

Table S1. Proteins significantly altered in neuroblastoma cells transfected with GIT2 siRNA.

Protein Uniprot IDs are displayed that demonstrated a significant (>2 SD from mean) expression alteration (siRNAGIT2/con) measured using a cross-over medium/heavy SILAC doublet experiment. An average normalized ratio of protein expression from siRNA GIT2 versus control (from the SILAC doublet label-swap) was log2 transformed for data visualization (N ratio). The simple expression ratio of the specific protein after siRNA GIT2 treatment compared control cells is also indicated.

Protein Description	Uniprot ID	average log(N-ratio)	siRNA GIT2/con
Nucleolar and coiled-body phosphoprotein 1	Q14978-2	0.65	1.57
Putative uncharacterized protein CGI-59	C9JXK6	0.44	1.36
Neutral alpha-glucosidase AB	Q14697-1	0.43	1.34
Histone H3	Q5TEC6	0.40	1.32
LDLR chaperone MESD	Q14696	0.33	1.26
Phosducin-like protein 3	Q9H2J4	0.27	1.21
Peroxiredoxin-4	Q13162	0.26	1.20
Protein FAM3C	Q92520	0.26	1.20
Sulfotransferase 1A1	P50225	0.24	1.18
Succinate dehydrogenase [ubiquinone] iron-sulfur subunit	P21912	0.24	1.18
Tubulin-tyrosine ligase-like protein 12	Q14166	0.24	1.18
Aspartate aminotransferase, mitochondrial;Transaminase A	P00505	0.22	1.17
DERP12 (Dermal papilla derived protein 12)	Q8TE01	0.21	1.15
Thymosin beta-4-like protein 3	Q0P5N8	0.21	1.15
Activator of 90 kDa heat shock protein ATPase homolog 1	O95433	0.21	1.15
ATPase family AAA domain-containing protein 3A	Q9NV17-1	0.21	1.15
Density-regulated protein	C9JW58	0.20	1.15
Enhancer of mRNA-decapping protein 3	Q96F86	0.20	1.15
Oxidoreductin-1-L-alpha	Q96HE7	0.20	1.15
Bisphosphate 3'-nucleotidase 1	O95861-2	0.20	1.15
Coiled-coil domain-containing protein 124	Q96CT7	0.20	1.15
Leucine aminopeptidase 3	P28838-1	0.19	1.14
Microtubule-associated protein 1B	P46821	0.19	1.14
Prefoldin subunit 4	Q9NQP4	0.19	1.14
Mitochondrial ATP-dependent protease Lon	P36776	0.19	1.14
60S ribosomal protein L14	P50914	0.19	1.14
Membrane-organizing extension spike protein	P26038	0.18	1.13
Histone H3.1	P68431	0.17	1.12
PHD finger-like domain-containing protein 5A	Q7RTV0	0.18	1.13

Signal recognition particle 14 kDa protein	P37108	0.18	1.13
NAD(P) transhydrogenase, mitochondria	Q13423	0.18	1.13
Creatine kinase U-type, mitochondrial	P12532-2	0.18	1.13
14-3-3 protein gamma	P61981	0.17	1.13
Laminin subunit gamma-1	P11047	0.17	1.13
Histone H4	P62805	0.17	1.13
Eukaryotic translation initiation factor 3 subunit F	B3KSH1	0.17	1.13
TRAF6-regulated IKK activator 1 beta Uev1A	Q13404-4	-0.17	0.89
Protein tyrosine phosphatase-like protein PTPLAD1	Q9P035	-0.17	0.89
ADP-ribosylation factor 1	P84077	-0.17	0.89
PEST proteolytic signal-containing nuclear protein	Q8WW12-1	-0.18	0.89
High-mobility group box 1 variant	P09429	-0.18	0.88
60S ribosomal protein L13a	P40429	-0.18	0.88
Chromatin-modifying protein 2a	O43633	-0.18	0.88
Phosphofructokinase 1	Q01813	-0.18	0.88
70 kDa peroxisomal membrane protein	B4DL07	-0.19	0.88
High-mobility group nucleosome binding domain 1	P05114	-0.20	0.87
33 kDa VAMP-associated protein	A6NDZ0	-0.20	0.87
Core histone macro-H2A.1	O75367-1	-0.20	0.87
Histone H2A type 1-B/E	P04908	-0.20	0.87
Adenylyl cyclase-associated protein	B4DNA3	-0.21	0.86
Spinocerebellar ataxia type 10 protein	Q9UBB4	-0.21	0.86
ATP synthase subunit delta, mitochondrial	P30049	-0.21	0.86
Synaptobrevin-3	Q15836	-0.21	0.86
Histone H2A type 1	P0C0S8	-0.22	0.86
Mitochondrial import inner membrane translocase subunit TIM44	O43615	-0.22	0.86
Guanine nucleotide binding protein (G protein), gamma 12	Q9UBI6	-0.22	0.86
Nuclear pore complex protein Nup50	Q9UKX7	-0.23	0.86
Mediator of DNA damage checkpoint protein 1	Q14676-1	-0.23	0.85
Nuclear ubiquitous casein/cyclin-dependent kinases substrate	Q9H1E3-1	-0.23	0.85
Fanconi anemia group I protein	Q9NVI1-3	-0.23	0.85
DnaJ homolog subfamily C member 8	O75937	-0.24	0.85
Histone H2A type 2-B	Q8IUE6	-0.25	0.84
Neuron-specific enolase	P09104	-0.25	0.84
Heterochromatin protein 1 homolog alpha	P45973	-0.26	0.84
26S proteasome non-ATPase regulatory subunit 7	P51665	-0.28	0.82
14-3-3 protein eta	Q04917	-0.30	0.81
Ras-related protein Rab-5B	P61020	-0.32	0.80
Splicing factor, arginine-serine-rich 15	C9J1W7	-0.32	0.80
Peptidyl-prolyl cis-trans isomerase FKBP8	Q14318-2	-0.42	0.75

