Supplementary table 1. The characteristics of subjects in gene expression profile sequencing experiment

Sample ID	Group	Gender	Age, years	Serum uric acid, μmol/L
1	Case	Female	59	375
2	Case	Female	65	367
3	Case	Male	47	600
4	Case	Male	56	423
5	Control	Female	59	193
6	Control	Female	48	219
7	Control	Female	48	226
8	Control	Female	53	231
9	Control	Male	59	197
10	Control	Male	59	188
11	Control	Male	52	247
12	Control	Male	63	272

Note: the cases were defined as hyperuricemia status, i.e. serum uric acid (SUA) > 420 μmol/L for males and SUA > 360 μmol/L for females

Supplementary table 2. The top results of over-represented gene sets potentially related to serum uric acid using GSEA tool

Gene Set Name	Description	Genes in Gene Set (K)	Genes in Overlap (k)	k/K	FDR q-value
GO-Biological process, Molecular function					
GO_NEUROGENESIS	Generation of cells within the nervous system.	1674	218	0.13	2.47E-45
GO_NEURON_DIFFERENTIATION	The process in which a relatively unspecialized cell acquires specialized features of a neuron.	1406	183	0.13	1.47E-37
GO_TRANSCRIPTION_REGULATOR_ACTIVITY	A molecular function that controls the rate, timing and/or magnitude of transcription of genetic information. The function of transcriptional regulators is to modulate gene expression at the transcription step so that they are expressed in the right cell at the right time and in the right amount throughout the life of the cell and the organism.	1987	223	0.11	2.17E-36
GO_BIOLOGICAL_ADHESION	The attachment of a cell or organism to a substrate, another cell, or other organism. Biological adhesion includes intracellular attachment between membrane regions.	1481	181	0.12	1.04E-33
GO_SEQUENCE_SPECIFIC_DNA_BINDING	Interacting selectively and non-covalently with DNA of a specific nucleotide composition, e.g. GC-rich DNA binding, or with a specific sequence motif or type of DNA e.g. promotor binding or rDNA binding.	1691	196	0.12	1.21E-33
GO_DNA_BINDING_TRANSCRIPTION_FACTOR_ACTIVITY	Interacting selectively and non-covalently with a specific double-stranded genomic DNA sequence (sometimes referred to as a motif) within the regulatory region of a gene to modulate transcription. Regulatory regions include promoters (proximal and distal) and enhancers. Genes are transcriptional units, and include bacterial operons.	1529	179	0.12	4.71E-31

GO_CELL_PROJECTION_ORGANIZATION	A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of a prolongation or process extending from a cell, e.g. a flagellum or axon.	1588	178	0.11	1.47E-28
GO_REGULATORY_REGION_NUCLEIC_ACID_BINDING	Interacting selectively and non-covalently with a nucleic acid region that regulates a nucleic acid-based process. Such processes include transcription, DNA replication, and DNA repair.	1472	169	0.11	2.98E-28
GO_CELL_CELL_ADHESION	The attachment of one cell to another cell via adhesion molecules.	884	124	0.14	4.00E-28
GO_CELL_MORPHOGENESIS	The developmental process in which the size or shape of a cell is generated and organized.	1041	136	0.13	6.86E-28
GO_CELL_CELL_SIGNALING	Any process that mediates the transfer of information from one cell to another. This process includes signal transduction in the receiving cell and, where applicable, release of a ligand and any processes that actively facilitate its transport and presentation to the receiving cell. Examples include signaling via soluble ligands, via cell adhesion molecules and via gap junctions.	1809	191	0.11	1.12E-27
GO_ANIMAL_ORGAN_MORPHOGENESIS	Morphogenesis of an animal organ. An organ is defined as a tissue or set of tissues that work together to perform a specific function or functions. Morphogenesis is the process in which anatomical structures are generated and organized. Organs are commonly observed as visibly distinct structures, but may also exist as loosely associated clusters of cells that work together to perform a specific function or functions.	1084	137	0.13	1.03E-26
GO_CELL_CELL_ADHESION_VIA_PLASMA_MEMBRANE_ADHESION_MOLECULES	The attachment of one cell to another cell via adhesion molecules that are at least partially embedded in the plasma membrane.	277	65	0.23	1.18E-26

