit 1	SF3A1	sp Q15459	0.7	0.0	0.5	0.8	-0.6	#DIV/0!	2
Q2L6G8;G8JLQ2;Q155	Corneodesmosin	CDSN	tr Q2L6G8	0.0	5.8	2.2	0.0	#DIV/0!	#NUM!	2
Q2M2H8;A0A0J9YX77	Probable maltase-glucoamylase-like protein LOC9343	MGAM	sp Q2M2H8	6.4	0.0	0.0	2.8	#NUM!	#DIV/0!	2
Q5BK9Y;G3XAI9;HOYH	Protein FAM133B;Protein FAM133A	FAM133B;F	sp Q5BK9Y	5.0	0.0	0.0	3.5	#NUM!	#DIV/0!	2
Q7L4I2-2;Q7L4I2	Arginine/serine-rich coiled-coil protein 2	RSRC2	sp Q7L4I2-	6.1	0.0	0.0	1.8	#NUM!	#DIV/0!	2
Q8ND56-3;Q8ND56-2	Protein LSM14 homolog A	LSM14A	sp Q8ND56-	83.1	12.5	13.6	25.2	-2.6	1.0	2
Q8WVK2;B8ZZ98	U4/U6.U5 small nuclear ribonucleoprotein 27 kDa pr	SNRNP27	sp Q8WVK	7.1	0.0	0.0	6.6	#NUM!	#DIV/0!	2
Q96FQ6	Protein S100-A16	S100A16	sp Q96FQ6	0.0	2.3	0.9	0.0	#DIV/0!	#NUM!	2
Q9NWB6-3;Q9NWB6-	Arginine and glutamate-rich protein 1	ARGLU1	sp Q9NWB6	16.9	0.0	1.0	7.6	-4.0	#DIV/0!	2
Q9NY12-2;Q9NY12	H/ACA ribonucleoprotein complex subunit 1	GAR1	sp Q9NY12	18.9	2.4	3.0	18.9	-2.6	3.0	2
Q9NZT1	Calmodulin-like protein 5	CALML5	sp Q9NZT1	0.0	1.9	3.5	0.0	#DIV/0!	#NUM!	2
U3KQK0;Q99880;Q99	Histone H2B;Histone H2B type 1-L;Histone H2B type 1	HIST1H2BN	tr U3KQK0	0.0	1.1	0.0	0.9	#DIV/0!	-0.3	2
A0A075B6H6;P01834	Ig kappa chain C region	IGKC	tr A0A075	0.0	1.1	0.0	0.0	#DIV/0!	#NUM!	1
A0A087WWS6		IFNA13	tr A0A087	6.8	0.0	0.0	0.0	#NUM!	#DIV/0!	1
A0A087WVY3;P3041	NK-tumor recognition protein;Putative peptidyl-proh	NKTR	tr A0A087	4.8	0.0	0.0	3.7	#NUM!	#DIV/0!	1
A0A087X106;CON_O	Keratin, type II cuticular Hb6;Keratin, type II cuticular	KRT81;KRT1	tr A0A087	0.0	0.3	0.4	0.0	#DIV/0!	#NUM!	1
A0A0A0MSI0;Q06830	Peroxioredoxin-1	PRDX1	tr A0A0A0	0.0	0.4	0.5	0.0	#DIV/0!	#NUM!	1
A0A0G2JRN3;A0A0241	Alpha-1-antitrypsin;Short peptide from AAT	SERPINA1	tr A0A0G2	0.5	0.0	0.0	0.3	#NUM!	#DIV/0!	1
A1A5B4-3;A1A5B4	Anoctamin-9	ANO9	sp A1A5B4	223.4	0.0	0.0	187.4	#NUM!	#DIV/0!	1
B1AN99;P35030-5;P3	Trypsin-3	PRSS3	tr B1AN99	46.3	138.8	8.3	78.7	-2.5	-0.8	1
B4DYP1			tr B4DYP1	0.0	1.1	0.0	0.0	#DIV/0!	#NUM!	1
B6VEX4;A0A0A0MRT6	Abl interactor 1	ABI1	tr B6VEX4	2.0	0.0	0.0	1.2	#NUM!	#DIV/0!	1
D6RB45;A0A1B0GX04	Matrin-3	MATR3	tr D6RB45	0.0	0.2	0.0	0.0	#DIV/0!	#NUM!	1
E9PIZ2;Q8N3Y3	Glycosyltransferase-like protein LARGE2;Xylosyltrans	GYLTL1B	tr E9PIZ2	2.3	0.0	0.0	2.0	#NUM!	#DIV/0!	1
