**The process of whole exome sequencing and quality control**

Peripheral blood was collected from all participants, and genomic DNA was extracted according to a standard phenol–chloroform procedure. Exome sequencing was performed by Macrogen (http://www.macrogen.com/), a commercial service. DNA sample was prepared according to the Illumina Protocol. Targeted enrichment was performed with TruSeq Exome Enrichment Kit optimized for Illumina sequencing. Briefly, genomic DNA was sheared to 350-400 base pair using Illumina adapters. The fragment was end repaired and polyA was ligated to the 3'and 5' end and Illumina adapters. The size selected product was PCR amplified, and the final product was validated using the Agilent Bioanalyzer. Two steps of hybridization and wash were needed for construction. PCR was used to amplify the enriched DNA library for sequencing which produced 101bp end reads, approximately 6-10 billion base calls were generated for each sample. PCR was performed with the same PCR primer cocktail used in TruSeq DNA Sample Preparation. The Enrichment Kit is designed to cover 62 Mb exomic sequences. Quality control of raw data was conducted by FastQC software(1). Raw read data were visualized using the Integrative Genome Viewer (IGV)(2).

**Quality control (QC):**

*Individual level QC:* Individual level quality control was conducted on raw and clean variant to make sure avoiding false positive variants. A suite of per-individual metrics, which included the total number of alternate alleles, dbSNP coverage (build137), and Transition/Transversion (Ti/Tv) ratio, and variant quality recalibration (VQSR) were calculated. From available exome data, we extracted common variants and estimated per-individual heterozygosity, pairwise relatedness, and sex-check using PLINK(3). We also use EIGENSOFT (4) to perform population stratification analysis. After calculating all of metrics above, we remove 6 samples (3 cases and 3 controls), and delete these samples for following analysis.

*Variants QC:* Variants quality control was conducted by KGGSeq software (5). These parameters were included (1) Variants were kept if the minimum overall sequencing quality scores≧50 (--seq-qual 50) and the minimum overall mapping quality score≧20 (--seq-mq 20); (2) The minimal genotyping quality per genotype≧30 (--gty-qual 30) and the minimal read depth per genotype≧30 (--gty-qual 30); (3) The fraction of the reads carrying alternative allele≦5% at a reference-allele homozygous genotype (--gty-af-ref 0.05), the fraction of the reads carrying alternative allele≧25% at a heterozygous genotype (--gty-af-het 0.25), and the fraction of the reads carrying alternative allele≧75% at a alternative-allele homozygous genotype(--gty-af-alt 0.75); (4) Minimal observed number of non-missing genotypes in all samples as 50 (--min-obs 50); (5) Variants in controls with the Hardy-Weinberg test p value≧0.00001 (--hwe-control 1.0E-5); (6) Variants with "FILTER" matching the VQSR labels.

**References**

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| --- | --- | --- |
| **Supplementary Table1** 15 brain regions were used to compute the coexpression network | | |
| STR | Striatum |  |
| MD | Mediodorsal nucleus of thalamus |  |
| AMY | Amygdaloid complex |  |
| HIP | Hippocampus |  |
| A1C | Primary auditory cortex | Neocortical regions |
| M1C | Primary motor cortex |
| S1C | Primary somatosensory cortex |
| V1C | Primary visual cortex |
| DFC | Dorsolateral prefrontal cortex |
| MFC | Anterior (rostral) cingulate (medial prefrontal) cortex |
| OFC | Orbital frontal cortex |
| VFC | Ventrolateral prefrontal cortex |
| ITC | Inferolateral temporal cortex |
| STC | Posterior (caudal) superior temporal cortex |
| IPC | Posteroinferior (ventral) parietal cortex |

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Supplementary Table 2**  The correlation coefficient among 5 original FA variables | | | | | | | |
| Brain areas | PUN\_R | PUN\_L | ACC\_L | ACC\_R | EN |  |
| PUN\_R | 1 | 0.85 | 0.58 | 0.585 | 0.682 |  |
| PUN\_L | 0.85 | 1 | 0.617 | 0.608 | 0.692 |  |
| ACC\_L | 0.58 | 0.617 | 1 | 0.632 | 0.504 |  |
| ACC\_R | 0.585 | 0.608 | 0.632 | 1 | 0.52 |  |
| EN | 0.682 | 0.692 | 0.504 | 0.52 | 1 |  |

PUN: precuneus; ACC: anterior cingulate cortex; EN: extra-nuclear; R: right; L: left

