THE LANCET Neurology

Supplementary webappendix

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Supplement to: Epi4K consortium, Epilepsy Phenome/Genome Project. Ultra-rare genetic variation in common epilepsies: a case-control sequencing study. *Lancet Neurol* 2017; **16:** 135–43.

Supplementary Appendix. Ultra-rare genetic variation in the common epilepsies: a case-control sequencing study

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Supplemental Method: IGM Bioinformatics Pipeline

After quality filtering the raw sequence data using CASAVA (Illumina, Inc., San Diego, CA), the Illumina lane-level FASTQ files were aligned to the Human Reference Genome (NCBI Build37/hg19) using the Burrows-Wheeler Alignment Tool (BWA).[1] Picard (http://picard.sourceforge.net) was used to remove duplicate reads and process these lane-level SAM files, resulting in a sample-level BAM file that was used for variant calling. Variant and genotype calling was performed using the GATK software with local re-alignment around insertion/deletion variants and base quality recalibration for variants.[2]

Variants were required to be among the consensus coding sequence public transcripts (CCDS release 14).[3] Variants were further required to have: i) at least 10-fold coverage, ii) quality score (QUAL) of at least 50, iii) genotype quality (GQ) score of at least 20, iv) quality by depth (QD) score of at least 2, v) mapping quality (MQ) score of at least 40, vi) read position rank sum (RPRS) score greater than -3, vii) mapping quality rank sum (MQRS) score greater than -6, viii) indels were required to have a maximum Fisher's strand bias (FS) of 200, ix) variants were screened according to VQSR tranche calculated using the known SNV sites from HapMap v3.3, dbSNP, and the Omni chip array from the 1000 Genomes Project to "PASS" SNVs were required to achieve a tranche of 99.9% for SNVs in genomes and exomes and 99% for indels in genomes, x) for heterozygous genotypes, the alternative allele ratio was required to be ≥25%. Finally, variants were excluded if they were among a predefined list of known sequencing artifacts or if they were marked by EVS (http://evs.gs.washington.edu/EVS/)[4] or ExAC (http://exac.broadinstitute.org/about)[5] as being problematic variants. Variants were annotated to Ensembl 73 [6] using SnpEff.[7]

The case and control populations were pre-screened with both KING[8] and PLINK[9] to ensure only unrelated (up to second-degree) samples were used. Any exomes with gender discordance between clinically-reported and X:Y coverage ratios were removed, as were contaminated samples according to VerifyBamID.[10] European genetic ancestry was confirmed using both self-reported ethnicity and principal component predicted ethnicity as calculated using EIGENSTRAT.[11] Further, to be eligible, samples were required to have greater than 85% of the 33.27 Mbps of CCDS (release 14) covered with at least 10-fold coverage.

Supplemental Method: Principal components analysis of ancestry

Principal component analysis was performed on 10,423 ethnically diverse samples that were sequenced at the Institute for Genomic Medicine (IGM), Columbia University, including 2,185 patients with epilepsy (Figure S1A). To generate eigenvectors, we used uncorrelated (r^2<0.1) polymorphic markers from the Illumina HumanCore chip that overlap protein-coding exons and are well covered by whole-exome sequencing. To be considered well covered, the variant site had to achieve a genotype missingness rate <5%, (i.e., only variants where at least 95% of the samples had at least 10-fold coverage were used). The total genotyping rate across the well covered polymorphic exonic markers for the case and control collection was 0.9984.

Classifying the 10,423 sequenced samples into a major geographic ancestry group was achieved using EIGENSTRAT[11] to generate principal components (PCs) based on 3,459 well covered exonic polymorphic markers. To derive our PC predicted genetic ethnicities, we ran a multinomial logistic regression model that used PC axes 1 – 6 as the independent variables and was trained on 2,821 individuals with pre-defined genetic ancestry across six ancestry groups. Each of the 10,423 sequenced samples was then assigned its own probability estimate for each of six ancestry groups (European, African American, Latino, East Asian, South Asian and Middle Eastern), with the sum of probabilities equalling one.

