Supplementary Information

Genome-wide profiling of multiple histone methylations in olfactory cells: further implications for cellular susceptibility to oxidative stress in schizophrenia

Shin-ichi Kano[1], Carlo Colantuoni[1, 2, *], Fang Han[2], Zhifeng Zhou[3], Qiaoping Yuan[3], Ashley Wilson[1], Yoichiro Takayanagi[4], Yohan Lee[5], Judith Rapoport[5], William Eaton[4], Nicola Cascella[1], Hongkai Ji[2], David Goldman[3], and Akira Sawa[1]

[1]Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA

[2]Department of Biostatistics, Johns Hopkins University School of Public Health, Baltimore, MD 21205, USA

[3]Laboratory of Neurogenetics, National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD 20892, USA

[4]Department of Mental Health, Johns Hopkins University School of Public Health, Baltimore, MD 21205, USA

[5]Child Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20892, USA

*Present address: Lieber Institute for Brain Development

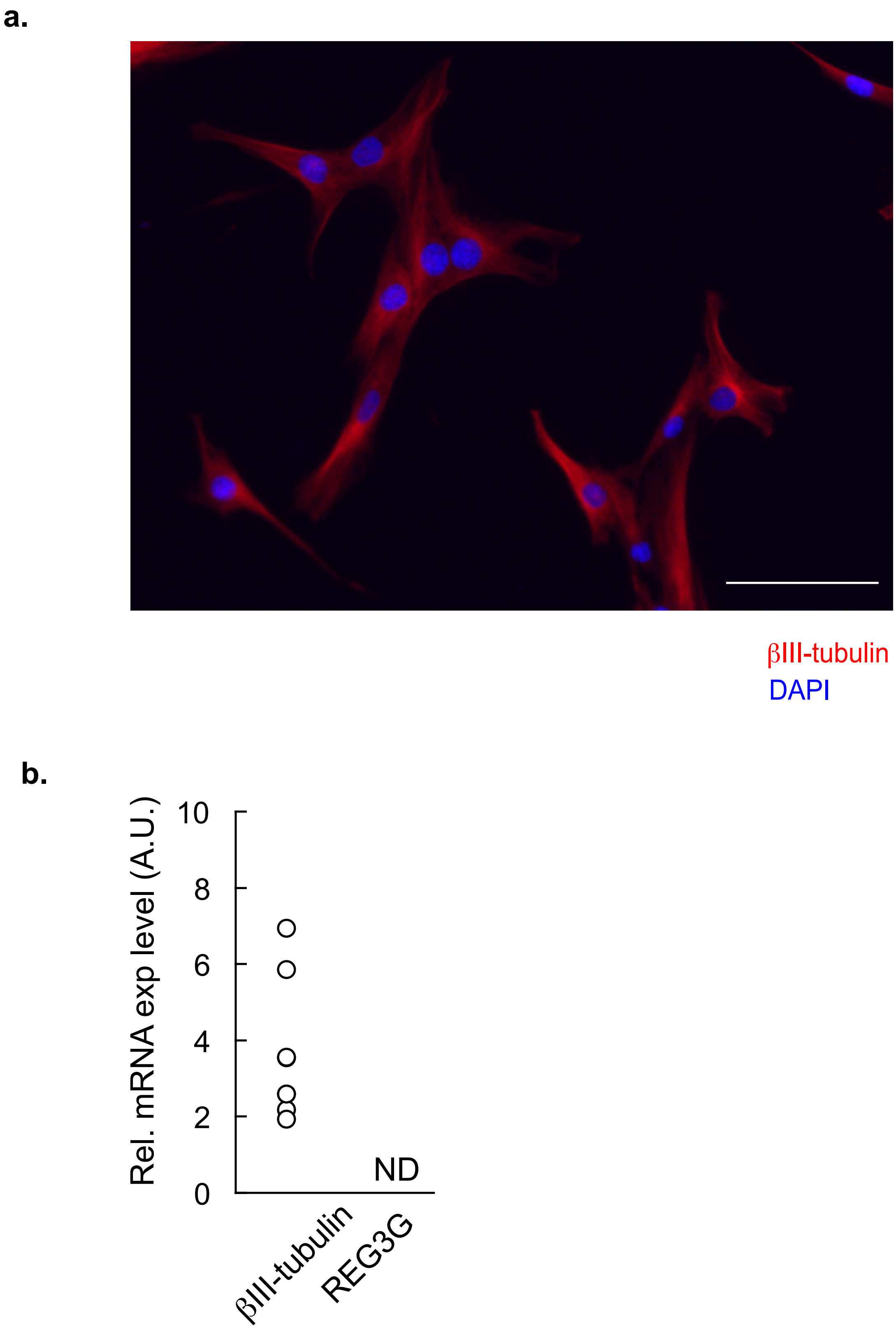
Supplementary information content

Acknowledgements, Supplementary Figures 1-3, Supplementary Figure legends, Supplementary Tables 1-7, Supplementary Methods and Materials, and Additional References.

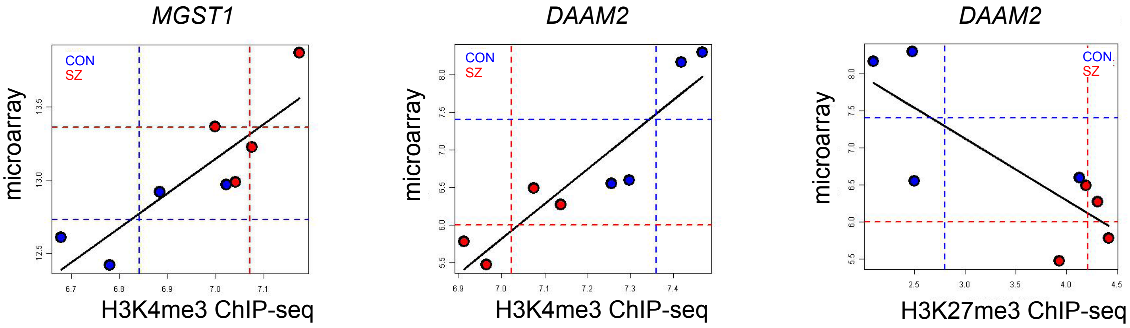
Acknowledgements

We thank Dr. Pamela Talalay, and Yukiko Lema for their critical readings and manuscript organization. This work was supported by grants from the US National Institutes of Health (MH-084018, MH-94268 Silvo O. Conte center, MH-069853, MH-085226, MH-088753, and MH-092443 to A.S.), as well as grants from Stanley (A.S.), S-R (A.S.), RUSK (A.S.), NARSAD (A.S.), JHU-BSI (A.S.), and MSCRF (A.S.). S. K. was supported by Uehara foundation, Kanae foundation, and JSPS, and is currently supported by NIH Pathway to Independence Award (K99MH093458) and NARSAD Young Investigator award (the Hammerschlag Family Investigator).

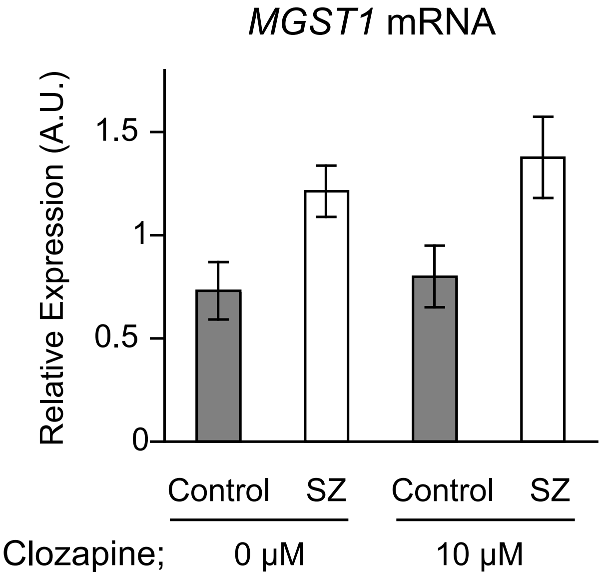
Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure legends

Supplementary Figure 1: Characterization of olfactory cells. (**a**) Representative picture of olfactory cells. Nearly all the olfactory cells are homogeneously stained with βIII-tubulin (in red), a marker for immature neurons. Blue, DAP1 staining for the nucleus, Scale bar: 100 μm. (**b**) No expression of regenerating islet-derived 3-gamma (*REG3G)* gene, a respiratory epithelium marker, in olfactory cells. Quantitative RT-PCR was performed to examine the expression level of βIII-tubulin (*TUBB3)* and *REG3G* genes in olfactory cells (control, n=4; SZ, n=4) as previously described. The data was shown as relative expression against β-actin mRNA. ND, not detected.

Supplementary Figure 2: Representative correlation data of ChIP-seq and microarrays. Shown are several representative correlation data. Microsomal glutathione *S*-transferase 1 (MGST1) is localized to endoplasmic reticulum and outer mitochondrial membranes where it is believed to protect these membranes from oxidative stress. Dishevelled associated activator of morphogenesis 2 (DAAM2) is involved in Wnt signaling and recently reported to modulate the formation of Wnt receptor complexes in canonical Wnt signal transduction. Note that reciprocal changes occurred in H3K4me3 and H3K27me3 signals at *DAAM2* gene promoters. Con, controls; SZ, schizophrenia.

Supplementary Figure 3: No obvious effects of clozapine on *MGST1* mRNA expression in olfactory cells. Olfactory cells from control and SZ subjects (control, n=4; SZ, n=4) were cultured in the presence of DMSO (vehicle) or 10 μM clozapine for 48 h. *MGST1* mRNA expression was analyzed by quantitative RT-PCR. The data was shown as relative expression of *MGST1* mRNA against β-actin mRNA. Error bars indicate s.e.m.

Supplementary Table 1: Demographics of SZ patients and control subjects

I.D.	Age	Gender	Race	Smoking	Disease duration	Antipsychotic medications [chlorpromazine equivalents mg]	Other medication
C#1	29	F	AA	No	---	---	---
C#2	28	M	C	No	---	---	---
C#3	46	M	C	No	---	---	---
C#4	49	M	C	Yes	---	---	---
SZ#1	44	M	AA	Yes	19	Fluphenazine 5 mg + Seroquel 400 mg **[750 mg]**	Citalopram 20 mg, Trihexyphen 5 mg, Lamictal 25 mg
SZ#2	45	M	AA	No	15	Zyprexa 15 mg **[300 mg]**	Metformin 500 mg,Pravachol 20 mg, Benadryl 50 mg, Lisinopril 5 mg, Cosopt and Alphagan
SZ#3	19	F	C	No	0.5	Zyprexa 10 mg + Clozapine 100 mg **[400 mg]**	None
SZ#4	34	M	AA	No	17	Zyprexa 30 mg **[600 mg]**	Lipitor 40 mg

Abbreviation: F/M, Female/Male; AA/C, African American/Caucasian

Note that there are no significant differences between SZ patients and control subjects in age, gender, race, and rate of smoking habits.

Supplementary Table 2: Genes with significant correlation ($p<0.05$) between ChIP seq and mciroarray data among the genes showing SZ-associated changes ($p<0.05$)

GeneSymbol	GeneName	Chr	Start	End	Strand	ChIP seq (H3K4me3)			ChIP seq (H3K27me3)			Microarray			ChIP seq vs Microarray	
						FC ($\log_2$)	D-stat	p-value	FC ($\log_2$)	D-stat	p-value	FC ($\log_2$)	D-stat	p-value	r	p-value
MGST1	microsomal glutathione S-transferase 1	chr12	16390978	16392978	+	0.23	1.68	4.7E-02				0.63	2.78	1.5E-02	0.87	5.5E-03
		chr12	16390845	16392845	+	0.23	1.86	3.1E-02				0.63	2.78	1.5E-02	0.86	6.0E-03
		chr12	16390342	16392342	+	0.25	1.80	3.6E-02				0.63	2.78	1.5E-02	0.85	8.2E-03
WSB1	WD repeat and SOCS box-containing 1	chr17	22644232	22646232	+	0.16	2.00	2.3E-02				0.51	3.51	5.3E-03	0.80	1.8E-02
ING3	inhibitor of growth family, member 3	chr7	120377052	120379052	+				-0.73	-2.16	7.8E-03	0.39	4.72	1.3E-03	-0.81	1.5E-02
TAF15	TAF15 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 68kDa	chr17	31159600	31161600	+	0.23	2.19	1.6E-02				0.35	2.47	2.5E-02	0.78	2.1E-02
AP1GBP1	AP1 gamma subunit binding protein 1	chr17	33042558	33044558	-	0.26	2.31	1.2E-02				0.26	2.71	1.7E-02	0.81	1.5E-02
RNF31	ring finger protein 31	chr14	23685498	23687498	+	0.12	1.68	4.6E-02				0.05	2.66	1.8E-02	0.75	3.2E-02
ACO1	aconitase 1, soluble	chr9	32373657	32375657	+				0.89	1.58	3.9E-02	-0.24	-3.11	9.3E-03	-0.85	1.5E-02
C10orf125	chromosome 10 open reading frame 125	chr10	135020518	135022518	-	-0.20	-1.67	4.8E-02				-0.31	-2.66	1.9E-02	0.92	1.1E-03
MFI2	antigen p97 (melanoma associated) identified by monoclonal antibodies 133.2 and 96.5	chr3	198240038	198242038	-	-0.28	-2.41	9.9E-03				-0.42	-4.11	2.5E-03	0.78	2.2E-02
SMARCD3	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 3	chr7	150575681	150577681	-	-0.18	-1.84	3.2E-02				-0.44	-2.39	2.8E-02	0.78	2.3E-02
FAM117A	family with sequence similarity 117, member A	chr17	45195517	45197517	-	-0.32	-3.38	1.8E-03				-0.44	-2.63	1.9E-02	0.88	4.3E-03
RHOD	ras homolog gene family, member D	chr11	66579896	66581896	+	-0.29	-1.99	2.5E-02				-0.52	-2.36	3.0E-02	0.89	2.9E-03
APLP1	amyloid beta (A4) precursor-like protein 1	chr19	41050240	41052240	+	-0.26	-2.30	1.2E-02				-0.52	-2.25	3.6E-02	0.76	2.8E-02
EIF4E3	eukaryotic translation initiation factor 4E family member	chr3	71884464	71886464	-	-0.30	-1.90	2.8E-02				-0.53	-2.43	2.7E-02	0.72	4.4E-02
HSPC159	galectin-related protein	chr2	64534165	64536165	+	-0.20	-2.29	1.2E-02				-0.57	-3.77	3.8E-03	0.76	2.7E-02
JUP	junction plakoglobin	chr17	37195474	37197474	-	-0.28	-2.79	4.4E-03				-0.58	-2.81	1.5E-02	0.87	5.3E-03
HIP1	huntingtin interacting protein 1	chr7	75205214	75207214	-	-0.22	-1.89	2.9E-02				-0.61	-2.05	5.0E-02	0.92	1.1E-03
C16orf5	chromosome 16 open reading frame 5	chr16	4527816	4529816	-	-0.32	-2.57	8.1E-03				-0.67	-2.24	3.6E-02	0.72	4.5E-02
DNASE1L1	deoxyribonuclease I-like 1	chrX	153289768	153291768	-	-0.31	-1.90	2.8E-02				-0.98	-3.26	7.5E-03	0.81	1.4E-02
LPXN	leupaxin	chr11	58098909	58100909	-	-0.25	-1.81	3.5E-02				-1.16	-2.27	3.4E-02	0.74	3.4E-02
DAAM2	dishevelled associated activator of morphogenesis 2	chr6	39867770	39869770	+	-0.34	-2.98	3.3E-03				-1.40	-2.63	1.9E-02	0.92	1.3E-03
									1.41	2.35	4.8E-03	-1.40	-2.63	1.9E-02	-0.79	2.0E-02
NMNAT2	nicotinamide nucleotide adenylyltransferase 2	chr1	181653359	181655359	-	-0.22	-2.06	2.1E-02				-1.78	-2.73	1.7E-02	0.81	1.6E-02