**Supplementary Table3** The correlation coefficient between the first component and any of 5 original FA

|  |  |  |  |
| --- | --- | --- | --- |
| First Component | Brain regions | Coefficients |  |
| PC1 | ACC\_L | -0.625 | Case |
| PC1 | ACC\_R | -0.602 | Case |
| PC1 | EN | -0.767 | Case |
| PC1 | PUN\_L | -0.976 | Case |
| PC1 | PUN\_R | -0.936 | Case |
| PC1 | ACC\_L | -0.566 | Control |
| PC1 | ACC\_R | -0.569 | Control |
| PC1 | EN | -0.673 | Control |
| PC1 | PUN\_L | -0.952 | Control |
| PC1 | PUN\_R | -0.928 | Control |

PUN: precuneus; ACC: anterior cingulate cortex; EN: extra-nuclear; R: right; L: left

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Supplementary Table 4** Subnetwork with 207 genes | | | | | |  |  |
| SF3A3 | MICA | LIPC | SUMO2 | PSMB8 | UBASH3B | NGEF | TRIM8 |
| CHRM4 | GGA3 | MGRN1 | RERE | PSMB3 | GRHPR | PCF11 | EIF2B4 |
| INPP5B | GLYCTK | EEF1A2 | TRIM39 | UBE2D2 | DNAJA3 | TSEN2 | FANCL |
| TRIM10 | PTBP2 | SMARCD1 | ZKSCAN4 | RNF5 | SERPING1 | ZCCHC7 | RRAS |
| ENO1 | DNAJA1 | PBRM1 | HIST1H2BE | HSPD1 | MATR3 | EIF2AK2 | IRF3 |
| OTUD7B | DLST | PLCB2 | LSM1 | AMFR | PCGF6 | ASH2L | ARHGAP1 |
| RNF165 | ALAS1 | PLCL1 | CLIC1 | PTN | HIST1H4C | PSMD6 |  |
| LASP1 | L3MBTL2 | ISYNA1 | HLA-B | GPD1 | HIST1H4B | BAG4 |  |
| MED19 | HIST1H1E | NUDT21 | SEC11A | PRKCD | HIST1H4A | BCL2L12 |  |
| MAGOH | EHMT2 | CLP1 | HIST1H4I | FANCA | HIST1H4E | TSSK6 |  |
| HLA-G | CSNK2B | DFNA5 | SETD8 | RAF1 | HIST1H4D | LTB |  |
| HLA-F | LSM2 | GIGYF2 | SETD7 | CHEK1 | HIST1H4H | PLEKHO1 |  |
| VPS37B | HSPA1L | SREBF2 | PRPF3 | EP300 | HIST1H4J | TAF5 |  |
| ALDH5A1 | DCP1B | NFKBIA | UBA52 | AKT3 | HIST1H4K | SUPT7L |  |
| THOC7 | NRGN | RBBP5 | RPL13A | HIST1H3I | HIST1H4L | HIST1H2BF |  |
| PPM1G | ST13 | CXXC1 | HIST1H3A | HIST1H3H | NRBP1 | HIST1H2BC |  |
| PUF60 | MYO5B | DHX16 | HIST1H2AB | HIST1H3G | CPNE7 | HIST1H2BI |  |
| CTNND1 | PACSIN3 | GTF2H4 | FXR1 | ZNF408 | CDK2AP1 | EIF4E2 |  |
| ACTR1A | PPARG | HSPA1A | RFWD3 | RPL29 | NFKBIE | HIST1H2BM |  |
| RANGAP1 | ING1 | PSME4 | HIST1H3D | RPLP1 | DCP1A | ACVR2B |  |
| GLG1 | MKL1 | LTA | HIST1H3B | RPS11 | TNF | TRIM26 |  |
| TRIM31 | SFMBT1 | DNAJB1 | HIST1H3C | RPS13 | SYNJ1 | MDC1 |  |
| TCF19 | HIST1H2BA | ATXN7 | PRMT1 | GNL3 | ZBTB5 | ADIPOR2 |  |