Table S2. GO term analysis of GIT2 siRNA-modulated proteins. Gene Ontology (GO) term enrichment analysis was performed using standard GO-term biological process algorithms with WebGestalt (version 2). GO term IDs, number of observed enriched proteins (Observed) and enrichment probability ($p < 0.05$) value (p value) is indicated for each significantly-enriched GO term.

GO term description	GO term ID	Observed	p value
cellular response to stress	GO:0033554	8	0.0296
protein-DNA complex assembly	GO:0065004	5	0.0055
chromatin assembly	GO:0031497	4	0.0138
nucleosome assembly	GO:0006334	4	0.0119
purine ribonucleoside triphosphate catabolic process	GO:0009207	2	0.0303
glucose catabolic process	GO:0006007	3	0.0307
glycolysis	GO:0006096	3	0.0256
acetyl-CoA catabolic process	GO:0046356	2	0.0367
ATP catabolic process	GO:0006200	2	0.0256
I-kappaB kinase/NF-kappaB cascade	GO:0007249	4	0.0367

Table S3. Proteins significantly altered in cells transfected with Flag-GIT2 cDNA. Protein Uniprot IDs are displayed that demonstrated a significant (>2 SD from mean) expression alteration (F-GIT2/con) measured using a cross-over medium/heavy SILAC doublet experiment. An average normalized ratio of protein expression from siRNA GIT2 versus control (from the SILAC doublet label-swap) was \log_2 transformed for data visualization (N-ratio). The simple expression ratio of the specific protein after siRNA GIT2 treatment compared control cells is also indicated.

Protein Description	Uniprot ID	Average log(N-ratio)	F-GIT2/con
Isoform 2 of C-terminal-binding protein 2	P56545-2	1.64	3.11
Dermal papilla derived protein 12	Q8TE01	1.35	2.56
Gastric-associated differentially-expressed protein YA61P	Q9NZ23	1.14	2.20
G2/mitotic-specific cyclin-B1	P14635	0.75	1.68
Isoform Long of Antigen KI-67	P46013-1	0.71	1.63
Aspartate aminotransferase, mitochondrial	P00505	0.42	1.34
Histone H3	Q5TEC6	0.35	1.27
Isoform 1 of Proteasome subunit alpha type-3	P25788-1	0.33	1.26
Kinesin family member 2C	Q99661-1	0.33	1.26
Eukaryotic translation initiation factor 3 subunit H	B3KS98	0.32	1.25
Histone H3.1	P68431	0.32	1.25
Histone H4	P62805	0.31	1.24
Transmembrane protein 165	Q9HC07	0.29	1.22
zinc finger protein 207 isoform c	Q59G94	0.29	1.22
Squalene synthetase	P37268	0.28	1.21
Ubiquitin-conjugating enzyme E2 S	Q16763	0.28	1.21
DNA topoisomerase 1	P11387	0.28	1.21
Isoform 2 of Transcription elongation factor SPT5	O00267-1	0.27	1.21
FUS interacting protein (Serine/arginine-rich) 1	O75494-1	0.27	1.21
Isoform 1 of Minor histocompatibility antigen H13	Q8TCT9-1	0.27	1.20
Non-histone chromosomal protein HMG-17	P05204	0.27	1.20
Eukaryotic translation initiation factor 1	P41567	0.27	1.20
Protein tyrosine phosphatase-like protein PTPLAD1	Q9P035	0.26	1.20
Msx2-interacting protein	Q96T58	0.26	1.20
Isoform 1 of Replication factor C subunit 1	P35251-1	0.25	1.19
Asparagine synthetase [glutamine-hydrolyzing]	P08243	0.25	1.19
Isoform 4 of 4F2 cell-surface antigen heavy chain	P08195-4	0.25	1.19
Isoform 1 of Golgin subfamily A member 3	Q08378-1	0.24	1.18
Non-histone chromosomal protein HMG-14	A6NEL0	0.23	1.18