Supplemantary Table 3: 545 pathways altered in SZ patients (ChIP-seq)

pathway	p-value	q-value
ZERBINI_RESPONSE_TO_SULINDAC_UP	<1.00E-16	<1.00E-16
TURASHVILI_BREAST_NORMAL_DUCTAL_VS_LOBULAR_DN	<1.00E-16	<1.00E-16
TURASHVILI_BREAST_CARCINOMA_DUCTAL_VS_LOBULAR_DN	<1.00E-16	<1.00E-16
CASORELLI_APL_SECONDARY_VS_DE_NOVO_DN	<1.00E-16	<1.00E-16
GARGALOVIC_RESPONSE_TO_OXIDIZED_PHOSPHOLIPIDS_LIGHTYELLOW_DN	<1.00E-16	<1.00E-16
TONKS_TARGETS_OF_RUNX1_RUNX1T1_FUSION_SUSTAINED_IN_MONOCYTE_DN	<1.00E-16	<1.00E-16
TONKS_TARGETS_OF_RUNX1_RUNX1T1_FUSION_SUSTAINDED_IN_ERYTHROCYTE_DN	<1.00E-16	<1.00E-16
ELVIDGE_HIF2A_TARGETS_UP	<1.00E-16	<1.00E-16
CASTELLANO_HRAS_TARGETS_UP	<1.00E-16	<1.00E-16
BERENJENO_TRANSFORMED_BY_RHOA_REVERSIBLY_UP	<1.00E-16	<1.00E-16
LINDGREN_BLADDER_CANCER_CLUSTER_2A_UP	<1.00E-16	<1.00E-16
GAUSSMANN_MLL_AF4_FUSION_TARGETS_B_DN	<1.00E-16	<1.00E-16
GAUSSMANN_MLL_AF4_FUSION_TARGETS_D_DN	<1.00E-16	<1.00E-16
LUCAS_HNF4A_TARGETS_DN	<1.00E-16	<1.00E-16
TURJANSKI_MAPK8_AND_MAPK9_TARGETS	<1.00E-16	<1.00E-16
TURJANSKI_MAPK7_TARGETS	<1.00E-16	<1.00E-16
NAGY_PCAF_COMPONENTS_HUMAN	<1.00E-16	<1.00E-16
NAKAMURA_BRONCHIAL_AND_BRONCHIOLAR_EPITHELIA	<1.00E-16	<1.00E-16
GALLUZZI_PREVENT_MITOCHONDIAL_PERMEABILIZATION	<1.00E-16	<1.00E-16
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_21	<1.00E-16	<1.00E-16
HEIDENBLAD_AMPLIFIED_IN_BONE_CANCER	<1.00E-16	<1.00E-16
BEGUM_TARGETS_OF_PAX3_FOXO1_FUSION_AND_PAX3	<1.00E-16	<1.00E-16
KORKOLA_EMBRYONAL_CARCINOMA	<1.00E-16	<1.00E-16
SCHRAMM_INHBA_TARGETS_DN	<1.00E-16	<1.00E-16
FUNG_IL2_TARGETS_WITH_STAT5_BINDING_SITES	<1.00E-16	<1.00E-16
RUGO_STRESS_RESPONSE_SUBSET_F	<1.00E-16	<1.00E-16
SASAKI_TARGETS_OF_TP73_AND_TP63	<1.00E-16	<1.00E-16
MAINA_HYPOXIA_VHL_TARGETS_UP	<1.00E-16	<1.00E-16
KONDO_HYPOXIA	<1.00E-16	<1.00E-16
JIANG_CORE_DUPLICON_GENES	<1.00E-16	<1.00E-16
CAFFAREL_RESPONSE_TO_THC_24HR_3_UP	<1.00E-16	<1.00E-16
STARK_BRAIN_22Q11_DELETION	<1.00E-16	<1.00E-16
DER_IFN_GAMMA_RESPONSE_DN	<1.00E-16	<1.00E-16
COLLER_MYC_TARGETS_DN	<1.00E-16	<1.00E-16
OSAWA_TNF_TARGETS	<1.00E-16	<1.00E-16
PARK_HSC_MARKERS	<1.00E-16	<1.00E-16
ROETH_TERT_TARGETS_DN	<1.00E-16	<1.00E-16
STAEGE_EWING_FAMILY_TUMOR	<1.00E-16	<1.00E-16
MCCOLLUM_GELDANAMYCIN_RESISTANCE_UP	<1.00E-16	<1.00E-16
KYNG_DNA_DAMAGE_BY_4NQO_OR_GAMMA_RADIATION	<1.00E-16	<1.00E-16
KYNG_ENVIRONMENTAL_STRESS_RESPONSE_NOT_BY_UV_IN_WS	<1.00E-16	<1.00E-16
KANG_CISPLATIN_RESISTANCE_DN	<1.00E-16	<1.00E-16
CLAUS_PGR_POSITIVE_MENINGIOMA_UP	<1.00E-16	<1.00E-16
WALLACE_PROSTATE_CANCER_DN	<1.00E-16	<1.00E-16
SARRIO_EPITHELIAL_MESENCHYMAL_TRANSITION_DN	<1.00E-16	<1.00E-16
GALI_TP53_TARGETS_APOPTOTIC_DN	<1.00E-16	<1.00E-16
BASSO_HAIRY_CELL_LEUKEMIA_UP	<1.00E-16	<1.00E-16
BOQUEST_STEM_CELL_DN	<1.00E-16	<1.00E-16
BOQUEST_STEM_CELL_CULTURED_VS_FRESH_UP	<1.00E-16	<1.00E-16
ALONSO_METASTASIS_EMT_DN	<1.00E-16	<1.00E-16
KRISHNAN_FURIN_TARGETS_UP	<1.00E-16	<1.00E-16
FERRARI_RESPONSE_TO_FENRETINIDE_DN	<1.00E-16	<1.00E-16
BRUNEAU_HEART_GREAT_VESSELS_AND_VALVULOGENESIS	<1.00E-16	<1.00E-16
KAPOSI_LIVER_CANCER_POOR_SURVIVAL_DN	<1.00E-16	<1.00E-16
OKAMOTO_LIVER_CANCER_MULTICENTRIC_OCCURRENCE_UP	<1.00E-16	<1.00E-16
YANAGISAWA_LUNG_CANCER_RECURRENCE	<1.00E-16	<1.00E-16
WEBER_METHYLATED_ICP_IN_SPERM_UP	<1.00E-16	<1.00E-16
GUTIERREZ_WALDENSTROEMS_MACROGLOBULINEMIA_1_UP	<1.00E-16	<1.00E-16
MOOTHA_PYR	<1.00E-16	<1.00E-16
LY_AGING_OLD_UP	<1.00E-16	<1.00E-16
ZEMBUTSU_SENSITIVITY_TO_FLUOROURACIL	<1.00E-16	<1.00E-16
NIELSEN_SYNOVIAL_SARCOMA_UP	<1.00E-16	<1.00E-16
DASU_IL6_SIGNALING_DN	<1.00E-16	<1.00E-16
BANDRES_RESPONSE_TO_CARMUSTIN_WITHOUT_MGMT_24HR_DN	<1.00E-16	<1.00E-16
U12_DEPENDENT_SPLICEOSOME	<1.00E-16	<1.00E-16
GLUCAN_METABOLIC_PROCESS	<1.00E-16	<1.00E-16
HETEROPHILIC_CELL_ADHESION	<1.00E-16	<1.00E-16
MONOCARBOXYLIC_ACID_TRANSPORT	<1.00E-16	<1.00E-16
NEGATIVE_REGULATION_OF_CYTOKINE_BIOSYNTHETIC_PROCESS	<1.00E-16	<1.00E-16
OXIDOREDUCTASE_ACTIVITY_ACTING_ON_SULFUR_GROUP_OF_DONORS	<1.00E-16	<1.00E-16
RNA_POLYMERASE_II_TRANSCRIPTION_MEDIATOR_ACTIVITY	<1.00E-16	<1.00E-16
METABOTROPIC_GLUTAMATEGABA_B_LIKE_RECEPTOR_ACTIVITY	<1.00E-16	<1.00E-16
MANNOSYLTRANSFERASE_ACTIVITY	<1.00E-16	<1.00E-16

CALCIUM_ION_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	<1.00E-16	<1.00E-16
HISTONE_DEACETYLASE_BINDING	<1.00E-16	<1.00E-16
IVANOVA_HEMATOPOIESIS_STEM_CELL_SHORT_TERM	<1.00E-16	<1.00E-16
NIELSEN_LIPOSARCOMA_UP	<1.00E-16	<1.00E-16
MOOTHA_ROS	<1.00E-16	<1.00E-16
BYSTRYKH_HEMATOPOIESIS_STEM_CELL_FGF3	<1.00E-16	<1.00E-16
CHESLER_BRAIN_D6MIT150_QTL_CIS	<1.00E-16	<1.00E-16
CHESLER_BRAIN_QTL_TRANS	<1.00E-16	<1.00E-16
CHESLER_BRAIN_D6MIT150_QTL_TRANS	<1.00E-16	<1.00E-16
GGCGGCA,MIR-371	<1.00E-16	<1.00E-16
module_0	<1.00E-16	<1.00E-16
module_390	<1.00E-16	<1.00E-16
module_407	<1.00E-16	<1.00E-16
module_454	<1.00E-16	<1.00E-16
module_496	<1.00E-16	<1.00E-16
KEGG_SULFUR_METABOLISM	<1.00E-16	<1.00E-16
BIOCARTA_ACE2_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_NEUROTRANSMITTERS_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_FEEDER_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_GLYCOLYSIS_PATHWAY	<1.00E-16	<1.00E-16
REACTOME_CYTOSOLIC_SULFONATION_OF_SMALL_MOLECULES	<1.00E-16	<1.00E-16
REACTOME_HORMONE_LIGAND_BINDING_RECEPTORS	<1.00E-16	<1.00E-16
chr1p11	<1.00E-16	<1.00E-16
chr11q	<1.00E-16	<1.00E-16
chr6p11	<1.00E-16	<1.00E-16
chr4q33	<1.00E-16	<1.00E-16
chrxq11	<1.00E-16	<1.00E-16
chr21q21	<1.00E-16	<1.00E-16
chr13q21	<1.00E-16	<1.00E-16
chr4p13	<1.00E-16	<1.00E-16
chr3p13	<1.00E-16	<1.00E-16
chr2q	<1.00E-16	<1.00E-16
chr1p	<1.00E-16	<1.00E-16
chr3q11	<1.00E-16	<1.00E-16
chr3q	<1.00E-16	<1.00E-16
chr4q11	<1.00E-16	<1.00E-16
TSAI_DNAJB4_TARGETS_DN	1.11E-16	5.64E-15
MURAKAMI_UV_RESPONSE_1HR_DN	1.11E-16	5.64E-15
TAKAYAMA_BOUND_BY_AR	2.22E-16	1.10E-14
YANG_BREAST_CANCER_ESR1_BULK_UP	2.22E-16	1.10E-14
REACTOME_SIGNALLING_TO_P38_VIA_RIT_AND_RIN	2.22E-16	1.10E-14
REGULATION_OF_GENE_SPECIFIC_TRANSCRIPTION	3.33E-16	1.63E-14
GOUYER_TUMOR_INVASIVENESS	4.44E-16	2.16E-14
chr19q12	5.55E-16	2.68E-14
YAGUE_PRETUMOR_DRUG_RESISTANCE_UP	7.77E-16	3.72E-14
CELLULAR_RESPONSE_TO_STRESS	8.88E-16	4.21E-14
PASTURAL_RIZ1_TARGETS_UP	1.44E-15	6.79E-14
LOPEZ_MESOTHELIOMA_SURVIVAL_WORST_VS_BEST_DN	2.22E-15	1.04E-13
OLIGOSACCHARYL_TRANSFERASE_COMPLEX	4.88E-15	2.26E-13
THUM_MIR21_TARGETS_HEART_DISEASE_DN	5.66E-15	2.60E-13
LE_SKI_TARGETS_DN	1.51E-14	6.87E-13
MCCOLLUM_GELDANAMYCIN_RESISTANCE_DN	2.03E-14	9.10E-13
V$SEF1_C	2.02E-14	9.10E-13
REGULATION_OF_SYNAPSE_STRUCTURE_AND_ACTIVITY	2.13E-14	9.47E-13
PUJANA_BREAST_CANCER_WITH_BRCA1_MUTATED_DN	4.11E-14	1.81E-12
XU_RESPONSE_TO_TRETINOIN_DN	5.01E-14	2.19E-12
TYROSINE_PHOSPHORYLATION_OF_STAT_PROTEIN	5.44E-14	2.36E-12
PEPPER_CHRONIC_LYMPHOCYTIC_LEUKEMIA_DN	7.09E-14	3.06E-12
REACTOME_ZINC_INFLUX_INTO_CELLS_BY_THE_SLC39_GENES_FAMILY	7.39E-14	3.16E-12
LIPID_KINASE_ACTIVITY	7.48E-14	3.17E-12
PEPTIDE_METABOLIC_PROCESS	7.79E-14	3.28E-12
YE_METASTATIC_LIVER_CANCER	8.76E-14	3.66E-12
CHANG_POU5F1_TARGETS_DN	1.01E-13	4.20E-12
FERRARI_RESPONSE_TO_FENRETINIDE_UP	1.02E-13	4.20E-12
MARTIN_INTERACT_WITH_HDAC	1.49E-13	6.11E-12
chr6q26	1.86E-13	7.55E-12
module_283	2.01E-13	8.10E-12
ST_PAC1_RECEPTOR_PATHWAY	2.61E-13	1.04E-11
CASTELLANO_HRAS_AND_NRAS_TARGETS_UP	3.19E-13	1.27E-11
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_12	3.35E-13	1.32E-11
HOEGERKORP_CD44_TARGETS_TEMPORAL_UP	3.56E-13	1.40E-11
COLLIS_PRKDC_REGULATORS	3.83E-13	1.49E-11
NUCLEOTIDE_SUGAR_METABOLIC_PROCESS	4.37E-13	1.69E-11
BIOPOLYMER_BIOSYNTHETIC_PROCESS	4.87E-13	1.87E-11
NEGATIVE_REGULATION_OF_MYELOID_CELL_DIFFERENTIATION	5.85E-13	2.23E-11
REACTOME_NOTCH_HLH_TRANSCRIPTION_PATHWAY	5.95E-13	2.25E-11
RAY_ALZHEIMERS_DISEASE	6.37E-13	2.40E-11

ST_INTERLEUKIN_13_PATHWAY	6.93E-13	2.57E-11
ST_IL_13_PATHWAY	6.93E-13	2.57E-11
ZHAN_VARIABLE_EARLY_DIFFERENTIATION_GENES_UP	7.99E-13	2.95E-11
HOEGERKORP_CD44_TARGETS_DIRECT_UP	8.90E-13	3.26E-11
GARGALOVIC_RESPONSE_TO_OXIDIZED_PHOSPHOLIPIDS_BLACK_DN	1.64E-12	5.97E-11
DAZARD_UV_RESPONSE_CLUSTER_G5	1.74E-12	6.29E-11
module_144	1.78E-12	6.40E-11
SU_SALIVARY_GLAND	1.94E-12	6.94E-11
SMALL_CONJUGATING_PROTEIN_BINDING	2.51E-12	8.92E-11
REACTOME_MTORC1_MEDIATED_SIGNALLING	2.60E-12	9.16E-11
UBIQUITIN_BINDING	2.76E-12	9.68E-11
HOEGERKORP_CD44_TARGETS_DIRECT_DN	3.07E-12	1.07E-10
ZERBINI_RESPONSE_TO_SULINDAC_DN	3.34E-12	1.16E-10
BIOCARTA_PLATELETAPP_PATHWAY	3.39E-12	1.17E-10
AACGGTT,MIR-451	3.56E-12	1.22E-10
DETECTION_OF_BIOTIC_STIMULUS	3.86E-12	1.31E-10
NEGATIVE_REGULATION_OF_RESPONSE_TO_STIMULUS	3.96E-12	1.34E-10
KYNG_ENVIRONMENTAL_STRESS_RESPONSE_NOT_BY_UV_IN_OLD	4.76E-12	1.60E-10
WEBER_METHYLATED_HCP_IN_SPERM_UP	4.80E-12	1.60E-10
MANN_RESPONSE_TO_AMIFOSTINE_DN	5.10E-12	1.69E-10
module_260	5.85E-12	1.93E-10
MA_PITUITARY_FETAL_VS_ADULT_UP	7.09E-12	2.33E-10
INTERLEUKIN_8_PRODUCTION	1.01E-11	3.30E-10
module_514	1.03E-11	3.35E-10
chr9q12	1.11E-11	3.59E-10
chr2p	1.38E-11	4.42E-10
WILLIAMS_ESR1_TARGETS_DN	2.03E-11	6.46E-10
BENPORATH_ES_CORE_NINE	2.72E-11	8.58E-10
chr8q	2.72E-11	8.58E-10
LU_TUMOR_VASCULATURE_DN	4.22E-11	1.32E-09
GALI_TP53_TARGETS_APOPTOTIC_UP	4.26E-11	1.33E-09
REICHERT_G1S_REGULATORS_AS_PI3K_TARGETS	5.02E-11	1.56E-09
SEMBA_FHIT_TARGETS_UP	1.06E-10	3.27E-09
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_29	1.79E-10	5.50E-09
GOERING_BLOOD_HDL_CHOLESTEROL_QTL_CIS	2.22E-10	6.78E-09
REACTOME_CLASS_C3_METABOTROPIC_GLUTAMATE_PHEROMONE_RECEPTORS	2.37E-10	7.18E-09
REACTOME_DEATH_RECEPTOR_SIGNALLING	2.58E-10	7.80E-09
module_140	2.64E-10	7.94E-09
MARTINELLI_IMMATURE_NEUTROPHIL_UP	2.70E-10	8.05E-09
CHANG_IMMORTALIZED_BY_HPV31_UP	3.16E-10	9.37E-09
REACTOME_OTHER_SEMAPHORIN_INTERACTIONS	3.38E-10	1.00E-08
BACOLOD_RESISTANCE_TO_ALKYLATING_AGENTS_UP	3.68E-10	1.08E-08
WEBER_METHYLATED_HCP_IN_FIBROBLAST_UP	5.54E-10	1.62E-08
REGULATION_OF_GTPASE_ACTIVITY	5.84E-10	1.70E-08
LUI_THYROID_CANCER_CLUSTER_4	6.49E-10	1.88E-08
REACTOME_BILE_SALT_AND_ORGANIC_ANION_SLC_TRANSPORTERS	6.84E-10	1.97E-08
NIELSEN_GIST_AND_SYNOVIAL_SARCOMA_UP	7.09E-10	2.03E-08
SINGLE_STRANDED_RNA_BINDING	7.42E-10	2.11E-08
PURINE_RIBONUCLEOTIDE_METABOLIC_PROCESS	7.96E-10	2.26E-08
HORMONE_BINDING	9.32E-10	2.62E-08
module_571	9.33E-10	2.62E-08
TURJANSKI_MAPK14_TARGETS	9.83E-10	2.75E-08
SA_G2_AND_M_PHASES	1.07E-09	2.97E-08
KORKOLA_CHORIOCARCINOMA_UP	1.31E-09	3.63E-08
AMIT_EGF_RESPONSE_20_HELA	1.40E-09	3.87E-08
SHIRAISHI_PLZF_TARGETS_DN	1.54E-09	4.23E-08
ATPASE_ACTIVITY_COUPLED_TO_TRANSMEMBRANE_MOVEMENT_OF_IONS_PHOSPHORYLATIVE	1.59E-09	4.35E-08
chr7q	1.94E-09	5.26E-08
NIKOLSKY_BREAST_CANCER_20P13_AMPLICON	2.14E-09	5.75E-08
DEVELOPMENTAL_GROWTH	2.13E-09	5.75E-08
PENG_GLUTAMINE_DEPRIVATION_UP	2.26E-09	6.05E-08
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_9	2.96E-09	7.87E-08
BUCKANOVICH_T_LYMPHOCYTE_HOMING_ON_TUMOR_UP	3.06E-09	8.06E-08
INTERACTION_WITH_HOST	3.04E-09	8.06E-08
ELLWOOD_MYC_TARGETS_UP	3.54E-09	9.29E-08
PURINE_NUCLEOTIDE_METABOLIC_PROCESS	4.07E-09	1.06E-07
module_391	4.62E-09	1.20E-07
SCHURINGA_STAT5A_TARGETS_UP	5.59E-09	1.45E-07
WHITESIDE_CISPLATIN_RESISTANCE_DN	6.55E-09	1.69E-07
REACTOME_RETROGRADE_NEUROTROPHIN_SIGNALLING	7.31E-09	1.88E-07
GUTIERREZ_WALDENSTROEMS_MACROGLOBULINEMIA_1_DN	7.41E-09	1.89E-07
ZHAN_EARLY_DIFFERENTIATION_GENES_UP	8.76E-09	2.23E-07
FOCAL_ADHESION	1.09E-08	2.75E-07
SIMBULAN_UV_RESPONSE_NORMAL_UP	1.17E-08	2.95E-07
module_501	1.20E-08	3.02E-07
REACTOME_ACTIVATION_OF_THE_AP1_FAMILY_OF_TRANSCRIPTION_FACTORS	1.25E-08	3.12E-07
RAY_TARGETS_OF_P210_BCR_ABL_FUSION_UP	1.63E-08	4.06E-07