GO_HOMOPHILIC_CELL_ADHESION_VIA_PLASMA_MEMBRANE_ADHESION_MOLECULES	The attachment of a plasma membrane adhesion molecule in one cell to an identical molecule in an adjacent cell.	168	51	0.30	2.42E-26
GO_POSITIVE_REGULATION_OF_CELLULAR_BIOSYNTHETIC_PROCESS	Any process that activates or increases the frequency, rate or extent of the chemical reactions and pathways resulting in the formation of substances, carried out by individual cells.	1967	197	0.10	8.46E-26
GO_NEURON_DEVELOPMENT	The process whose specific outcome is the progression of a neuron over time, from initial commitment of the cell to a specific fate, to the fully functional differentiated cell.	1143	139	0.12	1.48E-25
GO_CELL_MORPHOGENESIS_INVOLVED_IN_DIFFERENTIATION	The change in form (cell shape and size) that occurs when relatively unspecialized cells, e.g. embryonic or regenerative cells, acquire specialized structural and/or functional features that characterize the cells, tissues, or organs of the mature organism or some other relatively stable phase of the organism's life history.	753	108	0.14	2.59E-25
GO_REGULATION_OF_NERVOUS_SYSTEM_DEVELOPMENT	Any process that modulates the frequency, rate or extent of nervous system development, the origin and formation of nervous tissue.	957	124	0.13	3.76E-25
GO_CYTOSKELETON_ORGANIZATION	A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of cytoskeletal structures.	1396	156	0.11	5.78E-25
GO_CYTOSKELETAL_PROTEIN_BINDING	Interacting selectively and non-covalently with any protein component of any cytoskeleton (actin, microtubule, or intermediate filament cytoskeleton).	979	125	0.13	8.09E-25
Canonical pathways					
REACTOME_NEURONAL_SYSTEM	Neuronal System	410	65	0.16	3.48E-16
REACTOME_EXTRACELLULAR_MATRIX_ORGANIZATION	Extracellular matrix organization	301	45	0.15	6.01E-10

REACTOME_SIGNALING_BY_RHO_GTPASES	Signaling by Rho GTPases	454	56	0.12	1.73E-09
REACTOME_TRANSMISSION_ACROSS_CHEMICAL_SYNAPSES	Transmission across Chemical Synapses	269	41	0.15	1.73E-09
NABA_MATRISOME	Ensemble of genes encoding extracellular matrix and extracellular matrix-associated proteins	1026	94	0.09	4.21E-09
REACTOME_RHO_GTPASE_CYCLE	Rho GTPase cycle	140	28	0.20	4.89E-09
REACTOME_DEVELOPMENTAL_BIOLOGY	Developmental Biology	1131	96	0.08	1.17E-07
PID_RHOA_REG_PATHWAY	Regulation of RhoA activity	46	15	0.33	1.61E-07
REACTOME_NERVOUS_SYSTEM_DEVELOPMENT	Nervous system development	580	60	0.10	1.61E-07
REACTOME_G_ALPHA_12_13_SIGNALLING_EVENTS	G alpha (12/13) signalling events	80	19	0.24	2.71E-07
NABA_CORE_MATRISOME	Ensemble of genes encoding core extracellular matrix including ECM glycoproteins, collagens and proteoglycans	275	37	0.13	2.71E-07
REACTOME_NRAGE_SIGNALS_DEATH_THROUGH_JNK	NRAGE signals death through JNK	59	16	0.27	6.13E-07
KEGG_CALCIUM_SIGNALING_PATHWAY	Calcium signaling pathway	178	28	0.16	7.41E-07
KEGG_AXON_GUIDANCE	Axon guidance	129	23	0.18	1.48E-06
REACTOME_SIGNALING_BY_RECEPTOR_TYROSINE_KINASES	Signaling by Receptor Tyrosine Kinases	504	52	0.10	1.49E-06