Isoform 2 of Kinesin-like protein KIF23	A8MTR8	0.23	1.17
Isoform 2 of RNA-binding protein 10	P98175-1	0.23	1.17
Isoform 2 of Putative ribosomal RNA methyltransferase NOP2	A8MQ38	0.23	1.17
Transcription factor A, mitochondrial	Q00059	0.22	1.17
Isoform 1 of Erlin-2	O94905-1	0.22	1.16
Isoform 1 of Nucleolar RNA helicase 2	Q9NR30-1	0.21	1.15
39S ribosomal protein L10, mitochondrial	A6NGJ4	0.20	1.15
mRNA turnover protein 4 homolog	Q9UKD2	0.20	1.15
Isoform 1 of Surfeit locus protein 4	O15260-1	0.19	1.14
Isoform 1 of H/ACA ribonucleoprotein complex subunit 1	Q9NY12-1	0.18	1.14
Isoform 1 of Tryptophanyl-tRNA synthetase	P23381-1	0.18	1.14
Isoform 1 of Far upstream element-binding protein 1	B4DT31	0.18	1.13
Isoform 2 of UPF0488 protein C8orf33	Q9H7E9-2	0.18	1.13
Uncharacterized protein C7orf50	Q9BRJ6	0.18	1.13
Dolichyl-diphosphooligosaccharide-protein glycosyltransferase	P46977	0.18	1.13
Palmitoyl-protein thioesterase 1	Q5T0S6	0.18	1.13
Isoform 5 of AP-3 complex subunit delta-1	O14617-5	-0.17	0.89
Prolyl endopeptidase	P48147	-0.17	0.89
Serpin B6	B2RBA8	-0.17	0.89
Isoform 1 of Kinectin	Q86UP2-1	-0.18	0.89
Acetyl-CoA acetyltransferase, cytosolic	Q9BWD1	-0.18	0.88
Isoform Long of Glucose-6-phosphate 1-dehydrogenase	P11413-2	-0.18	0.88
Golgin B1	B2ZZ91	-0.19	0.88
Isocitrate dehydrogenase [NADP] cytoplasmic	O75874	-0.19	0.88
Condensin complex subunit 3	Q9BPX3	-0.19	0.88
Long-chain-fatty-acid-CoA ligase 3	O95573	-0.19	0.88
26S proteasome non-ATPase regulatory subunit 12	O00232	-0.21	0.86
Importin-9	Q96P70	-0.22	0.86
Brix domain-containing protein 2	Q8TDN6	-0.24	0.85
Tubulin-specific chaperone E	B7Z3P1	-0.27	0.83
WW domain-binding protein 11	Q9Y2W2	-0.34	0.79
Nucleolar protein 56	O00567	-0.52	0.70
Membrane-associated progesterone receptor component 2	O15173	-0.56	0.68
Casein kinase 2, beta polypeptide	Q5SRQ6	-0.64	0.64
UPF0727 protein C6orf115	Q9P1F3	-1.13	0.46
Isoform 1 of Titin	Q8WZ42-8	-1.19	0.44

Table S4. GO term analysis of Flag-GIT2-modulated proteins. Gene Ontology (GO) term enrichment analysis was performed using standard GO-term biological process algorithms with WebGestalt (version 2). GO term IDs, number of observed enriched proteins (Observed) and enrichment probability ($p < 0.05$) value (p value) is indicated for each significantly-enriched GO term.

GO term description	GO term ID	Observed	<i>p</i> value
cell cycle	GO:0007049	9	0.0052
ribonucleoprotein complex biogenesis	GO:0022613	5	0.0045
RNA processing	GO:0006396	5	0.0454
nuclear division	GO:0000280	4	0.0199
ncRNA processing	GO:0034470	3	0.0477
chromosome condensation	GO:0030261	2	0.0304
DNA-dependent DNA replication	GO:0006261	2	0.0491
proteasomal protein catabolic process	GO:0010498	3	0.0176
regulation of ubiquitin-protein ligase activity	GO:0051438	3	0.0096
aspartate family amino acid biosynthetic process	GO:0009067	2	0.0095

Table S5. Functional Network Analysis of total siRNA/FLAG-GIT2 modulated proteins.

Functional networks of the GIT2-regulated proteins were created using Ingenuity Pathway Analysis (IPA). Focus molecules represent the proteins that meet the applied statistical cutoffs ($p<0.05$) and map to the Global Molecular Network sets from IPA.