REGULATION_OF_PROTEIN_POLYMERIZATION	2.16E-08	5.35E-07
NAKAJIMA_EOSINOPHIL	2.33E-08	5.75E-07
chr18q22	2.59E-08	6.37E-07
GRAHAM_CML_DIVIDING_VS_NORMAL_DIVIDING_DN	2.92E-08	7.13E-07
DACOSTA_LOW_DOSE_UV_RESPONSE_VIA_ERCC3_XPCS_DN	3.06E-08	7.45E-07
CLIMENT_BREAST_CANCER_COPY_NUMBER_DN	3.30E-08	7.99E-07
module_293	3.37E-08	8.14E-07
ACETYLGALACTOSAMINYLTRANSFERASE_ACTIVITY	3.41E-08	8.18E-07
PROTEIN_MATURATION	3.42E-08	8.19E-07
IIZUKA_LIVER_CANCER_PROGRESSION_G1_G2_UP	3.48E-08	8.28E-07
LYSOSOMAL_TRANSPORT	3.49E-08	8.28E-07
CHANDRAN_METASTASIS_TOP50_DN	3.86E-08	9.12E-07
SECRETORY_GRANULE	4.38E-08	1.03E-06
IIZUKA_LIVER_CANCER_PROGRESSION_G2_G3_DN	4.99E-08	1.17E-06
MOROSETTI_FACIOSCAPULOHUMERAL_MUSCULAR_DISTROPHY_DN	6.02E-08	1.40E-06
NIELSEN_MALIGNAT_FIBROUS_HISTIOCYTOMA_UP	6.09E-08	1.41E-06
BYSTRYKH_HEMATOPOIESIS_STEM_CELL_FLI1	7.08E-08	1.64E-06
KORKOLA_YOLK_SAC_TUMOR_DN	7.45E-08	1.72E-06
module_143	8.29E-08	1.90E-06
FRASOR_TAMOXIFEN_RESPONSE_DN	9.25E-08	2.11E-06
GENE_SILENCING	9.60E-08	2.18E-06
EXTRINSIC_TO_PLASMA_MEMBRANE	1.03E-07	2.34E-06
WEST_ADRENOCORTICAL_TUMOR_MARKERS_DN	1.08E-07	2.44E-06
chr22q	1.14E-07	2.57E-06
YANG_BREAST_CANCER_ESR1_DN	1.17E-07	2.62E-06
BIOCARTA_RANMS_PATHWAY	1.18E-07	2.63E-06
AGTGCGT,MIR-521	1.37E-07	3.03E-06
CYCLASE_ACTIVITY	1.40E-07	3.10E-06
CELL_MATRIX_JUNCTION	1.57E-07	3.46E-06
BIOCARTA_PLCE_PATHWAY	1.72E-07	3.79E-06
REGULATION_OF_BLOOD_PRESSURE	1.76E-07	3.85E-06
VITAMIN_BINDING	1.86E-07	4.06E-06
NAKAMURA_LUNG_CANCER	2.02E-07	4.37E-06
NAKAMURA_LUNG_CANCER_MARKERS	2.02E-07	4.37E-06
BIOCARTA_PITX2_PATHWAY	2.37E-07	5.11E-06
SHIRAISHI_PLZF_TARGETS_UP	2.47E-07	5.30E-06
CELLULAR_RESPONSE_TO_EXTRACELLULAR_STIMULUS	2.70E-07	5.77E-06
TESAR_ALK_TARGETS_HUMAN_ES_4D_DN	3.05E-07	6.49E-06
POSITIVE_REGULATION_OF_CYTOSKELETON_ORGANIZATION_AND_BIOGENESIS	3.58E-07	7.59E-06
CAFFAREL_RESPONSE_TO_THC_8HR_5_DN	3.61E-07	7.64E-06
chr5q	3.72E-07	7.84E-06
SPERMATID_DEVELOPMENT	4.08E-07	8.56E-06
NEUTRAL_AMINO_ACID_TRANSPORT	4.30E-07	8.99E-06
FUNG_IL2_SIGNALING_1	4.47E-07	9.31E-06
DONATO_CELL_CYCLE_TRETINOIN	5.17E-07	1.07E-05
module_396	5.17E-07	1.07E-05
NIKOLSKY_BREAST_CANCER_10Q22_AMPLICON	5.62E-07	1.16E-05
chr12q11	5.74E-07	1.18E-05
BIOCARTA_CELL2CELL_PATHWAY	5.92E-07	1.21E-05
REGULATION_OF_RAS_GTPASE_ACTIVITY	6.12E-07	1.25E-05
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_13	6.74E-07	1.36E-05
MCCABE_HOXC6_TARGETS_UP	6.69E-07	1.36E-05
ANDROGEN_RECEPTOR_SIGNALING_PATHWAY	7.42E-07	1.50E-05
PROTEIN_SERINE_THREONINE_PHOSPHATASE_COMPLEX	7.93E-07	1.59E-05
EMBRYO_IMPLANTATION	8.23E-07	1.65E-05
ZAIDI_OSTEOBLAST_TRANSCRIPTION_FACTORS	8.42E-07	1.68E-05
BIOCARTA_CCR5_PATHWAY	8.43E-07	1.68E-05
MYOBLAST_DIFFERENTIATION	8.72E-07	1.73E-05
PIEPOLI_LGI1_TARGETS_UP	8.90E-07	1.76E-05
MONOSACCHARIDE_BINDING	9.26E-07	1.82E-05
DING_LUNG_CANCER_MUTATED_RECURRENTLY	1.01E-06	1.97E-05
STEROID_DEHYDROGENASE_ACTIVITY	1.04E-06	2.02E-05
STEROID_DEHYDROGENASE_ACTIVITY_ACTING_ON_THE_CH_OH_GROUP_OF_DONORSNAD_OR	1.04E-06	2.02E-05
module_402	1.03E-06	2.02E-05
KANG_GIST_WITH_PDGFRA_UP	1.05E-06	2.03E-05
WONG_IFNA2_RESISTANCE_UP	1.18E-06	2.27E-05
REACTOME_ACTIVATION_OF_RAC	1.31E-06	2.52E-05
LIU_CDX2_TARGETS_DN	1.35E-06	2.56E-05
GOUYER_TATI_TARGETS_UP	1.35E-06	2.56E-05
MUNSHI_MULTIPLE_MYELOMA_DN	1.35E-06	2.56E-05
XU_RESPONSE_TO_TRETINOIN_AND_NSC682994_DN	1.36E-06	2.58E-05
PHOSPHOLIPID_TRANSPORTER_ACTIVITY	1.54E-06	2.91E-05
BOYAULT_LIVER_CANCER_SUBCLASS_G23_DN	1.59E-06	2.99E-05
BIERIE_INFLAMMATORY_RESPONSE_TGFB1	1.69E-06	3.17E-05
DAVIES_MULTIPLE_MYELOMA_VS_MGUS_UP	1.72E-06	3.21E-05
MAP_KINASE_KINASE_KINASE_ACTIVITY	1.98E-06	3.68E-05
chr13q33	2.09E-06	3.87E-05

module_431	2.11E-06	3.91E-05
GAUTSCHI_SRC_SIGNALING	2.25E-06	4.14E-05
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_27	2.29E-06	4.21E-05
chr16q11	2.60E-06	4.77E-05
CHEOK_RESPONSE_TO_MERCAPTOPURINE_AND_HD_MTX_UP	3.07E-06	5.61E-05
MIZUKAMI_HYPOXIA_DN	3.15E-06	5.74E-05
REGULATION_OF_MUSCLE_CONTRACTION	3.36E-06	6.10E-05
MONOSACCHARIDE_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	3.41E-06	6.17E-05
REACTOME_SOS_MEDIATED_SIGNALLING	3.97E-06	7.16E-05
KAUFFMANN_MELANOMA_RELAPSE_DN	4.14E-06	7.42E-05
PROTEIN_AMINO_ACID_O_LINKED_GLYCOSYLATION	4.14E-06	7.42E-05
CELL_SUBSTRATE_ADHERENS_JUNCTION	4.34E-06	7.76E-05
module_457	4.72E-06	8.40E-05
NEUTRAL_AMINO_ACID_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	5.03E-06	8.93E-05
SUGAR_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	5.11E-06	9.05E-05
chr14q	5.20E-06	9.17E-05
DEACETYLASE_ACTIVITY	5.48E-06	9.64E-05
PROTEIN_DEACETYLASE_ACTIVITY	5.54E-06	9.71E-05
module_73	5.78E-06	1.01E-04
SHARMA_ASTROCYTOMA_WITH_NF1_SYNDROM	5.86E-06	1.02E-04
REACTOME_ERKS_ARE_INACTIVATED	6.47E-06	1.12E-04
BIOCARTA_TRKA_PATHWAY	6.51E-06	1.13E-04
PETRETTO_BLOOD_PRESSURE_DN	6.74E-06	1.16E-04
chr7p12	6.83E-06	1.17E-04
chr1q43	7.06E-06	1.21E-04
SMID_BREAST_CANCER_RELAPSE_IN_LIVER_DN	7.21E-06	1.23E-04
BIOCARTA_TGFB_PATHWAY	7.39E-06	1.26E-04
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_7	7.59E-06	1.29E-04
INTEGRAL_TO_GOLGI_MEMBRANE	7.83E-06	1.33E-04
HEIDENBLAD_AMPLIFIED_IN_SOFT_TISSUE_CANCER	8.52E-06	1.44E-04
REACTOME_APOPTOTIC_CLEAVAGE_OF_CELL_ADHESION_PROTEINS	8.58E-06	1.45E-04
SPHINGOID_METABOLIC_PROCESS	8.77E-06	1.47E-04
HOFMANN_MYELODYSPLASTIC_SYNDROM_HIGH_RISK_UP	8.88E-06	1.49E-04
NIKOLSKY_BREAST_CANCER_1Q32_AMPLICON	9.09E-06	1.52E-04
PROTEIN_STABILIZATION	9.16E-06	1.52E-04
IGARASHI_ATF4_TARGETS_UP	9.46E-06	1.57E-04
BIOCARTA_FIBRINOLYSIS_PATHWAY	1.00E-05	1.66E-04
LOPEZ_EPITHELIOID_MESOTHELIOMA	1.01E-05	1.67E-04
KOBAYASHI_RESPONSE_TO_ROMIDEPSIN	1.02E-05	1.68E-04
ANTIPORTER_ACTIVITY	1.05E-05	1.72E-04
REACTOME_SIGNALING_BY_TGF_BETA	1.06E-05	1.74E-04
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_5	1.08E-05	1.77E-04
RESPONSE_TO_STEROID_HORMONE_STIMULUS	1.12E-05	1.82E-04
REGULATION_OF_TRANSFORMING_GROWTH_FACTOR_BETA_RECEPTOR_SIGNALING_PATHWAY	1.15E-05	1.86E-04
RODRIGUES_DCC_TARGETS_UP	1.22E-05	1.96E-04
FRASOR_RESPONSE_TO_SERM_OR_FULVESTRANT_UP	1.31E-05	2.12E-04
ST_GRANULE_CELL_SURVIVAL_PATHWAY	1.34E-05	2.15E-04
CHEN_HOXA5_TARGETS_6HR_UP	1.41E-05	2.27E-04
ZHANG_RESPONSE_TO_CANTHARIDIN_UP	1.43E-05	2.29E-04
SMIRNOV_CIRCULATING_ENDOTHELIOCYTES_IN_CANCER_DN	1.44E-05	2.29E-04
WU_HBX_TARGETS_1_DN	1.45E-05	2.30E-04
NIELSEN_GIST_VS_SYNOVIAL_SARCOMA_UP	1.45E-05	2.30E-04
BUDHU_LIVER_CANCER_METASTASIS_UP	1.47E-05	2.32E-04
module_173	1.48E-05	2.34E-04
CELLULAR_RESPONSE_TO_NUTRIENT_LEVELS	1.55E-05	2.44E-04
module_495	1.63E-05	2.56E-04
YEMELYANOV_GR_TARGETS_DN	1.71E-05	2.68E-04
AMYLOID_PRECURSOR_PROTEIN_METABOLIC_PROCESS	1.74E-05	2.71E-04
SU_THYMUS	1.79E-05	2.78E-04
chr3p23	1.81E-05	2.81E-04
WONG_IFNA2_RESISTANCE_DN	1.82E-05	2.81E-04
REGULATION_OF_CELL_CELL_ADHESION	1.88E-05	2.89E-04
IIZUKA_LIVER_CANCER_PROGRESSION_L1_G1_UP	2.01E-05	3.10E-04
POSITIVE_REGULATION_OF_T_CELL_PROLIFERATION	2.05E-05	3.14E-04
PROTEIN_TARGETING_TO_MITOCHONDRION	2.11E-05	3.22E-04
CALVET_IRINOTECAN_SENSITIVE_VS_RESISTANT_UP	2.18E-05	3.33E-04
KUMAMOTO_RESPONSE_TO_NUTLIN_3A_UP	2.24E-05	3.41E-04
REGULATION_OF_JNK_CASCADE	2.26E-05	3.43E-04
REACTOME_FACILITATIVE_NA_INDEPENDENT_GLUCOSE_TRANSPORTERS	2.38E-05	3.59E-04
ZEMBUTSU_SENSITIVITY_TO_CISPLATIN	2.40E-05	3.62E-04
IVANOV_MUTATED_IN_COLON_CANCER	2.49E-05	3.74E-04
STEROID_HORMONE_RECEPTOR_BINDING	2.56E-05	3.84E-04
module_377	2.56E-05	3.84E-04
BIOCARTA_ARENRF2_PATHWAY	2.67E-05	3.98E-04
LOPEZ_MESOTELIOMA_SURVIVAL_TIME_DN	2.75E-05	4.10E-04
MARTINELLI_IMMATURE_NEUTROPHIL_DN	2.89E-05	4.28E-04
NEGATIVE_REGULATION_OF_SECRETION	2.89E-05	4.28E-04

