Supplemental Materials Contents

Supplemental Methods

Additional Sample Details

Our sample for this report is composed of 87 subjects with bipolar disorder ("BP") originally collected as part of the Chicago, Hopkins, National Institute of Mental Health Intermural Program ("CHIP") BP study and 931 BP subjects originally collected as part of the NIMH Genetics Initiative Bipolar Disorder Collaborative study [1-3]. There are 119 male and 268 female attempter subjects, and 291 male and 340 female non-attempter subjects present in the study population.

Target Library Creation

NimbleGen SeqCap EZ (NimbleGen, Madison WI) paired-end libraries were prepared for each subject following standard protocols. Briefly, 1-3µg fragmented whole genomic DNA was prepared for each subject using a Covaris S2 (Covaris, Woburn MA) with a 10% duty cycle, an intensity setting of 5, and 200 cycles per burst for 90s at 4^{o} C. Each fragmented sample was then end-repaired and ligated with either paired-end barcoded DNA adapters from Integrated DNA Technologies (IDT, Coralville IA) or with NEXTflex DNA barcode adapters from Bioo Scientific (Austin TX). Barcoded samples were then filtered for size via a 2% agarose gel in 1X TAE buffer and either 0.5 µg/mL ethidium bromide or 0.01% SYBR Gold (Life Technologies, Grand Island NY). ~300bp DNA fragments were sliced and extracted from the gel. Libraries were then amplified via 8 cycles of PCR using Phusion High-Fidelity PCR Master Mix (New England Biolabs, Ipswich MA). Annealing temperatures for the PCR were set at 65^{o} C for samples prepared with full-length paired-end primers or at 60^{o} C for partial-length primers.

Following preparation, a 400bp unimodal sample peak was confirmed via a Bioanalyzer DNA 1000 kit (Agilent Technologies, Santa Clara CA). Samples were quantified via a NanoDrop 1000 Spectrophotometer (Thermo Scientific, Waltham MA) with the requirement that at least 1µg of

sample to be present for non-multiplexed capture or 500/250/166ng DNA per subject in multiplexed 2/4/6 subject capture experiments, respectively.

Target Design and Capture

Our 1,018 BP subjects were each hybridized to one of three different arrays. The SeqCap EZ Exome v1 (NimbleGen, Madison WI) array was used to capture the first 30 attempter and 57 non-attempter BP subject samples. The version 2 SeqCap EZ array was used to capture an additional 15 attempter and 56 non-attempter BP subject samples. For the third and fourth years of our sequencing experiments, version 2 SeqCap EZ (NimbleGen, Madison WI) was used with the addition of custom targets designed to capture regulatory regions (1kb promoters/full UTR regions) for 1,422 post-synaptic density genes [4] and 57 genes that have been previously associated with BP disorder. The customized version 2 SeqCap EZ array was used to capture the remaining 342 attempter and 518 non-attempter BP subjects. Overall target coverage of the SeqCap EZ Exome (NimbleGen, Madison WI) kits was approximately 26.2 Mb (~16,000 transcripts), 36.0 Mb (~30,000 transcripts), and 54.3 Mb (~30,000 transcripts) for SeqCap EZ version 1, 2, and customized 2, respectively.

All hybridizations were performed with either 1µg of the DNA library from a single sample (initial non-multiplexed experiments) or with 1µg total pooled DNA libraries equally distributed by mass among the pooled samples followed by post-hybridization following the instructions in the SeqCap EZ Exome guide (NimbleGen, Madison WI). Briefly, the post hybridization products were washed and enriched in duplicate 18 cycle PCR reactions. Duplicate PCR products were then pooled together, washed, and quality tested with Bioanalyzer DNA 1000 kits (DNA quantity and fragment size).

Sequencing and Initial Quality Control

Two different sequencing platforms were used in this project: samples prepared with SeqCap EZ Exome version 1 (NimbleGen, Madison WI) were sequenced at one sample per lane using a GA-IIx sequencer (Illumina, San Diego CA), while samples prepared with the version 2 and version 2+custom capture targets were sequenced using HiSeq 2000 sequencers (Illumina, San Diego CA) using 2, 4, or 6 pooled samples. All samples were sequenced using paired-end 76-cycle runs. Only samples assessed to have ≥20X coverage depth in ≥70% of the capture targets were included within the final dataset. It was noted that samples failing to meet the 20X/70% threshold that were sequenced with the Illumina GA-IIx could often be pooled together and reanalyzed to gain greater depth of coverage (thus allowing re-inclusion of these samples in downstream analysis). Samples failing the 20X/70% metric when sequenced with the increased data collection capacity of the HiSeq 2000 generally did not see improvement if pooling/re-sequencing attempts were applied. An elevated level of detected PCR duplicates and/or diminished 2X sequencing depth coverage of targets detected in these samples was strongly suggestive of low library complexity, and such samples were either excluded from the study or re-sequenced from recreated libraries.

Sample Alignment, Calling, and Quality Control Pipeline

A semi-automated sample processing pipeline was constructed to prepare all samples for analysis. Individual samples were separated by barcode through the CASAVA version 1.8 software package (Illumina, San Diego CA). Sample FASTQ output files were individually aligned against the hg19/GRCh37 build via the Burrows Wheeler Aligner [5] version 0.6.2 aln module with a seed length of 30. Resultant SAM files were converted to BAM files and processed via SAMtools [6] version 0.1.18. BAMtools [7] version 2.1.1 was used to remove unpaired reads and Picard version 1.88 (http://broadinstittute.github.io/picard) was used to remove duplicate reads from the BAM files. Reads with low mapping quality were then removed

by BAMtools [7] followed by indexing via SAMtools [6]. The genome analysis toolkit (GATK) [8] version 2.6-5 was then used to realign sequences around suspected and known DNA insertion and deletion (indel) sites and to perform base recalibration of predicted variant sites based on dbSNP version 138 and 1000 Genomes known sites.

Following the initial data preparation, the GATK Reducereads tool generated reduced BAM files. The reduced files were then simultaneously genotyped as a single group (all study subjects genotyped at once) for SNPs and indels using the GATK unified genotyper package. The GATK was used for group variant recalibration around called SNPs and indels. Initial flagging and removal of low-quality SNPs was performed based on the combined examination of quality-depth (QD), mapping quality rank sum (MQRankSum), read position rank sum (ReadPosRankSum), fisher based strand bias (FS), mapping quality (MQ), and haplotype score (HaplotypeScore) based assessments during the recalibration step. In addition, all detected indels and tri/quad allelic sites were removed from the final analyzed dataset due to the technological limitations involved with accurately calling these complex alleles.

Variant-Level Quality Control Measures

Several additional levels of quality control were employed to remove questionable variant calls from the dataset. All subject genotype calls that had a call depth of less than 10 or a genotype quality ("GQ") score of 20 or less were removed from the dataset by setting them to missing in the variant call file ("VCF"). All variants that were flagged during GATK [8] variant recalibration checks for any reason were removed. Variants failing a Hardy-Weinberg check via a p-value of $< 1*10^{-6}$ were also removed. Finally, any variants missing calls in ≥10% of all subjects post call QC were removed from the dataset.

Systematic bias in variant calling between study groups (attempters and non-attempters) was assessed by examining the average number of variants that arose in a single subject within the

study population (“singletons”). On average, 227.7 singletons were observed per attempter and 224.0 singletons per non-attempter. Performing a t-test on these distributions led to a p-value of 0.29 when assuming equal variance and a p-value of 0.29 if assuming unequal variance. These results demonstrate no evidence of significant calling bias between the groups.

Finally, assessments of the final quality-checked dataset were made via two methods. First, the distribution of individual variant test results was plotted against the expected results for a sample of this size as a QQ-plot (Fig S2). This QQ assessment showed no broad deviations from the expected p-values, suggesting little or no underlying population structure contribution to our results. Second, exome genotypes were compared against overlapping available GWAS genotypes [9, 10] for all subjects in the study. 10,251 variants were covered in the exome that were also genotyped within the GWAS study. A call mismatch rate of 0.33% (16,379,480 matched calls, 54,170 mismatched calls) was noted in the comparison of these studies, suggesting very high quality calls within the prepared exome data.

Subject Quality Assessment

Subjects were assessed for population stratification using principal component analysis via the software packages EIGENSTRAT and SMARTPCA within the EIGENSOFT package [11]. Only variants with a minor allele frequency (“MAF”) >0.05 which were successfully typed in ≥95% of the study sample and were not in linkage disequilibrium (LD) were used for this analysis. The first two principal components for the subjects are represented within Fig S1 and demonstrate an equal distribution of each subject population with no other discernible outliers.

In addition, subjects were assessed for correct sex via the PLINK [12] v1.07 “--check-sex” method. This method assesses the ratio of X chromosome homozygote SNP calls to all X chromosome calls against expected values for males and females against the labeled sex of each subject in the data. We used a set of X chromosome variants with MAF>0.05 and which

were successfully called in ≥95% of our subject population to perform this check and flag any mislabeled subjects for removal from the final dataset.

Statistical Analyses Details

All variants detected in the dataset, regardless of allele frequency, were assessed for association with suicidal behavior via the logistic regression package "logistf" [13] which included the correction for the covariates of sex, assay/platform, and the first five components of the principal component analysis for each subject (for a single variant result overview see Table S6). Functional variants were assessed using two minor allele frequency ("MAF") thresholds for all gene and pathway tests: functional variants with MAF≤0.05 ("MAF05") and functional variants with MAF≤0.01 ("MAF01"). The MAF of any given variant was determined by examining the frequency within our complete dataset in addition to the listed frequency in the European 1000 genomes October 2014 release dataset [14], the non-Finnish European Exome Aggregation Consortium version 0.3 (Exome Aggregation Consortium ("ExAC"), Cambridge, MA (URL: http://exac.broadinstitute.org) (accessed March, 2015)), and/or the European NHLBI GO Exome Sequencing Project (http://evs.gs.washington.edu/EVS/; version SIV2) subjects, where available.

Variants were also selected for inclusion in gene- and pathway-level analyses based on a variety of functional annotations. Variants were annotated for coding regions via ANNOVAR [15] (version 2015Mar22). Coding functional variants were classified into one of two groups: disruptive coding and broad coding functional variants [16]. The disruptive coding classification refers to any identified stopgain/nonsense, frameshift, or essential splice site mutations. The broad coding classification encompasses the complete set of disruptive variants as well as any non-synonymous variants predicted to be functional by at least one of the following packages: SIFT [17], polyphen2 (HVAR and HDIV) [18], LRT [19], Mutation Taster [20], and VEST [21].

Variants to be included within the regulatory gene- and pathway-level analyses were selected based on functional classification within the “regulome” database (“regDB”) [22]. Variant selection was based on two described score thresholds that represent variants “likely to affect the binding of regulatory elements” (regDB scores of 1 and 2; “regulatory narrow”) and those that are “less likely to affect binding” due to less overlapping evidence (regDB scores of 3-6) [22]. For consistency, we refer to these groups as regulatory narrow and regulatory broad. The regulatory broad classification includes all regulatory narrow variants (regDB scores 1-6).

