

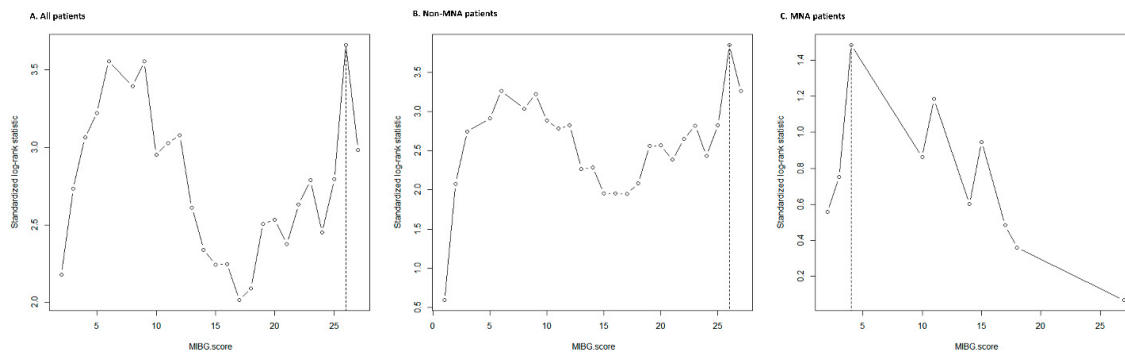


Figure S1. Optimal cut-point values of the Curie score obtained from maximally selected log-rank statistics.

Table S1. Treatment regimens.

Regimen	Drug	Dosage	Schedule	Comments
Induction				
CEDC ^a	Cisplatin	60 mg/m ² /day	Day 0	
	Etoposide	100 mg/m ² /day	Day 2, 5	
	Doxorubicin	30 mg/m ² /day	Days 2	
	Cyclophosphamide	30 mg/kg/day	Days 3,4	
ICE ^a	Ifosfamide	1,200 mg/m ² /day	Days 0–4	
	Carboplatin	400 mg/m ² /day	Days 0,1	
	Etoposide	100 mg/m ² /day	Days 0–4	
Consolidation				
First HDCT	Carboplatin	60 mg/m ² /day	Days, –7, –6, –5	
	Etoposide	100 mg/m ² /day	Days, –7, –6, –5	
	Cyclophosphamide	30 mg/m ² /day	Days, –4, –3, –2	
Second HDCT	Thiotepa	100 mg/m ² /day	Days, –6, –5, –4	
	Melphalan	30 mg/m ² /day	Days, –3, –2	
	TBI	3.33 Gy/day	Days, –3, –2, –1	
	or ¹³¹ I-MIBG Tx	12 or 18 mCi/kg	Days –21	NB–2004 study NB–2009, 2014 study
Maintenance				
Immunotherapy	Interleukin-2		For 5 days every 4 weeks	10 cycles from week 9 of HDCT2
Differentiation Tx	13-cis-retinoic acid	125 mg/m ² /day	For 14 days every 4 weeks	10 cycles from week 9 of HDCT2

MIBG, metaiodobenzylguanidine; HDCT, high-dose chemotherapy. ^a The chemotherapy dose was adjusted for patients younger than 24 months of age, i.e., kilogram-based dose for <6 months age, 70% of dose based on the body surface area for 6–11 months of age, 80% dose for 12–17 months of age and dose for 18–23 months of age.

Table S2. Prognostic significance of individual and different combinations of metastatic sites.

Predictor	Unadjusted		Adjusted ^a	
	sHR (95% CI)	p value	sHR (95% CI)	p value
BM	2.24 (0.94–5.35)	0.071	1.62 (0.62–4.23)	0.320
Bone	1.70 (0.52–5.57)	0.380	1.47 (0.42–5.18)	0.550
Distant lymph nodes	1.40 (0.75–2.60)	0.290	1.28 (0.65–2.49)	0.480
Liver	1.49 (0.72–3.62)	0.380	1.52 (0.73–3.18)	0.260
Skin	0.96 (0.13–7.25)	0.970	1.01 (0.22–4.74)	0.990
Lung ^b	2.32 (1.02–5.28)	0.044	2.22 (0.92–5.35)	0.076
CNS ^c	1.68 (0.62–4.61)	0.310	1.32 (0.25–6.87)	0.740
Other	2.85 (1.51–5.39)	0.001	2.34 (1.12–4.90)	0.023
MSI ^d	1.56 (1.22–2.01)	<0.001	2.30 (1.17–4.54)	0.012

Abbreviations: sHR, subdistributional hazard ratio; CI, confidence interval; BM, bone marrow; CNS, central nervous system; MSI, metastatic site index. ^a Adjusted for *MYCN* amplification and modified Curie score. ^b Direct invasion from thoracic tumors or pleural involvement was excluded. ^c Only parenchymal or leptomeningeal lesions are considered CNS metastases. ^d Metastatic site index (MSI) is a score based on the number of metastatic system/compartments involved (potentially up to 8: bone marrow, bone, distant lymph nodes, liver, skin, lung, CNS and other).