chrxq27	3.00E-05	4.44E-04
AUXILIARY_TRANSPORT_PROTEIN_ACTIVITY	3.01E-05	4.44E-04
OUELLET_OVARIAN_CANCER_INVASIVE_VS_LMP_DN	3.13E-05	4.60E-04
REACTOME_VIRAL_DSRNA_TLR3_TRIF_COMPLEX_ACTIVATES_RIP1	3.14E-05	4.60E-04
VERRECCHIA_RESPONSE_TO_TGFB1_C4	3.22E-05	4.71E-04
REGULATION_OF_HEART_CONTRACTION	3.41E-05	4.97E-04
FOURNIER_ACINAR_DEVELOPMENT_EARLY_DN	3.44E-05	5.00E-04
NAKAMURA_ALVEOLAR_EPITHELIUM	3.52E-05	5.10E-04
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_1	3.53E-05	5.10E-04
IIZUKA_LIVER_CANCER_PROGRESSION_L0_L1_DN	3.55E-05	5.13E-04
BIOCARTA_TOB1_PATHWAY	3.59E-05	5.17E-04
BYSTRYKH_HEMATOPOIESIS_STEM_CELL_IL3RA	3.83E-05	5.50E-04
DISTECHE_ESCAPED_FROM_X_INACTIVATION	3.88E-05	5.56E-04
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_16	3.99E-05	5.70E-04
V$EVI1_01	4.06E-05	5.79E-04
module_178	4.12E-05	5.85E-04
HINATA_NFKB_TARGETS_KERATINOCYTE_DN	4.42E-05	6.27E-04
INTERFERON_GAMMA_BIOSYNTHETIC_PROCESS	4.54E-05	6.42E-04
CASTELLANO_HRAS_AND_NRAS_TARGETS_DN	4.64E-05	6.55E-04
NGO_MALIGNANT_GLIOMA_1P_LOH	4.90E-05	6.89E-04
REACTOME_STEROID_HORMONE_BIOSYNTHESIS	4.97E-05	6.98E-04
SYNAPTOGENESIS	5.30E-05	7.42E-04
PROTEIN_SERINE_THREONINE_TYROSINE_KINASE_ACTIVITY	5.45E-05	7.61E-04
AEROBIC_RESPIRATION	5.61E-05	7.80E-04
chr19p	5.60E-05	7.80E-04
SCHUHMACHER_MYC_TARGETS_DN	5.80E-05	8.00E-04
HSC_MATURE_FETAL	5.80E-05	8.00E-04
REACTOME_RNA_POLYMERASE_III_TRANSCRIPTION_TERMINATION	5.79E-05	8.00E-04
PASTURAL_RIZ1_TARGETS_DN	5.85E-05	8.05E-04
AMINO_ACID_DERIVATIVE_BIOSYNTHETIC_PROCESS	5.92E-05	8.12E-04
MURAKAMI_UV_RESPONSE_1HR_UP	6.44E-05	8.80E-04
BIOCARTA_IL3_PATHWAY	6.44E-05	8.80E-04
LIU_CMYB_TARGETS_DN	7.28E-05	9.90E-04
FUNG_IL2_SIGNALING_2	7.28E-05	9.90E-04
chr3q24	7.38E-05	9.98E-04
chr13q22	7.37E-05	9.98E-04
REGULATION_OF_INTERFERON_GAMMA_BIOSYNTHETIC_PROCESS	7.40E-05	9.99E-04
STEGMEIER_PRE-MITOTIC_CELL_CYCLE_REGULATORS	7.50E-05	1.01E-03
HU_ANGIOGENESIS_UP	7.84E-05	1.05E-03
TRACEY_RESISTANCE_TO_IFNA2_DN	7.88E-05	1.06E-03
RESPONSE_TO_TOXIN	7.93E-05	1.06E-03
ENDOTHELIAL_CELL_PROLIFERATION	8.11E-05	1.08E-03
CELL_SOMA	8.34E-05	1.11E-03
chr11p	8.35E-05	1.11E-03
ZEMBUTSU_SENSITIVITY_TO_NIMUSTINE	8.54E-05	1.13E-03
GRAHAM_CML_QUIESCENT_VS_CML_DIVIDING_DN	8.77E-05	1.16E-03
BIOGENIC_AMINE_METABOLIC_PROCESS	8.82E-05	1.16E-03
BIOCARTA_P35ALZHEIMERS_PATHWAY	8.90E-05	1.17E-03
LIPID_HOMEOSTASIS	9.37E-05	1.23E-03
STEROL_BINDING	9.54E-05	1.25E-03
DNA_MODIFICATION	9.63E-05	1.26E-03
MODY_HIPPOCAMPUS_POSTNATAL	9.71E-05	1.27E-03
CELLULAR_MONOVALENT_INORGANIC_CATION_HOMEOSTASIS	9.77E-05	1.27E-03
NIKOLSKY_BREAST_CANCER_19P13_AMPLICON	9.98E-05	1.30E-03
REACTOME_ASSOCIATION_OF_LICENSING_FACTORS_WITH_THE_PREREPLICATIVE_COMPLEX	1.00E-04	1.30E-03
module_190	1.02E-04	1.32E-03
OXFORD_RALA_AND_RALB_TARGETS_UP	1.02E-04	1.32E-03
AMINOPEPTIDASE_ACTIVITY	1.03E-04	1.33E-03
PETRETTO_BLOOD_PRESSURE_UP	1.04E-04	1.33E-03
TESAR_ALK_TARGETS_HUMAN_ES_5D_DN	1.05E-04	1.34E-03
module_513	1.07E-04	1.37E-03
INTERFERON_GAMMA_PRODUCTION	1.11E-04	1.41E-03
PYEON_HPV_POSITIVE_TUMORS_DN	1.13E-04	1.44E-03
CGGTGTG,MIR-220	1.13E-04	1.44E-03
CGTCTTA,MIR-208	1.14E-04	1.44E-03
ALDO_KETO_REDUCTASE_ACTIVITY	1.15E-04	1.45E-03
GCGCCTT,MIR-525,MIR-524	1.16E-04	1.46E-03
REGULATION_OF_CELLULAR_PH	1.19E-04	1.50E-03
TURJANSKI_MAPK1_AND_MAPK2_TARGETS	1.24E-04	1.55E-03
BIOCARTA_VDR_PATHWAY	1.42E-04	1.78E-03
REACTOME_HUMAN_TAK1_ACTIVATES_NFKB_BY_PHOSPHORYLATION_AND_ACTIVATION_OF_IKK	1.49E-04	1.86E-03
WANG_RESPONSE_TO_PACLITAXEL_VIA_MAPK8_UP	1.50E-04	1.87E-03
LIU_BREAST_CANCER	1.53E-04	1.90E-03
module_539	1.55E-04	1.92E-03
KEGG_RIBOFLAVIN_METABOLISM	1.59E-04	1.97E-03
NIELSEN_SYNOVIAL_SARCOMA_DN	1.60E-04	1.97E-03
SMALL_CONJUGATING_PROTEIN_SPECIFIC_PROTEASE_ACTIVITY	1.73E-04	2.13E-03

CYCLIC_NUCLEOTIDE_METABOLIC_PROCESS	1.74E-04	2.14E-03
KYNG_ENVIRONMENTAL_STRESS_RESPONSE_NOT_BY_GAMMA_IN_WS	1.77E-04	2.17E-03
REGULATION_OF_PROTEIN_SECRETION	1.83E-04	2.24E-03
REACTOME_GLUCURONIDATION	1.84E-04	2.24E-03
GNF2_TNFSF10	1.90E-04	2.31E-03
VERNELL_RETINOBLASTOMA_PATHWAY_DN	1.91E-04	2.33E-03
module_423	1.98E-04	2.40E-03
SHI_SPARC_TARGETS_DN	2.00E-04	2.43E-03
KEGG_TERPENOID_BACKBONE_BIOSYNTHESIS	2.04E-04	2.46E-03
MEINHOLD_OVARIAN_CANCER_LOW_GRADE_UP	2.11E-04	2.55E-03
chr13q31	2.17E-04	2.61E-03
module_470	2.19E-04	2.63E-03
MARSON_FOXP3_TARGETS_STIMULATED_DN	2.28E-04	2.73E-03
POSITIVE_REGULATION_OF_ANGIOGENESIS	2.35E-04	2.81E-03
AMIT_DELAYED_EARLY_GENES	2.36E-04	2.82E-03
BIOCARTA_CTL_PATHWAY	2.38E-04	2.83E-03
module_231	2.39E-04	2.85E-03
PROTEIN_IMPORT_INTO_NUCLEUS_TRANSLOCATION	2.41E-04	2.86E-03
BOYLAN_MULTIPLE_MYELOMA_PCA1_DN	2.44E-04	2.89E-03
REACTOME_CALCITONIN_LIKE_LIGAND_RECEPTORS	2.47E-04	2.92E-03
NEGATIVE_REGULATION_OF_ANGIOGENESIS	2.49E-04	2.93E-03
NF_KAPPAB_BINDING	2.49E-04	2.93E-03
AMUNDSON_DNA_DAMAGE_RESPONSE_TP53	2.54E-04	2.98E-03
MITOTIC_SPINDLE_ORGANIZATION_AND_BIOGENESIS	2.58E-04	3.02E-03
BIOCARTA_SKP2E2F_PATHWAY	2.79E-04	3.27E-03
LUI_THYROID_CANCER_CLUSTER_3	2.87E-04	3.35E-03
NEBEN_AML_WITH_FLT3_OR_NRAS_DN	2.94E-04	3.42E-03
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_22	3.01E-04	3.49E-03
CGCAAAA,MIR-450	3.07E-04	3.56E-03
KIM_RESPONSE_TO_TSA_AND_DECITABINE_DN	3.14E-04	3.62E-03
TCGATGG,MIR-213	3.14E-04	3.62E-03
FOURNIER_ACINAR_DEVELOPMENT_EARLY_UP	3.21E-04	3.69E-03
RODRIGUES_THYROID_CARCINOMA_UP	3.33E-04	3.82E-03
LOPEZ_MESOTHELIOMA_SURVIVAL_WORST_VS_BEST_UP	3.36E-04	3.85E-03
MILICIC_FAMILIAL_ADENOMATOUS_POLYPOSIS_DN	3.38E-04	3.87E-03
module_335	3.40E-04	3.89E-03
OHASHI_AURKB_TARGETS	3.48E-04	3.97E-03
REACTOME_CDC6_ASSOCIATION_WITH_THE_ORC:ORIGIN_COMPLEX	3.57E-04	4.06E-03
BIOCARTA_SRCRPTP_PATHWAY	3.76E-04	4.27E-03
SCHLESINGER_METHYLATED_IN_COLON_CANCER	3.94E-04	4.46E-03
REGULATION_OF_ENDOTHELIAL_CELL_PROLIFERATION	4.05E-04	4.58E-03
ROY_WOUND_BLOOD_VESSEL_DN	4.12E-04	4.64E-03
chr17q	4.12E-04	4.64E-03
REGULATION_OF_T_CELL_PROLIFERATION	4.17E-04	4.69E-03
VACUOLAR_TRANSPORT	4.18E-04	4.69E-03
NUCLEOTIDE_BIOSYNTHETIC_PROCESS	4.21E-04	4.72E-03
CERAMIDE_METABOLIC_PROCESS	4.36E-04	4.87E-03
REACTOME_A_THIRD_PROTEOLYTIC_CLEAVAGE_RELEASES_NICD	4.46E-04	4.97E-03
COFACTOR_TRANSPORTER_ACTIVITY	4.56E-04	5.08E-03
NIELSEN_LEIOMYOSARCOMA_DN	4.92E-04	5.46E-03
REGULATION_OF_HORMONE_SECRETION	4.95E-04	5.48E-03
CATION_TRANSPORTING_ATPASE_ACTIVITY	4.94E-04	5.48E-03
KEGG_TAURINE_AND_HYPOTAURINE_METABOLISM	5.12E-04	5.65E-03
REACTOME_BASE_FREE_SUGAR_PHOSPHATE_REMOVAL_VIA_THE_SINGLE_NUCLEOTIDE_REPL	5.18E-04	5.71E-03
CARBOHYDRATE_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	5.36E-04	5.90E-03
MILICIC_FAMILIAL_ADENOMATOUS_POLYPOSIS_UP	5.54E-04	6.08E-03
SULFUR_COMPOUND_BIOSYNTHETIC_PROCESS	5.76E-04	6.31E-03
HETEROGENEOUS_NUCLEAR_RIBONUCLEOPROTEIN_COMPLEX	5.80E-04	6.34E-03
module_540	6.05E-04	6.60E-03
ROZANOV_MMP14_CORRELATED	6.10E-04	6.63E-03
MURAKAMI_UV_RESPONSE_6HR_DN	6.09E-04	6.63E-03
NEGATIVE_REGULATION_OF_PHOSPHORYLATION	6.18E-04	6.70E-03
WANG_ESOPHAGUS_CANCER_PROGRESSION_UP	6.33E-04	6.85E-03
ENDOCYTIC_VESICLE	6.33E-04	6.85E-03
EPITHELIAL_TO_MESENCHYMAL_TRANSITION	6.35E-04	6.85E-03
LAMB_CCND1_TARGETS	6.50E-04	6.99E-03
chr9p12	6.51E-04	6.99E-03
BIOCARTA_ASBCELL_PATHWAY	6.60E-04	7.08E-03
CHANDRAN_METASTASIS_TOP50_UP	6.90E-04	7.39E-03
NUCLEAR_CHROMATIN	6.97E-04	7.45E-03
VITAMIN_METABOLIC_PROCESS	7.12E-04	7.59E-03
TASTE_RECEPTOR_ACTIVITY	7.14E-04	7.60E-03
chr11p12	7.19E-04	7.64E-03
CHIN_BREAST_CANCER_COPY_NUMBER_UP	7.27E-04	7.71E-03
REACTOME_GLUTAMATE_NEUROTRANSMITTER_RELEASE_CYCLE	7.35E-04	7.78E-03
TESAR_ALK_TARGETS_HUMAN_ES_5D_UP	7.54E-04	7.97E-03
OXIDOREDUCTASE_ACTIVITY_ACTING_ON_THE_CH_NH_GROUP_OF_DONORS	7.61E-04	8.03E-03

FINAK_BREAST_CANCER_SDPP_SIGNATURE	7.95E-04	8.37E-03
chr5p14	8.16E-04	8.57E-03
MODY_HIPPOCAMPUS_NEONATAL	8.36E-04	8.77E-03
BUCKANOVICH_T_LYMPHOCYTE_HOMING_ON_TUMOR_DN	8.40E-04	8.79E-03
FRIDMAN_SENESCENCE_DN	8.55E-04	8.93E-03
REACTOME_SYNTHESIS_OF_BILE_ACIDS_AND_BILE_SALTS_VIA_24_HYDROXYCHOLESTEROL	8.86E-04	9.24E-03
SPINDLE_POLE	9.10E-04	9.47E-03
ACTIN_FILAMENT_BUNDLE_FORMATION	9.15E-04	9.51E-03
NUCLEOBASENUCLEOSIDENUCLEOTIDE_AND_NUCLEIC_ACID_TRANSMEMBRANE_TRANSPORTE	9.41E-04	9.76E-03
CARBOXY_LYASE_ACTIVITY	9.48E-04	9.81E-03

Supplemantary Table 4: 517 pathways altered in SZ patients (gene expression microarray)

pathway	p-value	q-value
PYEON_HPV_POSITIVE_TUMORS_DN	<1.00E-16	<1.00E-16
KORKOLA_YOLK_SAC_TUMOR_DN	<1.00E-16	<1.00E-16
KOBAYASHI_EGFR_SIGNALING_6HR_UP	<1.00E-16	<1.00E-16
PIEPOLI_LGI1_TARGETS_DN	<1.00E-16	<1.00E-16
LIU_CMYB_TARGETS_DN	<1.00E-16	<1.00E-16
PEPPER_CHRONIC_LYMPHOCYTIC_LEUKEMIA_DN	<1.00E-16	<1.00E-16
LINDGREN_BLADDER_CANCER_CLUSTER_2A_UP	<1.00E-16	<1.00E-16
GAUSSMANN_MLL_AF4_FUSION_TARGETS_B_DN	<1.00E-16	<1.00E-16
ZIRN_TRETINOIN_RESPONSE_DN	<1.00E-16	<1.00E-16
IVANOV_MUTATED_IN_COLON_CANCER	<1.00E-16	<1.00E-16
TURJANSKI_MAPK1_AND_MAPK2_TARGETS	<1.00E-16	<1.00E-16
TURJANSKI_MAPK8_AND_MAPK9_TARGETS	<1.00E-16	<1.00E-16
TURJANSKI_MAPK7_TARGETS	<1.00E-16	<1.00E-16
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_9	<1.00E-16	<1.00E-16
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_22	<1.00E-16	<1.00E-16
PATTERSON_DOCETAXEL_RESISTANCE	<1.00E-16	<1.00E-16
XU_HGF_TARGETS_REPRESSED_BY_AKT1_UP	<1.00E-16	<1.00E-16
XU_AKT1_TARGETS_48HR	<1.00E-16	<1.00E-16
DACOSTA_LOW_DOSE_UV_RESPONSE_VIA_ERCC3_XPCS_UP	<1.00E-16	<1.00E-16
HEIDENBLAD_AMPLICON_12P11_12_UP	<1.00E-16	<1.00E-16
MANN_RESPONSE_TO_AMIFOSTINE_DN	<1.00E-16	<1.00E-16
SIMBULAN_UV_RESPONSE_NORMAL_UP	<1.00E-16	<1.00E-16
GOUYER_TATI_TARGETS_UP	<1.00E-16	<1.00E-16
STARK_BRAIN_22Q11_DELETION	<1.00E-16	<1.00E-16
PENG_GLUTAMINE_DEPRIVATION_UP	<1.00E-16	<1.00E-16
IIZUKA_LIVER_CANCER_PROGRESSION_G1_G2_UP	<1.00E-16	<1.00E-16
WONG_IFNA2_RESISTANCE_DN	<1.00E-16	<1.00E-16
OSAWA_TNF_TARGETS	<1.00E-16	<1.00E-16
SCHURINGA_STAT5A_TARGETS_UP	<1.00E-16	<1.00E-16
XU_RESPONSE_TO_TRETINOIN_DN	<1.00E-16	<1.00E-16
RORIE_TARGETS_OF_EWSR1_FLI1_FUSION_DN	<1.00E-16	<1.00E-16
MARSON_FOXP3_TARGETS_STIMULATED_DN	<1.00E-16	<1.00E-16
KYNG_ENVIRONMENTAL_STRESS_RESPONSE_NOT_BY_UV_IN_WS	<1.00E-16	<1.00E-16
GALI_TP53_TARGETS_APOPTOTIC_DN	<1.00E-16	<1.00E-16
BOQUEST_STEM_CELL_DN	<1.00E-16	<1.00E-16
YAGUE_PRETUMOR_DRUG_RESISTANCE_DN	<1.00E-16	<1.00E-16
CONRAD_GERMLINE_STEM_CELL	<1.00E-16	<1.00E-16
THUM_MIR21_TARGETS_HEART_DISEASE_DN	<1.00E-16	<1.00E-16
KRISHNAN_FURIN_TARGETS_UP	<1.00E-16	<1.00E-16
KRISHNAN_FURIN_TARGETS_DN	<1.00E-16	<1.00E-16
FIRESTEIN_CTNNB1_PATHWAY_AND_PROLIFERATION	<1.00E-16	<1.00E-16
PALOMERO_GSI_SENSITIVITY_UP	<1.00E-16	<1.00E-16
MARTINELLI_IMMATURE_NEUTROPHIL_DN	<1.00E-16	<1.00E-16
RAY_TARGETS_OF_P210_BCR_ABL_FUSION_UP	<1.00E-16	<1.00E-16
LEE_NAIVE_T_LYMPHOCYTE	<1.00E-16	<1.00E-16
VALK_AML_WITH_T_8_21_TRANSLOCATION	<1.00E-16	<1.00E-16
BOYAULT_LIVER_CANCER_SUBCLASS_G23_DN	<1.00E-16	<1.00E-16
SEIKE_LUNG_CANCER_POOR_SURVIVAL	<1.00E-16	<1.00E-16
TSAI_DNAJB4_TARGETS_DN	<1.00E-16	<1.00E-16
DORN_ADENOVIRUS_INFECTION_24HR_UP	<1.00E-16	<1.00E-16
EXTERNAL_SIDE_OF_PLASMA_MEMBRANE	<1.00E-16	<1.00E-16
GROWTH_CONE	<1.00E-16	<1.00E-16
REGULATION_OF_DEFENSE_RESPONSE	<1.00E-16	<1.00E-16
TISSUE_MORPHOGENESIS	<1.00E-16	<1.00E-16
SYNAPTOGENESIS	<1.00E-16	<1.00E-16
ISOPRENOID_METABOLIC_PROCESS	<1.00E-16	<1.00E-16
FEMALE_GAMETE_GENERATION	<1.00E-16	<1.00E-16
REGULATION_OF_LIPID_METABOLIC_PROCESS	<1.00E-16	<1.00E-16
PHOSPHOLIPASE_C_ACTIVATION	<1.00E-16	<1.00E-16
MAINTENANCE_OF_CELLULAR_LOCALIZATION	<1.00E-16	<1.00E-16
NEGATIVE_REGULATION_OF_ANGIOGENESIS	<1.00E-16	<1.00E-16
MONOCARBOXYLIC_ACID_TRANSPORT	<1.00E-16	<1.00E-16
INTERLEUKIN_8_BIOSYNTHETIC_PROCESS	<1.00E-16	<1.00E-16
PEPTIDE_METABOLIC_PROCESS	<1.00E-16	<1.00E-16
FEEDING_BEHAVIOR	<1.00E-16	<1.00E-16
INTERLEUKIN_2_PRODUCTION	<1.00E-16	<1.00E-16
INTERLEUKIN_8_PRODUCTION	<1.00E-16	<1.00E-16
MORPHOGENESIS_OF_AN_EPITHELIUM	<1.00E-16	<1.00E-16
KERATINOCYTE_DIFFERENTIATION	<1.00E-16	<1.00E-16
BILE_ACID_METABOLIC_PROCESS	<1.00E-16	<1.00E-16
ESTABLISHMENT_OF_VESICLE_LOCALIZATION	<1.00E-16	<1.00E-16
LYSOSOMAL_TRANSPORT	<1.00E-16	<1.00E-16
POSITIVE_REGULATION_OF_DNA_METABOLIC_PROCESS	<1.00E-16	<1.00E-16