Gene-level tests were performed using all variants within the four specified classifications based on gene boundaries as defined by the ANNOVAR annotation using Ensembl transcripts (Ensembl version 75, Feb 2014) [23] on the hg19/GRCh37 assembly. The genes were then assessed via two methods: gene burden tests and sequence kernel association tests (SKAT). Gene burden tests were accomplished by collapsing variant signals using the CMC variant collapsing method over subjects as has been described elsewhere [24]. Briefly, each gene locus was assessed for the presence or absence of functional variants. Any subject with one or more functional variants within the given gene locus was classified as a “1” for the burden test of that gene, whereas subjects with no functional variants in the given gene locus were classified as a “0” for the burden test of the gene. The collapsed values were then assessed along with all covariates using Firth’s corrected penalized logistic regression [25] via the R package “logistf” [13] version 1.21 for all genes. SKAT tests utilized the SKAT R package, version 1.1.2, using the “davies” method [26] for all autosomal genes. The SKAT examines each variant site within a multivariate model to allow individual sites to have varying directional effects on the test result [26]. All gene-level analyses included the covariates of sex, the first five components from our sample PCA analysis, and the sample processing platform/array group.

Pathway-level analyses were performed on a primary selection of 33 existing pathways defined in the literature and online resources. These pathways were selected based on suspected

importance within suicidal behavior risk and/or due to general importance to brain structure and function (Table S4). In addition, a secondary set of pathway analyses were performed on 3,621 pathways selected primarily from the MSigDB v5.1 [27]. These pathways were selected to represent well-described biological pathways (collections H and C2), shared motifs (collection C3), and gene ontology pathways (collection C5).

The complete pathways (including sex chromosome genes) were assessed for direct genetic association with suicidal behavior via the PLINK/SEQ v0.10 package “SMP” method. This method utilized all dataset genes assessed using the PLINK/SEQ “burden” test with 1 million permutations and correcting for platform/assay via the –strata PLINK/SEQ command. The SMP method includes a correction for the background variation distribution across all genes for a given analysis. Top results were also corrected for past diagnoses of alcohol dependence within all subjects in a secondary analysis.

Finally, the SMP analyses were corrected for multiple testing via a 500 attempter/non-attempter label swapping permutations. This involved repeating all SMP analyses across each functional variant set and MAF threshold 500 times with randomly swapped attempter/non-attempter labels for each subject and comparing these randomized results against the primary SMP analysis results, generating an empirical p-value for each result. Note that only 500 permutations were run due to the computational burden of performing these analyses.

Power Calculations

Individual and gene-based power calculations were performed using Quanto version 1.2.4 [28]. Program settings were as follows: a mismatched case/control ratio of 1:1.6 with 387 cases, “gene only” hypothesis, log-additive mode of inheritance with allele frequencies of 0.01 to 0.05 by 0.01 steps for single variants and allele frequencies of 0.02 to 0.1 by 0.02 steps for gene based tests were used. P0 and kP were placed at 0.046 (4.6% estimated population disease

prevalence [29]) with RG being plotted from values of 1-5 for genes and 1-8 for single variants. Significance levels were estimated at the liberal $2.5*10^{-6}$ and standard $5.0*10^{-8}$ for genes and single variants, respectively. Plots of the resulting power calculations are available in Figs S3 and S4 for single variant and gene tests, respectively.

Sample Set Acknowledgements

Data and biomaterials for the CHIP sample were collected at Johns Hopkins, NIMH intramural program, and University of Chicago from 1988 to 2010, under the direction of Ray DePaulo, along with James Potash, Francis McMahon, and Elliot Gershon. This work was supported by NIH grants R01 MH-042243 (Drs. DePaulo and Potash) and R01 MH-061613 (Dr. Gershon); by the National Alliance for Research on Schizophrenia and Depression; by the Stanley Medical Research Institute; and by the NIMH Intramural Research Program (Dr. McMahon).

Genome-wide SNP genotyping of the NIMH samples was performed through the Genetic Association Information Network under the direction of The Bipolar Genome Study (BiGS) Consortium. The Principal Investigators and Co-Investigators were: University of California San Diego, La Jolla, CA, John R. Kelsoe, M.D. (PI), Tiffany A. Greenwood, Ph.D., Thomas B. Barrett, M.D., Ph.D., Caroline M. Nievergelt, Ph.D., Rebecca McKinney, Paul D. Shilling, Ph.D.; Scripps Research Institute, La Jolla, CA: Nicholas Schork, Ph.D. (PI), Erin N. Smith, Ph.D., Cinnamon S. Bloss, Ph.D.; Indiana University, Bloomington, IN, John I. Nurnberger, Jr., M.D. (PI), Howard J. Edenberg, Ph.D., Tatiana Foroud, Ph.D., Daniel M. Koller; University of Chicago, Chicago, IL, Elliot Gershon, M.D. (PI), Chunyu Liu, Ph.D., Judith A. Badner, Ph.D.; Rush University Medical Center, Chicago, IL, William A. Scheftner, M.D.; Howard University, Washington, DC, William B. Lawson, M.D. (PI), Evaristus A. Nwulia, M.D., Maria Hipolito, M.D.; University of Iowa, Iowa City, IA, William Coryell, M.D. (PI); Washington University, St. Louis, MO, John Rice, Ph.D. (PI); University of California San Francisco, San Francisco, CA, William Byerley, M.D. (PI); National Institute of Mental Health, Bethesda, MD, Francis McMahon, M.D.

(PI), Thomas G. Schulze, M.D.; University of Pennsylvania, Philadelphia, PA, Wade Berrettini, M.D., Ph.D. (PI); Johns Hopkins University, Baltimore, MD, James B. Potash, M.D. (PI), Peter P. Zandi, Ph.D., Pamela B. Mahon, Ph.D.; University of Michigan, Ann Arbor, MI, Melvin G. McInnis, M.D. (PI), Sebastian Zöllner, Ph.D., Peng Zhang; The Translational Genomics Research Institute, Phoenix, AZ, David Craig, Ph.D. (PI), Szabolics Szelinger.

Data and biomaterials were collected in four projects that participated in the National Institute of Mental Health (NIMH) Bipolar Disorder Genetics Initiative. From 1991-98, the Principal Investigators and Co-Investigators were: Indiana University, Indianapolis, IN, U01 MH46282, John Nurnberger, M.D., Ph.D., Marvin Miller, M.D., and Elizabeth Bowman, M.D.; Washington University, St. Louis, MO, U01 MH46280, Theodore Reich, M.D., Allison Goate, Ph.D., and John Rice, Ph.D.; Johns Hopkins University, Baltimore, MD U01 MH46274, J. Raymond DePaulo, Jr., M.D., Sylvia Simpson, M.D., MPH, and Colin Stine, Ph.D.; NIMH Intramural Research Program, Clinical Neurogenetics Branch, Bethesda, MD, Elliot Gershon, M.D., Diane Kazuba, B.A., and Elizabeth Maxwell, M.S.W.

Data and biomaterials were collected as part of ten projects that participated in the National Institute of Mental Health (NIMH) Bipolar Disorder Genetics Initiative. From 1999-03, the Principal Investigators and Co-Investigators were: Indiana University, Indianapolis, IN, R01 MH59545, John Nurnberger, M.D., Ph.D., Marvin J. Miller, M.D., Elizabeth S. Bowman, M.D., N. Leela Rau, M.D., P. Ryan Moe, M.D., Nalini Samavedy, M.D., Rif El-Mallakh, M.D. (at University of Louisville), Husseini Manji, M.D. (at Wayne State University), Debra A. Glitz, M.D. (at Wayne State University), Eric T. Meyer, M.S., Carrie Smiley, R.N., Tatiana Foroud, Ph.D., Leah Flury, M.S., Danielle M. Dick, Ph.D., Howard Edenberg, Ph.D.; Washington University, St. Louis, MO, R01 MH059534, John Rice, Ph.D., Theodore Reich, M.D., Allison Goate, Ph.D., Laura Bierut, M.D. ; Johns Hopkins University, Baltimore, MD, R01 MH59533, Melvin McInnis M.D. , J. Raymond DePaulo, Jr., M.D., Dean F. MacKinnon, M.D., Francis M. Mondimore, M.D., James

B. Potash, M.D., Peter P. Zandi, Ph.D., Dimitrios Avramopoulos M.D., Ph.D., and Jennifer Payne, M.D.; University of Pennsylvania, PA, R01 MH59553, Wade Berrettini M.D., Ph.D.; University of California at Irvine, CA, R01 MH60068, William Byerley M.D., and Mark Vawter M.D.; University of Iowa, IA, R01 MH059548, William Coryell M.D. , and Raymond Crowe M.D. ; University of Chicago, IL, R01 MH59535, Elliot Gershon, M.D., Judith Badner Ph.D. , Francis McMahon M.D. , Chunyu Liu Ph.D., Alan Sanders M.D., Maria Caserta, Steven Dinwiddie M.D., Tu Nguyen, Donna Harakal; University of California at San Diego, CA, R01 MH59567, John Kelsoe, M.D., Rebecca McKinney, B.A.; Rush University, IL, R01 MH059556, William Scheftner M.D. , Howard M. Kravitz, D.O., M.P.H., Diana Marta, B.S., Annette Vaughn-Brown, MSN, RN, and Laurie Bederow, MA; NIMH Intramural Research Program, Bethesda, MD, 1Z01MH002810-01, Francis J. McMahon, M.D., Layla Kassem, PsyD, Sevilla Detera-Wadleigh, Ph.D., Lisa Austin, Ph.D., Dennis L. Murphy, M.D.