| FSD2 | HIST1H2AA | NFX1 | PSMA6 | BAG1 | SRF | HSPE1 |  |
| F2 | DDB2 | TRIM54 | HLA-C | HSP90AB1 | RBX1 | DENR |  |
|  | PBX3 | CHCHD2 | PIAS2 | HSPA1B | CNTN2 | IDH3B |  |
|  | NCAN | HIST1H2BB | CCHCR1 | HIST1H3J | LIPG | PSPH |  |
|  |  | INHBA | RBL2 | CDC5L | VARS | YLPM1 |  |
|  |  | DIP2A | PSMB9 | TTC23 | DGKI | MAD1L1 |  |
|  |  |  | TRIM27 | TAP1 | DGKZ | EI24 |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Supplementary Table 5** Genes in four modules for PGC-1 | | | | |
| Yellow module | Blue module | Brown module | Turquoise module | Turquoise module |
| BCL2L12 | HSP90AB1 | RPS11 | EEF1A2 | TAF5 |
| CDK2AP1 | DNAJA1 | RPL29 | LASP1 | NFX1 |
| CLIC1 | CHCHD2 | UBA52 | ACTR1A | GIGYF2 |
| DGKI | PSMB3 | RPL13A | NCAN | MKL1 |
| ENO1 | MATR3 | RPLP1 | SREBF2 | LIPG |
| GRHPR | NUDT21 | RPS13 | PBX3 | PCF11 |
| HLA-B | SUMO2 | PPM1G | CTNND1 | ZCCHC7 |
| HLA-C | UBE2D2 | PUF60 | DNAJB1 | CLP1 |
| HLA-F | HSPD1 | PRMT1 | NGEF | PRPF3 |
| HLA-G | PTBP2 | RNF5 | AMFR | CHEK1 |
| IRF3 | RBX1 | LSM2 | IDH3B | SETD8 |
| L3MBTL2 | EI24 | ISYNA1 | SMARCD1 | DCP1B |
| LTB | ST13 | CSNK2B | AKT3 | MDC1 |
| MICA | ALAS1 | EHMT2 | PBRM1 | EIF2AK2 |
| NFKBIA | TRIM8 | PLEKHO1 | ZBTB5 | SFMBT1 |
| PIAS2 | GLG1 | MED19 | RANGAP1 | ZKSCAN4 |
| PSMB8 | SF3A3 | VPS37B | VARS | DFNA5 |
| PSMB9 | THOC7 | CXXC1 | RAF1 | ACVR2B |
| PSPH | GNL3 | ADIPOR2 | NRBP1 | FANCA |
| PTN | CDC5L | SEC11A | DLST | TSEN2 |
| RRAS | LSM1 | CNTN2 | YLPM1 | DIP2A |
| SERPING1 | FXR1 | TRIM26 | RNF165 | CPNE7 |
| TAP1 | HSPE1 | GTF2H4 | DNAJA3 | DGKZ |
| TTC23 | DENR | TRIM39 | MGRN1 | PLCB2 |
|  | PSMA6 | SUPT7L | SRF | HIST1H4E |
|  | EIF4E2 | EIF2B4 | RERE | GPD1 |
|  | MAGOH | BAG4 | NRGN | HIST1H2BC |
|  | ASH2L | MAD1L1 | ING1 | INHBA |
|  | RBBP5 | NFKBIE | TRIM27 | HIST1H4H |
|  | BAG1 | DDB2 | EP300 | ATXN7 |
|  | FANCL | SYNJ1 | RBL2 | PRKCD |
|  | ARHGAP1 | ZNF408 | GGA3 | MYO5B |
|  | PSMD6 | PLCL1 | DHX16 | TRIM54 |
|  | SETD7 | CCHCR1 | ALDH5A1 | PPARG |
|  | UBASH3B | HIST1H3D | PSME4 | FSD2 |
|  | PACSIN3 | OTUD7B | CHRM4 |  |
|  | INPP5B | HIST1H4I | TCF19 |  |
|  | PCGF6 | HIST1H2BF | RFWD3 |  |
|  | GLYCTK | TSSK6 | DCP1A |  |
|  |  |  |  |  |

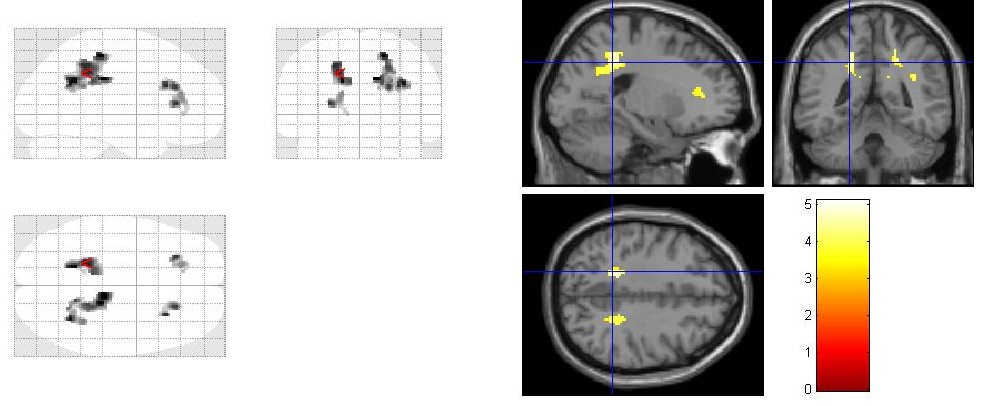
**Supplementary Table 6** GO Enrichment Analysis of Genes in each module