VESICLE_LOCALIZATION	<1.00E-16	<1.00E-16
MAINTENANCE_OF_CELLULAR_PROTEIN_LOCALIZATION	<1.00E-16	<1.00E-16
POSITIVE_REGULATION_OF_ANGIOGENESIS	<1.00E-16	<1.00E-16
NEGATIVE_REGULATION_OF_MYELOID_CELL_DIFFERENTIATION	<1.00E-16	<1.00E-16
ACTIN_FILAMENT_BASED_MOVEMENT	<1.00E-16	<1.00E-16
GENE_SILENCING	<1.00E-16	<1.00E-16
REGULATION_OF_ENDOTHELIAL_CELL_PROLIFERATION	<1.00E-16	<1.00E-16
VITAMIN_BINDING	<1.00E-16	<1.00E-16
NON_MEMBRANE_SPANNING_PROTEIN_TYROSINE_KINASE_ACTIVITY	<1.00E-16	<1.00E-16
ORGANIC_ANION_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	<1.00E-16	<1.00E-16
HYDROLASE_ACTIVITY_HYDROLYZING_N_GLYCOSYL_COMPOUNDS	<1.00E-16	<1.00E-16
3_5_CYCLIC_NUCLEOTIDE_PHOSPHODIESTERASE_ACTIVITY	<1.00E-16	<1.00E-16
DEAMINASE_ACTIVITY	<1.00E-16	<1.00E-16
TRANSMEMBRANE_RECEPTOR_PROTEIN_PHOSPHATASE_ACTIVITY	<1.00E-16	<1.00E-16
PROTEIN_SERINE_THREONINE_TYROSINE_KINASE_ACTIVITY	<1.00E-16	<1.00E-16
TRANSITION_METAL_ION_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	<1.00E-16	<1.00E-16
WHITESIDE_CISPLATIN_RESISTANCE_DN	<1.00E-16	<1.00E-16
ABE_VEGFA_TARGETS	<1.00E-16	<1.00E-16
BYSTRYKH_HEMATOPOIESIS_STEM_CELL_FLI1	<1.00E-16	<1.00E-16
V$HOXA3_01	<1.00E-16	<1.00E-16
AGCGCTT,MIR-518F,MIR-518E,MIR-518A	<1.00E-16	<1.00E-16
CGGTGTG,MIR-220	<1.00E-16	<1.00E-16
ACCGAGC,MIR-423	<1.00E-16	<1.00E-16
CGTCTTA,MIR-208	<1.00E-16	<1.00E-16
module_96	<1.00E-16	<1.00E-16
module_140	<1.00E-16	<1.00E-16
module_141	<1.00E-16	<1.00E-16
module_211	<1.00E-16	<1.00E-16
module_283	<1.00E-16	<1.00E-16
module_328	<1.00E-16	<1.00E-16
module_354	<1.00E-16	<1.00E-16
module_376	<1.00E-16	<1.00E-16
module_390	<1.00E-16	<1.00E-16
module_401	<1.00E-16	<1.00E-16
module_410	<1.00E-16	<1.00E-16
module_423	<1.00E-16	<1.00E-16
module_465	<1.00E-16	<1.00E-16
module_467	<1.00E-16	<1.00E-16
module_470	<1.00E-16	<1.00E-16
module_543	<1.00E-16	<1.00E-16
module_545	<1.00E-16	<1.00E-16
KEGG_PRIMARY_BILE_ACID_BIOSYNTHESIS	<1.00E-16	<1.00E-16
KEGG_RENIN_ANGIOTENSIN_SYSTEM	<1.00E-16	<1.00E-16
KEGG_ASTHMA	<1.00E-16	<1.00E-16
BIOCARTA_ASBCELL_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_CYTOKINE_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_EPONFKB_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_FEEDER_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_FIBRINOLYSIS_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_IL17_PATHWAY	<1.00E-16	<1.00E-16
BIOCARTA_PTC1_PATHWAY	<1.00E-16	<1.00E-16
REACTOME_A_THIRD_PROTEOLYTIC_CLEAVAGE_RELEASES_NICD	<1.00E-16	<1.00E-16
REACTOME_BASE_FREE_SUGAR_PHOSPHATE_REMOVAL_VIA_THE_SINGLE_NUCLEOTIDE_REPL	<1.00E-16	<1.00E-16
REACTOME_COMMON_PATHWAY	<1.00E-16	<1.00E-16
REACTOME_E2F_ENABLED_INHIBITION_OF_PRE_REPLICATION_COMPLEX_FORMATION	<1.00E-16	<1.00E-16
REACTOME_FACILITATIVE_NA_INDEPENDENT_GLUCOSE_TRANSPORTERS	<1.00E-16	<1.00E-16
REACTOME_P75NTR_RECRUITS_SIGNALLING_COMPLEXES	<1.00E-16	<1.00E-16
REACTOME_P75NTR_SIGNALS_VIA_NFKB	<1.00E-16	<1.00E-16
REACTOME_PHASE_1_FUNCTIONALIZATION	<1.00E-16	<1.00E-16
REACTOME_PHOSPHORYLATION_OF_CD3_AND_TCR_ZETA_CHAINS	<1.00E-16	<1.00E-16
REACTOME_RECYCLING_OF_BILE_ACIDS_AND_SALTS	<1.00E-16	<1.00E-16
REACTOME_RESOLUTION_OF_AP_SITES_VIA_THE_SINGLE_NUCLEOTIDE_REPLACEMENT_PATHW	<1.00E-16	<1.00E-16
REACTOME_TRANSLOCATION_OF_ZAP70_TO_IMMUNOLOGICAL_SYNAPSE	<1.00E-16	<1.00E-16
REACTOME_JNK_PHOSPHORYLATION_AND_ACTIVATION_MEDIATED_BY_ACTIVATED_HUMAN_TAK	<1.00E-16	<1.00E-16
REACTOME_BILE_SALT_AND_ORGANIC_ANION_SLC_TRANSPORTERS	<1.00E-16	<1.00E-16
REACTOME_GLUCURONIDATION	<1.00E-16	<1.00E-16
REACTOME_SHCMEDIATED_CASCADE	<1.00E-16	<1.00E-16
REACTOME_GAP_JUNCTION_ASSEMBLY	<1.00E-16	<1.00E-16
REACTOME_GAP_JUNCTION_DEGRADATION	<1.00E-16	<1.00E-16
REACTOME_APOPTOSIS_INDUCED_DNA_FRAGMENTATION	<1.00E-16	<1.00E-16
chr13q11	<1.00E-16	<1.00E-16
chryp11	<1.00E-16	<1.00E-16
chr2q22	<1.00E-16	<1.00E-16
chr2p	<1.00E-16	<1.00E-16
chr19p	<1.00E-16	<1.00E-16
chr12p	<1.00E-16	<1.00E-16
chr5p14	<1.00E-16	<1.00E-16

chr11p12	<1.00E-16	<1.00E-16
chr2p15	<1.00E-16	<1.00E-16
chr3p13	<1.00E-16	<1.00E-16
chr13q33	<1.00E-16	<1.00E-16
chr1p	<1.00E-16	<1.00E-16
chr6p	<1.00E-16	<1.00E-16
chr4q11	<1.00E-16	<1.00E-16
ST_INTERLEUKIN_13_PATHWAY	<1.00E-16	<1.00E-16
ST_IL_13_PATHWAY	<1.00E-16	<1.00E-16
SA_FAS_SIGNALING	<1.00E-16	<1.00E-16
TONKS_TARGETS_OF_RUNX1_RUNX1T1_FUSION_ERYTHROCYTE_DN	1.11E-16	4.53E-15
FARMER_BREAST_CANCER_CLUSTER_8	1.11E-16	4.53E-15
WALLACE_PROSTATE_CANCER_DN	1.11E-16	4.53E-15
GUTIERREZ_WALDENSTROEMS_MACROGLOBULINEMIA_1_DN	1.11E-16	4.53E-15
CHIARETTI_T_ALL_RELAPSE_PROGNOSIS	1.11E-16	4.53E-15
T_CELL_PROLIFERATION	1.11E-16	4.53E-15
WONG_ENDMETRIUM_CANCER_UP	2.22E-16	8.95E-15
KANG_CISPLATIN_RESISTANCE_DN	2.22E-16	8.95E-15
TCGATGG,MIR-213	3.33E-16	1.33E-14
NEGATIVE_REGULATION_OF_BINDING	5.55E-16	2.21E-14
BIOCARTA_KREB_PATHWAY	8.88E-16	3.52E-14
KYNG_ENVIRONMENTAL_STRESS_RESPONSE_NOT_BY_4NQO_IN_OLD	9.99E-16	3.93E-14
BIOCARTA_GRANULOCYTES_PATHWAY	1.33E-15	5.21E-14
SENSORY_PERCEPTION_OF_CHEMICAL_STIMULUS	3.22E-15	1.25E-13
LUCAS_HNF4A_TARGETS_DN	3.55E-15	1.37E-13
ENDOTHELIAL_CELL_MIGRATION	4.11E-15	1.58E-13
CARBOHYDRATE_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	4.88E-15	1.87E-13
WONG_IFNA2_RESISTANCE_UP	7.66E-15	2.91E-13
NEGATIVE_REGULATION_OF_TRANSCRIPTION_FACTOR_ACTIVITY	1.22E-14	4.62E-13
SASAKI_TARGETS_OF_TP73_AND_TP63	1.52E-14	5.72E-13
MAINA_HYPOXIA_VHL_TARGETS_UP	1.71E-14	6.39E-13
JIANG_CORE_DUPLICON_GENES	1.73E-14	6.44E-13
REACTOME_CREB_PHOSPHORYLATION_THROUGH_THE_ACTIVATION_OF_CAMKII	2.92E-14	1.08E-12
TURJANSKI_MAPK14_TARGETS	3.00E-14	1.10E-12
BALLIF_DEVELOPMENTAL_DISABILITY_P16_P12_DELETION	3.56E-14	1.30E-12
NEGATIVE_REGULATION_OF_DNA_BINDING	6.06E-14	2.21E-12
module_65	6.20E-14	2.24E-12
chr6q15	7.41E-14	2.67E-12
REACTOME_SYNTHESIS_OF_BILE_ACIDS_AND_BILE_SALTS_VIA_7ALPHA_HYDROXYCHOLESTER	8.73E-14	3.12E-12
REACTOME_SYNTHESIS_OF_BILE_ACIDS_AND_BILE_SALTS	9.66E-14	3.44E-12
SCIAN_INVERSED_TARGETS_OF_TP53_AND_TP73_UP	1.46E-13	5.19E-12
HISTONE_METHYLTRANSFERASE_ACTIVITY	5.01E-13	1.77E-11
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_27	5.49E-13	1.92E-11
POSITIVE_REGULATION_OF_CELL_MIGRATION	8.88E-13	3.10E-11
GNF2_TTN	1.39E-12	4.84E-11
MIZUKAMI_HYPOXIA_UP	1.58E-12	5.46E-11
LOPEZ_MESOTHELIOMA_SURVIVAL_UP	1.65E-12	5.67E-11
NUCLEAR_REPLICATION_FORK	1.73E-12	5.89E-11
module_428	1.73E-12	5.89E-11
FOURNIER_ACINAR_DEVELOPMENT_LATE_UP	2.25E-12	7.62E-11
module_560	2.40E-12	8.09E-11
NIKOLSKY_BREAST_CANCER_14Q22_AMPLICON	3.50E-12	1.17E-10
REGULATION_OF_MEMBRANE_POTENTIAL	4.02E-12	1.34E-10
RICKMAN_HEAD_AND_NECK_CANCER_D	4.28E-12	1.41E-10
REACTOME_APOPTOTIC_CLEAVAGE_OF_CELL_ADHESION_PROTEINS	4.27E-12	1.41E-10
UNFOLDED_PROTEIN_RESPONSE	4.86E-12	1.60E-10
REACTOME_CD28_DEPENDENT_PI3K_AKT_SIGNALING	5.80E-12	1.90E-10
KORKOLA_TERATOMA_DN	7.66E-12	2.49E-10
LAU_APOPTOSIS_CDKN2A_DN	9.79E-12	3.17E-10
RESPIRATORY_GASEOUS_EXCHANGE	1.35E-11	4.35E-10
MONOSACCHARIDE_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	1.36E-11	4.35E-10
FINETTI_BREAST_CANCER_KINOME_GREEN	1.43E-11	4.57E-10
chr2q34	1.58E-11	5.03E-10
SUGAR_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	1.86E-11	5.88E-10
FUNG_IL2_TARGETS_WITH_STAT5_BINDING_SITES	1.92E-11	6.05E-10
BIOCARTA_EIF2_PATHWAY	1.96E-11	6.15E-10
LEE_INTRATHYMIC_T_PROGENITOR	2.13E-11	6.64E-10
VITAMIN_TRANSPORT	2.31E-11	7.18E-10
MONTERO_THYROID_CANCER_POOR_SURVIVAL_UP	2.37E-11	7.34E-10
CHESLER_BRAIN_QTL_TRANS	2.95E-11	9.09E-10
BYSTRYKH_SCP2_QTL	3.51E-11	1.07E-09
chr14q	3.51E-11	1.07E-09
KYNG_ENVIRONMENTAL_STRESS_RESPONSE_NOT_BY_UV_IN_OLD	3.54E-11	1.07E-09
REACTOME_COPI_MEDIATED_TRANSPORT	4.33E-11	1.31E-09
LIPID_KINASE_ACTIVITY	6.25E-11	1.88E-09
HEDVAT_ELF4_TARGETS_UP	8.51E-11	2.55E-09
CASPASE_REGULATOR_ACTIVITY	1.05E-10	3.12E-09