Data and biomaterials were collected as part of eleven projects (Study 40) that participated in the National Institute of Mental Health (NIMH) Bipolar Disorder Genetics Initiative. From 2003-2007, the Principal Investigators and Co-Investigators were: Indiana University, Indianapolis, IN, R01 MH59545, John Nurnberger, M.D., Ph.D., Marvin J. Miller, M.D., Elizabeth S. Bowman, M.D., N. Leela Rau, M.D., P. Ryan Moe, M.D., Nalini Samavedy, M.D., Rif El-Mallakh, M.D. (at University of Louisville), Husseini Manji, M.D. (at Johnson and Johnson), Debra A. Glitz, M.D. (at Wayne State University), Eric T. Meyer, Ph.D., M.S. (at Oxford University, UK), Carrie Smiley, R.N., Tatiana Foroud, Ph.D., Leah Flury, M.S., Danielle M. Dick, Ph.D (at Virginia Commonwealth University), Howard Edenberg, Ph.D.; Washington University, St. Louis, MO, R01 MH059534, John Rice, Ph.D., Theodore Reich, M.D., Allison Goate, Ph.D., Laura Bierut, M.D. K02 DA21237; Johns Hopkins University, Baltimore, M.D., R01 MH59533, Melvin McInnis, M.D., J. Raymond DePaulo, Jr., M.D., Dean F. MacKinnon, M.D., Francis M. Mondimore, M.D., James B. Potash, M.D., Peter P. Zandi, Ph.D., Dimitrios Avramopoulos M.D.,Ph.D., and

Jennifer Payne, M.D.; University of Pennsylvania, PA, R01 MH59553, Wade Berrettini, M.D., Ph.D.; University of California at San Francisco, CA, R01 MH60068, William Byerley, M.D., and Sophia Vinogradov, M.D.; University of Iowa, IA, R01 MH059548, William Coryell, M.D., and Raymond Crowe, M.D.; University of Chicago, IL, R01 MH59535, Elliot Gershon, M.D., Judith Badner, Ph.D., Francis McMahon, M.D., Chunyu Liu, Ph.D., Alan Sanders, M.D., Maria Caserta, Steven Dinwiddie, M.D., Tu Nguyen, Donna Harakal; University of California at San Diego, CA, R01 MH59567, John Kelsoe, M.D., Rebecca McKinney, B.A.; Rush University, IL, R01 MH059556, William Scheftner, M.D., Howard M. Kravitz, D.O., M.P.H., Diana Marta, B.S., Annette Vaughn-Brown, M.S.N., R.N., and Laurie Bederow, M.A.; NIMH Intramural Research Program, Bethesda, MD, 1Z01MH002810-01, Francis J. McMahon, M.D., Layla Kassem, Psy.D., Sevilla Detera-Wadleigh, Ph.D., Lisa Austin, Ph.D., Dennis L. Murphy, M.D.; Howard University, William B. Lawson, M.D., Ph.D., Evarista Nwulia, M.D., and Maria Hipolito, M.D.

Supplemental Figures

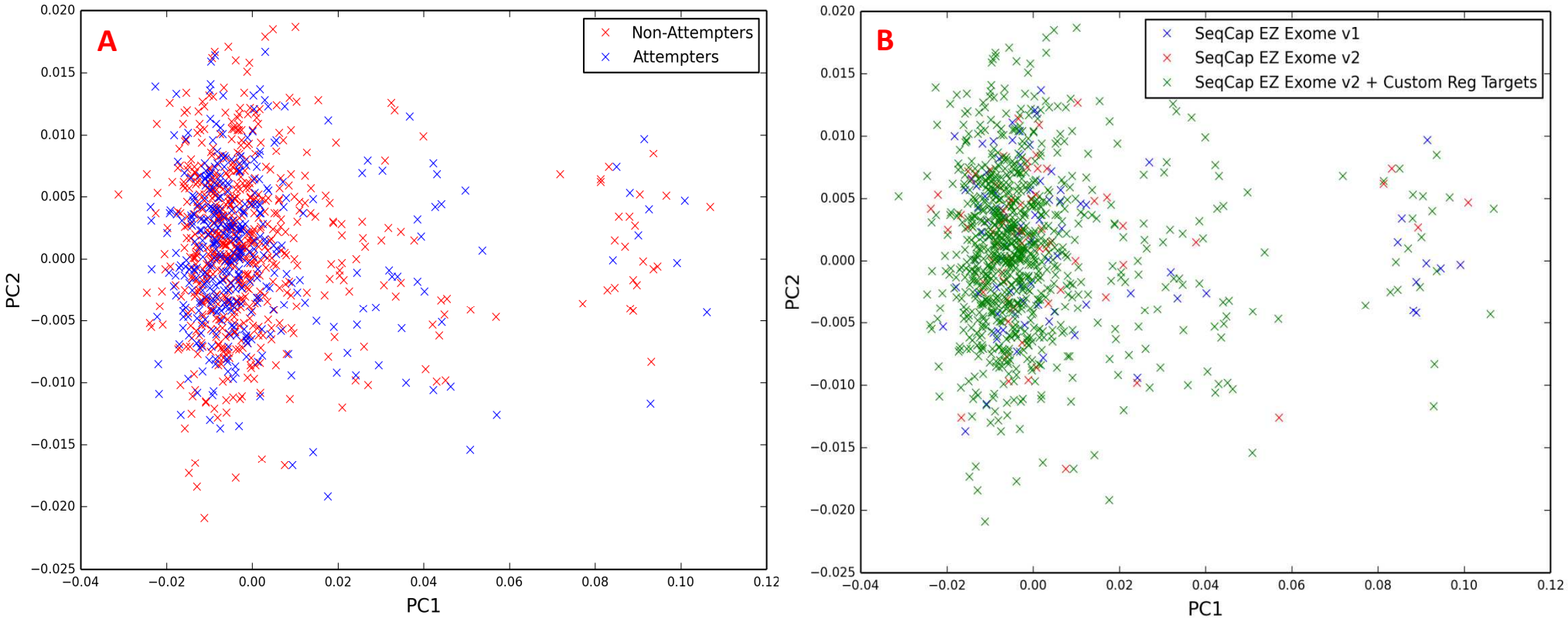

Fig S1: Principal component analysis plots of the first two components for each subject. Panel A presents the subjects labeled by suicide attempt status where red = BP subjects with no history of suicide attempt (631 subjects); dark blue = BP subjects with a history of suicide attempt (387 subjects). Panel B labels subjects by the sequencing array they were genotyped with where blue = BP subjects processed in the first year of sequencing using the Illumina SeqCap EZ Exome Array v1 (87 subjects), red = BP subjects processed in the second year of sequencing using the SeqCap EZ Exome v2 (71 subjects), and green = BP subjects processed in the third and fourth years of sequencing using the SeqCap EZ Exome v2 + custom regulatory sequence targets (860 subjects).

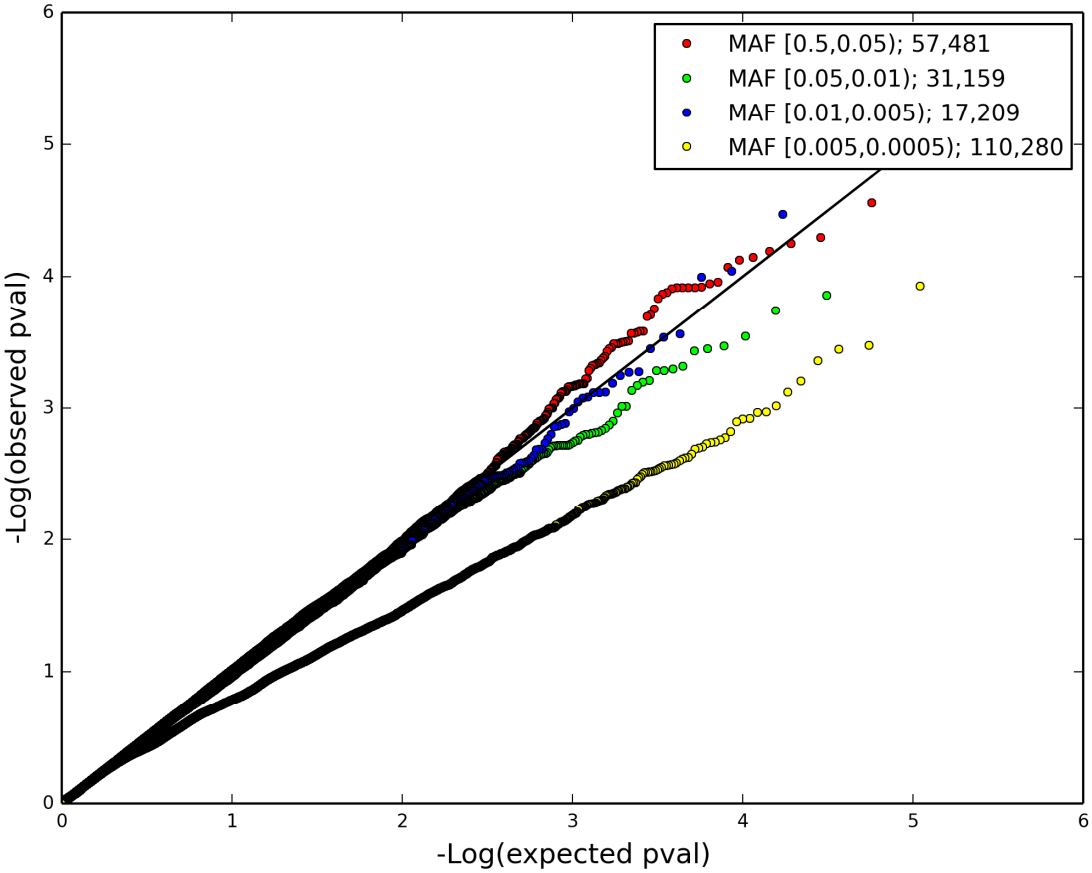

Fig S2: Individual variant QQ-plot for all subjects with a history of suicide attempt (387 subjects) versus all non-attempter subjects (631 subjects). The solid line represents the expected p-value distribution and the colored points represent observed single variant data at different minor allele frequency (MAF) ranges, as labeled. The value at the right of each MAF range is the number of unique sites that were identified within the dataset in the MAF range.

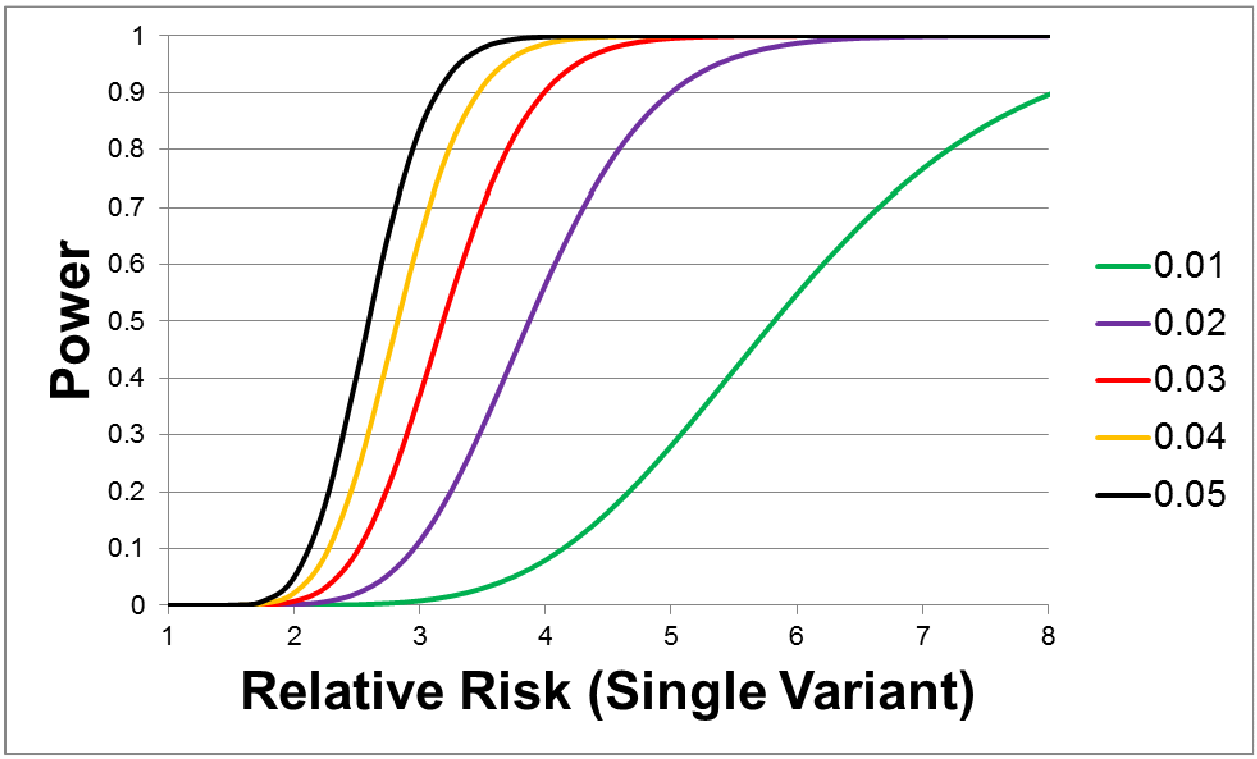

Fig S3: Power calculations for 387 attempters and 631 non-attempters for single variant test significance (Bonferroni $p=5*10^{-8}$). Each colored line represents a different risk allele minor allele frequency, the X axis representing the relative risk of the variant to be detected, and the Y axis representing the power for detection of the given variant rarity and relative risk.

