**Supplementary Tables**

**Supplementary Table S1.** The 11 criteria for substance use disorders.

| **No.** | **Categories of Behavior** | **Criteria for Substance Use Disorders (SUD)\*** |
| --- | --- | --- |
| 1 | Impaired control | Used larger amounts or longer: Taking the drug in greater quantities or over prolonged periods of time |
| 2 | Repeated attempts to control use and/or quit: Wanting to cut or avoid using the substance, but they haven't been successful |
| 3 | Much time spent using: Spending a lot of time to get, using, or recover from substance using |
| 4 | Craving: Cravings and encourages the substance to be used |
| 5 | Social impairment | Activities given up to use: Not able to do what you can do at home, at work, or at school that you once liked because of substance use |
| 6 | Social or interpersonal problems related to use: Continuing to use, even though it creates issues in your relationships or conflicts with others |
| 7 | Neglected major roles to use: Giving up and refusing to perform significant social, occupational or recreational functions as a result of substance use |
| 8 | Risky use | Hazardous use: Using substances again and again, including though you or others are in danger |
| 9 | Social or interpersonal problems related to use: Continuing to use, even though you know that you have a physical or psychological condition which may have been triggered or exacerbated by the substance |
| 10 | Pharmacological indicators | Tolerance: Need more substance to have the effect you like |
| 11 | Withdrawal: Development of withdrawal symptoms and signs of withdrawal, which can be eased by taking more of the substance |

**Supplementary Table S2.** Genetic information and results for Hardy-Weinberg equilibrium tests of the 14 selected SNPs.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CHR | Position | Locus | SNP | Function | Minor Allele | Major Allele | MAF | PHWE1 | PHWE2 |
| 5 | 141623077 | *HDAC3* | rs145973883 | intron | A | C | 0.11  | 0.66  | 0.32  |
| 5 | 141624420 | *HDAC3* | rs56221992 | intron | T | C | 0.11  | 0.78  | 0.91  |
| 5 | 141624764 | *HDAC3* | rs11741808 | intron | G | A | 0.10  | 0.17  | 0.49  |
| 5 | 141626120 | *HDAC3* | rs2547547 | intron | G | A | 0.10  | 0.43  | 1.00  |
| 5 | 141626786 | *HDAC3* | rs188494342 | intron | G | A | 0.17  | 0.84  | 0.77  |
| 5 | 141626788 | *HDAC3* | rs374763242 | intron | G | A | 0.09  | 0.52  | 0.90  |
| 5 | 141631309 | *HDAC3* | rs2735188 | intron | C | T | 0.10  | 0.21  | 0.34  |
| 5 | 141631779 | *HDAC3* | rs2545025 | intron | C | A | 0.10  | 0.09  | 0.72  |
| 5 | 141632446 | *HDAC3* | rs76686252 | intron | A | G | 0.08  | 0.09  | 0.65  |
| 5 | 141632663 | *HDAC3* | rs12655779 | intron | G | A | 0.10  | 0.13  | 1.00  |
| 5 | 141634927 | *HDAC3* | rs2530223 | coding-synonymous | C | T | 0.35  | 0.52  | 0.96  |
| 5 | 141636721 | *HDAC3* | rs1421896 | intron | G | T | 0.32  | 0.90  | 0.74  |
| 5 | 141637772 | *HDAC3* | rs976552 | intron | C | A | 0.16  | 0.75  | 0.65  |
| 5 | 141639543 | *HDAC3* | rs14251 | untranslated-3 | A | C | 0.14  | 0.75  | 0.46  |

SNP, single nucleotide polymorphism; CHR, chromosome; MAF, minor allele frequency; HWE, Hardy-Weinberg equilibrium. PHWE1: *P* value for HWE tests conducted in cases; PHWE2: *P* value for HWE tests conducted in controls.