MARTIN_INTERACT_WITH_HDAC	1.39E-10	4.13E-09
GABA_RECEPTOR_ACTIVITY	2.46E-10	7.27E-09
module_236	2.61E-10	7.69E-09
BANDRES_RESPONSE_TO_CARMUSTIN_WITHOUT_MGMT_24HR_DN	2.65E-10	7.77E-09
ANION_CATION_SYMPORTER_ACTIVITY	2.89E-10	8.42E-09
GAUTSCHI_SRC_SIGNALING	3.02E-10	8.79E-09
GLUCOSE_CATABOLIC_PROCESS	4.34E-10	1.26E-08
POTASSIUM_CHANNEL_REGULATOR_ACTIVITY	4.42E-10	1.27E-08
BANDRES_RESPONSE_TO_CARMUSTIN_MGMT_24HR_DN	4.45E-10	1.28E-08
BOQUEST_STEM_CELL_CULTURED_VS_FRESH_UP	4.55E-10	1.30E-08
NUCLEAR_UBIQUITIN_LIGASE_COMPLEX	4.57E-10	1.30E-08
REACTOME_TRAFFICKING_OF_GLUR2_CONTAINING_AMPA_RECEPTORS	4.90E-10	1.39E-08
module_407	5.03E-10	1.42E-08
KEGG_TAURINE_AND_HYPOTAURINE_METABOLISM	5.57E-10	1.56E-08
REGULATION_OF_PEPTIDYL_TYROSINE_PHOSPHORYLATION	6.36E-10	1.78E-08
CHASSOT_SKIN_WOUND	6.39E-10	1.78E-08
VACUOLAR_TRANSPORT	1.26E-09	3.48E-08
MURATA_VIRULENCE_OF_H_PILORI	1.27E-09	3.50E-08
module_58	1.32E-09	3.63E-08
MAP_KINASE_KINASE_KINASE_ACTIVITY	1.53E-09	4.18E-08
WEBER_METHYLATED_HCP_IN_SPERM_DN	1.73E-09	4.73E-08
TURASHVILI_BREAST_NORMAL_DUCTAL_VS_LOBULAR_DN	1.85E-09	5.02E-08
GLUCOSAMINE_METABOLIC_PROCESS	2.05E-09	5.56E-08
PHOSPHATASE_INHIBITOR_ACTIVITY	2.12E-09	5.73E-08
REACTOME_ACTIVATION_OF_THE_AP1_FAMILY_OF_TRANSCRIPTION_FACTORS	2.17E-09	5.83E-08
BIOCARTA_IL4_PATHWAY	2.99E-09	8.00E-08
NIELSEN_GIST_AND_SYNOVIAL_SARCOMA_UP	3.77E-09	1.01E-07
module_424	4.73E-09	1.26E-07
SCHUHMACHER_MYC_TARGETS_DN	5.17E-09	1.37E-07
OHM_EMBRYONIC_CARCINOMA_DN	6.23E-09	1.64E-07
DNA_DAMAGE_RESPONSESIGNAL_TRANSDUCTION_BY_P53_CLASS_MEDIATOR	1.02E-08	2.69E-07
DEFENSE_RESPONSE_TO_VIRUS	1.19E-08	3.10E-07
INOSITOL_OR_PHOSPHATIDYLINOSITOL_PHOSPHODIESTERASE_ACTIVITY	1.21E-08	3.16E-07
ZHAN_VARIABLE_EARLY_DIFFERENTIATION_GENES_UP	1.22E-08	3.16E-07
REACTOME_UNFOLDED_PROTEIN_RESPONSE	1.23E-08	3.17E-07
REACTOME_ACTIVATED_TAK1_MEDIATES_P38_MAPK_ACTIVATION	1.25E-08	3.20E-07
POSITIVE_REGULATION_OF_CYTOKINE_PRODUCTION	1.38E-08	3.54E-07
module_130	1.45E-08	3.70E-07
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_15	1.66E-08	4.23E-07
TRICARBOXYLIC_ACID_CYCLE_INTERMEDIATE_METABOLIC_PROCESS	1.68E-08	4.26E-07
CASTELLANO_HRAS_AND_NRAS_TARGETS_DN	1.90E-08	4.81E-07
BIOCARTA_IL5_PATHWAY	2.05E-08	5.16E-07
KUROKAWA_LIVER_CANCER_EARLY_RECURRENCE_DN	2.36E-08	5.90E-07
N_ACETYLGLUCOSAMINE_METABOLIC_PROCESS	2.49E-08	6.21E-07
TIAN_TNF_SIGNALING_NOT_VIA_NFKB	2.80E-08	6.96E-07
REACTOME_HORMONE_SENSITIVE_LIPASE_HSL_MEDIATED_TRIACYLGLYCEROL_HYDROLYSIS	3.21E-08	7.95E-07
INTERCALATED_DISC	3.22E-08	7.96E-07
WAESCH_ANAPHASE_PROMOTING_COMPLEX	3.53E-08	8.68E-07
KEGG_PROXIMAL_TUBULE_BICARBONATE_RECLAMATION	3.56E-08	8.74E-07
FUCOSYLTRANSFERASE_ACTIVITY	3.75E-08	9.17E-07
RESPONSE_TO_STEROID_HORMONE_STIMULUS	3.87E-08	9.43E-07
SPHINGOLIPID_BIOSYNTHETIC_PROCESS	3.95E-08	9.59E-07
PARK_HSC_MARKERS	4.86E-08	1.17E-06
module_429	5.02E-08	1.21E-06
REACTOME_REGULATION_OF_RHEB_GTPASE_ACTIVITY_BY_AMPK	5.66E-08	1.36E-06
REACTOME_MRNA_DECAY_BY_3_TO_5_EXORIBONUCLEASE	5.91E-08	1.41E-06
HASLINGER_B_CLL_WITH_MUTATED_VH_GENES	6.16E-08	1.47E-06
PDZ_DOMAIN_BINDING	6.74E-08	1.60E-06
ROETH_TERT_TARGETS_UP	6.77E-08	1.60E-06
ST_PAC1_RECEPTOR_PATHWAY	7.49E-08	1.77E-06
BIOCARTA_PARKIN_PATHWAY	7.68E-08	1.80E-06
REACTOME_FGFR_LIGAND_BINDING_AND_ACTIVATION	8.63E-08	2.02E-06
REACTOME_NRIF_SIGNALS_CELL_DEATH_FROM_THE_NUCLEUS	9.30E-08	2.17E-06
chrxq27	9.39E-08	2.18E-06
FUNG_IL2_SIGNALING_1	1.01E-07	2.33E-06
chr6q13	1.09E-07	2.52E-06
GUTIERREZ_WALDENSTROEMS_MACROGLOBULINEMIA_1_UP	1.14E-07	2.62E-06
MALE_GONAD_DEVELOPMENT	1.24E-07	2.83E-06
TURJANSKI_MAPK11_TARGETS	1.28E-07	2.93E-06
PROTEIN_MATURATION	1.45E-07	3.31E-06
COFACTOR_TRANSPORT	1.52E-07	3.45E-06
FINAK_BREAST_CANCER_SDPP_SIGNATURE	1.67E-07	3.79E-06
REACTOME_XENOBIOTICS	1.72E-07	3.87E-06
KONDO_HYPOXIA	2.06E-07	4.64E-06
PROTEIN_IMPORT_INTO_NUCLEUS_TRANSLOCATION	2.16E-07	4.85E-06
MONOCARBOXYLIC_ACID_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	2.62E-07	5.84E-06
REACTOME_NOTCH_HLH_TRANSCRIPTION_PATHWAY	2.88E-07	6.41E-06

INNATE_IMMUNE_RESPONSE	2.95E-07	6.56E-06
GNF2_SERPINI2	3.04E-07	6.72E-06
PERIPHERAL_NERVOUS_SYSTEM_DEVELOPMENT	3.07E-07	6.76E-06
CASORELLI_APL_SECONDARY_VS_DE_NOVO_DN	3.75E-07	8.23E-06
CHESLER_BRAIN_D6MIT150_QTL_CIS	3.77E-07	8.26E-06
REACTOME_PECAM1_INTERACTIONS	3.79E-07	8.27E-06
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_24	5.42E-07	1.18E-05
module_404	5.59E-07	1.21E-05
DNA_MODIFICATION	6.95E-07	1.50E-05
CELLULAR_RESPONSE_TO_EXTRACELLULAR_STIMULUS	7.05E-07	1.52E-05
chr1p12	8.35E-07	1.80E-05
BIOCARTA_CACAM_PATHWAY	8.47E-07	1.81E-05
POSITIVE_REGULATION_OF_EPITHELIAL_CELL_PROLIFERATION	8.97E-07	1.92E-05
NEUTRAL_AMINO_ACID_TRANSPORT	1.01E-06	2.16E-05
module_31	1.10E-06	2.33E-05
RODRIGUES_DCC_TARGETS_UP	1.22E-06	2.57E-05
GOUYER_TATI_TARGETS_DN	1.30E-06	2.73E-05
module_540	1.33E-06	2.80E-05
MATTIOLI_MULTIPLE_MYELOMA_SUBGROUPS	1.36E-06	2.86E-05
MAINTENANCE_OF_PROTEIN_LOCALIZATION	1.49E-06	3.12E-05
GLYCOSPHINGOLIPID_METABOLIC_PROCESS	1.65E-06	3.43E-05
TYROSINE_PHOSPHORYLATION_OF_STAT_PROTEIN	2.05E-06	4.27E-05
SITE_OF_POLARIZED_GROWTH	2.24E-06	4.64E-05
REGULATION_OF_TYROSINE_PHOSPHORYLATION_OF_STAT_PROTEIN	2.27E-06	4.69E-05
VERRECCHIA_RESPONSE_TO_TGFB1_C6	2.46E-06	5.07E-05
WANG_RECURRENT_LIVER_CANCER_DN	2.51E-06	5.15E-05
module_39	2.61E-06	5.33E-05
TRACEY_RESISTANCE_TO_IFNA2_DN	2.73E-06	5.57E-05
chr4q24	2.80E-06	5.69E-05
KEGG_TASTE_TRANSDUCTION	2.81E-06	5.69E-05
CAFFAREL_RESPONSE_TO_THC_24HR_3_UP	3.24E-06	6.54E-05
IIZUKA_LIVER_CANCER_PROGRESSION_L1_G1_UP	3.67E-06	7.40E-05
ARYLSULFATASE_ACTIVITY	3.71E-06	7.45E-05
REACTOME_ADENYLATE_CYCLASE_ACTIVATING_PATHWAY	3.74E-06	7.49E-05
REGULATION_OF_NEUROGENESIS	3.97E-06	7.92E-05
LIANG_HEMATOPOIESIS_STEM_CELL_NUMBER_QTL	3.99E-06	7.94E-05
HEMATOPOIETIN_INTERFERON_CLASSD200_DOMAIN_CYTOKINE_RECEPTOR_BINDING	4.21E-06	8.35E-05
BIOCARTA_SRCRPTP_PATHWAY	4.22E-06	8.35E-05
HASLINGER_B_CLL_WITH_CHROMOSOME_12_TRISOMY	4.38E-06	8.64E-05
GALE_APL_WITH_FLT3_MUTATED_DN	4.52E-06	8.89E-05
SCHWAB_TARGETS_OF_BMYB_S427G_DN	4.88E-06	9.55E-05
SCHWAB_TARGETS_OF_BMYB_I624M_DN	4.88E-06	9.55E-05
REACTOME_GAMMA_CARBOXYLATION_TRANSPORT_AND_AMINO_TERMINAL_CLEAVAGE_OF_PR	4.90E-06	9.57E-05
KUMAMOTO_RESPONSE_TO_NUTLIN_3A_UP	5.03E-06	9.77E-05
COLLIS_PRKDC_REGULATORS	5.17E-06	0.000100231
KANG_FLUOROURACIL_RESISTANCE_DN	5.22E-06	0.000100866
MONOOXYGENASE_ACTIVITY	5.32E-06	0.000102532
GLAND_DEVELOPMENT	5.36E-06	0.000102967
TRANSITION_METAL_ION_TRANSPORT	5.61E-06	0.000107498
module_194	5.66E-06	0.000107843
module_464	5.65E-06	0.000107843
NIKOLSKY_BREAST_CANCER_19P13_AMPLICON	5.75E-06	0.00010932
module_538	6.17E-06	0.000116896
GNF2_IGF1	6.21E-06	0.000117366
PHOSPHOLIPID_TRANSPORTER_ACTIVITY	6.56E-06	0.000123674
GLUTATHIONE_TRANSFERASE_ACTIVITY	6.63E-06	0.000124714
REICHERT_G1S_REGULATORS_AS_PI3K_TARGETS	6.66E-06	0.000124887
IIZUKA_LIVER_CANCER_PROGRESSION_L0_L1_UP	7.03E-06	0.000131401
ISHIKAWA_STING_SIGNALING	7.29E-06	0.000135516
SYNAPTIC_VESICLE	7.29E-06	0.000135516
REACTOME_NA_CL_DEPENDENT_NEUROTRANSMITTER_TRANSPORTERS	8.16E-06	0.000151248
GHO_ATF5_TARGETS_UP	8.34E-06	0.000154275
CELLULAR_RESPONSE_TO_STRESS	9.79E-06	0.000180492
ACETYLGALACTOSAMINYLTRANSFERASE_ACTIVITY	1.00E-05	0.000184534
NIKOLSKY_BREAST_CANCER_10Q22_AMPLICON	1.10E-05	0.00020164
BIOCARTA_SODD_PATHWAY	1.13E-05	0.00020752
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_12	1.16E-05	0.000211454
KEGG_FOLATE_BIOSYNTHESIS	1.24E-05	0.000224791
ONDER_CDH1_TARGETS_3_UP	1.27E-05	0.000229771
chr13q21	1.28E-05	0.000232331
module_450	1.31E-05	0.000236493
REGULATION_OF_MYELOID_CELL_DIFFERENTIATION	1.43E-05	0.000257549
chr4q22	1.47E-05	0.00026357
CDC42_PROTEIN_SIGNAL_TRANSDUCTION	1.50E-05	0.000268408
NEGATIVE_REGULATION_OF_IMMUNE_SYSTEM_PROCESS	1.51E-05	0.00026963
PHOSPHORUS_OXYGEN_LYASE_ACTIVITY	1.53E-05	0.000272143
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_7	1.59E-05	0.000281577

module_563	1.69E-05	0.000299058
CHANG_POU5F1_TARGETS_UP	1.70E-05	0.000299976
HONRADO_BREAST_CANCER_BRCA1_VS_BRCA2	1.71E-05	0.000301923
module_264	1.97E-05	0.000345441
SCHLESINGER_H3K27ME3_IN_NORMAL_AND_METHYLATED_IN_CANCER	2.04E-05	0.000357266
REACTOME_GRB2_SOS_PROVIDES_LINKAGE_TO_MAPK_SIGNALING_FOR_INTERGRINS_	2.15E-05	0.000376624
LOPEZ_MESOTHELIOMA_SURVIVAL_OVERALL_UP	2.18E-05	0.000380971
module_148	2.30E-05	0.000400118
NIKOLSKY_BREAST_CANCER_1Q32_AMPLICON	2.31E-05	0.000400988
FOCAL_ADHESION_FORMATION	2.44E-05	0.000422233
CYCLIC_NUCLEOTIDE_PHOSPHODIESTERASE_ACTIVITY	2.62E-05	0.000451841
MA_PITUITARY_FETAL_VS_ADULT_UP	2.62E-05	0.000451841
OLIGOSACCHARYL_TRANSFERASE_COMPLEX	2.74E-05	0.000471026
REGULATION_OF_T_CELL_PROLIFERATION	2.87E-05	0.000491522
KERLEY_RESPONSE_TO_CISPLATIN_DN	2.90E-05	0.000495387
DETECTION_OF_CHEMICAL_STIMULUS	2.99E-05	0.00050977
SHIRAISHI_PLZF_TARGETS_DN	3.01E-05	0.000512273
REACTOME_PKA_ACTIVATION	3.22E-05	0.000545501
HORMONE_BINDING	3.40E-05	0.000575773
module_0	3.47E-05	0.000584892
REGULATION_OF_CHROMOSOME_ORGANIZATION_AND_BIOGENESIS	3.61E-05	0.000607277
module_135	3.70E-05	0.000621021
DNA_DAMAGE_RESPONSESIGNAL_TRANSDUCTION_RESULTING_IN_INDUCTION_OF_APOPTOSIS	3.86E-05	0.000647134
PRODUCTION_OF_MOLECULAR_MEDIATOR_OF_IMMUNE_RESPONSE	3.90E-05	0.000651299
chr22q	3.93E-05	0.000655634
MARSON_FOXP3_TARGETS_STIMULATED_UP	3.99E-05	0.000662796
CYCLASE_ACTIVITY	4.01E-05	0.000664561
EHLERS_ANEUPLOIDY_DN	4.05E-05	0.000669949
XU_RESPONSE_TO_TRETINOIN_UP	4.19E-05	0.000691542
HSC_MATURE_FETAL	4.22E-05	0.000694802
G2_M_TRANSITION_OF_MITOTIC_CELL_CYCLE	4.24E-05	0.000696812
LEI_MYB_TARGETS	4.34E-05	0.000711107
CARBONATE_DEHYDRATASE_ACTIVITY	4.55E-05	0.000744567
BACOLOD_RESISTANCE_TO_ALKYLATING_AGENTS_UP	4.62E-05	0.000752699
TOMLINS_METASTASIS_UP	5.65E-05	0.000920018
PHOTORECEPTOR_CELL_MAINTENANCE	5.73E-05	0.000930316
CHIANG_LIVER_CANCER_SUBCLASS_UNANNOTATED_UP	5.79E-05	0.000937238
chrxq11	6.19E-05	0.000999614
INTERLEUKIN_1_SECRETION	6.25E-05	0.001006388
YAO_TEMPORAL_RESPONSE_TO_PROGESTERONE_CLUSTER_4	6.29E-05	0.00101125
ANION_TRANSPORT	7.01E-05	0.00112351
DYSTROPHIN_ASSOCIATED_GLYCOPROTEIN_COMPLEX	7.30E-05	0.001168278
AMINO_SUGAR_METABOLIC_PROCESS	7.47E-05	0.001192767
YAO_HOXA10_TARGETS_VIA_PROGESTERONE_DN	7.49E-05	0.00119308
module_478	8.65E-05	0.001374383
NEUROPEPTIDE_BINDING	8.82E-05	0.001394804
NEUROPEPTIDE_RECEPTOR_ACTIVITY	8.82E-05	0.001394804
LE_SKI_TARGETS_DN	9.23E-05	0.001456892
BIOCARTA_RANMS_PATHWAY	9.73E-05	0.001531226
GOERING_BLOOD_HDL_CHOLESTEROL_QTL_CIS	0.000100144	0.001568928
GLYCOLIPID_METABOLIC_PROCESS	0.000100034	0.001568928
GTCTACC,MIR-379	0.000100964	0.001574831
REACTOME_EFFECTS_OF_PIP2_HYDROLYSIS	0.000100987	0.001574831
PROTEIN_STABILIZATION	0.000102233	0.001590601
POSITIVE_REGULATION_OF_CYTOKINE_BIOSYNTHETIC_PROCESS	0.000106027	0.001645852
REACTOME_STEROID_HORMONE_BIOSYNTHESIS	0.000107255	0.001661098
REACTOME_RAS_ACTIVATION_UOPN_CA2_INFUX_THROUGH_NMDA_RECEPTOR	0.000112629	0.001740351
VERRECCHIA_RESPONSE_TO_TGFB1_C4	0.000113967	0.001753016
BIOCARTA_CARDIACEGF_PATHWAY	0.000113792	0.001753016
REACTOME_NF_KB_IS_ACTIVATED_AND_SIGNALS_SURVIVAL	0.000117828	0.001808305
WANG_RESPONSE_TO_FORSKOLIN_DN	0.000118297	0.00181139
FERRARI_RESPONSE_TO_FENRETINIDE_DN	0.000119716	0.001828981
DNA_REPLICATION_INITIATION	0.000123841	0.001887743
LU_TUMOR_VASCULATURE_DN	0.000125618	0.001910522
MICROVILLUS	0.000132138	0.002005179
LY_AGING_OLD_UP	0.000134657	0.002038826
REACTOME_PHOSPHOLIPASE_CMEDIATED_CASCADE	0.00013528	0.002039142
chr11p	0.000135081	0.002039142
EHLERS_ANEUPLOIDY_UP	0.000141464	0.002127619
AGCGCAG,MIR-191	0.000141997	0.002130898
BIOCARTA_41BB_PATHWAY	0.000143264	0.002145151
BIOCARTA_ARAP_PATHWAY	0.000150832	0.002253496
HU_ANGIOGENESIS_UP	0.000152375	0.002271533
KYNG_ENVIRONMENTAL_STRESS_RESPONSE_NOT_BY_GAMMA_IN_OLD	0.000157403	0.002341333
HEME_BIOSYNTHETIC_PROCESS	0.000179822	0.002668932
chr2q	0.000189346	0.002804141
MONTERO_THYROID_CANCER_POOR_SURVIVAL_DN	0.000191039	0.002823037