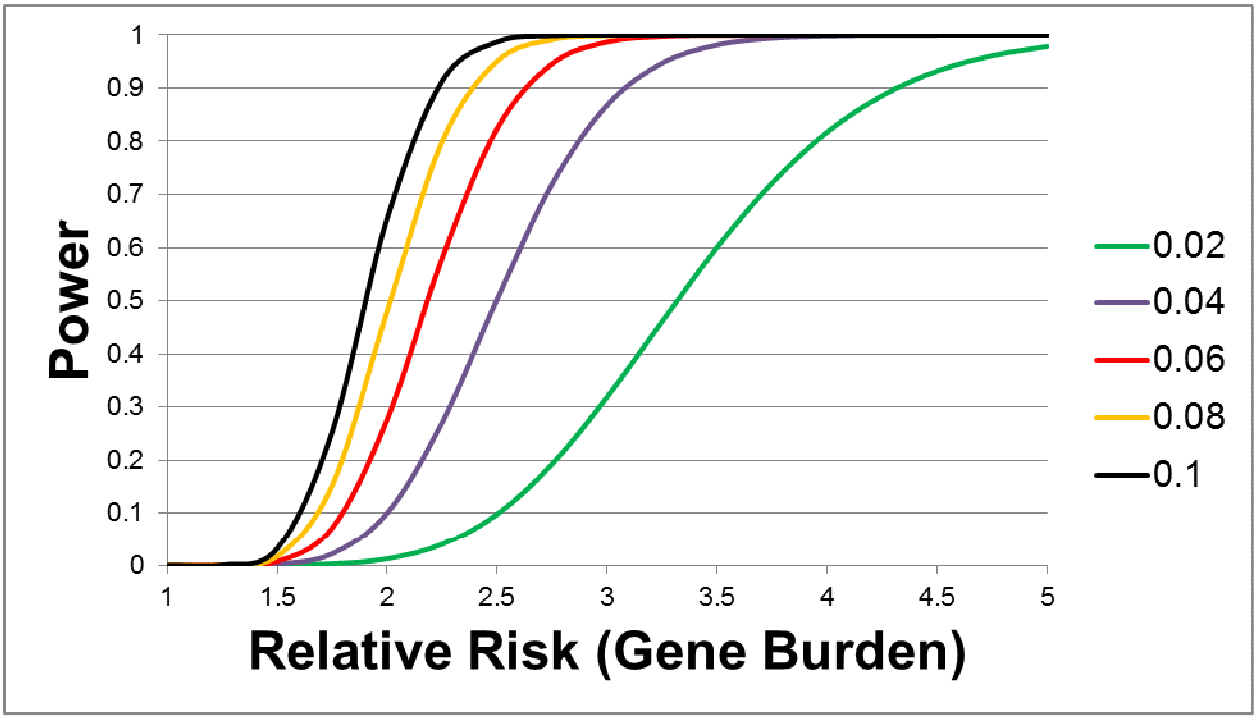

Fig S4: Power calculations for 387 attempters and 631 non-attempters for gene burden test significance (Bonferroni $p=2.6*10^{-6}$). Each colored line represents a different collapsed risk allele minor allele frequency (the cumulative frequenting of all rare functional variants collapsed by subject), the X axis represents the relative risk of the collapsed variants to be detected, and the Y axis represents the power for detection of the given collapsed variant rarity and relative risk.

Supplemental Tables

Table S1: Best Results for Genes Found to be Associated with Suicide in Published Studies

Gene Symbol (References)	Variant Set	Set P-value	Burden Odds Ratio	Predicted Gene Function
ABI3BP [30]	Code Broad MAF05 SKAT	0.060	0.77	Poorly characterized; may be involved in cell fate determination
ACE [31-33]	Code Broad MAF01 SKAT	0.32	1.3	Initiate vasopressin (increase in blood pressure)
ACP1 [34]	Reg Broad MAF01 SKAT	0.066	1.1	Acid phosphatase that may act in regulating WNT signaling
ADRA2A [35-40]	-	-	-	Alpha-2a adrenergic; paralog of HTR2A
AKT1 [41, 42]	Code Broad MAF01 SKAT	0.82	1.1	Mediator of growth factor induced neuronal survival
BDNF [43-55]	Reg Broad MAF01 Burden	0.0045	1.8	Promotes survival and differentiation of neurons
CCKBR [56, 57]	Code Broad MAF01 Burden	0.59	1.5	Receptor for the CCK neuropeptide
CLOCK [58]	Code Broad MAF05 SKAT	0.093	0.52	A core mediator of the circadian clock cycle
COMT [59-68]	Code Broad MAF05 SKAT	0.44	1.4	Degradation of dopamine, norepinephrine, and epinephrine
CREB1 [69]	Code Broad MAF01 SKAT	0.82	1.2	DNA transcription factor
CRHBP [70, 71]	Code Broad MAF01 Burden	0.92	1.1	Suppresses CRH (and thus HPA) activity
CRHR1 [70, 72-75]	-	-	-	Mediates numerous CRH responses
CRHR2 [75, 76]	Code Broad MAF05 Burden	0.27	0.74	Mediates numerous CRH responses
CRP [77]	Code Disrupt MAF01 Burden	0.33	4.4	Mediates several inflammatory processes
DISC1 [78]	Reg Broad MAF05 Burden	0.035	0.72	Mediates cortical development processes
DNMT3B [79]	Code Broad MAF05 SKAT	0.13	1.4	DeNovo methyltransferase activity
DRD2 [80-83]	Code Broad MAF01 SKAT	0.45	1.6	Mediates dopamine response by opposing DRD1
EFEMP1 [84]	Code Broad MAF01 Burden	0.090	0.14	Activates EGFR signaling, with possible roles in cell migration/adhesion
FAM110C [34]	Code Broad MAF01 Burden	0.87	0.76	Poorly characterized; may play a role in cell spread/migration
FAM150B [34]	-	-	-	Poorly characterized
FKBP5 [71, 85-91]	Reg Broad MAF01 Burden	0.094	1.4	Immune regulation mediation
FTO [92]	Code Broad MAF01 Burden	0.24	0.37	Alkylated DNA and RNA repair
GABRG2 [93]	Code Broad MAF01 SKAT	0.82	1.1	Receptor for Gamma-Aminobutyric Acid
HTR1A [94-96]	Code Broad MAF01 Burden	0.74	0.87	Serotonergic response mediation
HTR2A [97-103]	Code Broad MAF01 Burden	0.50	2.2	Serotonergic response mediation

Table S1 Previously Associated Genes

LSAMP [104]	Reg Broad MAF05 SKAT	0.071	4.1	Guides neuronal connections in development
MAOA [105-108]	Reg Broad MAF05 Burden	0.084	2.2	Degrades serotonin and other monoamines
MAPK1 [69]	Reg Broad MAF05 Burden	0.15	0.68	Regulation of cellular division and life-cycle
NGFR [109]	-	-	-	Mediates neuronal survival
NOS1 [110-112]	Code Broad MAF01 Burden	0.84	0.95	Smooth muscle and neurotransmission regulation
NTRK2 [40, 54, 113-118]	Code Broad MAF01 Burden	0.095	0.42	Central/peripheral nervous development
ODC1 [119]	Code Broad MAF01 Burden	0.40	0.62	A central enzyme in the urea cycle
SAT1 [120-124]	-	-	-	Core enzyme in polyamine catabolism
SH3YL1 [34]	Code Broad MAF05 Burden	0.49	0.60	Poorly characterized; may regulate cell migration
SKA2 [125]	Code Broad MAF05 SKAT	0.41	0.64	Mediates microtubule binding for chromosome organization in mitosis
SLC6A4 [59, 103, 106, 126-151]	Code Broad MAF01 Burden	0.12	3.4	Serotonin uptake from synapse
TAAR6 [152]	Code Broad MAF05 SKAT	0.83	0.95	Trace amine reception
TBC1D25 (OATL1) [123]	Code Broad MAF05 Burden	0.35	0.70	Autophagosome maturation
TIMELESS [58]	Code Broad MAF05 Burden	0.42	1.4	Regulates DNA replication and the circadian cycle
TPH1 [98, 150, 153-170]	Code Broad MAF05 SKAT	0.30	0.60	Core enzyme for serotonin biosynthesis
TPH2 [166, 171-183]	Code Disrupt MAF01 Burden	0.19	7.3	Core enzyme for serotonin biosynthesis

Table S1: This table outlines the results from our data of the gene level analyses. The best p-values from all analyses are presented and have been corrected for the covariates of sex, analysis platform, and the first five principal component analyses. Comparisons were all made of suicide attempters (n=387) vs non-attempters (n=631). References represent papers with positive evidence for association of the gene/region with suicidal behavior. Any value listed as "-" could not be calculated due to insufficient detected functional variation for analysis within the gene locus. All listed genes were captured by the arrays.