Network Number	Functions	Network Score	Focus Molecules
1	<i>Cellular Assembly and Organization</i>	66	ABCD3
	<i>Cellular Function and Maintenance</i>		ASNS
	<i>DNA Replication, Recombination, and Repair</i>		BRIX1
			CBX5
			CCNB1
			FANCI
			FDFT1
			FKBP8
			H2AFY
			HIST1H2AB/HIST1H2AE
			HIST1H2AG (includes others)
			HIST1H3A (includes others)
			HIST1H4A (includes others)
			HMGN1
			HMGN2
			MKI67
			NOLC1
			NOP2
			NOP56
			PRDX4
			PTPLAD1
			RPL14
			SRP14 (includes EG:20813)
			TMSB10/TMSB4X
			TOP1
			UBE2V1
2	<i>Cellular Assembly and Organization</i>	57	ARF1
	<i>Cellular Function and Maintenance</i>		CAP1
	<i>Cellular Compromise</i>		CSNK2B
			EDC3 (includes EG:315708)
			EIF3F
			EIF3H
			HMGB1
			KIF23

			KIF2C
			LOC100505793/SRSF10
			LONP1
			MAP1B
			MSN
			PFDN4
			PSMA3
			PSMD7
			PSMD12
			RFC1
			SLC3A2
			TBCE
			TTN (includes EG:22138)
			VAPA
			WBP11
			YWHAG
			YWAH
			ZNF207
3	Cancer	29	AHSA1
	<i>Cell Cycle</i>		ATXN10
	<i>Hair and Skin Development and Function</i>		C6orf115
			DENR
			ENO2
			HM13
			MESDC2
			PCNP
			PFKP
			RAB5B
			RBM10
			SDHB
			SULT1A1
			SUPT5H
			TTLL12
4	<i>Cell Cycle</i>	20	ATAD3A/ATAD3B
	<i>Reproductive System Development and Function</i>		ATP5D
	<i>Gene Expression</i>		FAM3C
			GANAB
			HIST2H2AB
			IPO9
			MDC1
			NNT
			PHF5A
			SPEN
			UBE2S

			VAMP3
5	<i>Cell Signaling</i>	17	BPNT1
	<i>Molecular Transport</i>		CHMP2A
	<i>Vitamin and Mineral Metabolism</i>		CKMT1A/CKMT1B
			EIF1
			GNG12
			GOLGA3
			LAMC1
			LAP3
			PGRMC2
			TIMM44
6	<i>Cell Cycle</i>	15	CCDC124
	<i>Skeletal and Muscular System Development and Function</i>		CTBP2
	<i>Organ Morphology</i>		DNAJC8
			ERO1L
			GOT2
			PDCL3
			PFKL
			SCAF4
			TMEM165

Table S6. IPA Canonical Signaling Pathway analysis of total combined siRNA/FLAG-GIT2

modulated proteins. Canonical signaling pathway analysis was performed upon the total complement of GIT2 ‘constellation’ proteins significantly affected by either GIT2 expression potentiation or reduction. For significant population of a specific canonical signaling pathway, at least two inclusive proteins were required, with an enrichment probability of <0.05.

Canonical Signaling Pathways	-log(p-value)	Ratio	Proteins
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	2.68E+00	6.12E-02	YWHAG,YWHAH,CCNB1
ATM Signaling	2.36E+00	5.08E-02	MDC1,CBX5,CCNB1
EIF2 Signaling	2.32E+00	2.44E-02	EIF3H,EIF3F,EIF1,RPL14,RPL13A
Protein Ubiquitination Pathway	2.43E+00	2.23E-02	PSMA3,PSMD7,DNAJC8,PSMD12,UBE2V1,UBE2S
IGF-1 Signaling	1.72E+00	2.83E-02	YWHAG,YWHAH,CSNK2B
Myc Mediated Apoptosis Signaling	1.34E+00	3.28E-02	YWHAG,YWHAH
Role of BRCA1 in DNA Damage Response	1.33E+00	3.08E-02	MDC1,RFC1
ERK5 Signaling	1.30E+00	3.12E-02	YWHAG,YWHAH
Mitotic Roles of Polo-Like Kinase	1.30E+00	3.08E-02	KIF23,CCNB1
Hypoxia Signaling in the Cardiovascular System	1.28E+00	3.08E-02	UBE2V1,UBE2S
Huntington's Disease Signaling	1.44E+00	1.69E-02	SDHB,VAMP3,UBE2S,GNG12
Actin Cytoskeleton Signaling	1.44E+00	1.66E-02	TMSB10/TMSB4X,TTN,GNG12,MSN
Regulation of eIF4 and p70S6K Signaling	1.26E+00	1.70E-02	EIF3H,EIF3F,EIF1