Table S3. Characteristics of patients for RNA-Seq analysis.

Characteristics	RNA sample (<i>n</i> = 25)	Others (<i>n</i> = 105)	p-value
Sex. No. (%)			
Male	20 (80)	57 (54)	0.034
Age at diagnosis, mean ± SD	4.9 ± 2.6	4.4 ± 3.0	0.458
Primary tumor site, No (%)			0.860
Abdomen/Pelvis	23 (92)	94 (90)	
Primary tumor volume (cm ³), mean ± SD	325 ± 396	350 ± 393	0.777
<i>MYCN</i> status			
Nonamplified	23 (92)	72 (73)	0.077
Amplified	2 (8)	27 (20)	
Cytogenetics, No. (%)			
1p deletion	19 (79)	44 (80)	1.000
11q deletion	11 (46)	12 (22)	0.059
17q gain	6 (26)	16 (29)	1.000
INPC			1.000
Favorable	6 (25)	22 (23)	
Unfavorable	18 (75)	75 (77)	
Curie score at diagnosis, mean ± SD	14.3 ± 11.0	13.5 ± 10.7	0.733
Response to induction treatment, No. (%)			0.166
Complete response	6 (24)	45 (43)	
Very good partial response	5 (20)	24 (23)	
Partial response	13 (52)	28 (27)	
Mixed response	0	2 (2)	
Stable disease	0	4 (4)	
Progressive disease	1 (4)	2 (2)	

Abbreviations: INPC, International Neuroblastoma Pathology Classification; SD, standard deviation.

Table S4. Differentially expressed genes between patients with low and high metastatic burden.

	Gene Name	Log ₂ (fold change)	P value	FDR
Down-regulated	<i>FAM151A</i>	-4.153784656	1.01E-06	0.015892
	<i>PAX7</i>	-3.323674818	0.00017	0.209025
	<i>FDCSP</i>	-4.459497745	0.000504	0.255283
	<i>MAGEA1</i>	-4.225267699	0.000452	0.255283
	<i>SDK2</i>	-2.318223576	0.000568	0.264813
	<i>SLC17A7</i>	-1.838057332	0.000689	0.292807
	<i>CSAG1</i>	-3.338727913	0.001031	0.305655
	<i>RP11-529K1.3</i>	-2.396452916	0.001023	0.305655
	<i>PLEC</i>	-1.543008079	0.000881	0.305655
	<i>CTAG2</i>	-4.063645168	0.002333	0.32981
	<i>ALX1</i>	-3.8211702	0.001792	0.32981
	<i>XAGE1C</i>	-3.371049802	0.001979	0.32981
	<i>XAGE1E</i>	-3.369198581	0.001978	0.32981
	<i>XAGE1A</i>	-3.236800008	0.001618	0.32981
	<i>CP</i>	-2.502895198	0.002406	0.32981
	<i>ISLR2</i>	-2.310967438	0.00134	0.32981
	<i>ZBTB20</i>	-1.880308778	0.001976	0.32981
	<i>C1orf95</i>	-1.693227193	0.002143	0.32981
	<i>TUBA3C</i>	-3.469798412	0.00262	0.333735
	<i>RSC1A1</i>	-3.167977549	0.003216	0.343777
	<i>NPFFR2</i>	-2.801977346	0.002939	0.343777
	<i>ABCA7</i>	-1.521702671	0.003126	0.343777
	<i>TPTE</i>	-2.269247269	0.00423	0.37347
	<i>ANKRD33B</i>	-1.575120709	0.004514	0.380294
	<i>ZNF80</i>	-2.324200658	0.004721	0.390455
	<i>MAGEA6</i>	-3.651662116	0.004974	0.399244
	<i>CTAG1B</i>	-1.78515239	0.005408	0.409445
	<i>HLA-DRB5</i>	-2.994055715	0.005635	0.411874
	<i>CDH1</i>	-2.613623571	0.00567	0.412125
	<i>MAGEA12</i>	-3.331860724	0.006389	0.432767
	<i>STRA6</i>	-1.857751499	0.006518	0.435164
	<i>GP1BA</i>	-3.483631324	0.006755	0.436819
	<i>KEL</i>	-2.25973468	0.006747	0.436819
	<i>IGFL4</i>	-2.688758243	0.007036	0.438892
	<i>MAGEA3</i>	-3.434153605	0.007189	0.441152
	<i>IL17REL</i>	-2.313892101	0.007324	0.442071
	<i>ENTHD1</i>	-2.689621917	0.007386	0.442725
	<i>EHF</i>	-2.404255566	0.00741	0.442725
	<i>SCN5A</i>	-1.942418932	0.007741	0.447231
	<i>CTAG1A</i>	-2.48748255	0.008384	0.462104
	<i>KIF21B</i>	-1.836564468	0.00882	0.469643
	<i>PLCH2</i>	-1.819999509	0.008973	0.469643
	<i>ADRA1A</i>	-1.689082933	0.008757	0.469643
	<i>MYBPC2</i>	-2.484164428	0.009026	0.469658
	<i>OR7D2</i>	-2.147383601	0.009514	0.483196
	<i>KCNC3</i>	-2.20992386	0.009666	0.483344
Up-regulated	<i>PCDHA1</i>	1.740932287	0.001185894	0.329810196
	<i>SULT1A2</i>	2.119078124	0.002010513	0.329810196
	<i>LY6H</i>	3.784993658	0.001724316	0.329810196
	<i>GPR143</i>	1.996851721	0.008914896	0.469642767
	<i>LMO3</i>	2.4134251	0.008936518	0.469642767