For a sample to pass the requirement of European genetic ancestry, we required the probability of being European to be greater than 0.50 and furthermore that the sample was within the boundary defined by the major principal components 1 and 2 of: [PC1: -0.008 to -0.003] and [PC2: -0.01 to 0.005] (Figure S1B; Table S3).

Supplemental Method: Site-based opportunity to call variants

The sequence real-estate of the consensus coding sequence (CCDS, release 14) public transcripts amasses 33,266,994 unique bases (sites), among which we included two base-pair intronic extensions to accommodate each exon's canonical splice sites.

To help alleviate the noise caused by inconsistently covered sites we performed the following steps for each of our three case-control comparisons to prune 'noisy' protein-coding sites out of our tests:

1) For each of the 33.27Mbp sites, the percentage of case and control samples that had at least 10-fold coverage was calculated.

2) For each nucleotide site, the difference between the case and control percentages was then calculated as the |absolute difference|. Thus, for each nucleotide site a single positive value was generated, which reflects the difference in the opportunity to have called a variant at that precise site between cases and controls. This was done regardless of whether the site was variant or non-variant in the combined case control population.

3) We then calculated the mean |absolute difference| from the 33.27 million comparisons. The mean is then subtracted from the |absolute difference| values for each site to reflect the deviation from mean difference, which is then squared to define the variation value for each of the 33.27 million sites. The resulting variation estimates across the 33.27 million sites were then sorted from largest to smallest and plotted as a cumulative sum of variation plot (Figure S8). In this plot, the y-axis reflects the cumulative sum of variation explained and the x-axis reflects the cumulative percentage of the 33.27Mbp sequence.

4) The plot is then shifted on a 45 degree angle to find the peak maximum point. That is the y-axis is replaced by (y-x). Plotting the new y against x, the subjective function is plotted. Here, the x value at which y is maximized points us to the suggested cut-off index.

5) After having isolated the single (max) point, we refer back to the corresponding |absolute difference| that is annotated to the nucleotide site reflecting that point. For our three case populations the corresponding |absolute difference| for the case compared to control comparisons equalled 0.052 (GGE), 0.051 (familial NAFE), and 0.064 (sporadic NAFE). In summary, this process uses the cumulative sum of variation plot to identify a single point at which we account for most of the variation while reducing the amount of sites that will be pruned out.

6) We then find the precise nucleotide sites that have |absolute difference| greater than 5.2% (using the GGE example) and remove those sites from the genic boundaries. For familial GGE this translated to 8.94% of sites pruned out (Figure S8); for familial NAFE 8.33% of sites were pruned out and similarly 8.30% of sites were pruned out for sporadic NAFE analyses. All genic collapsing analyses relied on these post-pruning genic boundaries.

Supplemental Method: Quantile-quantile probability plots and genomic inflation factor (λ)

Quantile-quantile plots were generated using a permutation-based expected probabilities distribution. To achieve this, for each model (matrix) we randomly permuted the case and control labels of the original configuration and then recomputed the Fisher's Exact test for all genes. This was repeated 1,000 times. For each of the 1,000 permutations we ordered the p-values and then took the mean of each rank-ordered estimate across the 1,000 permutations, i.e., the average 1^{st} order statistic, the average 2^{nd} order statistic, etc. These then represent the empirical estimates of the expected ordered p-values (expected -log10(p-values)). This empirical-based expected p-value distribution no longer depends on an assumption that the p-values are uniformly distributed under the null. For each matrix, we plot the permutation-based expected distribution relative to the observed order statistic to get our permutation-based QQ plot (Figure S2).

Moreover, to get more reliable estimates of lambda, our lambda inflation factors were estimated based on the same procedure as defined in the 'estlambda' method in R package genABEL using default regression method, but instead of assuming uniformity of expected p-value distributions, we use the permutated p-values as described above for QQ plots to represent the expected distribution. Our permutation-based approach is more computationally intensive, but is more representative of the true null distribution of Fisher's Exact p-values for the given case-control configurations in this study. An R package QQperm is available to generate such permutation-based QQ plots and lambda estimates.