REACTOME_RNA_POLYMERASE_III_CHAIN_ELONGATION	0.000195736	0.002886153
chr18q22	0.000203754	0.002997848
GUTIERREZ_CHRONIC_LYMPHOCYTIC_LEUKEMIA_UP	0.000206547	0.003027857
BODY_FLUID_SECRETION	0.000206689	0.003027857
BIOGENIC_AMINE_METABOLIC_PROCESS	0.000211066	0.003085306
ZIRN_TRETINOIN_RESPONSE_WT1_DN	0.000224585	0.003275839
module_71	0.000227446	0.003310434
ADP_BINDING	0.000232461	0.003376173
MOTOR_ACTIVITY	0.000240858	0.003485514
chr9p11	0.00024102	0.003485514
LYSOSOMAL_MEMBRANE	0.000248659	0.003588325
CAFFAREL_RESPONSE_TO_THC_8HR_5_UP	0.000250338	0.003604869
AMUNDSON_GAMMA_RADIATION_RESISTANCE	0.00025222	0.003624252
VACUOLAR_MEMBRANE	0.000256192	0.003673536
SIALYLTRANSFERASE_ACTIVITY	0.000269826	0.003860854
REACTOME_GLUCAGON_TYPE_LIGAND_RECEPTORS	0.000278951	0.003982997
NLS_BEARING_SUBSTRATE_IMPORT_INTO_NUCLEUS	0.000300945	0.004287997
KEGG_GLYOXYLATE_AND_DICARBOXYLATE_METABOLISM	0.000308826	0.004391042
COLLIS_PRKDC_SUBSTRATES	0.000313205	0.004443966
CLAUS_PGR_POSITIVE_MENINGIOMA_UP	0.000315433	0.004466219
SCIAN_CELL_CYCLE_TARGETS_OF_TP53_AND_TP73_UP	0.00031684	0.00447677
module_186	0.000317689	0.004479417
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_25	0.000347108	0.004884051
DORN_ADENOVIRUS_INFECTION_32HR_UP	0.000350386	0.004919948
PHOSPHOLIPASE_A2_ACTIVITY	0.000369577	0.005178674
REGULATION_OF_SYNAPSE_STRUCTURE_AND_ACTIVITY	0.00037471	0.005239742
WEBER_METHYLATED_HCP_IN_FIBROBLAST_DN	0.000379607	0.00529728
V$MEF2_04	0.000391005	0.005433924
module_173	0.000390691	0.005433924
REACTOME_G_ALPHA_Z_SIGNALLING_EVENTS	0.00041223	0.005717153
module_534	0.000420029	0.005813412
module_21	0.00042375	0.005852938
GOUYER_TUMOR_INVASIVENESS	0.000433714	0.005978358
NEGATIVE_REGULATION_OF_CYTOSKELETON_ORGANIZATION_AND_BIOGENESIS	0.000436479	0.006004254
DORN_ADENOVIRUS_INFECTION_48HR_UP	0.000449921	0.0061766
CYTOSOLIC_PART	0.000456652	0.006256313
BERENJENO_TRANSFORMED_BY_RHOA_REVERSIBLY_UP	0.000465321	0.006362209
REACTOME_CYTOCHROME_P450_ARRANGED_BY_SUBSTRATE_TYPE	0.000472991	0.006454032
LIU_BREAST_CANCER	0.000477257	0.006499147
chr5q15	0.000479546	0.006517208
BUCKANOVICH_T_LYMPHOCYTE_HOMING_ON_TUMOR_UP	0.00048401	0.006564684
CORNIFIED_ENVELOPE	0.000505407	0.006841193
MOROSETTI_FACIOSCAPULOHUMERAL_MUSCULAR_DISTROPHY_DN	0.000506616	0.006843868
LIPID_HOMEOSTASIS	0.000522278	0.007041392
BRUSH_BORDER	0.0005302	0.007133984
chr8q11	0.000561465	0.007539677
KEGG_SULFUR_METABOLISM	0.000564545	0.007566024
ABDULRAHMAN_KIDNEY_CANCER_VHL_DN	0.000571595	0.007645371
REGULATION_OF_RAS_GTPASE_ACTIVITY	0.000576337	0.007693582
REACTOME_HORMONE_BIOSYNTHESIS	0.000597682	0.007962815
chr9p21	0.000636713	0.008466157
STEGMEIER_PRE-MITOTIC_CELL_CYCLE_REGULATORS	0.000658911	0.008744138
RNA_ELONGATION	0.000662771	0.008778143
GNF2_CD14	0.000668714	0.008839569
APICAL_PLASMA_MEMBRANE	0.000671816	0.008863257
BIOCARTA_THELPER_PATHWAY	0.000713077	0.009389316
REACTOME_STEROID_HORMONES	0.00072101	0.009475331
ZHANG_RESPONSE_TO_CANTHARIDIN_UP	0.000723193	0.009485598
AGTGCGT,MIR-521	0.000731562	0.009576808

Supplemantary Table 5: 72 pathways commonly changed in ChIP-seq and gene expression microarray

pathway	p-value	q-value
LINDGREN_BLADDER_CANCER_CLUSTER_2A_UP	<1.00E-16	<1.00E-16
GAUSSMANN_MLL_AF4_FUSION_TARGETS_B_DN	<1.00E-16	<1.00E-16
TURJANSKI_MAPK8_AND_MAPK9_TARGETS	<1.00E-16	<1.00E-16
TURJANSKI_MAPK7_TARGETS	<1.00E-16	<1.00E-16
STARK_BRAIN_22Q11_DELETION	<1.00E-16	<1.00E-16
OSAWA_TNF_TARGETS	<1.00E-16	<1.00E-16
KYNG_ENVIRONMENTAL_STRESS_RESPONSE_NOT_BY_UV_IN_WS	<1.00E-16	<1.00E-16
GALI_TP53_TARGETS_APOPTOTIC_DN	<1.00E-16	<1.00E-16
BOQUEST_STEM_CELL_DN	<1.00E-16	<1.00E-16
KRISHNAN_FURIN_TARGETS_UP	<1.00E-16	<1.00E-16
MONOCARBOXYLIC_ACID_TRANSPORT	<1.00E-16	<1.00E-16
module_390	<1.00E-16	<1.00E-16
BIOCARTA_FEEDER_PATHWAY	<1.00E-16	<1.00E-16
chr3p13	<1.00E-16	<1.00E-16
chr1p	<1.00E-16	<1.00E-16
chr4q11	<1.00E-16	<1.00E-16
TSAI_DNAJB4_TARGETS_DN	1.11E-16	5.64E-15
THUM_MIR21_TARGETS_HEART_DISEASE_DN	5.66E-15	2.60E-13
XU_RESPONSE_TO_TRETINOIN_DN	5.01E-14	2.19E-12
PEPPER_CHRONIC_LYMPHOCYTIC_LEUKEMIA_DN	7.09E-14	3.06E-12
PEPTIDE_METABOLIC_PROCESS	7.79E-14	3.28E-12
module_283	2.01E-13	8.10E-12
NEGATIVE_REGULATION_OF_MYELOID_CELL_DIFFERENTIATION	5.85E-13	2.23E-11
ST_INTERLEUKIN_13_PATHWAY	6.93E-13	2.57E-11
ST_IL_13_PATHWAY	6.93E-13	2.57E-11
MANN_RESPONSE_TO_AMIFOSTINE_DN	5.10E-12	1.69E-10
INTERLEUKIN_8_PRODUCTION	1.01E-11	3.30E-10
chr2p	1.38E-11	4.42E-10
module_140	2.64E-10	7.94E-09
REACTOME_BILE_SALT_AND_ORGANIC_ANION_SLC_TRANSPORTERS	6.84E-10	1.97E-08
PENG_GLUTAMINE_DEPRIVATION_UP	2.26E-09	6.05E-08
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_9	2.96E-09	7.87E-08
SCHURINGA_STAT5A_TARGETS_UP	5.59E-09	1.45E-07
WHITESIDE_CISPLATIN_RESISTANCE_DN	6.55E-09	1.69E-07
SIMBULAN_UV_RESPONSE_NORMAL_UP	1.17E-08	2.95E-07
RAY_TARGETS_OF_P210_BCR_ABL_FUSION_UP	1.63E-08	4.06E-07
IIZUKA_LIVER_CANCER_PROGRESSION_G1_G2_UP	3.48E-08	8.28E-07
LYSOSOMAL_TRANSPORT	3.49E-08	8.28E-07
BYSTRYKH_HEMATOPOIESIS_STEM_CELL_FLI1	7.08E-08	1.64E-06
KORKOLA_YOLK_SAC_TUMOR_DN	7.45E-08	1.72E-06
GENE_SILENCING	9.60E-08	2.18E-06
VITAMIN_BINDING	1.86E-07	4.06E-06
GOUYER_TATI_TARGETS_UP	1.35E-06	2.56E-05
BOYAULT_LIVER_CANCER_SUBCLASS_G23_DN	1.59E-06	2.99E-05
chr13q33	2.09E-06	3.87E-05
BIOCARTA_FIBRINOLYSIS_PATHWAY	1.00E-05	0.000165543
WONG_IFNA2_RESISTANCE_DN	1.82E-05	0.000281381
REACTOME_FACILITATIVE_NA_INDEPENDENT_GLUCOSE_TRANSPORTERS	2.38E-05	0.000359465
IVANOV_MUTATED_IN_COLON_CANCER	2.49E-05	0.000374019
MARTINELLI_IMMATURE_NEUTROPHIL_DN	2.89E-05	0.000428147
SYNAPTOGENESIS	5.30E-05	0.000741522
PROTEIN_SERINE_THREONINE_TYROSINE_KINASE_ACTIVITY	5.45E-05	0.000761356
chr19p	5.60E-05	0.000780348
LIU_CMYB_TARGETS_DN	7.28E-05	0.000990347
PYEON_HPV_POSITIVE_TUMORS_DN	0.000112996	0.001436164
CGGTGTG,MIR-220	0.000113378	0.001437777
CGTCTTA,MIR-208	0.000114007	0.001442513
TURJANSKI_MAPK1_AND_MAPK2_TARGETS	0.000123828	0.001552841
REACTOME_GLUCURONIDATION	0.000183713	0.002243987
module_423	0.000197567	0.002397641
module_470	0.000219183	0.002631669
MARSON_FOXP3_TARGETS_STIMULATED_DN	0.000228259	0.002734823
POSITIVE_REGULATION_OF_ANGIOGENESIS	0.000235215	0.002812193
NEGATIVE_REGULATION_OF_ANGIOGENESIS	0.000248998	0.002927367
MYLLYKANGAS_AMPLIFICATION_HOT_SPOT_22	0.000300619	0.003490613
REGULATION_OF_ENDOTHELIAL_CELL_PROLIFERATION	0.000404714	0.004576887
REACTOME_A_THIRD_PROTEOLYTIC_CLEAVAGE_RELEASES_NICD	0.000445673	0.004970361
REACTOME BASE FREE SUGAR PHOSPHATE REMOVAL VIA THE SINGLE NUCLEOTIDE REPL	0.000517699	0.005705973
BIOCARTA_ASBCELL_PATHWAY	0.00066021	0.007083021
chr11p12	0.000718845	0.007639469
chr5p14	0.00081571	0.008572032

Supplementary Table 6: No race-associated difference in pathways (ChIP-seq)

pathway	p-value	q-value
NIKOLSKY_BREAST_CANCER_17Q11_Q21_AMPLICON	0.000158289	0.375524621
RESPONSE_TO_TOXIN	0.000174617	0.375524621
NAM_FXYD5_TARGETS_DN	0.000209996	0.375524621
MORF_DDB1	0.000380695	0.472290788
SULFURIC_ESTER_HYDROLASE_ACTIVITY	0.000595949	0.472290788
RASHI_RESPONSE_TO_IONIZING_RADIATION_3	0.000621829	0.472290788
MACROMOLECULAR_COMPLEX_DISASSEMBLY	0.000831024	0.472290788
KEGG_PURINE_METABOLISM	0.001275578	0.472290788
MORF_PPP5C	0.001339673	0.472290788
KEGG_NUCLEOTIDE_EXCISION_REPAIR	0.001481486	0.472290788
GINESTIER_BREAST_CANCER_20Q13_AMPLIFICATION_DN	0.001559754	0.472290788
PROTEIN_COMPLEX_DISASSEMBLY	0.001752054	0.472290788
CELLULAR_PROTEIN_COMPLEX_DISASSEMBLY	0.001771966	0.472290788
chr11q12	0.001954902	0.472290788
REACTOME_NUCLEOTIDE_EXCISION_REPAIR	0.001993975	0.472290788
ST_INTERLEUKIN_13_PATHWAY	0.001995981	0.472290788
ST_IL_13_PATHWAY	0.001995981	0.472290788
V$USF2_Q6	0.002042061	0.472290788
MORF_PRKAG1	0.002136326	0.472290788
PHOSPHOLIPASE_A2_ACTIVITY	0.002215713	0.472290788
MORF_HEAB	0.002385815	0.472290788
GCM_VAV1	0.002405021	0.472290788
LASTOWSKA_NEUROBLASTOMA_COPY_NUMBER_DN	0.002412944	0.472290788
REACTOME_GLOBAL_GENOMIC_NER	0.00244041	0.472290788
BIOCARTA_EIF_PATHWAY	0.002448087	0.472290788
CARBOXYLESTERASE_ACTIVITY	0.002540846	0.472290788
REACTOME_POST_NMDA_RECEPTOR_ACTIVATION_EVENTS	0.002610959	0.472290788
REACTOME_GRB2_SOS_PROVIDES_LINKAGE_TO_MAPK_SIGNALING_FOR_IN	0.002638743	0.472290788
REACTOME_PI3K_AKT_SIGNALLING	0.002739341	0.472290788
VERRECCHIA_RESPONSE_TO_TGFB1_C3	0.002751703	0.472290788
GNF2_MLF1	0.002920097	0.472290788
WEIGEL_OXIDATIVE_STRESS_RESPONSE	0.003002357	0.472290788
NIKOLSKY_BREAST_CANCER_16Q24_AMPLICON	0.00303828	0.472290788
CHOI_ATL_CHRONIC_VS_ACUTE_DN	0.003075832	0.472290788
RESPONSE_TO_UV	0.003150465	0.472290788
module_72	0.003169306	0.472290788
module_120	0.003266468	0.473613954
REACTOME_RNA_POLYMERASE_III_TRANSCRIPTION_INITIATION	0.003439953	0.47722301
NIKOLSKY_BREAST_CANCER_6P24_P22_AMPLICON	0.003669912	0.47722301
chr22q13	0.003776371	0.47722301
chr6q14	0.003927351	0.47722301
MORF_IKBKG	0.003941263	0.47722301
MICROTUBULE_ASSOCIATED_COMPLEX	0.004023771	0.47722301
TRANSCRIPTION_FACTOR_COMPLEX	0.004056758	0.47722301
HISTONE_DEACETYLASE_COMPLEX	0.004064347	0.47722301
GNF2_CCNA1	0.004451406	0.47722301
PRODUCTION_OF_MOLECULAR_MEDIATOR_OF_IMMUNE_RESPONSE	0.004666881	0.47722301
RESPONSE_TO_LIGHT_STIMULUS	0.00474438	0.47722301
WATANABE_RECTAL_CANCER_RADIOTHERAPY_RESPONSIVE_DN	0.005070008	0.47722301
XENOBIOTIC_METABOLIC_PROCESS	0.005080839	0.47722301
V$AP2_Q3	0.005120358	0.47722301
MORF_BMI1	0.005127757	0.47722301
WANG_CLIM2_TARGETS_UP	0.005204985	0.47722301
GATTGGY_V$NFY_Q6_01	0.005230706	0.47722301
RODRIGUES_THYROID_CARCINOMA_UP	0.005262964	0.47722301
MORF_TERF1	0.005411688	0.47722301
REACTOME_TRANSCRIPTION_COUPLED_NER	0.005555197	0.47722301
chr2q14	0.005563771	0.47722301
V$MAX_01	0.005628594	0.47722301
chr16p11	0.005644857	0.47722301
CHIN_BREAST_CANCER_COPY_NUMBER_DN	0.005705828	0.47722301
REACTOME_REGULATION_OF_INSULIN_SECRETION_BY_ACETYLCHOLINE	0.005715528	0.47722301
CALCIUM_ION_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	0.005791776	0.47722301
TRANSCRIPTION_ELONGATION_REGULATOR_ACTIVITY	0.005835394	0.47722301
OSMAN_BLADDER_CANCER_DN	0.005842536	0.47722301
BIOCARTA_CXCR4_PATHWAY	0.005906083	0.47722301
WEBER_METHYLATED_HCP_IN_SPERM_UP	0.006206823	0.47722301
chr8p11	0.006216954	0.47722301
module_13	0.006267465	0.47722301
NIKOLSKY_BREAST_CANCER_5P15_AMPLICON	0.006279201	0.47722301
CTTTGTA,MIR-524	0.006661768	0.47722301
V$MYB_Q6	0.00672545	0.47722301
GGGCGGR_V$SP1_Q6	0.006808503	0.47722301