Table S2: Sample Demographics

Attribute	Group	Attempters	Non-Attempters	P-value
Sex	Female	268 (69.3%)	340 (53.9%)	$1.1*10^{-6}$
	Male	119 (30.7%)	291 (46.1%)	$1.1*10^{-6}$
Age	Mean Interview Age	42.0	41.4	0.45
Education	Mean Years of Schooling	14.4	15.0	$5.2*10^{-4}$
Diagnosis	BPI	343 (88.6%)	599 (94.9%)	$3.2*10^{-4}$
	SABP	44 (11.4%)	31 (4.9%)	$1.8*10^{-4}$
	BP Otherwise Affected	0 (0.0%)	1 (0.16%)	1.0
Comorbidities	Alcohol Dependence	160 (41.3%)	157 (24.9%)	$4.9*10^{-8}$
	Substance Abuse	84 (21.7%)	75 (11.9%)	$3.9*10^{-5}$

Table S4: Primary Pathways Hypothesized to be of Importance to Suicidal Behavior Risk

Pathway	Source	Number of Genes	Best Burden P-value	Odds Ratio	Variant Set
Glutamatergic Synapse	KEGG [184]	115	0.52	0.91	Coding Disruptive MAF01
Hypothalamic-Pituitary-Adrenal (HPA) Axis	Breen et al. [185]	22	0.040	6.5	Coding Disruptive MAF01
Ion-Channels: All Ion Channels	Purcell et al. [16]	237	0.35	0.99	Coding Broad MAF01
Ion-Channels: Cholinergic Receptor Genes	Purcell et al. [16]	16	0.41	0.89	Coding Disruptive MAF01
Ion-Channels: GABA Receptor Genes	Purcell et al. [16]	20	0.19	1.0	Coding Broad MAF05
Ion-Channels Ionotropic Glutamate Receptor Genes	Purcell et al. [16]	14	0.12	1.0	Coding Broad MAF05
Ion-Channels: Potassium Inwardly Rectifying Channel Genes	Purcell et al. [16]	14	0.81	0.98	Coding Broad MAF05
Ion-Channels: Serotonin Receptor Genes	Purcell et al. [16]	16	0.46	0.88	Coding Broad MAF01
Ion-Channels Twin Pore Potassium Channel Genes	Purcell et al. [16]	14	0.48	1.1	Coding Broad MAF05
Ion-Channels Voltage-Gated Calcium Channel Genes	Purcell et al. [16]	26	0.11	2.4	Coding Disruptive MAF01
Ion-Channels Voltage-Gated Potassium Channel Genes	Purcell et al. [16]	50	0.24	1.0	Coding Broad MAF01
Ion-Channels Voltage-Gated Sodium Channel Genes	Purcell et al. [16]	14	0.22	0.97	Coding Broad MAF01
Neuronal ARC	Purcell et al. [16]	28	0.94	0.78	Coding Broad MAF01
Neuronal Cytoplasm	Purcell et al. [16]	271	0.86	0.86	Coding Disruptive MAF01
Neuronal Early Endosomes	Purcell et al. [16]	17	0.71	0.90	Coding Broad MAF01
Neuronal Endoplasmic Reticulum	Purcell et al. [16]	97	0.095	1.4	Coding Disruptive MAF01
Neuronal ER Golgi-Derived Vesicles	Purcell et al. [16]	94	0.12	1.6	Coding Disruptive MAF01
Neuronal Golgi	Purcell et al. [16]	31	0.54	1.1	Coding Disruptive MAF01
Neuronal Mglur5	Purcell et al. [16]	39	0.76	1.0	Coding Broad MAF05
Neuronal Mitochondrion	Purcell et al. [16]	197	0.70	0.95	Coding Broad MAF01
Neuronal NMDAR Network	Purcell et al. [16]	61	0.13	1.2	Coding Broad MAF01
Neuronal Nucleus	Purcell et al. [16]	167	0.098	1.0	Coding Broad MAF05
Neuronal Plasma Membrane	Purcell et al. [16]	50	0.26	1.1	Coding Disruptive MAF01
Neuronal Pre-Synapse	Purcell et al. [16]	431	0.72	1.0	Coding Disruptive MAF01
Neuronal Pre-Synaptic Active Zone	Purcell et al. [16]	173	0.60	1.1	Coding Broad MAF01
Neuronal PSD	Purcell et al. [16]	685	0.48	1.1	Coding Disruptive MAF01
Neuronal PSD-95	Purcell et al. [16]	65	0.66	0.82	Coding Disruptive MAF01
Neuronal Recycling Endosomes Trans-Golgi Network	Purcell et al. [16]	68	0.50	1.1	Coding Broad MAF01
Neuronal Synaptic Vesicle	Purcell et al. [16]	344	0.54	1.0	Coding Broad MAF01
Primary Brain-expressed	Pirooznia et al. [186]	13,128	0.48	1.0	Coding Broad MAF05
Serotonergic Synapse	Judy et al. [187], KEGG [184]	20	0.51	1.6	Coding Disruptive MAF01
Synaptome	Bayes et al. [4]	1,461	0.18	1.0	Regulatory Broad MAF05
WNT Signaling	KEGG [184]	154	0.31	1.2	Coding Disruptive MAF05

Table S5: Average On-Target Sample Quality Metrics

Metric	Sequencing Platform / Array	Attempters	Non-Attempters
Average Sequenced Sites Per Sample	GA-IIx / SeqCap EZ v1	26,400,929	26,401,298
	HiSeq / SeqCap EZ v2	36,172,446	36,172,543
	HiSeq / SeqCap EZ v2+	47,656,051	47,655,952
Average per Site Read Depth	GA-IIx / SeqCap EZ v1	56.9	56.5
	HiSeq / SeqCap EZ v2	72.0	66.3
	HiSeq / SeqCap EZ v2+	75.0	74.3
Sites with Read Depth ≥ 1	GA-IIx / SeqCap EZ v1	95.7%	95.7%
	HiSeq / SeqCap EZ v2	95.5%	95.7%
	HiSeq / SeqCap EZ v2+	97.9%	97.9%
Sites with Read Depth ≥ 10	GA-IIx / SeqCap EZ v1	88.4%	88.4%
	HiSeq / SeqCap EZ v2	92.0%	91.8%
	HiSeq / SeqCap EZ v2+	94.7%	94.6%
Average Minor Allele Calls	GA-IIx / SeqCap EZ v1	15,709	15,664
	HiSeq / SeqCap EZ v2	23,742	23,386
	HiSeq / SeqCap EZ v2+	27,589	27,415
Average Singleton Variants	GA-IIx / SeqCap EZ v1	160	152
	HiSeq / SeqCap EZ v2	197	204
	HiSeq / SeqCap EZ v2+	235	234
Average Ti/Tv	GA-IIx / SeqCap EZ v1	3.08	3.06
	HiSeq / SeqCap EZ v2	2.96	2.96
	HiSeq / SeqCap EZ v2+	2.83	2.83

Table S5: Reported sample metrics averaged over all individuals in Attempter (N=387) and Non-Attempter (N=631) subjects. Ti/Tv represents the ratio of transition variants to transversion variants. “Sites” represent single on-target base pairs identified via sequence alignment and analysis. The referenced sequence platforms and arrays are described above within the supplemental materials and methods.

Table S6: Top Individual Variants (P<0.0001); Suicide Attempters versus Non-Attempters

SNP ID	hg19 Location	P-Value	Odds Ratio	Gene	Position/Function	Attempter MAF	Non-Attempter MAF
rs2215955	chr7:38469039	$2.8*10^{-5}$	0.61	*AMPH*	Non-Synonymous (V→F)	0.24	0.33
rs11214703	chr11:113561025	$3.4*10^{-5}$	8.9	*TMPRSS5*	Synonymous	0.023	0.0028
rs45585336	chr14:20528682	$5.1*10^{-5}$	2.0	*OR4L1*	Non-Synonymous (I→T)	0.12	0.066
rs45584133	chr14:20528250	$5.6*10^{-5}$	1.9	*OR4L1*	Non-Synonymous (G→V)	0.12	0.066
rs3752252	chr20:59829847	$6.4*10^{-5}$	1.5	*CDH4*	Intronic	0.43	0.33
rs17851444	chr3:9920138	$7.2*10^{-5}$	0.54	*CIDEC*	Synonymous	0.079	0.14
rs9677004	chr19:58117083	$7.5*10^{-5}$	1.6	*ZNF530*	Non-Synonymous (T→A)	0.21	0.14
rs3742732	chr14:77942316	$8.5*10^{-5}$	1.9	*ISM2*	Synonymous	0.12	0.067
rs151147550	chr21:31768847	$9.1*10^{-5}$	15	*KRTAP13-1*	Non-Synonymous (R→H)	0.013	0.00079

Table S7: All Top Gene Results (P<0.01)

Gene	Chromosome	hg19 Start	hg19 Stop	Cytogenetic Band	Uncorrected P-value	Odds Ratio	Variant Set
CDK11A	1	1634169	1655766	p36.33	0.0061	1.0	MAF01 Coding Broad SKAT
TNFRSF8	1	12123434	12204264	p36.22	0.0046	1.1	MAF05 Coding Broad SKAT
AADACL4	1	12704566	12727097	p36.21	0.0087	3.0	MAF01 Coding Broad Burden
PRDM2	1	14026693	14151574	p36.21	0.0086	2.7	MAF01 Coding Broad Burden
WNT4	1	22443798	22470462	p36.12	0.0031	4.3	MAF01 Coding Broad SKAT
FUCA1	1	24171567	24194784	p36.11	0.0046	3.5	MAF01 Coding Broad Burden
PPT1	1	40538379	40563375	p34.2	0.0052	4.5	MAF01 Coding Broad SKAT
LRRC41	1	46726868	46769280	p34.1	0.0071	2.3	MAF01 Coding Broad SKAT
RPF1	1	84944942	84963473	p22.3	0.0019	2.0	MAF05 Coding Broad Burden
OLFM3	1	102268130	102462586	p21.1	0.0074	1.0	MAF01 Coding Broad SKAT
PROK1	1	110993822	110999976	p13.3	0.0083	3.6	MAF01 Coding Broad SKAT
CHIA	1	111833484	111863188	p13.2	0.0015	2.0	MAF01 Coding Broad SKAT
CCT3	1	156278759	156337664	q22	0.0080	8.1	MAF01 Coding Broad SKAT
OR6Y1	1	158516918	158517895	q23.1	0.0093	0.39	MAF05 Coding Broad Burden
OLFML2B	1	161952982	161993644	q23.3	0.0048	0.067	MAF01 Coding Broad Burden
PRDX6	1	173446405	173457946	q25.1	0.0070	2.0	MAF05 Regulatory Broad Burden
RC3H1	1	173900352	173991435	q25.1	0.0090	1.6	MAF05 Coding Broad SKAT
IER5	1	181057638	181059977	q25.3	0.0059	3.7	MAF01 Coding Broad SKAT
COLGALT2	1	183898796	184006863	q25.3	0.00039	3.1	MAF05 Coding Broad Burden
RGS21	1	192286122	192336415	q31.2	0.0095	1.5	MAF05 Coding Broad SKAT
C1orf106	1	200860176	200884863	q32.1	0.00020	1.9	MAF01 Coding Broad SKAT
C1orf35	1	228288427	228293112	q42.13	0.0096	1.1	MAF05 Coding Broad SKAT
GNPAT	1	231376953	231413719	q42.2	0.00043	27	MAF01 Regulatory Broad Burden
CEP170	1	243287730	243418650	q43	0.0091	16	MAF01 Regulatory Broad Burden
C1orf100	1	244515937	244552965	q44	0.00076	5.6	MAF05 Coding Broad SKAT
SMYD3	1	245912642	246670614	q44	0.0056	1.6	MAF01 Coding Broad SKAT
ROCK2	2	11319887	11488456	p25.1	0.0032	0.66	MAF05 Regulatory Broad SKAT
OTOF	2	26680071	26781566	p23.3	0.0064	1.6	MAF05 Coding Broad Burden
CAPN14	2	31395924	31456724	p23.1	0.0081	5.1	MAF01 Coding Broad SKAT
HEATR5B	2	37195526	37311485	p22.2	0.0043	2.2	MAF01 Coding Broad SKAT
CDKL4	2	39402787	39456729	p22.1	0.0049	2.0	MAF01 Coding Broad SKAT
SRBD1	2	45615819	45839304	p21	0.0058	2.3	MAF01 Coding Broad Burden
NRXN1	2	50145643	51259674	p16.3	0.0071	1.2	MAF01 Regulatory Broad SKAT
PROKR1	2	68870721	68882708	p13.3	0.0099	2.4	MAF01 Coding Broad SKAT
PCBP1	2	70314585	70316332	p13.3	0.00095	2.5	MAF05 Regulatory Broad SKAT
RNF181	2	85822848	85824736	p11.2	0.0047	4.2	MAF01 Coding Broad SKAT
GNLY	2	85912298	85925977	p11.2	0.0034	4.7	MAF01 Coding Broad Burden
SULT1C3	2	108863651	108881807	q12.3	0.0011	2.1	MAF05 Coding Broad SKAT
KIF5C	2	149632819	149883273	q23.1	0.0040	5.4	MAF01 Coding Broad SKAT
HDLBP	2	242166679	242256476	q37.3	0.0070	0.95	MAF01 Regulatory Narrow SKAT
EDEM1	3	5229331	5261642	p26.1	0.0094	1.6	MAF01 Coding Broad SKAT