Supplemental Method: Gene-set enrichment testing

Given the noise coming from the presence of background genetic variation in genes, it can be difficult for our current sample sizes to detect a significantly elevated rate of qualifying variants when testing individual genes (Figure S3). Thus, we also assessed enrichment among six biologically informed gene-sets (Table S14) that were chosen and described in our earlier studies of the epileptic encephalopathies.[12]

The six gene-sets were:
1) 43 established dominant human epilepsy genes[13] (Figure S4, Table S5)
2) The subset of 33 dominant epilepsy genes that have been securely implicated with epileptic encephalopathies
3) 209 genes coding for ion channels (IUPHAR)[14]
4) 823 FMRP-associated genes[15]
5) 78 synaptic transmission genes[16]
6) 235 mouse orthologs linked with seizure phenotypes in the Mouse Genome Database[17]

P-values are from a logistic regression model that regresses the case/control status of a sample on the presence (1) or absence (0) of at least one qualifying variant among the corresponding gene set. We provide the corresponding OR and its 95% CI. All tests are based on the Primary model. To ensure all our gene-set tests properly accounted for background variation, we applied a logistic regression model where the *P* values controlled for two background variation covariates. The first covariate we controlled for was the individual's total exome-wide number (tally) of qualifying variants from the Primary analysis (Table 1), minus the variants found in the gene-set being assessed. The second covariate corrected for the presumed neutral variation in the gene-set of interest by counting up the total number of synonymous annotated variants an individual had in the specific gene-set being assessed. We included gender as a third covariate.

Supplemental Method: Gene selection for qualifying variant Sanger validation

The candidate genes were selected based on meeting three criteria: i) were among the top 20 genes for familial GGE/NAFE case enrichment, ii) had at least four case carriers, and iii) were among the 25% most intolerant genes based on at least two of three genic intolerance metrics used: the residual variation intolerance score (RVIS) based on the EVS and subsequently the ExAC implementations (http://genic-intolerance.org/),[18] and the genic constraint score.[19]

The seven candidate genes emerging from the GGE analyses were: *ARNT2, ATP1A3, CACNA1B, COPB1, CUX1*, *KEAP1* and *SLC9A2*. Two additional candidate genes were selected from the familial GGE analyses on the basis of research interest: *GRIA4* and *KCNQ5*. The two candidate genes from the familial NAFE analyses were: *FNIP1* and *TYRO3*. Two additional candidate genes were selected from the familial NAFE analyses on the basis of research interest: *C5orf42* and *SLC12A5*. We also Sanger sequenced qualifying variants that were found among the following established epilepsy genes: *CDKL5*, *CHD2*, *CHRNB2*, *DEPDC5*, *DNM1*, *EEF1A2*, *GABRA1*, *GABRB3*, *GABRG2*, *GRIN2A*, *KCNA2, KCNQ2*, *KCNT1*, *LGI1*, *PCDH19*, *SCN1A, SCN2A, SCN8A* and *SLC2A1*.

Supplemental Method: Conditional analyses to assess the relative contribution of increasing minor allele frequencies on epilepsy risk

To assess the relative contribution of variants with different minor allele frequencies (MAF) on epilepsy risk, we developed a multivariable logistic regression model that relates disease risk to the presence of variants of a given frequency within 43 known dominant epilepsy genes. Specifically, we divided variants into five, mutually exclusive, categories:

1) Ultra-rare variants predicted to be probably damaging by PolyPhen-2, inframe indels or have a loss-of-function effect, with MAF up to 0.05% in the test population, and absent in EVS and ExAC reference cohorts (MAF = 0%);

2) Not in category 1, predicted to be probably damaging by PolyPhen-2, inframe indels or have a loss-of-function effect, with MAF up to 0.05% in the test population and less than 0.005% in ExAC;

3) Not in categories 1 or 2, predicted to be probably damaging by PolyPhen-2, inframe indels or have a loss-of-function effect, with MAF up to 0.1% in the test population and up to 0.1% in ExAC;

4) Ultra-rare synonymous annotated variants, with MAF up to 0.05% in the test population (i.e., up to four alleles in the combined case and control test population), and absent in EVS and ExAC reference cohorts (MAF = 0%);

5) No variant qualifying for categories 1-4.