Table S5. Differentially expressed genes between patients with low and high metastatic burden in the non-MYCN amplification (MNA) subgroup.

	Gene Name	Log ₂ (fold change)	P value	FDR
Down-regulated	<i>FAM151A</i>	-4.04175	4.09E-06	0.01051
	<i>PAX7</i>	-3.82958	4.68E-06	0.01051
	<i>TSPEAR</i>	-2.99112	4.00E-05	0.037003
	<i>ANKRD33B</i>	-1.8745	8.28E-05	0.065027
	<i>MAGEA1</i>	-4.74031	0.000152	0.077148
	<i>KISS1R</i>	-1.94125	0.00084	0.178306
	<i>RP11-529K1.3</i>	-2.53041	0.001111	0.206196
	<i>ZBTB20</i>	-1.80925	0.001542	0.230113
	<i>CSAG1</i>	-3.29065	0.00171	0.234916
	<i>CTAG1A</i>	-2.94693	0.001698	0.234916
	<i>DNAJC5G</i>	-2.76385	0.001816	0.234916
	<i>SLC17A7</i>	-1.76354	0.001965	0.239075
	<i>FDCSP</i>	-4.14753	0.002137	0.246939
	<i>SDK2</i>	-2.2666	0.002268	0.250713
	<i>MBD6</i>	-1.63333	0.002232	0.250713
	<i>MAGEA6</i>	-3.76836	0.003591	0.281457
	<i>PAGE2B</i>	-3.22185	0.003752	0.281457
	<i>TBX1</i>	-2.1758	0.003797	0.281457
	<i>PLEC</i>	-1.62616	0.003574	0.281457
	<i>CTAG2</i>	-4.12586	0.004034	0.292099
	<i>ISLR2</i>	-1.84972	0.004197	0.29355
	<i>ADRA1A</i>	-1.93233	0.004633	0.306003
	<i>LAMA5</i>	-1.51653	0.004625	0.306003
	<i>XAGE1A</i>	-2.93906	0.005124	0.317753
	<i>TGIF2LX</i>	-2.46893	0.005573	0.318284
	<i>XAGE1C</i>	-3.08077	0.00587	0.320152
	<i>XAGE1E</i>	-3.07882	0.00587	0.320152
	<i>C1orf95</i>	-1.75586	0.005869	0.320152
	<i>PLCH2</i>	-2.04674	0.006041	0.322401
	<i>CTAG1B</i>	-1.88515	0.006206	0.322942
	<i>SYCE1</i>	-3.06809	0.006802	0.328035
	<i>SPDYE2</i>	-2.92582	0.00687	0.328035
	<i>TUBA3C</i>	-3.41744	0.007324	0.336524
	<i>MAGEA12</i>	-3.29575	0.007351	0.336786
	<i>CP</i>	-2.56143	0.008165	0.349597
	<i>SLC9A3</i>	-2.37399	0.008436	0.354459
	<i>ALX1</i>	-3.33167	0.008684	0.355366
	<i>RSC1A1</i>	-3.23033	0.008696	0.355366
	<i>TPTE</i>	-2.25218	0.009376	0.363788
Up-regulated	<i>PRR16</i>	1.642109	0.000829	0.178306
	<i>RCAN2</i>	1.744963	0.005168	0.317753
	<i>NDN</i>	1.790537	0.000338	0.120579
	<i>C10orf107</i>	1.875407	0.008721	0.355366
	<i>PCDHA1</i>	1.900439	0.001583	0.231292
	<i>PCDH7</i>	1.955574	0.002171	0.247406
	<i>LMO3</i>	2.057861	0.008351	0.352314
	<i>DDX43</i>	2.101648	0.001946	0.238933
	<i>SULT1A2</i>	2.141738	0.007732	0.343123
	<i>EDIL3</i>	2.754512	0.000274	0.107751
	<i>LY6H</i>	3.71531	0.005291	0.317753

Table S6. Significant gene sets between patients with low and high metastatic burden.