WP_PREIMPLANTATION_EMBRYO	Preimplantation Embryo	60	15	0.25	4.83E-06
REACTOME_HEMOSTASIS	Hemostasis	678	62	0.09	4.99E-06
WP_PATHWAYS_REGULATING_HIPPO_SIGNALING	Pathways Regulating Hippo Signaling	99	19	0.19	6.70E-06
REACTOME_NEUROTRANSMITTER_RECEPTORS_AND_POSTSYNAPTIC_SIGNAL_TRANSMISSION	Neurotransmitter receptors and postsynaptic signal transmission	205	28	0.14	1.17E-05
REACTOME_CELL_DEATH_SIGNALLING_VIA_NRAGE_NRIF_AND_NADE	Cell death signalling via NRAGE, NRIF and NADE	76	16	0.21	1.82E-05

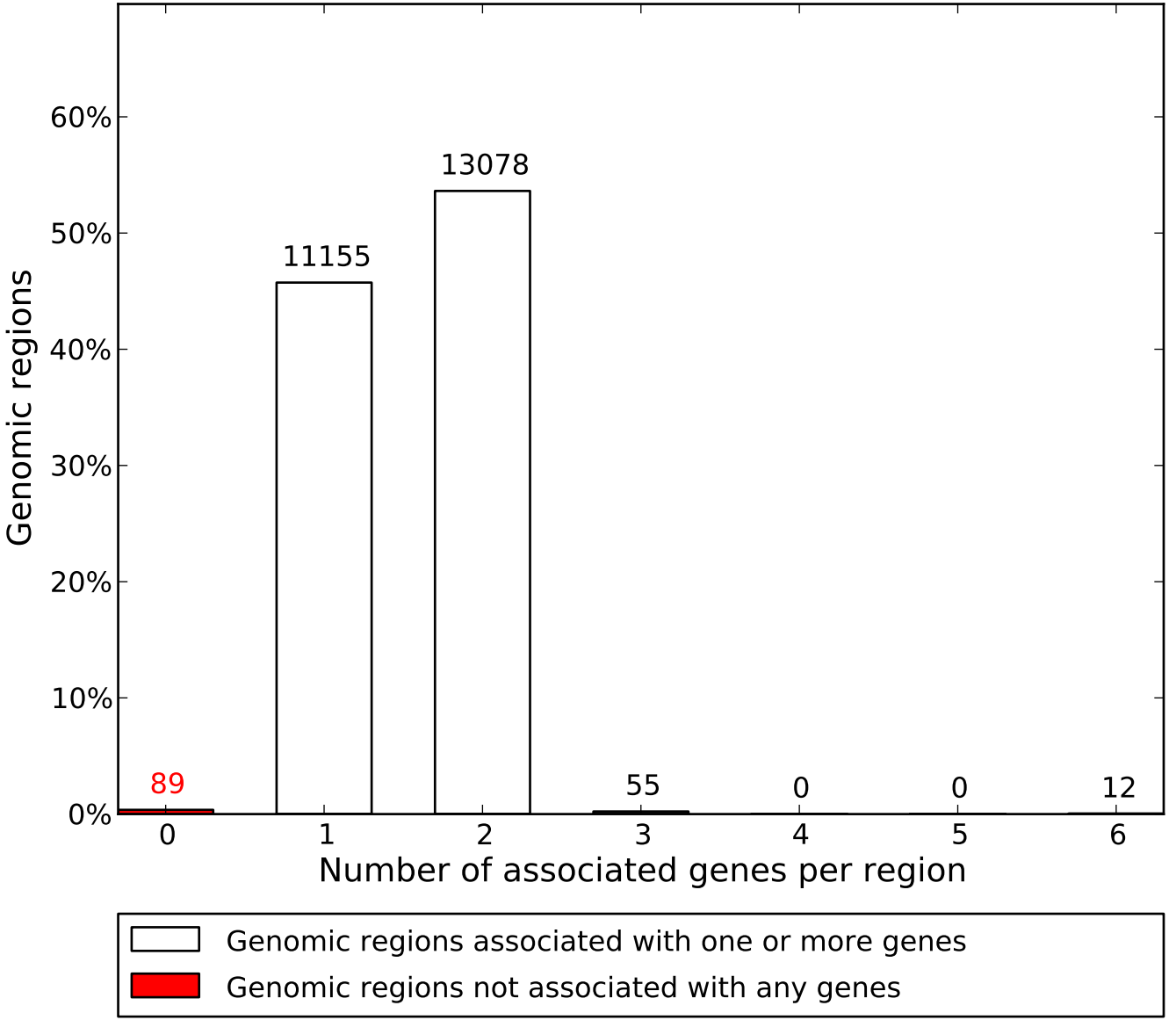
Note: Collections included Canonical pathways of C2: curated gene sets, and GO biological process and GO molecular function of C5: ontology gene sets in MSigDB database