Let X_{ij} be an indicator of whether individual *i* has a type *j* variant in any of the 43 disease genes, i.e.,

$$X_{ij} = \begin{cases} 1, & \text{if individual } i \text{ has a type } j \text{ variant among the 43 disease genes,} \\ 0, & \text{otherwise} \end{cases}$$

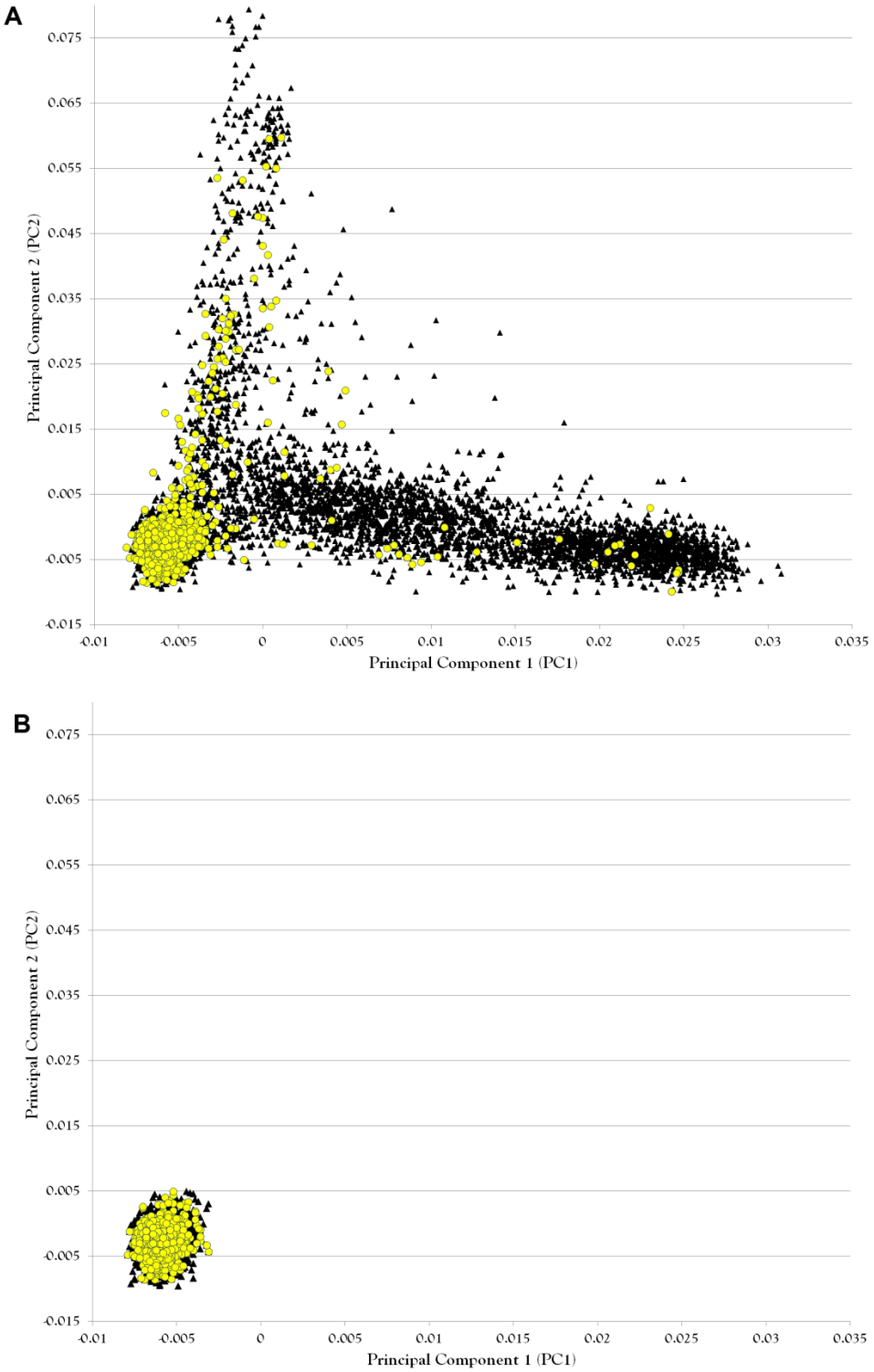
and $D_i = 1$ if individual *i* has epilepsy and $D_i = 0$ otherwise. We fit the following multivariable logistic regression model:

$$logit(\Pr(D_i = 1)) = \beta_0 + \beta_1 X_{i1} + \beta_2 X_{i2} + \beta_3 X_{i3} + \beta_4 X_{i4}.$$