	Gene Set Name	log2FC	P value	FDR
Down-regulated	GO_ARRESTIN_FAMILY_PROTEIN_BINDING	-0.549	0.0000000	0.0004
	GO_POSITIVE_REGULATION_OF_ACTION_POTENTIAL	-0.495	0.0000115	0.0345
	GO_ADP_RIBOSYLATION_FACTOR_BINDING	-0.608	0.0000424	0.0548
	GO_SPINAL_CORD_ASSOCIATION_NEURON_DIFFERENTIATION	-0.477	0.0000461	0.0548
	GO_AP_2_ADAPTOR_COMPLEX_BINDING	-0.502	0.0001952	0.1010
	GO_POSITIVE_REGULATION_OF_ACTIN_FILAMENT_BASED_MOVEMENT	-0.548	0.0003439	0.1278
	BIOCARTA_ION_PATHWAY	-0.563	0.0004024	0.1306
	GO_NEURAL_PLATE_DEVELOPMENT	-0.411	0.0004782	0.1364
	GO_REGULATION_OF_AUTOPHAGOSOME_MATURATION	-0.428	0.0005492	0.1433
	GO_NEGATIVE_REGULATION_OF_LOW_DENSITY_LIPOPROTEIN_PARTICLE_CLEARANCE	-0.571	0.0007795	0.1795
	GO_ESTABLISHMENT_OF_LYMPHOCYTE_POLARITY	-0.472	0.0007698	0.1795
	BIOCARTA_PPARG_PATHWAY	-0.425	0.0007505	0.1795
	GO_CYTOSKELETAL_ANCHORING_AT_NUCLEAR_MEMBRANE	-0.578	0.0012505	0.1880
	GO_MEMBRANE_DEPOLARIZATION_DURING_AV_NODE_CELL_ACTION_POTENTIAL	-0.476	0.0010827	0.1880
	GO_REGULATION_OF_NEURON_PROJECTION_ARBORIZATION	-0.458	0.0010631	0.1880
	GO_RESPONSE_TO_IMMUNE_RESPONSE_OF_OTHER_ORGANISM_INVOLVED_IN_SYMBIOTIC_INTERACTION	-0.466	0.0017664	0.2079
Up-regulated	GO_RIBOSOME_DISASSEMBLY	0.635	0.0000048	0.0289
	GO_CYSTEINE_METABOLIC_PROCESS	0.421	0.0000103	0.0345
	GO_RIBONUCLEOPROTEIN_COMPLEX_DISASSEMBLY	0.428	0.0000180	0.0431
	GO_SIGNAL_RECOGNITION_PARTICLE_ENDOPLASMIC_RETICULUM_TARGETING	0.647	0.0000220	0.0441
	GO_NUCLEOTIDE_EXCISION_REPAIR_DNA_DAMAGE_RECOGNITION	0.455	0.0000325	0.0548
	GO_CYCLOSPORIN_A_BINDING	0.477	0.0000548	0.0548
	GO_TRNA_SPLICING_LIGASE_COMPLEX	0.534	0.0000519	0.0548
	GO_PROTEIN_REFOLDING	0.408	0.0000669	0.0574
	GO_MALATE_METABOLIC_PROCESS	0.546	0.0001577	0.0902
	GO_PROLINE_BIOSYNTHETIC_PROCESS	0.547	0.0001503	0.0902
	GO_ANDROGEN_BIOSYNTHETIC_PROCESS	0.490	0.0002371	0.1095
	GO_SIGNAL_RECOGNITION_PARTICLE	0.479	0.0003834	0.1278
	REACTOME_ATF6_ATF6_ALPHA_ACTIVATES_CHAPERONES	0.414	0.0005047	0.1364
	GO_FATTY_ACID_ALPHA_OXIDATION	0.526	0.0005113	0.1364
	GO_EGO_COMPLEX	0.590	0.0004892	0.1364
	GO_MALATE_DEHYDROGENASE_ACTIVITY	0.506	0.0008154	0.1795
	GO_PREFOLDIN_COMPLEX	0.515	0.0008256	0.1795
	GO_PURINE_RIBONUCLEOSIDE_SALVAGE	0.564	0.0008822	0.1795