E9PLA6;E9PIH8;E9PI	Serp1n H1	SERPINH1	tr E9PLA6	0.0	0.1	0.0	0.0	#DIV/0!	#NUM!	1
F8VV32;A0A0A4J259	Lysozyme;Lysozyme C	LYZ	tr F8VV32	3.5	5.5	5.2	10.3	0.6	0.9	1
F8VZ99;P05783	Keratin, type I cytoskeletal 18	KRT18	tr F8VZ99	0.0	0.6	0.0	0.0	#DIV/0!	#NUM!	1
G3V258		ADCY4	tr G3V258	7.2	0.0	0.0	4.0	#NUM!	#DIV/0!	1
HOY5C3;P32004-3;P3	Neural cell adhesion molecule L1	L1CAM	tr HOY5C3	74.2	0.0	0.0	58.8	#NUM!	#DIV/0!	1
HOY8D1;A6XMV8;CON	Putative trypsin-6;Trypsin-2;Trypsin-1;Alpha-trypsin	PRSS1;PRSS	tr HOY8D1	147.3	49.8	15.9	79.5	-3.2	0.7	1
HOYMP2;HOYL71;H3B	Mothers against decapentaplegic homolog	SMAD3	tr HOYMP2	4.2	0.0	0.0	5.1	#NUM!	#DIV/0!	1
H7C5C2;Q14188-7;Q1	Transcription factor Dp-2	TFDP2	tr H7C5C2	0.0	481.3	51.5	0.0	#DIV/0!	#NUM!	1
I3L1B1;O43896	Kinesin-like protein;Kinesin-like protein KIF1C	KIF1C	tr I3L1B1	0.0	9.1	0.0	0.0	#DIV/0!	#NUM!	1
J3QL74;J3QLI2;O4382	Zinc finger and BTB domain-containing protein 14	ZBTB14	tr J3QL74	2657.2	2.0	1.5	12.9	-10.8	2.3	1
M0QZK8;O75223-3;O	Gamma-glutamylcyclotransferase	GGCT	tr M0QZK8	0.3	1.0	1.1	0.0	1.7	#NUM!	1
O75319	RNA/RNP complex-1-interacting phosphatase	RNUP11	sp O75319	1.2	0.0	0.0	1.2	#NUM!	#DIV/0!	1
O75343	Guanylate cyclase soluble subunit beta-2	GUICY1B2	sp O75343	27.1	0.0	0.0	19.2	#NUM!	#DIV/0!	1
O75400-2;O75400-3	Pre-mRNA-processing factor 40 homolog A	PRPF40A	sp O75400-	1.3	0.0	0.0	4.0	#NUM!	#DIV/0!	1
O75874	Isocitrate dehydrogenase [NADP] cytoplasmic	IDH1	sp O75874	0.0	1.5	0.0	0.0	#DIV/0!	#NUM!	1
O75901	Ras association domain-containing protein 9	RASSF9	sp O75901	2.8	0.0	0.0	2.9	#NUM!	#DIV/0!	1
O95497	Pantetheinase	VNN1	sp O95497	2.3	0.0	0.0	2.7	#NUM!	#DIV/0!	1
P04259	Keratin, type II cytoskeletal 6B	KRT6B	sp P04259	6.7	108.3	30.0	31.8	2.2	-1.8	1
P07858	Cathepsin B;Cathepsin B light chain;Cathepsin B heav	CTSB	sp P07858	0.0	0.8	0.0	0.0	#DIV/0!	#NUM!	1
P09210;P08263	Glutathione S-transferase A2;Glutathione S-transferas	GSTA2;GST	sp P09210	0.1	0.0	0.1	0.5	-0.4	#DIV/0!	1
P17066;P48741	Heat shock 70 kDa protein 6;Putative heat shock 70 kI	HSPA6;HSP	sp P17066	3.0	4.0	3.4	2.3	0.2	-0.8	1
P26006;P26006-1	Integrin alpha-3;Integrin alpha-3 heavy chain;Integrin	ITGA3	sp P26006	0.0	425.8	61.6	0.0	#DIV/0!	#NUM!	1