In this model β_1 through β_4 represent the additive increase in the log-odds of an individual having variants in groups 1-4 relative to individuals in group 5 (i.e., individuals without a variant in groups 1-4). Thus, each parameter is relative to the same baseline group and naturally adjusted for variation in the other groups. Further, X_{i4} is included in the model to explicitly adjust for any variation in background ultra-rare neutral variation in the set of 43 dominant epilepsy genes between cases and controls.

Supplementary Figure S1: Principal components analysis of ancestry

(A) Principal components 1 and 2 for 10,423 ethnically diverse samples (black triangles), including 2,185 patients with epilepsy (yellow circles). **(B)** Samples were retained if the principal-component multinomial model probability of being European was greater than 0.50 (supplemental methods) and furthermore the sample was within the quadrant boundary defined by PCs 1 and 2 as: [PC1: -0.008 to -0.003] and [PC2: -0.01 to 0.005].

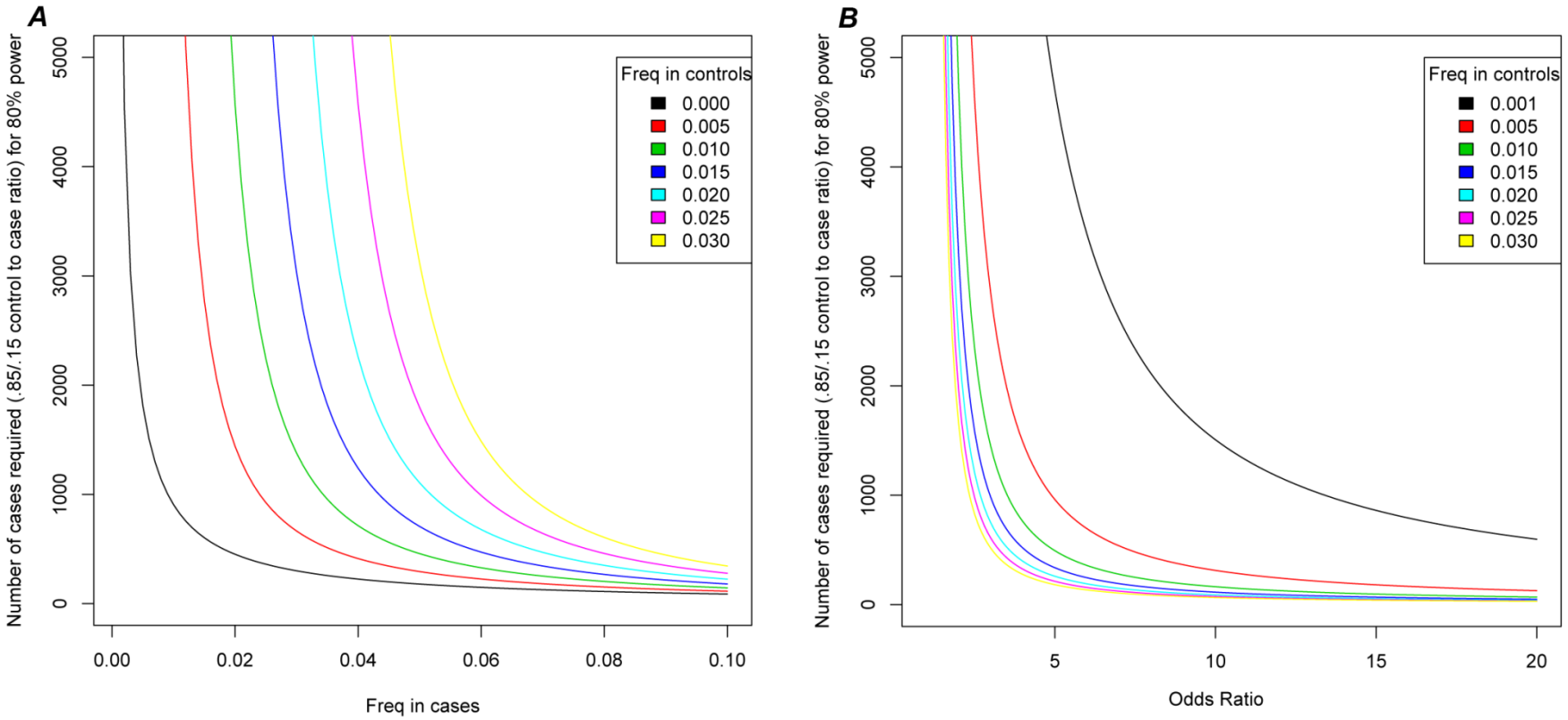


Supplementary Figure S2: Quantile-quantile plots.

(A-E) Permutation-based quantile-quantile plots from the analysis of 640 familial GGE cases to 3,877 control exomes. **(A)** Primary analysis: qualifying variants have a MAF<0.05% in test data and are absent among external reference cohorts. Variants are annotated as LoF, inframe indels or missense variants predicted to be "probably damaging" by PolyPhen-2 (HumDiv). The genomic inflation factor λ is 1.108. **(B)** Qualifying variants are putative LoF variants with a MAF <0.1% in internal and external population data. The genomic inflation factor λ is 1.056. **(C)** Qualifying variants have a MAF <0.1% in internal case and control data. Variants are annotated as loss-of-function, inframe indels or missense variants predicted to be "probably damaging" by PolyPhen-2 (HumDiv). The genomic inflation factor λ is 1.062. **(D)** Qualifying variants have a MAF <0.05% in internal case and control data, and are absent among external reference cohorts. Variants are annotated as synonymous. The