GO_PROTEASOME_REGULATORY_PARTICLE_BASE_SUBCOMPLEX	0.522	0.0009681	0.1845
GO_PROTEIN_DENEDDYLATION	0.448	0.0009937	0.1864
GO_MITOCHONDRIAL_RNA_MODIFICATION	0.424	0.0013180	0.1880
GO_HYPEROSMOTIC_SALINITY_RESPONSE	0.450	0.0013330	0.1880
GO_TRANSLATION_TERMINATION_FACTOR_ACTIVITY	0.464	0.0012943	0.1880
GO_AMP_BIOSYNTHETIC_PROCESS	0.472	0.0013778	0.1880
GO_RNA_IMPORT_INTO_MITOCHONDRION	0.532	0.0011609	0.1880
GO_ESCRT_COMPLEX_DISASSEMBLY	0.419	0.0013945	0.1881
REACTOME_SUMO_IS_CONJUGATED_TO_E1_UBA2:SAE1	0.470	0.0015154	0.1936
GO_POSITIVE_REGULATION_OF_PROTEIN_MONOUBIQUITINATION	0.488	0.0015229	0.1936
REACTOME_ALPHA_OXIDATION_OF_PHYTANATE	0.512	0.0016586	0.1991
GO_REGULATION_OF_CILIUM_BEAT_FREQUENCY	0.404	0.0018452	0.2116
BIOCARTA_AHSP_PATHWAY	0.521	0.0018507	0.2116
GO_GONADAL_MESODERM_DEVELOPMENT	0.563	0.0020124	0.2246
GO_7S_RNA_BINDING	0.531	0.0021160	0.2277
HALLMARK_OXIDATIVE_PHOSPHORYLATION	0.412	0.0022386	0.2326
GO_SUCKLING_BEHAVIOR	0.463	0.0022517	0.2326
GO_FREE_UBIQUITIN_CHAIN_POLYMERIZATION	0.443	0.0023919	0.2361
GO_MITOCHONDRIAL_TRNA_METHYLATION	0.459	0.0024582	0.2361
KEGG_PROTEIN_EXPORT	0.496	0.0024565	0.2361
GO_THIOREDOXIN_PEROXIDASE_ACTIVITY	0.533	0.0024212	0.2361

Table S7. Significant gene sets between patients with low and high metastatic burden in the non-MNA subgroup.

Gene Set Name		log 2FC	P value	FD R
Down-regulated	GO_ADP_RIBOSYLATION_FACTOR_BINDING	-0.6	0.000	0.01
		65	0051	3806
	GO_ARRESTIN_FAMILY_PROTEIN_BINDING	-0.5	0.000	0.01
		39	0057	3806
	GO_NEURAL_PLATE_DEVELOPMENT	-0.5	0.000	0.01
		09	0058	3806
	GO_ATP_BINDING_CASSETTE_ABC_TRANSPORTER_COMPLEX	-0.7	0.000	0.01
		50	0126	6390
	BIOCARTA_ION_PATHWAY	-0.6	0.000	0.01
		48	0137	6390
	GO_POSITIVE_REGULATION_OF_ACTION_POTENTIAL	-0.5	0.000	0.01
		17	0111	6390
	GO_CONVERGENT_EXTENSION_INVOLVED_IN_ORGANOGENESIS	-0.4	0.000	0.01
		12	0209	8852
	GO_SPINAL_CORD_ASSOCIATION_NEURON_DIFFERENTIATION	-0.4	0.000	0.05
		95	1254	3772
	BIOCARTA_PITX2_PATHWAY	-0.4	0.000	0.05
		18	1229	3772
	GO_POSITIVE_REGULATION_OF_ACTIN_FILAMENT_BASED_MOVEMENT	-0.5	0.000	0.05
		88	1698	7253
	GO_ROUNDABOUT_BINDING	-0.4	0.000	0.05
		93	1593	7253
	GO_RRNA_GUANINE_METHYLTRANSFERASE_ACTIVITY	-0.5	0.000	0.05
		82	2157	7759
	GO_REGULATION_OF_AUTOPHAGOSOME_MATURATION	-0.4	0.000	0.05
		61	2266	7759
	GO_MODULATION_OF_MICROTUBULE_CYTOSKELETON_INVOLVED_IN_CEREBRAL_CORTEX_RADIAL_GLIA_GUIDED_MIGRATION	-0.5	0.000	0.08
		41	4903	4072
	GO_AP_2_ADAPTOR_COMPLEX_BINDING	-0.5	0.000	0.08
		14	5029	5026
	GO_NEURAL_PLATE_MORPHOGENESIS	-0.4	0.000	0.08
		97	5295	5895