The top 20 Canonical pathways gene sets and 20 GO gene sets (FDR q-value < 0.01) were presented in the table

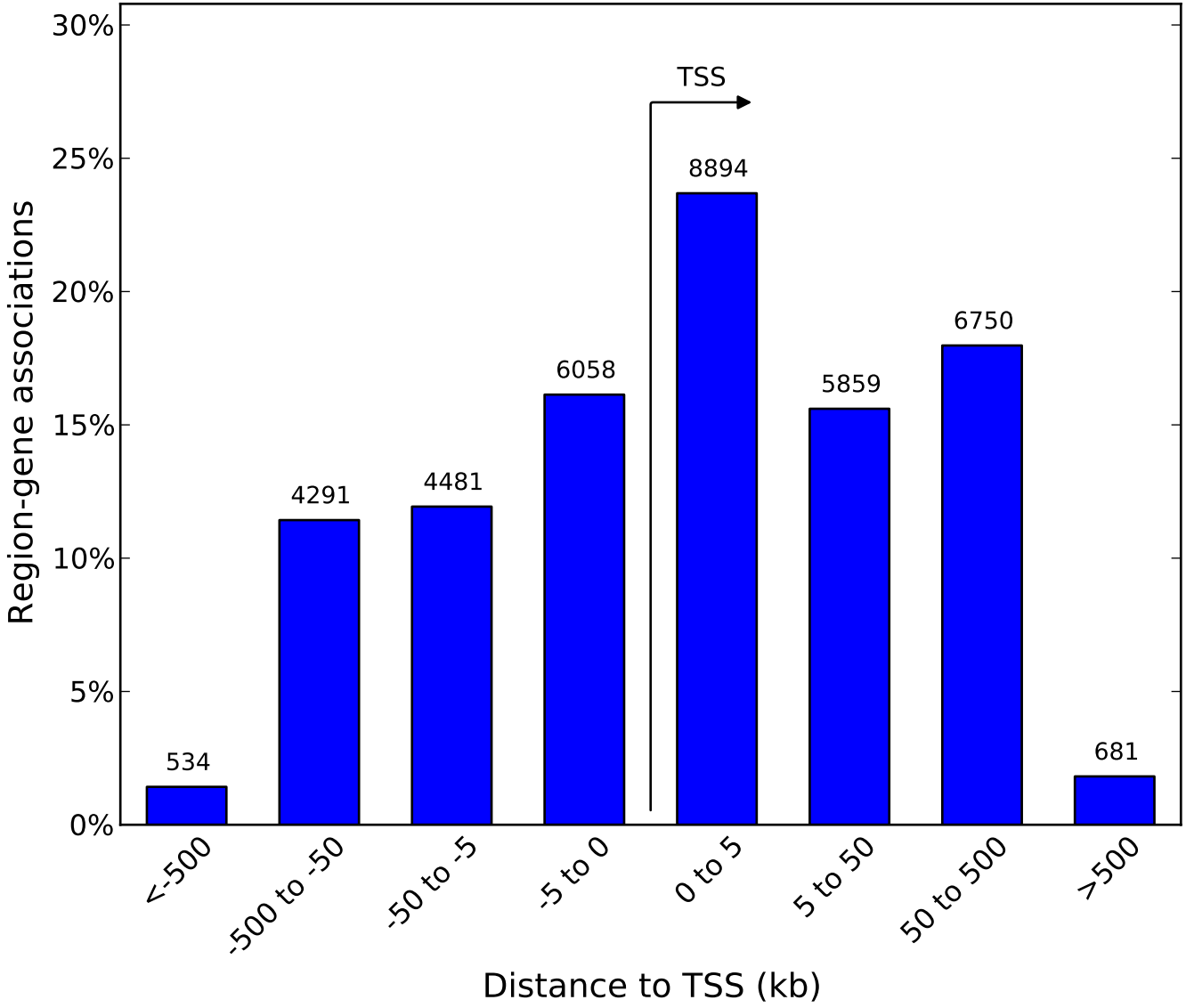
Genes in Overlap (k): the number of genes in the intersection of the query set with a set from MSigDBet