**Supplementary Table S3.** Detailed results of the single marker-based association analyses.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CHR | SNP | A1 | A2 | TEST | AFF | UNAFF | χ2 | DF | *P* |
| 5 | rs145973883 | A | C | GENO | 16/236/969 | 30/428/1870 | 0.477  | 2 | 0.788  |
| 5 | rs145973883 | A | C | ALLELIC | 268/2174 | 488/4168 | 0.410  | 1 | 0.522  |
| 5 | rs56221992 | T | C | GENO | 15/256/950 | 26/437/1865 | 2.600  | 2 | 0.273  |
| 5 | rs56221992 | T | C | ALLELIC | 286/2156 | 489/4167 | 2.408  | 1 | 0.121  |
| 5 | rs11741808 | G | A | GENO | 15/198/1008 | 26/413/1889 | 1.363  | 2 | 0.506  |
| 5 | rs11741808 | G | A | ALLELIC | 228/2214 | 465/4191 | 0.769  | 1 | 0.380  |
| 5 | rs2547547 | G | A | GENO | 15/218/988 | 21/401/1906 | 1.113  | 2 | 0.573  |
| 5 | rs2547547 | G | A | ALLELIC | 248/2194 | 443/4213 | 0.749  | 1 | 0.387  |
| 5 | rs188494342 | G | A | GENO | 35/353/833 | 67/671/1590 | 0.003  | 2 | 0.998  |
| 5 | rs188494342 | G | A | ALLELIC | 423/2019 | 805/3851 | 0.001  | 1 | 0.973  |
| 5 | rs374763242 | G | A | GENO | 14/213/994 | 18/384/1926 | 1.839  | 2 | 0.399  |
| 5 | rs374763242 | G | A | ALLELIC | 241/2201 | 420/4236 | 1.365  | 1 | 0.243  |
| 5 | rs2735188 | C | T | GENO | 17/216/988 | 26/399/1903 | 0.709  | 2 | 0.701  |
| 5 | rs2735188 | C | T | ALLELIC | 250/2192 | 451/4205 | 0.547  | 1 | 0.460  |
| 5 | rs2545025 | C | A | GENO | 19/217/985 | 22/394/1912 | 3.132  | 2 | 0.209  |
| 5 | rs2545025 | C | A | ALLELIC | 255/2187 | 438/4218 | 1.948  | 1 | 0.163  |
| 5 | rs76686252 | A | G | GENO | 13/177/1031 | 14/316/1998 | 2.931  | 2 | 0.231  |
| 5 | rs76686252 | A | G | ALLELIC | 203/2239 | 344/4312 | 1.925  | 1 | 0.165  |
| 5 | rs12655779 | G | A | GENO | 19/223/979 | 21/402/1905 | 3.759  | 2 | 0.153  |
| 5 | rs12655779 | G | A | ALLELIC | 261/2181 | 444/4212 | 2.376  | 1 | 0.123  |
| 5 | rs2530223 | C | T | GENO | 134/557/530 | 292/1068/968 | 2.286  | 2 | 0.319  |
| 5 | rs2530223 | C | T | ALLELIC | 825/1617 | 1652/3004 | 2.031  | 1 | 0.154  |
| 5 | rs1421896 | G | T | GENO | 129/540/552 | 237/1001/1090 | 0.843  | 2 | 0.656  |
| 5 | rs1421896 | G | T | ALLELIC | 798/1644 | 1475/3181 | 0.734  | 1 | 0.392  |
| 5 | rs976552 | C | A | GENO | 28/327/866 | 65/631/1632 | 0.869  | 2 | 0.648  |
| 5 | rs976552 | C | A | ALLELIC | 383/2059 | 761/3895 | 0.517  | 1 | 0.472  |
| 5 | rs14251 | A | C | GENO | 28/327/866 | 43/518/1767 | 10.370  | 2 | 0.006  |
| 5 | rs14251 | A | C | ALLELIC | 383/2059 | 604/4052 | 9.836  | 1 | 0.002  |

SNP, single nucleotide polymorphism; CHR, chromosome; A1, tested allele (minor allele); A2, major allele; GENO, genotypic; AFF, counts for genotypes or alleles for patients; UNAFF, counts for genotypes or alleles for controls; DF, degree(s) of freedom.