GO_CYTOSKELETAL_ANCHORING_AT_NUCLEAR_MEMBRANE	-0.6	0.000	0.09
	38	6059	2976
REACTOME_NEGATIVE_REGULATION_OF_TCF_DEPENDENT_SIGNALING_BY_DVL_INTERACTING_PROTEINS	-0.7	0.000	0.09
	24	6749	7676
BIOCARTA_PPARG_PATHWAY	-0.4	0.000	0.09
	35	6967	9567
GO_GATOR1_COMPLEX	-0.5	0.000	0.10
	06	8073	8970
GO_NEGATIVE_REGULATION_OF_LOW_DENSITY_LIPOPROTEIN_PARTICLE_CLEARANCE	-0.5	0.001	0.12
	44	0435	9140
GO_NEGATIVE_REGULATION_OF_HISTONE_DEACETYLATION	-0.6	0.001	0.13
	70	1672	7368
GO_NEURONAL_ACTION_POTENTIAL_PROPAGATION	-0.4	0.001	0.13
	33	1883	8265
GO_ANTEROGRADE_DENDRITIC_TRANSPORT	-0.5	0.001	0.13
	48	3104	8910
BIOCARTA_PELP1_PATHWAY	-0.4	0.001	0.13
	55	2601	8910
GO_RADIAL_GLIA_GUIDED_MIGRATION_OF_PURKINJE_CELL	-0.6	0.001	0.15
	31	6921	3882
GO_KICSTOR_COMPLEX	-0.5	0.001	0.16
	61	8619	1962
GO_U3_SNORNA_BINDING	-0.4	0.002	0.17
	93	1965	9613
GO_CHONDROBLAST_DIFFERENTIATION	-0.4	0.002	0.17
	55	2483	9613
GO_NUCLEAR_MIGRATION_ALONG_MICROTUBULE	-0.6	0.002	0.18
	08	3689	1758
GO_NEURONAL_SIGNAL_TRANSDUCTION	-0.5	0.002	0.18
	95	4868	2274
GO_NEGATIVE_REGULATION_OF_SINGLE_STRANDED_VIRAL_RNA_REPLICATION_VIA_DOUBLE_STRANDED_DNA_INTERME DIATE	-0.4	0.002	0.18
	37	4524	2274
GO_NEGATIVE_REGULATION_OF_EXECUTION_PHASE_OF_APOPTOSIS	-0.4	0.002	0.18
	30	5981	3570
GO_SOFT_PALATE_DEVELOPMENT	-0.5	0.002	0.19
	23	9839	4961
GO_REGULATION_OF_NEURON_PROJECTION_ARBORIZATION	-0.4	0.002	0.19

		47	9291	4961
	GO_ESTABLISHMENT_OF_LYMPHOCYTE_POLARITY	-0.4	0.003	0.19
		37	1652	7505
	REACTOME_STAT5_ACTIVATION	-0.4	0.003	0.19
		25	1656	7505
	GO_L_LYSINE_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	-0.5	0.004	0.22
		29	6780	7671
	GO_GASTRIC_EMPTYING	-0.4	0.004	0.22
		62	6171	7671
	GO_PHOSPHATIDYLINOSITOL_TRANSPORTER_ACTIVITY	-0.4	0.005	0.23
		30	1467	4910
	GO_POSITIVE_REGULATION_OF_CREB_TRANSCRIPTION_FACTOR_ACTIVITY	-0.4	0.005	0.24
		51	3580	0182
	GO_MEMBRANE_DEPOLARIZATION_DURING_AV_NODE_CELL_ACTION_POTENTIAL	-0.4	0.005	0.24
		40	5009	2769
Up-regu lated	GO_CYSTEINE_METABOLIC_PROCESS	0.47	0.000	0.00
		5	0007	7829
	GO_TRNA_SPLICING_LIGASE_COMPLEX	0.60	0.000	0.01
		2	0031	3806
	GO_ENDOSOME_TRANSPORT_VIA_MULTIVESICULAR_BODY_SORTING_PATHWAY	0.40	0.000	0.01
		2	0111	6390
	GO_REGULATION_OF_GLUCOCORTICOID_RECEPTOR_SIGNALING_PATHWAY	0.62	0.000	0.01
		0	0087	6390
	REACTOME_ATF6_ATF6_ALPHA_ACTIVATES_CHAPERONE_GENES	0.47	0.000	0.01
		8	0152	6627
	GO_CYCLOSPORIN_A_BINDING	0.52	0.000	0.01
		7	0178	7796
	GO_RIBOSOME_DISASSEMBLY	0.66	0.000	0.02
		8	0354	8313
	GO_RIBONUCLEOPROTEIN_COMPLEX_DISASSEMBLY	0.46	0.000	0.02
		9	0424	9919
	GO_LATE_ENDOSOME_TO_VACUOLE_TRANSPORT	0.45	0.000	0.03
		7	0573	6179
	GO_SIGNAL_RECOGNITION_PARTICLE_ENDOPLASMIC_RETICULUM_TARGETING	0.66	0.000	0.03
		2	0603	6208
	GO_NUCLEOTIDE_EXCISION_REPAIR_DNA_DAMAGE_RECOGNITION	0.46	0.000	0.03
		1	0728	9702