Table S7 Top Genes

RP11-438J1.1	3	10291056	10327480	p25.3	0.0099	1.6	MAF01 Coding Broad SKAT
ENTPD3	3	40428647	40470110	p22.1	0.0071	3.3	MAF01 Coding Broad SKAT
NBEAL2	3	47021173	47051193	p21.31	0.0036	2.4	MAF01 Coding Broad Burden
SMARCC1	3	47626762	47823596	p21.31	0.0052	1.3	MAF01 Coding Broad SKAT
CDHR4	3	49828165	49837268	p21.31	0.0091	3.1	MAF05 Coding Broad Burden
TRAIP	3	49866034	49894007	p21.31	0.0099	0.076	MAF01 Coding Broad Burden
LRTM1	3	54952264	55001115	p14.3	0.0074	8.7	MAF01 Coding Broad Burden
OR5H2	3	98001732	98002676	q11.2	0.0043	3.7	MAF01 Coding Broad Burden
KIAA1524	3	108268716	108308491	q13.13	0.0083	1.1	MAF05 Coding Broad SKAT
GAP43	3	115342171	115440337	q13.31	0.0046	2.0	MAF05 Regulatory Broad SKAT
MYLK	3	123328896	123603178	q21.1	0.0079	0.97	MAF01 Coding Broad SKAT
OSBPL11	3	125247702	125313934	q21.2	0.0074	3.3	MAF01 Coding Broad SKAT
SLCO2A1	3	133651540	133771028	q22.2	0.0025	2.7	MAF01 Coding Broad SKAT
PRR23B	3	138737873	138739768	q23	0.0084	23	MAF01 Coding Broad Burden
MED12L	3	150803484	151154860	q25.1	0.0014	0.13	MAF01 Coding Broad Burden
IFT80	3	159974774	160117668	q25.33	0.0046	2.8	MAF01 Coding Broad SKAT
NAALADL2	3	174156363	175523428	q26.31	0.0051	4.9	MAF01 Coding Broad Burden
RTP1	3	186915274	186919253	q27.3	0.0041	0.064	MAF01 Coding Broad Burden
LRCH3	3	197518097	197615307	q29	0.0070	3.7	MAF01 Coding Broad Burden
HTT	4	3076408	3245676	p16.3	0.0025	1.9	MAF01 Regulatory Broad Burden
LRPAP1	4	3508103	3534286	p16.3	0.0074	0.50	MAF05 Coding Broad Burden
CLNK	4	10488019	10686489	p16.1	0.0028	2.9	MAF01 Coding Broad SKAT
RFC1	4	39289076	39367995	p14	0.0080	2.8	MAF01 Coding Broad SKAT
TMPRSS11B	4	69092371	69111438	q13.2	0.0036	3.5	MAF01 Coding Broad SKAT
ART3	4	76932337	77033955	q21.1	0.0080	3.4	MAF01 Coding Broad SKAT
PRDM5	4	121606074	121844025	q27	0.0055	2.9	MAF01 Coding Broad SKAT
GRIA2	4	158125334	158287227	q32.1	0.0034	23	MAF01 Coding Broad SKAT
MLF1IP	4	185615772	185655287	q35.1	0.0071	1.7	MAF01 Coding Broad SKAT
ACSL1	4	185676749	185747972	q35.1	0.0031	2.5	MAF01 Coding Broad SKAT
FAT1	4	187508937	187647876	q35.2	0.0069	1.5	MAF01 Coding Broad SKAT
PDZD2	5	31639517	32111037	p13.3	0.0069	1.5	MAF05 Coding Broad Burden
ADAMTS12	5	33523640	33892297	p13.2	0.0024	0.54	MAF05 Coding Broad Burden
RXFP3	5	33936491	33939023	p13.2	0.0025	3.0	MAF01 Coding Broad SKAT
SLC1A3	5	36606457	36688436	p13.2	0.0017	1.1	MAF05 Regulatory Broad SKAT
NNT	5	43602794	43707507	p12	0.00067	2.8	MAF01 Coding Broad SKAT
MAST4	5	65892176	66465423	q12.3	0.0044	1.7	MAF05 Coding Broad Burden
BHMT	5	78407602	78428108	q14.1	0.0014	2.6	MAF01 Coding Broad SKAT
ZFYVE16	5	79703832	79775169	q14.1	0.0045	2.6	MAF01 Coding Broad SKAT
RASGRF2	5	80256491	80525975	q14.1	0.0049	1.5	MAF01 Regulatory Broad SKAT
REEP5	5	112212084	112258236	q22.2	0.0035	2.7	MAF01 Regulatory Broad Burden
SEMA6A	5	115779312	115910630	q23.1	0.0077	0.41	MAF01 Coding Broad Burden
SLC12A2	5	127419458	127525380	q23.3	0.0057	2.7	MAF01 Coding Broad SKAT
SFXN1	5	174904065	174956745	q35.2	0.00081	1.7	MAF01 Regulatory Broad SKAT
BTN3A1	6	26402465	26415444	p22.2	0.0046	2.3	MAF01 Coding Broad SKAT
UHRF1BP1	6	34759857	34850915	p21.31	0.0054	3.3	MAF01 Coding Broad Burden
ENPP5	6	46126924	46138708	p21.1	0.0072	0.21	MAF01 Coding Broad Burden

DDX43	6	74104471	74127292	q13	0.0028	4.8	MAF01 Coding Broad SKAT
LIN28B	6	105404923	105531207	q16.3	0.0065	6.1	MAF01 Coding Broad Burden
SESN1	6	109307640	109416022	q21	0.0037	6.7	MAF01 Coding Broad SKAT
TRAF3IP2	6	111877657	111927481	q21	0.0082	0.16	MAF01 Coding Broad Burden
PHACTR2	6	143857982	144152322	q24.2	0.0062	4.3	MAF01 Coding Broad Burden
GRM1	6	146348782	146758734	q24.3	0.00023	2.8	MAF01 Coding Broad SKAT
PLEKHG1	6	150920999	151164799	q25.1	0.0064	2.1	MAF05 Coding Broad SKAT
SYNE1	6	152442819	152958936	q25.2	0.00058	1.9	MAF01 Regulatory Broad Burden
FNDC1	6	159590429	159693141	q25.3	0.0063	1.3	MAF01 Coding Broad SKAT
DGKB	7	14184674	15014402	p21.2	0.0089	1.7	MAF01 Regulatory Broad Burden
GPNMB	7	23275586	23314727	p15.3	0.0089	2.8	MAF01 Coding Disrupt SKAT
HOXA1	7	27132612	27135615	p15.2	0.0043	4.0	MAF01 Coding Broad SKAT
PLEKHA8	7	30067020	30170096	p14.3	0.0095	3.3	MAF01 Coding Broad SKAT
NT5C3A	7	33053742	33102409	p14.3	0.0087	6.1	MAF01 Coding Broad SKAT
BBS9	7	33168856	33645680	p14.3	0.0029	0.41	MAF05 Regulatory Broad Burden
ZNF680	7	63980262	64023484	q11.21	0.0063	0.15	MAF01 Coding Broad Burden
TRIM50	7	72726535	72742085	q11.23	0.0053	6.2	MAF01 Coding Broad Burden
CCDC146	7	76751751	76958850	q11.23	0.00090	2.2	MAF01 Coding Broad SKAT
GNAT3	7	80087987	80141336	q21.11	0.0084	0.078	MAF01 Coding Broad Burden
ARPC1B	7	98971872	98992424	q22.1	0.0077	0.52	MAF05 Coding Broad Burden
CYP3A43	7	99425636	99463718	q22.1	0.0055	2.0	MAF05 Coding Broad Burden
GPC2	7	99767229	99774995	q22.1	0.0078	3.2	MAF01 Coding Broad SKAT
SRPK2	7	104751151	105039755	q22.3	0.0033	3.1	MAF01 Coding Broad SKAT
LAMB1	7	107564244	107643700	q31.1	0.0034	1.2	MAF05 Coding Broad SKAT
CEP41	7	130033612	130082274	q32.2	0.0058	1.8	MAF01 Coding Broad SKAT
AGK	7	141250989	141355044	q34	0.0076	0.44	MAF01 Regulatory Broad SKAT
SLC4A2	7	150754297	150773614	q36.1	0.0043	4.0	MAF01 Coding Broad SKAT
ESYT2	7	158523686	158622944	q36.3	0.0078	15	MAF01 Regulatory Narrow SKAT
ZDHHC2	8	17013538	17082308	p22	0.0032	2.6	MAF01 Coding Broad SKAT
PBK	8	27667137	27695612	p21.1	0.0039	22	MAF01 Coding Broad Burden
WHSC1L1	8	38127215	38239790	p11.23	0.0080	0.32	MAF05 Coding Broad Burden
PXDNL	8	52232138	52722005	q11.23	0.0053	2.8	MAF05 Coding Disrupt Burden
KCNB2	8	73449626	73850584	q13.3	0.0065	20	MAF01 Regulatory Broad Burden
GDAP1	8	75233365	75401107	q21.11	0.0071	7.9	MAF01 Coding Broad Burden
CDH17	8	95139399	95229531	q22.1	0.0070	1.2	MAF01 Coding Broad SKAT
TBC1D31	8	124054208	124164393	q24.13	0.0014	1.4	MAF01 Coding Broad SKAT
NDRG1	8	134249414	134314265	q24.22	0.0048	2.4	MAF05 Regulatory Broad Burden
IL33	9	6215805	6257983	p24.1	0.0060	5.5	MAF01 Coding Broad SKAT
LURAP1L	9	12775020	12822130	p23	0.0016	3.4	MAF01 Coding Broad SKAT
C9orf3	9	97488983	97849441	q22.32	0.0080	1.8	MAF01 Coding Broad SKAT
ANKS6	9	101493611	101559247	q22.33	0.0029	2.8	MAF01 Coding Broad SKAT
STOM	9	124101355	124132531	q33.2	0.0049	0.89	MAF05 Regulatory Broad SKAT
GLE1	9	131266979	131304567	q34.11	0.0019	4.1	MAF05 Coding Broad Burden
NELFB	9	140149625	140167998	q34.3	0.0065	5.1	MAF01 Coding Broad SKAT
TAF3	10	7860467	8058590	p14	0.0037	19	MAF01 Coding Broad Burden
OTUD1	10	23728198	23731308	p12.2	0.0077	0.40	MAF05 Coding Broad Burden