K: the number of genes in the set from MSigDB

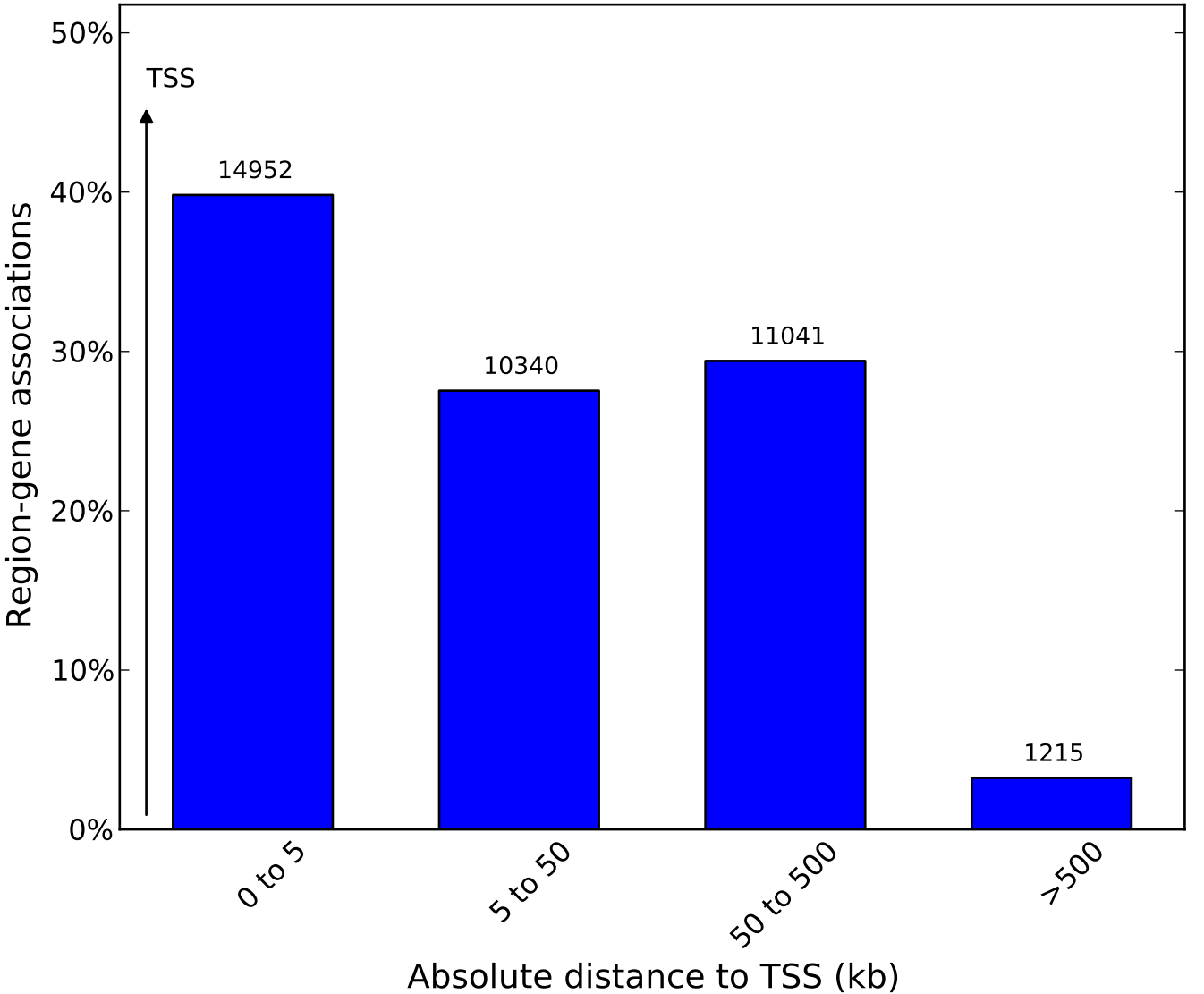
FDR q-value: the false discovery rate analog of hypergeometric P-value after correction for multiple hypothesis testing according to Benjamini and Hochberg



Supplementary figure 1



Supplementary figure 2



Supplementary figure 3