chr12q24	0.006810494	0.47722301
chr9q32	0.006925638	0.47722301
REACTOME_RNA_POLYMERASE_III_TRANSCRIPTION_INITIATION_FROM_TYPE	0.007084744	0.47722301
chr11q25	0.007139085	0.47722301
DER_IFN_GAMMA_RESPONSE_DN	0.007414527	0.47722301
chr1p34	0.007480348	0.47722301
chr2p12	0.007518727	0.47722301
ZHAN_MULTIPLE_MYELOMA_MS_DN	0.007768735	0.47722301
REACTOME_RESOLUTION_OF_AP_SITES_VIA_THE_SINGLE_NUCLEOTIDE_REI	0.00778489	0.47722301
BYSTRYKH_HEMATOPOIESIS_STEM_CELL_AND_BRAIN_QTL_TRANS	0.007820249	0.47722301
module_162	0.007878955	0.47722301
ACTWSNACTNY_UNKNOWN	0.007899197	0.47722301
NUCLEOTIDYLTRANSFERASE_ACTIVITY	0.008024497	0.47722301
GCM_DENR	0.008071434	0.47722301
CELL_MATRIX_JUNCTION	0.008086976	0.47722301
GRESHOCK_CANCER_COPY_NUMBER_UP	0.008100555	0.47722301
KAYO_AGING_MUSCLE_UP	0.008129232	0.47722301
GRESHOCK_CANCER_COPY_NUMBER_DN	0.008466888	0.47722301
MORF_ATRX	0.008490764	0.47722301
MOOTHA_PYR	0.008524166	0.47722301
MOOTHA_ROS	0.008524166	0.47722301
chr6p	0.008694809	0.47722301
WEBER_METHYLATED_IN_COLON_CANCER	0.008704693	0.47722301
REACTOME_P75NTR_RECRUITS_SIGNALLING_COMPLEXES	0.008754985	0.47722301
V$NMYC_01	0.008777011	0.47722301
V$ELF1_Q6	0.008806609	0.47722301
module_371	0.00897697	0.481590223
V$STAT3_02	0.009275291	0.489378808
ST_WNT_CA2_CYCLIC_GMP_PATHWAY	0.009508702	0.489378808
MORF_PHB	0.009582163	0.489378808
V$ZID_01	0.009724811	0.489378808
BIOCARTA_RARRXR_PATHWAY	0.009813981	0.489378808

Supplementary Table 7: No race-associated difference in pathways (gene expression microarray)

pathway	p-value	q-value
BRUNEAU_SEPTATION_ATRIAL	0.029059209	0.996279098
BIOCARTA_ACE2_PATHWAY	0.032564961	0.996279098
SMID_BREAST_CANCER_RELAPSE_IN_LIVER_UP	0.035072678	0.996279098
SEIKE_LUNG_CANCER_POOR_SURVIVAL	0.037160253	0.996279098
module_441	0.048071605	0.996279098
NEGATIVE_REGULATION_OF_MYELOID_CELL_DIFFERENTIATION	0.055298397	0.996279098
GNF2_MAPT	0.058385413	0.996279098
BUDHU_LIVER_CANCER_METASTASIS_DN	0.059640784	0.996279098
BIOCARTA_PLATELETAPP_PATHWAY	0.082633885	0.996279098

Supplementary Methods and Materials

Subjects and clinical assessment

Four subjects with schizophrenia and four age-, gender-, education-, and smoking habit-matched normal controls were recruited from our pool of patients and controls that we previously described (1). Patients were recruited from the outpatient psychiatric clinics of the Johns Hopkins Medical Institutions. The diagnosis was performed according to criteria of the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) (2). Normal controls were recruited from the general population through flyers posted at the Hopkins Hospital and an ad hoc advertisement placed in a local magazine. All subjects were administered the Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version (SCID-IV) (3). All patients were assessed with the Scales for the Assessment of Positive and Negative Symptoms (SAPS and SANS) (4) by a study psychiatrist who specializes in schizophrenia (NC). Subjects were excluded from the study if they had a history of traumatic brain injury with loss of consciousness for >1 h, a history of drug abuse within 6 months of the study or drug dependence within 12 months of the study, or a history of untreated major medical illnesses. The study was approved by the Johns Hopkins Institutional Review Board, and all subjects gave written consent for their participation.

Nasal biopsy and olfactory cell culture

Olfactory epithelium (OE) tissues were obtained by nasal biopsy as previously described (5). Dissociated olfactory cells were prepared as follows. First, OE tissue pieces were incubated with 2.4 U/mL Dispase II for 45 min at 37ºC, and mechanically minced into small pieces. Then, the tissue pieces were further treated with 0.25 mg/mL collagenase A for 10 min at 37ºC. Cells were gently suspended, and centrifuged to obtain pellets. Cell pellets were resuspended in D-MEM/F12 supplemented with 10% FBS and antibiotics (D-MEM/F12 medium), and tissue debris was removed by transferring only the cell suspension into a new tube. Cells were then plated on 6-well plates in fresh D-MEM/F12 medium. Cells floating or loosely attached to the plate were collected on days 2 and 7, and further incubated on 6-well plates until they reached confluency. Finally, cells were collected by gentle trypsinization, and stored in liquid nitrogen tank until further use. After recovery, cells were maintained in D-MEM/F12 medium and supplemented with fresh medium every 2-3 days. For immunofluorescence cell staining, these olfactory cells are stained nearly homogeneously with βIII-tubulin, a marker for immature neurons.

Chromatin immunoprecipitation (ChIP) and high-throughput sequencing

Chromatin immunoprecipitation (ChIP) assay was carried out with ChIP-grade antibodies against H3K4me3 (#ab8580, Abcam) and H3K27me3 (#07-449, Millipore) (6) and Magna ChIP™ G Chromatin Immunoprecipitation Kit (Millipore) following the manufacturer's protocol. Five million olfactory cells were harvested from 80-90% confluent culture, and fixed with formaldehyde. After quenching and washing with PBS, the nuclear fraction was prepared and resuspended in Nuclear lysis buffer. Suspensions were then extensively sonicated with Sonic Dismembrator Model 100 (Fisher Scientific). After centrifugation, supernatant fractions were diluted with ChIP dilution buffer, and incubated with protein G magnetic beads and anti-H3K4me3 or anti-H3K27me3 antibodies overnight at 4ºC. The samples were then washed with low-salt buffer, high-salt buffer, LiCl buffer, and TE buffer by using the magnetic separator. Finally, the samples were incubated at 62ºC overnight to reverse the cross-links and the chromatin complex was recovered from beads. DNA was purified by QIAQuick PCR purification kit (Qiagen) and eluted in EB buffer. Aliquots of equal volumes from the samples after sonication were kept as input controls. Then, genomic DNA fragments prepared by ChIP were blunted, ligated with adapter DNA, and amplified using ChIP-Seq DNA sample preparation Kit (Illumina). DNA fragments of 150 – 300 bp size were collected for the sequencing reaction. Finally, DNA samples were loaded onto a flow cell by using the Cluster Generation kit GAII and sequenced with 1G Genome analyzer (Illumina). Sequencing was performed with 8 individual samples loaded separately (4 normal controls and 4 patients with schizophrenia) on the same flow cell. We obtained 191-596 million 36-nucleotide reads per sample, among which about 50.9-78.7% of reads were mapped uniquely to locations in the reference human genome.

ChIP-seq data analysis

ChIP-seq reads were aligned to the hg18 version of the human genome and then analyzed using CisGenome algorithms (http://www.biostat.jhsph.edu/~hji/cisgenome/) (7, 8). For individual gene analysis, all ChIP-seq data are expressed as quantile-normalized (by using the "affy" package within BioConductor in the R statistical language), log2-transformed, reads observed within ±1,000 base pairs of known RefSeq transcriptional start sites (TSSs). Although included in the analysis, data from subject 1 were not included in the reference distribution for the H3K4me3 data, as they caused artifacts in the resulting distributions. Differential ChIP-seq signals were determined by standard and moderated t-statistics (Significance Analysis of Microarrays, SAM in the "siggenes" R package) along with False Discovery Rate (FDR) analysis. For pathway analysis, we used the reads within ±2,000 base pairs of known RefSeq TSSs. We first cleaned the data by log2 transformation of original counts and normalized them with quantile normalization and use of a C program. This gave us a continuous matrix with columns as subjects and rows as probes. Subsequently, we calculated the ratio of H3K4me3 signal levels to H3K27me3 signal levels (=[H3K4me3 signals]/[H3K27me3 signals]) in each RefSeq gene promoter and performed the Wald test to screen out all pathways that were significantly associated with the disease.

Microarray experiments

Total RNA was purified with RNeasy kit (Qiagen) from individual olfactory cells. The quality of RNA was 10 in RNA integrity number (RIN) score, which was assessed using a Bioanalyzer

RNA 6000 Nano Chip (Agilent Technologies). Microarray experiments were performed at the Johns Hopkins University Microarray Core Facility. Biotin-labeled cRNA was prepared by the Affymetrix 1-cycle amplification kit, and followed by hybridization and scanning. Fragmented biotin-labeled cRNA was hybridized on Affymetrix U133Plus2.0 chip at 45ºC overnight. Post-hybridization was done according to the Affymetrix instructions. The chips were stained with R-Phycoerythrin streptavidin (Invitrogen) and scanned for signal detection with the Affymetrix scanner.

Microarray data analysis

Data analysis was performed with custom code in the R statistical language and additional contributing packages within Bioconductor. Raw data were imported into a single AffyBatch object from CEL files. Additional data for probeset annotation was imported from metadata packages in the Bioconductor project. The position of probesets (3'-5' position within the mRNA) was used to assess RNA degradation in each sample after the GeneChip hybridization. RNA degradation plots were made using "AffyRNAdeg", "summaryAffyRNAdeg", and "plotAffyRNAdeg" functions in the “affy” package within Bioconductor. Both intensities in addition to ratios to the mean intensity for each array element were inspected using density plots, boxplots, and scatterplots. Intensities and ratios were visualized across the physical 2D surface of the arrays by generating GeneChip pseudo color images in order to investigate possible spatial artifacts. All raw intensities were normalized using quantile normalization-based algorithms in the “gcrma” package within Bioconductor. Following normalization, intensities and ratios were again inspected as described above. At all levels of analysis, dimension-reducing techniques including multidimensional scaling (MDS, with 1 minus Pearson's r as a distance metric), and principal components analysis (PCA) were used to identify outlier arrays and artifacts. After quality control, differential expression was determined by standard and moderated t-statistics (Significance Analysis of Microarrays, SAM in the “siggenes” R package) along with False Discovery Rate (FDR) analysis. For pathway analysis, the microarray data set was presented in a matrix similar to that used in ChIP-seq analysis: columns as subjects and rows as the probes.

Correlation analysis of ChIP-seq and microarray

ChIP-seq data were associated with expression data by cross-referencing RefSeq identifiers associated with Affymetrix probe sets with RefSeq identifiers associated with TSSs around which ChIP-seq data were tallied. This resulted in some ChIP-seq data being associated with more than one probe on the expression microarrays.

Pathway analysis

Pathway analysis was performed with 6767 gene groups extracted from the Molecular Signature Database v3.0 (MSigDB) (http://www.broadinstitute.org/gsea/msigdb/index.jsp). We consider a gene group (pathway) consisting of *G* genes and suppose that there are n SZ patient and n control samples. For each schizophrenia sample *i* and gene *g*, we compute x_{ig} = $\log_2$(normalized H3K4me3 ChIP-seq signal in TSS ± 2,000 bp) – $\log_2$(normalized H3K27me3 ChIP-seq signal in TSS ± 2,000 bp). Similarly, for each control sample *i* and gene *g*, we also compute compute y_{ig} = $\log_2$(normalized H3K4me3 ChIP-seq signal in TSS ± 2,000 bp) – $\log_2$(normalized H3K27me3 ChIP-seq signal in TSS ± 2,000 bp). Let $\mathbf{X}_i = (x_{i1}, \dots, x_{iG})'$ and $\mathbf{Y}_i = (y_{i1}, \dots, y_{iG})'$. The average histone modification signals for SZ and control group are

$$\overline{\mathbf{X}} = \frac{1}{n}\sum_{i=1}^{n}\mathbf{X}_i \quad \text{and} \quad \overline{\mathbf{Y}} = \frac{1}{n}\sum_{i=1}^{n}\mathbf{Y}_i$$

The average difference between SZ and control group is

$$\mathbf{D} = \overline{\mathbf{X}} - \overline{\mathbf{Y}} = (d_1, \dots, d_G)'$$

where

$$d_g = \frac{1}{n}\sum_{i=1}^{n} x_{ig} - \frac{1}{n}\sum_{i=1}^{n} y_{ig}$$

Here d_g is equivalent to measuring ΔK4-ΔK27 at gene *g*, where ΔK4 and ΔK27 are defined as the difference in the mean $\log_2$ ChIP-seq signals between SZ patients and control for H3K4me3 and H3K27me3, respectively. Since H3K4me3 and H3K27me3 are indicators for gene activation and repression, respectively, a positive d_g should correlate with up-regulated gene expression in SZ, and a negative d_g should correlate with down-regulated gene expression in schizophrenia. We want to test whether $\mathbf{D}$ is equal to zero, which would then imply that a pathway is not changed between SZ patients and controls. To do so, we used the generalized Wald test to assess the null hypothesis $H_0\colon \mathbf{D} = 0$ versus the alternative hypothesis $H_1\colon \mathbf{D} \neq 0$. Let $\mathbf{\Sigma}$ be the pooled sample covariance matrix of $\mathbf{X}$ and $\mathbf{Y}$, and $q = rank(\mathbf{\Sigma})$. Let $\mathbf{\Omega}$ be the pseudo-inverse of $\mathbf{\Sigma}$. The generalized Wald test computes the following test statistic:

$T = n\mathbf{D}'\mathbf{\Omega}\mathbf{D}/2$

Under the null hypothesis, the statistic above approximately follows a chi-square distribution χ_q^2 with *q* degrees of freedom. Therefore we use χ_q^2 to determine the p-value of the test. The same procedure was applied to all the gene groups (pathways), and the p-values were subsequently converted to q-values to adjust for multiple testing. The significance cut-off level was set at q=0.01, as the default choice by John Storey in their qvalue package (http://www.bioconductor.org/packages/2.9/bioc/vignettes/qvalue/inst/doc/manual.pdf).

Quantitative RT-PCR

Total RNA was isolated using RNEasy Mini kit (Qiagen) with on-column or post hoc DNase I treatment, and first-strand cDNA was synthesized with use of oligo (dT)20 primer and SuperScript III Reverse Transcriptase (both from Invitrogen). Quantitative real-time PCR was carried out with SYBR GreenER reagent (Invitrogen) on ABI PRISM® 7900HT Sequence

Detection System (Applied Biosystems). PCR was performed by the following protocol: 50°C, 2 min; 95°C, 10 min; and 95°C, 15 sec, 60°C, 1 min for 40 cycles plus a dissociation curve step at the last step to verify single amplicon in the reaction. Data were normalized by the expression levels of ACTB mRNA. Statistical analysis was performed using standard two-tailed t-test. The following gene-specific primers were used. βIII-tubulin (TUBB3) and REG3G primers are the same as those used in a previous publication (5).

MGST1, 5'-ACGTGTACGCAGAGCCCACC-3', 5'-TGGCTGTAGAGGGGTCGGGA-3'.
DAAM2, 5'-GTTCTCCAGCCCCATCCCGAAC-3', 5'-CAGACTCTGCATCGCAGCCATGG-3'.
LPXN, 5'-GCAGATGCTGGCAAGAAGCA-3', 5'-CCCCCAAGCATTGAGTCCAG-3'.
βIII-tubulin, 5'-ACGTGTGAGCTGCTCCTGTCT-3', 5'-AAAACCGTAAAACGTCAGGCC-3'
REG3G, 5'-TCCCTCCACCATCTTAAACCC-3', 5'-CAGAAATCCTGTGCTTCTTGACA-3'
β-actin, 5'- AGTCGGTTGGAGCGAGCATC -3', 5'- GGGGTGGCTTTTAGGATGGC -3'.

Immunocytochemistry

Olfactory cells were seeded on coverslips and fixed with PBS containing 4% paraformaldehyde for 15 min at room temperature. After washing with PBS, the cells were washed with PBS containing 0.1% Triton-X100 for 15 min at room temperature. After 1 h blocking in PBS containing 5% goat serum at room temperature, the cells were incubated with rabbit polyclonal anti-βIII tubulin (Covance) overnight at 4ºC. Then, after three washes with PBS, the cells were incubated for 2 h at room temperature with goat anti-rabbit IgG Alexa568 (Invitrogen). Nuclei were stained with DAPI (Invitrogen). Coverslips were mounted onto glass slides and visualized under an epifluorescence microscope (Zeiss).

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