KEGG_PROTEIN_EXPORT	0.59	0.000	0.03
	3	0703	9702
GO_PROTEIN_PEPTIDYL_PROLYL_ISOMERIZATION	0.42	0.000	0.05
	2	1675	7253
REACTOME_ATF6_ATF6_ALPHA_ACTIVATES_CHAPERONES	0.46	0.000	0.05
	3	1598	7253
GO_NEGATIVE_REGULATION_OF_MEMBRANE_POTENTIAL	0.51	0.000	0.05
	2	1717	7253
GO_ANDROGEN_BIOSYNTHETIC_PROCESS	0.51	0.000	0.05
	4	1467	7253
GO_PROLINE_BIOSYNTHETIC_PROCESS	0.54	0.000	0.05
	6	1641	7253
GO_COPI_VESICLE_COAT	0.44	0.000	0.05
	2	2372	7759
GO_POSTTRANSLATIONAL_PROTEIN_TARGETING_TO_ENDOPLASMIC_RETICULUM_MEMBRANE	0.44	0.000	0.05
	5	2295	7759
GO_AMP_BIOSYNTHETIC_PROCESS	0.56	0.000	0.05
	6	2406	7759
GO_3_HYDROXYACYL_COA_DEHYDROGENASE_ACTIVITY	0.57	0.000	0.05
	5	2185	7759
GO_RNA_IMPORT_INTO_MITOCHONDRION	0.59	0.000	0.05
	5	1872	7759
GO_PROTEIN_UFMYLATION	0.59	0.000	0.05
	6	2382	7759
REACTOME_WAX_AND_PLASMALOGEN_BIOSYNTHESIS	0.57	0.000	0.05
	9	2572	9363
GO_SIGNAL_RECOGNITION_PARTICLE	0.51	0.000	0.07
	0	3730	2317
REACTOME_SYNTHESIS_SECRETION_AND_INACTIVATION_OF_GLUCOSE_DEPENDENT_INSULINOTROPIC_POLYPEPTIDE_GIP	0.51	0.000	0.07
	4	3735	2317
GO_LATE_ENDOSOME_TO_VACUOLE_TRANSPORT_VIA_MULTIVESICULAR_BODY_SORTING_PATHWAY	0.55	0.000	0.07
	2	3735	2317
GO_COPII_VESICLE_COAT	0.51	0.000	0.07
	8	3962	5490
REACTOME_CYTOCHROME_C_MEDIATED_APOPTOTIC_RESPONSE	0.41	0.000	0.07
	7	4159	6815
GO_PROTEIN_PRENYLTRANSFERASE_ACTIVITY	0.41	0.000	0.08

	4	4708	2331
GO_REGULATION_OF_ENDOPLASMIC_RETICULUM_TUBULAR_NETWORK_ORGANIZATION	0.59	0.000	0.08
	0	4723	2331
GO_ENDOPLASMIC_RETICULUM_TUBULAR_NETWORK_MEMBRANE	0.54	0.000	0.08
	9	5295	5895
GO_POSITIVE_REGULATION_OF_PROTEIN_MONOUBIQUITINATION	0.55	0.000	0.09
	7	6038	2976
GO_PREFOLDIN_COMPLEX	0.54	0.000	0.09
	0	6754	7676
GO_PROTEIN_POLYUFBMYLATION	0.73	0.000	0.10
	8	7412	4675
GO_MITOCHONDRIAL_ACETYL_COA_BIOSYNTHETIC_PROCESS_FROM_PYRUVATE	0.71	0.000	0.10
	7	8352	8970
GO_MALATE_METABOLIC_PROCESS	0.46	0.001	0.12
	3	0435	9140
GO_OXIDOREDUCTASE_ACTIVITY_ACTING_ON_PAIRC_DONORS_WITH_INCORPORATION_OR_REDUCTION_OF_MOLECULAR_OXYGEN_REDUCED_ASCORBATE_AS_ONE_DONOR_AND_INCORPORATION_OF_ONE_ATOM_OF_OXYGEN	0.41	0.001	0.13
	6	2310	8910
REACTOME_ZINC_EFFLUX_AND_COMPARTMENTALIZATION_BY_THE_SLC30_FAMILY	0.47	0.001	0.13
	2	2980	8910
GO_PURINE_RIBONUCLEOSIDE_SALVAGE	0.59	0.001	0.13
	6	3240	8910
GO_FATTY_ACID_ALPHA_OXIDATION	0.57	0.001	0.13
	2	3501	9715
GO_CELLULAR_LIPID_BIOSYNTHETIC_PROCESS	0.42	0.001	0.14
	8	5798	7745
GO_PROTEASOME_REGULATORY_PARTICLE_BASE_SUBCOMPLEX	0.53	0.001	0.14
	9	5368	7745
GO_EGO_COMPLEX	0.63	0.001	0.15
	8	6542	2748
GO_MEDIUM_CHAIN_FATTY_ACID_CATABOLIC_PROCESS	0.51	0.001	0.16
	4	8394	1168
GO_POSITIVE_REGULATION_OF_MAINTENANCE_OF_SISTER_CHROMATID_COHESION	0.42	0.002	0.17
	0	2100	9613
GO_GLYCEROL_ETHER_BIOSYNTHETIC_PROCESS	0.43	0.002	0.17
	7	2232	9613
GO_REGULATION_OF_PROTEIN_MONOUBIQUITINATION	0.44	0.002	0.17
	0	2973	9613