CREM	10	35415719	35501886	p11.21	0.0059	3.6	MAF01 Coding Broad SKAT
CHAT	10	50817141	50901925	q11.23	0.0058	3.8	MAF01 Coding Broad Burden
A1CF	10	52559169	52645435	q11.23	0.0083	2.0	MAF01 Coding Broad SKAT
CFAP70	10	75013517	75118617	q22.2	0.000065	4.1	MAF01 Coding Broad SKAT
POLR3A	10	79734907	79789303	q22.3	0.0010	0.45	MAF05 Coding Broad SKAT
ANXA11	10	81910645	81965328	q22.3	0.0076	0.74	MAF05 Coding Broad SKAT
KIF20B	10	91461367	91534700	q23.31	0.0081	0.36	MAF01 Regulatory Narrow Burden
LZTS2	10	102756375	102767593	q24.31	0.0029	4.4	MAF01 Coding Broad SKAT
TECTB	10	114043493	114064793	q25.2	0.0062	1.6	MAF01 Coding Broad SKAT
AFAP1L2	10	116054583	116164515	q25.3	0.0074	5.5	MAF01 Coding Broad Burden
RAB11FIP2	10	119764427	119806114	q26.11	0.0050	3.5	MAF01 Coding Broad Burden
PTPRE	10	129705325	129884119	q26.2	0.0033	0.23	MAF01 Coding Broad Burden
PSMD13	11	236546	252983	p15.5	0.0044	8.8	MAF01 Coding Broad Burden
MUC5B	11	1244296	1283406	p15.5	0.0060	1.6	MAF01 Coding Broad Burden
KCNQ1	11	2465914	2870339	p15.5	0.0044	1.2	MAF01 Regulatory Narrow SKAT
OR51A4	11	4967355	4968356	p15.4	0.00093	0.46	MAF05 Coding Broad Burden
OR52N4	11	5775923	5776959	p15.4	0.0094	2.5	MAF01 Coding Broad Burden
OR10A6	11	7949180	7950209	p15.4	0.0049	0.51	MAF05 Coding Broad Burden
IPO7	11	9406169	9469673	p15.4	0.0076	2.3	MAF01 Regulatory Broad Burden
TSG101	11	18489883	18548779	p15.1	0.0038	6.8	MAF01 Coding Broad SKAT
BDNF	11	27676440	27743605	p14.1	0.0045	1.8	MAF01 Regulatory Broad Burden
KIAA1549L	11	33563618	33695648	p13	0.0063	2.5	MAF01 Coding Broad SKAT
CD59	11	33719807	33757991	p13	0.0030	1.6	MAF05 Regulatory Broad Burden
PACSIN3	11	47199076	47207994	p11.2	0.0039	3.1	MAF01 Coding Broad SKAT
FOLH1	11	49168187	49230222	p11.12	0.0046	2.5	MAF01 Coding Broad SKAT
OR5M11	11	56309746	56310757	q12.1	0.0031	5.5	MAF01 Coding Broad SKAT
OR5B3	11	58169937	58170882	q12.1	0.0056	0.54	MAF01 Coding Broad SKAT
TMEM132A	11	60691935	60704631	q12.2	0.0053	0.49	MAF05 Coding Broad Burden
PPP1R32	11	61248592	61258403	q12.2	0.0055	2.0	MAF05 Coding Broad Burden
KLC2	11	66024765	66035331	q13.2	0.0051	1.5	MAF01 Regulatory Broad SKAT
BRMS1	11	66104804	66112596	q13.2	0.0058	6.7	MAF01 Coding Broad SKAT
CABP4	11	67219877	67226699	q13.2	0.0087	0.074	MAF01 Coding Broad Burden
SHANK2	11	70313961	70963623	q13.4	0.00022	2.2	MAF05 Coding Broad Burden
FAT3	11	92085262	92629618	q14.3	0.0060	1.5	MAF05 Coding Broad Burden
ATM	11	108093211	108239829	q22.3	0.0097	0.63	MAF05 Coding Broad Burden
TMPRSS5	11	113558272	113577095	q23.2	0.0099	2.5	MAF01 Coding Broad SKAT
TREH	11	118528026	118550399	q23.3	0.0022	3.0	MAF05 Coding Broad Burden
ABCG4	11	119019722	119033360	q23.3	0.0041	21	MAF01 Coding Broad Burden
ZNF202	11	123594885	123612383	q24.1	0.0058	0.21	MAF05 Coding Broad Burden
VWA5A	11	123986069	124018428	q24.2	0.0038	1.3	MAF01 Coding Broad SKAT
SRPR	11	126132814	126139039	q24.2	0.0047	2.3	MAF05 Coding Broad SKAT
SLC6A13	12	329789	372039	p13.33	0.000061	3.6	MAF01 Coding Broad SKAT
FKBP4	12	2904119	2914576	p13.33	0.0079	15	MAF01 Regulatory Broad Burden
MFAP5	12	8789942	8815484	p13.31	0.0095	0.076	MAF01 Coding Broad Burden
GOLT1B	12	21654715	21671342	p12.1	0.0078	22	MAF01 Coding Broad Burden
CNTN1	12	41086244	41466220	q12	0.0087	2.5	MAF01 Coding Broad SKAT

FMNL3	12	50031724	50101948	q13.12	0.0078	0.073	MAF01 Regulatory Narrow Burden
KRT79	12	53215194	53228079	q13.13	0.0078	0.61	MAF05 Coding Broad Burden
SOAT2	12	53497302	53518322	q13.13	0.0085	2.9	MAF01 Coding Broad SKAT
OR6C68	12	55886147	55887100	q13.2	0.0089	0.16	MAF05 Coding Broad Burden
MARS	12	57869228	57911352	q13.3	0.0076	0.15	MAF01 Coding Broad Burden
USP15	12	62654119	62811211	q14.1	0.0023	0.30	MAF05 Regulatory Broad Burden
LEMD3	12	65563351	65642107	q14.3	0.0017	3.1	MAF01 Coding Broad SKAT
PPP1R12A	12	80167343	80329240	q21.31	0.00089	3.5	MAF01 Regulatory Broad SKAT
EEA1	12	93164413	93323107	q22	0.0056	1.6	MAF01 Coding Broad SKAT
FGD6	12	95470525	95611258	q22	0.0070	0.35	MAF01 Coding Broad Burden
APAF1	12	99038919	99129204	q23.1	0.0084	1.9	MAF05 Coding Broad SKAT
ALDH2	12	112204691	112247782	q24.12	0.0012	10	MAF01 Coding Broad Burden
MORN3	12	122089024	122110537	q24.31	0.0012	11	MAF01 Coding Broad Burden
RILPL1	12	123955925	124018265	q24.31	0.0036	8.7	MAF01 Coding Broad SKAT
ZNF140	12	133656424	133684130	q24.33	0.0084	17	MAF01 Coding Broad Burden
TPTE2	13	19997017	20110903	q12.11	0.0041	2.1	MAF01 Coding Broad SKAT
DCLK1	13	36345478	36705443	q13.3	0.00039	4.9	MAF01 Coding Broad SKAT
TNFSF11	13	43136872	43182149	q14.11	0.0024	2.4	MAF01 Coding Broad SKAT
COG3	13	46039060	46110765	q14.13	0.0053	3.5	MAF01 Coding Broad SKAT
LRCH1	13	47127303	47327175	q14.13	0.0093	1.4	MAF01 Coding Broad SKAT
DACH1	13	72012098	72441330	q21.33	0.0046	8.7	MAF01 Coding Broad Burden
KCTD12	13	77454312	77460540	q22.3	0.00077	1.6	MAF01 Regulatory Broad SKAT
OR4K2	14	20344391	20345468	q11.2	0.0050	3.1	MAF01 Coding Broad SKAT
METTL17	14	21457929	21465189	q11.2	0.0034	0.23	MAF05 Coding Broad Burden
EAPP	14	34985135	35008916	q13.1	0.0067	8.0	MAF01 Coding Broad Burden
RP11-407N17.3	14	39703106	39820397	q21.1	0.0015	0.24	MAF01 Coding Broad Burden
CTAGE5	14	39734488	39856156	q21.1	0.0033	0.26	MAF01 Coding Broad Burden
GPX2	14	65405870	65409531	q23.3	0.0033	0.34	MAF05 Coding Broad SKAT
ACTN1	14	69340860	69446157	q24.1	0.0079	0.60	MAF01 Regulatory Broad SKAT
ZFYVE1	14	73436159	73493920	q24.2	0.0032	2.5	MAF01 Coding Broad SKAT
NUMB	14	73741815	73930348	q24.3	0.0069	8.0	MAF01 Coding Broad Burden
WARS	14	100800125	100843142	q32.2	0.0071	2.5	MAF01 Coding Broad SKAT
ASPG	14	104552016	104579098	q32.33	0.0041	7.1	MAF01 Coding Broad SKAT
AHNAK2	14	105403581	105444694	q32.33	0.0013	1.0	MAF01 Coding Broad SKAT
AVEN	15	34158428	34331377	q14	0.00079	1.1	MAF05 Coding Broad SKAT
DUOX2	15	45384848	45406542	q21.1	0.0083	23	MAF01 Coding Disrupt Burden
CORO2B	15	68871308	69020145	q23	0.0051	1.4	MAF01 Coding Broad SKAT
GRAMD2	15	72452148	72490126	q23	0.0061	4.3	MAF01 Coding Broad Burden
FBXO22	15	76196200	76227609	q24.2	0.0014	0.056	MAF01 Coding Broad Burden
CHRNA5	15	78857862	78887611	q25.1	0.0028	0.061	MAF01 Coding Broad Burden
KLHL25	15	86302554	86338261	q25.3	0.0082	2.6	MAF01 Coding Broad SKAT
C16orf13	16	684429	686358	p13.3	0.0016	6.7	MAF01 Coding Broad SKAT
STUB1	16	730224	732870	p13.3	0.0038	2.6	MAF01 Regulatory Broad Burden
TSC2	16	2097466	2138716	p13.3	0.0089	0.63	MAF05 Regulatory Broad Burden
CASKIN1	16	2227184	2246526	p13.3	0.0084	2.7	MAF01 Regulatory Broad Burden
PAM16	16	4381550	4405608	p13.3	0.0080	1.1	MAF05 Regulatory Broad SKAT