**Supplemental Table S4.** The effects of SNP rs14251 on target gene *HDAC3*’s expression

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Gene | SNP | Ref\_allele | Alt\_allele | *P*-Value | NES | T-statistic | Tissue |
| *HDAC3* | rs14251 | C | A | 0.004  | 0.0800  | 2.90  | Esophagus - Mucosa |
| *HDAC3* | rs14251 | C | A | 0.015  | 0.0960  | 2.50  | Testis |
| *HDAC3* | rs14251 | C | A | 0.035  | -0.1100  | -2.10  | Brain - Frontal Cortex (BA9) |
| *HDAC3* | rs14251 | C | A | 0.037  | 0.1100  | 2.10  | Pituitary |
| *HDAC3* | rs14251 | C | A | 0.066  | 0.0400  | 1.80  | Skin - Not Sun Exposed (Suprapubic) |
| *HDAC3* | rs14251 | C | A | 0.110  | 0.0360  | 1.60  | Cells - Cultured fibroblasts |
| *HDAC3* | rs14251 | C | A | 0.110  | -0.0400  | -1.60  | Muscle - Skeletal |
| *HDAC3* | rs14251 | C | A | 0.150  | 0.0820  | 1.50  | Cells - EBV-transformed lymphocytes |
| *HDAC3* | rs14251 | C | A | 0.230  | -0.1000  | -1.20  | Brain - Amygdala |
| *HDAC3* | rs14251 | C | A | 0.230  | 0.0390  | 1.20  | Breast - Mammary Tissue |
| *HDAC3* | rs14251 | C | A | 0.250  | -0.0530  | -1.20  | Heart - Atrial Appendage |
| *HDAC3* | rs14251 | C | A | 0.290  | 0.0230  | 1.10  | Whole Blood |
| *HDAC3* | rs14251 | C | A | 0.300  | 0.0220  | 1.00  | Skin - Sun Exposed (Lower leg) |
| *HDAC3* | rs14251 | C | A | 0.310  | -0.0780  | -1.00  | Ovary |
| *HDAC3* | rs14251 | C | A | 0.310  | 0.0460  | 1.00  | Spleen |
| *HDAC3* | rs14251 | C | A | 0.330  | -0.0490  | -0.98  | Adrenal Gland |
| *HDAC3* | rs14251 | C | A | 0.350  | -0.0370  | -0.93  | Heart - Left Ventricle |
| *HDAC3* | rs14251 | C | A | 0.390  | 0.0490  | 0.87  | Artery - Coronary |
| *HDAC3* | rs14251 | C | A | 0.410  | -0.0450  | -0.83  | Brain - Hypothalamus |
| *HDAC3* | rs14251 | C | A | 0.440  | -0.0420  | -0.78  | Small Intestine - Terminal Ileum |
| *HDAC3* | rs14251 | C | A | 0.450  | 0.0320  | 0.76  | Pancreas |
| *HDAC3* | rs14251 | C | A | 0.490  | 0.0180  | 0.68  | Adipose - Subcutaneous |
| *HDAC3* | rs14251 | C | A | 0.520  | -0.0420  | -0.64  | Minor Salivary Gland |
| *HDAC3* | rs14251 | C | A | 0.520  | 0.0400  | 0.64  | Prostate |
| *HDAC3* | rs14251 | C | A | 0.530  | 0.0290  | 0.63  | Brain - Cortex |
| *HDAC3* | rs14251 | C | A | 0.540  | -0.0270  | -0.61  | Colon - Sigmoid |
| *HDAC3* | rs14251 | C | A | 0.570  | -0.0220  | -0.57  | Brain - Nucleus accumbens (basal ganglia) |
| *HDAC3* | rs14251 | C | A | 0.570  | 0.0160  | 0.57  | Lung |
| *HDAC3* | rs14251 | C | A | 0.590  | 0.0260  | 0.54  | Brain - Putamen (basal ganglia) |
| *HDAC3* | rs14251 | C | A | 0.670  | -0.0140  | -0.43  | Nerve - Tibial |
| *HDAC3* | rs14251 | C | A | 0.680  | -0.0310  | -0.42  | Brain - Substantia nigra |
| *HDAC3* | rs14251 | C | A | 0.680  | 0.0160  | 0.41  | Colon - Transverse |
| *HDAC3* | rs14251 | C | A | 0.720  | 0.0130  | 0.36  | Artery - Aorta |
| *HDAC3* | rs14251 | C | A | 0.720  | -0.0140  | -0.35  | Brain - Cerebellar Hemisphere |
| *HDAC3* | rs14251 | C | A | 0.740  | -0.0110  | -0.33  | Thyroid |
| *HDAC3* | rs14251 | C | A | 0.760  | -0.0170  | -0.31  | Brain - Hippocampus |
| *HDAC3* | rs14251 | C | A | 0.770  | -0.0210  | -0.30  | Brain - Anterior cingulate cortex (BA24) |
| *HDAC3* | rs14251 | C | A | 0.800  | 0.0110  | 0.25  | Stomach |
| *HDAC3* | rs14251 | C | A | 0.820  | -0.0073  | -0.23  | Adipose - Visceral (Omentum) |
| *HDAC3* | rs14251 | C | A | 0.840  | -0.0064  | -0.20  | Artery - Tibial |
| *HDAC3* | rs14251 | C | A | 0.880  | -0.0074  | -0.15  | Brain - Cerebellum |
| *HDAC3* | rs14251 | C | A | 0.880  | 0.0110  | 0.15  | Brain - Spinal cord (cervical c-1) |
| *HDAC3* | rs14251 | C | A | 0.880  | 0.0100  | 0.16  | Vagina |
| *HDAC3* | rs14251 | C | A | 0.890  | -0.0100  | -0.13  | Uterus |
| *HDAC3* | rs14251 | C | A | 0.960  | -0.0015  | -0.05  | Esophagus - Muscularis |
| *HDAC3* | rs14251 | C | A | 0.990  | 0.0003  | 0.01  | Brain - Caudate (basal ganglia) |
| *HDAC3* | rs14251 | C | A | 0.990  | 0.0007  | 0.02  | Liver |

SNP, single nucleotide polymorphism; Ref\_allele, reference allele; Alt\_allele, alternative allele; NES, normalized effect size; EBV, Epstein-Barr virus.

**Supplementary Figures**

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**Power=79.2%, RR=1.30**

**Supplementary Figure S1.** Statistical power as a function of genotype relative risk (RR).



**Supplementary Figure S2.** Protein-protein interaction (PPI) network based on *HDAC3* constructed by using STRING.