|  |  |  |
| --- | --- | --- |
| **GO Terms** | **Raw P value** | **Adjusted P Value** |
| **Yellow module** |  |  |
| antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-dependent | 1.60e-11 | 6.50e-09 |
| antigen processing and presentation of exogenous peptide antigen via MHC class I | 2.33e-11 | 9.46e-09 |
| antigen processing and presentation of peptide antigen via MHC class I | 1.26e-10 | 5.12e-08 |
| innate immune response | 3.15e-09 | 1.28e-06 |
| MHC class I receptor activity | 1.23e-08 | 7.87e-07 |
| MHC class I protein complex | 5.69e-11 | 4.38e-09 |
| MHC protein complex | 1.07e-09 | 8.24e-08 |
| **Blue module** |  |  |
| lysine N-methyltransferase activity | 0.0001 | 0.0008 |
| histone-lysine N-methyltransferase activity | 0.0001 | 0.0008 |
| macromolecular complex | 8.77e-05 | 0.0006 |
| **Brown module** |  |  |
| SRP-dependent cotranslational protein targeting to membrane | 3.68e-09 | 4.71e-07 |
| viral infectious cycle | 3.09e-08 | 2.17e-06 |
| histonemethyltransferase activity | 0.0001 | 0.0029 |
| proteinmethyltransferase activity | 0.0003 | 0.0043 |
| N-methyltransferase activity | 0.0003 | 0.0043 |
| S-adenosylmethionine-dependent methyltransferase activity | 0.0013 | 0.0123 |
| histone-lysine N-methyltransferase activity | 0.0032 | 0.0199 |
| lysine N-methyltransferase activity | 0.0035 | 0.0199 |
| protein-lysine N-methyltransferase activity | 0.0035 | 0.0199 |
| **Turquoise module** |  |  |
| RNA polymerase II core promoter proximal region sequence-specific DNA binding | 0.0001 | 0.0043 |
| core promoter proximal region DNA binding | 0.0005 | 0.0092 |
| phosphotransferase activity, alcohol group as acceptor | 0.0010 | 0.0158 |
| intracellular organelle | 9.98e-08 | 1.77e-06 |

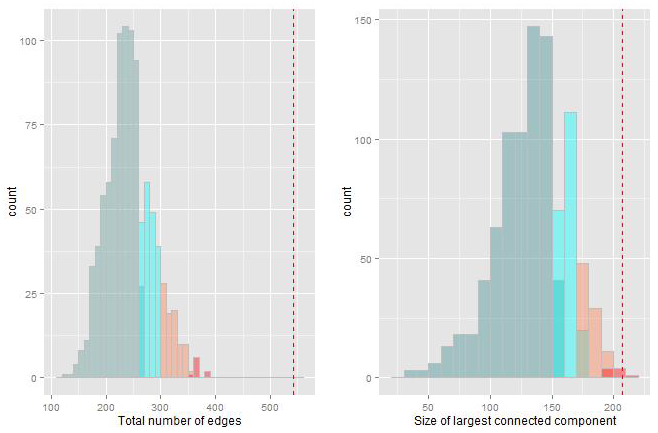
**Supplementary Figure 1** The plot of the first two principal components of 93 patients with schizophrenia and 134 controls

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**Supplementary Figure 2**  FA was significantly reduced in the left and right anterior cingulate cortex, left and right precuneus and extra-nuclear in patients with schizophrenia compared to controls in schizophrenic patients compared to controls (FDR corrected *p* < 0.01, cluster size ≥ 100).



**Supplementary Figure 3** The histograms are colored based on different percentiles: 70% (cyan), 90% (pink) and 99% (red), red dashed line shows the parameters of the sub-network in question.



**Supplementary Figure 4** Temporal patterns of gene expression as summarized by the average expression level of genes in each module.