GO_HYPEROSMOTIC_SALINITY_RESPONSE	0.46	0.002	0.17
	3	2832	9613
GO_PROTEIN_SERINE_THREONINE_PHOSPHATASE_INHIBITOR_ACTIVITY	0.50	0.002	0.17
	4	2915	9613
REACTOME_GLUCURONIDATION	0.53	0.002	0.17
	3	1609	9613
GO_OMEGA_HYDROXYLASE_P450_PATHWAY	0.45	0.002	0.18
	9	4075	1758
REACTOME_SYNTHESIS_OF_16_20_HYDROXYEICOSATETRAENOIC_ACIDS_HETE	0.45	0.002	0.18
	9	4075	1758
GO_PROTEIN_NEDDYLATION	0.60	0.002	0.18
	1	4767	2274
GO_PROTEIN_GERANYLGERANYLTRANSFERASE_ACTIVITY	0.46	0.002	0.18
	3	6016	3570
GO_THIOREDOXIN_PEROXIDASE_ACTIVITY	0.56	0.002	0.18
	2	6559	4952
GO_PROTEIN_DENEDDYLATION	0.41	0.002	0.19
	4	7894	1340
REACTOME_GOLGI_CISTERNAE_PERICENTRIOLAR_STACK_REORGANIZATION	0.41	0.002	0.19
	7	7799	1340
GO_REGULATION_OF_CENTRIOLE_ELONGATION	0.52	0.002	0.19
	0	8599	3843
GO_KINOCILIUM	0.42	0.003	0.19
	8	0386	5750
REACTOME_SUMO_IS_CONJUGATED_TO_E1_UBA2:SAE1	0.45	0.003	0.19
	6	1095	7505
GO_HOST_CELL_CYTOPLASM	0.46	0.003	0.19
	2	1756	7505
GO_FREE_UBIQUITIN_CHAIN_POLYMERIZATION	0.48	0.003	0.19
	6	2248	7505
GO_RIBOSOMAL_LARGE_SUBUNIT_BINDING	0.43	0.003	0.20
	4	4777	3639
GO_NEDD8_TRANSFERASE_ACTIVITY	0.54	0.003	0.20
	7	6609	8275
GO_SEQUENCE_SPECIFIC_MRNA_BINDING	0.44	0.003	0.20
	4	7370	8647
GO_ENDOSOME_TO_LYSOSOME_TRANSPORT_VIA_MULTIVESICULAR_BODY_SORTING_PATHWAY	0.51	0.003	0.20

	8	7268	8647
REACTOME_TRAFFICKING_OF_MYRISTOYLATED_PROTEINS_TO_THE_CILIUM	0.45	0.003	0.20
	9	7941	9880
GO_REGULATION_OF_CILIUM_BEAT_FREQUENCY	0.46	0.003	0.21
	0	8867	2942
REACTOME_ALPHA_OXIDATION_OF_PHYTANATE	0.54	0.004	0.21
	6	0242	6623
GO_TRANSLATION_TERMINATION_FACTOR_ACTIVITY	0.43	0.004	0.21
	4	1667	7834
GO_MITOCHONDRIAL_PROTON_TRANSPORTING_ATP_SYNTHASE_COMPLEX_ASSEMBLY	0.65	0.004	0.22
	5	2828	2555
GO_PURINE_NUCLEOSIDE_CATABOLIC_PROCESS	0.45	0.004	0.22
	7	4642	5176
REACTOME_VIF_MEDIATED_DEGRADATION_OF_APOBEC3G	0.41	0.004	0.22
	5	6592	7671
GO_GLYCOSIDE_METABOLIC_PROCESS	0.43	0.004	0.22
	1	7536	7671
HALLMARK_OXIDATIVE_PHOSPHORYLATION	0.44	0.004	0.22
	2	6257	7671
GO_REGULATION_OF_CILIUM_BEAT_FREQUENCY_INVOLVED_IN_CILIARY_MOTILITY	0.59	0.004	0.22
	7	7553	7671
GO_MITOCHONDRIAL_TRNA_METHYLATION	0.45	0.004	0.22
	6	8197	7777
BIOCARTA_AHSP_PATHWAY	0.56	0.005	0.23
	2	0309	1022
GO_POSTTRANSLATIONAL_PROTEIN_TARGETING_TO_MEMBRANE_TRANSLOCATION	0.69	0.005	0.23
	6	0027	1022
GO_7S_RNA_BINDING	0.51	0.005	0.24
	8	3623	0182
REACTOME_PROPIONYL_COA_CATABOLISM	0.67	0.005	0.24
	0	4207	1895