UBN1	16	4896666	4932361	p13.3	0.0071	0.21	MAF01 Coding Broad Burden
AC004381.6	16	20817751	20860987	p12.3	0.0027	1.3	MAF01 Coding Broad SKAT
TMEM219	16	29952206	29984373	p11.2	0.0074	5.5	MAF01 Coding Broad SKAT
CCDC102A	16	57546090	57570511	q21	0.0075	7.7	MAF01 Coding Broad Burden
TEPP	16	58010339	58022020	q21	0.00027	31	MAF01 Coding Broad Burden
ZNF319	16	58028572	58034357	q21	0.0056	4.8	MAF01 Coding Broad Burden
CDH11	16	64977656	65160015	q21	0.0084	0.30	MAF01 Coding Broad Burden
CDH3	16	68670092	68756519	q22.1	0.0059	3.2	MAF01 Coding Broad Burden
TAF1C	16	84211458	84220669	q24.1	0.0071	3.4	MAF01 Coding Broad Burden
ZNF778	16	89284118	89295363	q24.3	0.0040	1.0	MAF01 Coding Broad SKAT
NXN	17	702553	883010	p13.3	0.0039	2.5	MAF01 Coding Broad SKAT
MYO1C	17	1367392	1396106	p13.3	0.0099	1.8	MAF05 Coding Broad Burden
TMEM88	17	7758383	7759417	p13.1	0.0043	3.6	MAF01 Coding Broad SKAT
MPRIP	17	16945859	17120993	p11.2	0.0075	2.0	MAF01 Coding Broad SKAT
ALDH3A2	17	19551449	19580911	p11.2	0.0071	3.4	MAF01 Coding Broad SKAT
MYO18A	17	27400528	27507430	q11.2	0.0065	2.3	MAF01 Coding Broad Burden
GIT1	17	27900487	27921072	q11.2	0.0070	2.6	MAF01 Regulatory Broad Burden
MYO1D	17	30819540	31204195	q11.2	0.0055	0.28	MAF01 Coding Broad Burden
CCL16	17	34303529	34308532	q12	0.0090	0.42	MAF05 Coding Broad Burden
ATP6V0A1	17	40610862	40674629	q21.2	0.0044	2.3	MAF01 Regulatory Broad Burden
MTMR4	17	56566898	56595266	q22	0.0093	0.98	MAF01 Coding Broad SKAT
CBX2	17	77751931	77761782	q25.3	0.0069	0.96	MAF01 Coding Broad SKAT
TBC1D16	17	77906142	78009647	q25.3	0.0011	2.1	MAF05 Coding Broad Burden
EMILIN2	18	2847028	2915991	p11.32	0.0030	1.6	MAF05 Coding Broad SKAT
DSG1	18	28898052	28936992	q12.1	0.0051	1.6	MAF01 Coding Broad SKAT
DSG3	18	29027758	29058665	q12.1	0.00018	2.7	MAF01 Coding Broad SKAT
SLC25A52	18	29339525	29340843	q12.1	0.0096	3.1	MAF01 Coding Broad SKAT
LOXHD1	18	44056935	44236996	q21.1	0.00046	1.0	MAF05 Coding Broad SKAT
ZNF516	18	74069644	74207146	q23	0.0090	1.9	MAF01 Coding Broad SKAT
PPAP2C	19	281040	291393	p13.3	0.0097	0.29	MAF01 Coding Broad Burden
THEG	19	361750	376013	p13.3	0.0094	0.074	MAF01 Coding Broad Burden
POLRMT	19	617223	633597	p13.3	0.0012	26	MAF01 Coding Broad Burden
PRSS57	19	685521	695460	p13.3	0.0093	2.4	MAF01 Coding Broad SKAT
FSD1	19	4304597	4323840	p13.3	0.0052	3.4	MAF01 Regulatory Broad Burden
ZNF559	19	9434448	9461838	p13.2	0.0023	5.9	MAF01 Coding Broad SKAT
ICAM5	19	10400657	10407454	p13.2	0.0039	0.063	MAF01 Regulatory Broad Burden
ZNF823	19	11832080	11849824	p13.2	0.0036	1.9	MAF05 Coding Broad SKAT
CCDC130	19	13842574	13874110	p13.2	0.0014	11	MAF01 Coding Broad Burden
CC2D1A	19	14017014	14041692	p13.12	0.0073	1.6	MAF01 Coding Broad SKAT
OR7A17	19	14991138	14992264	p13.12	0.0099	0.51	MAF05 Coding Broad Burden
AP1M1	19	16308389	16346160	p13.11	0.0030	1.6	MAF01 Regulatory Broad SKAT
SUGP1	19	19386827	19431653	p13.11	0.0060	22	MAF01 Coding Broad SKAT
ZNF429	19	21679484	21739072	p12	0.0090	1.2	MAF05 Coding Broad SKAT
RHPN2	19	33469499	33555794	q13.11	0.00079	2.2	MAF05 Coding Broad Burden
ZNF780B	19	40534167	40562116	q13.2	0.0076	3.3	MAF05 Coding Disrupt Burden
CNTD2	19	40728115	40732597	q13.2	0.0057	6.9	MAF01 Coding Broad SKAT

Table S7 Top Genes

IRGQ	19	44088521	44100287	q13.31	0.0081	2.3	MAF05 Regulatory Narrow SKAT
ZNF221	19	44455375	44471861	q13.31	0.0015	3.6	MAF01 Coding Broad SKAT
ZNF222	19	44529494	44537265	q13.31	0.0099	2.9	MAF01 Coding Broad Burden
TRPM4	19	49660998	49715093	q13.33	0.0073	0.87	MAF01 Coding Broad SKAT
TSKS	19	50243010	50266587	q13.33	0.0055	1.7	MAF01 Coding Broad SKAT
SIGLEC12	19	51994611	52005043	q13.41	0.0081	0.32	MAF01 Coding Broad Burden
PPP2R1A	19	52693292	52730687	q13.41	0.0072	2.7	MAF01 Regulatory Broad Burden
ZNF534	19	52932440	52955568	q13.41	0.0087	0.79	MAF05 Coding Broad SKAT
ZNF835	19	57174020	57183151	q13.43	0.0087	1.9	MAF05 Coding Broad SKAT
ZNF530	19	58111253	58124090	q13.43	0.0028	1.2	MAF05 Coding Broad SKAT
CSNK2A1	20	459116	524465	p13	0.0028	6.0	MAF01 Regulatory Narrow SKAT
PYGB	20	25228705	25278650	p11.21	0.00047	0.11	MAF01 Coding Broad Burden
ZNF341	20	32319463	32380075	q11.22	0.0064	0.93	MAF01 Coding Broad SKAT
CPNE1	20	34213953	34252878	q11.22	0.0092	2.0	MAF01 Coding Broad SKAT
SLC32A1	20	37353105	37358015	q11.23	0.0099	5.8	MAF01 Coding Broad Burden
YWHAB	20	43514317	43537173	q13.12	0.0049	1.5	MAF05 Regulatory Broad Burden
KCNB1	20	47980414	48099184	q13.13	0.0077	19	MAF01 Coding Broad Burden
PHACTR3	20	58152564	58422766	q13.32	0.0087	1.9	MAF05 Coding Broad SKAT
EEF1A2	20	62119366	62130505	q13.33	0.00047	0.047	MAF01 Regulatory Broad Burden
ZBTB21	21	43406940	43430496	q22.3	0.0067	0.15	MAF01 Coding Broad Burden
UBASH3A	21	43824008	43867791	q22.3	0.0029	1.6	MAF01 Coding Broad SKAT
MYO18B	22	26138111	26427007	q12.1	0.0079	1.4	MAF01 Coding Broad SKAT
PDXP	22	38054734	38062941	q13.1	0.0062	0.81	MAF05 Coding Broad SKAT
MCHR1	22	41074754	41078818	q13.2	0.0022	0.30	MAF01 Coding Broad SKAT
MEI1	22	42095503	42195460	q13.2	0.0092	2.3	MAF01 Coding Broad SKAT
PACSIN2	22	43231418	43411151	q13.2	0.0047	1.5	MAF01 Regulatory Broad SKAT
PNPLA3	22	44319619	44360368	q13.31	0.00055	2.8	MAF01 Coding Broad SKAT
HDAC10	22	50683612	50689834	q13.33	0.0093	7.8	MAF01 Coding Broad Burden
PASD1	X	150732094	150845211	q28	0.0035	0.42	MAF05 Coding Broad Burden
LCA10	X	153146127	153154444	q28	0.0038	0.14	MAF05 Coding Broad Burden

Table S7: P-values are corrected for the covariates of sex, platform, and the first 5 PCA components but are not corrected for multiple testing.

Table S8: Top Variants Contributing to the Limonene and Pinene Degradation Pathway Result

SNP ID	hg19 Location	P-Value	Odds Ratio	Gene	Position/Function	Attempter MAF	Non-Attempter MAF
rs61737992	chr17:19575096	0.013	3.3	*ALDH3A2*	Non-Synonymous (P→S)	0.014	0.0032
rs61757684	chr5:125880710	0.033	3.4	*ALDH7A1*	Non-Synonymous (T→A)	0.012	0.0032
rs556650006	chr5:125930919	0.057	12	*ALDH7A1*	Non-Synonymous (L→P)	0.0028	0.0
rs199916968	chr3:184910322	0.086	9.6	*EHHADH*	Non-Synonymous (R→C)	0.0026	0.0
rs147086207	chr12:112221070	0.11	8.6	*ALDH2*	Non-Synonymous (D→H)	0.0026	0.0

Table S9: MAF01 Coding Broad Gene Burden Results Contributing to the Limonene and Pinene Degradation Pathway Result

Gene	Chromosome	hg19 Start	hg19 Stop	P-value	Odds Ratio	Attempter Collapsed Frequency	Non-Attempter Collapsed Frequency
ALDH2	12	38390661	38400658	0.0012	10	0.023	0.0016
ALDH3A2	17	19549449	19582911	0.011	3.4	0.031	0.0095
ALDH7A1	5	125875533	125933110	0.039	2.3	0.041	0.017
ALDH9A1	1	165629453	165670100	0.066	0.24	0.0026	0.013
ECHS1	10	135173984	135189193	0.12	4.0	0.010	0.0016
EHHADH	3	184906412	185001778	0.14	1.8	0.034	0.019
ALDH1B1	9	38390661	38400658	0.20	1.6	0.041	0.025
NAT6	3	50331833	50338852	0.26	0.39	0.0031	0.012
YOD1	1	207215194	207228325	0.30	2.6	0.0078	0.0016
HADHA	2	26411504	26469594	0.91	1.0	0.031	0.030

Collapsed frequencies refer to the frequency of individuals with at least one variant meeting the variant set criteria across the complete gene locus; P-values and odds ratios corrected for sex, platform, and the first 5 principal components for each subject. $p<1.0*10^{-6}$ (conservative) or $p<2.5*10^{-6}$ (liberal) required for significance via Bonferroni correction.

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