P30050-2;P30050	60S ribosomal protein L12	RPL12	sp P30050-	0.0	0.7	0.3	0.0	#DIV/0!	#NUM!	1
P35908	Keratin, type II cytoskeletal 2 epidermal	KRT2	sp P35908	855.5	6100.3	5414.0	2338.3	2.7	-1.4	1
P42081	T-lymphocyte activation antigen CD86	CD86	sp P42081	0.0	3.6	0.0	0.0	#DIV/0!	#NUM!	1
P52597	Heterogeneous nuclear ribonucleoprotein F;Heteroge	HNRNPF	sp P52597	0.8	0.0	0.0	0.7	#NUM!	#DIV/0!	1
P53396-3;P53396-2	P ATP-citrate synthase	ACLY	sp P53396-	0.0	0.2	0.0	0.1	#DIV/0!	-1.4	1
P60709;E5E9R0;E7E	Actin, cytoplasmic 1;Actin, cytoplasmic 1, N-terminal	ACTB	sp P60709	17.2	10.0	8.8	5.8	-1.0	-0.8	1
P62306	Small nuclear ribonucleoprotein F	SNRPF	sp P62306	1.0	0.5	0.0	0.0	#NUM!	#NUM!	1
P62805	Histone H4	HIST1H4A	sp P62805	0.3	0.8	1.0	0.2	1.8	-1.7	1
P63261;I3L130;I3L1	Actin, cytoplasmic 2;Actin, cytoplasmic 2, N-terminal	ACTG1	sp P63261	0.0	0.4	0.6	0.0	#DIV/0!	#NUM!	1
Q16584-2;Q16584	Mitogen-activated protein kinase kinase kinase 11	MAP3K11	sp Q16584-	4.7	2.8	3.0	0.0	-0.7	#NUM!	1
Q3B726	DNA-directed RNA polymerase I subunit RPA43	TWISTNB	sp Q3B726	0.8	0.0	0.0	0.9	#NUM!	#DIV/0!	1
Q562R1	Beta-actin-like protein 2	ACTBL2	sp Q562R1	0.0	3.6	4.2	0.0	#DIV/0!	#NUM!	1
Q6NXT1-2			sp Q6NXT1-	0.0	0.9	3.5	0.0	#DIV/0!	#NUM!	1
Q86X95-2;Q86X95	Corepressor interacting with RBP1	CIR1	sp Q86X95-	0.6	0.0	0.2	0.8	-1.4	#DIV/0!	1
Q86Y37-2;Q86Y37	CDK2-associated and cullin domain-containing protei	CACUL1	sp Q86Y37-	25.3	0.0	0.0	16.5	#NUM!	#DIV/0!	1
Q96AE7-2;Q96AE7	Tetratricopeptide repeat protein 17	TTC17	sp Q96AE7-	1.1	3428.6	0.0	1.2	#NUM!	-11.5	1
Q96NLO-2			sp Q96NLO-	23.8	0.0	0.0	49.5	#NUM!	#DIV/0!	1
Q96PE3-2;Q96PE3-4	C Type I inositol 3,4-bisphosphate 4-phosphatase	INPP4A	sp Q96PE3-	67.0	0.0	0.0	21.7	#NUM!	#DIV/0!	1
Q96RE9-3			sp Q96RE9-	0.0	7.3	85.5	0.0	#DIV/0!	#NUM!	1
Q9NP86	Calcium-binding protein 5	CABP5	sp Q9NP86	40.2	0.0	0.0	1.8	#NUM!	#DIV/0!	1
Q9UKX2	Myosin-2	MYH2	sp Q9UKX2	0.1	0.0	0.0	0.3	#NUM!	#DIV/0!	1
Q9UQG0	Endogenous retrovirus group K member 11 Pol protei	ERVK-11	sp Q9UQG0	3.3	0.6	0.0	0.0	#NUM!	#NUM!	1
Q9Y371-3			sp Q9Y371-	292.4	0.0	0.0	0.0	#NUM!	#DIV/0!	1
X6RJP6;P37802;P378	Transgelin-2	TAGLN2	tr X6RJP6	0.0	0.8	0.7	0.0	#DIV/0!	#NUM!	1