genomic inflation factor λ is 0.992. **(E-H)** Permutation-based quantile-quantile plots from the analysis of 525 familial NAFE cases to 3,877 control exomes. **(E)** Primary analysis: qualifying variants have a MAF<0.05% in internal case and control data, and are absent among external reference cohorts. Variants are annotated as LoF, inframe indels or missense variants predicted to be "probably damaging" by PolyPhen-2 (HumDiv). The genomic inflation factor λ is 1.082. **(F)** Qualifying variants are putative LoF variants with a MAF <0.1% in internal and external population data. The genomic inflation factor λ is 1.074. **(G)** Qualifying variants have a MAF <0.1% in internal case and control data. Variants are annotated as LoF, inframe indels or missense variants predicted to be "probably damaging" by PolyPhen-2 (HumDiv). The genomic inflation factor λ is 1.041. **(H)** Qualifying variants have a MAF <0.05% in internal case and control data, and are absent among external reference cohorts. Variants are annotated as synonymous. The genomic inflation factor λ is 1.000. **(I-L)** Permutation-based quantile-quantile plots from the analysis of 662 sporadic NAFE cases to 3,877 control exomes. **(I)** Qualifying variants have a MAF <0.05% in internal case and control data, and are absent among external reference cohorts. Variants are annotated as LoF, inframe indels or missense variants predicted to be "probably damaging" by PolyPhen-2 (HumDiv). The genomic inflation factor λ is 1.001. **(J)** Qualifying variants are putative LoF variants with a MAF <0.1% in internal and external population data. The genomic inflation factor λ is 0.996. **(K)** Qualifying variants have a MAF <0.1% in internal case and control data. Variants are annotated as LoF, inframe indels or missense variants predicted to be "probably damaging" by PolyPhen-2 (HumDiv). The genomic inflation factor λ is 1.026. **(L)** Qualifying variants have a MAF <0.05% in internal case and control data, and are absent among external reference cohorts. Variants are annotated as synonymous. The genomic inflation factor λ is 0.978.

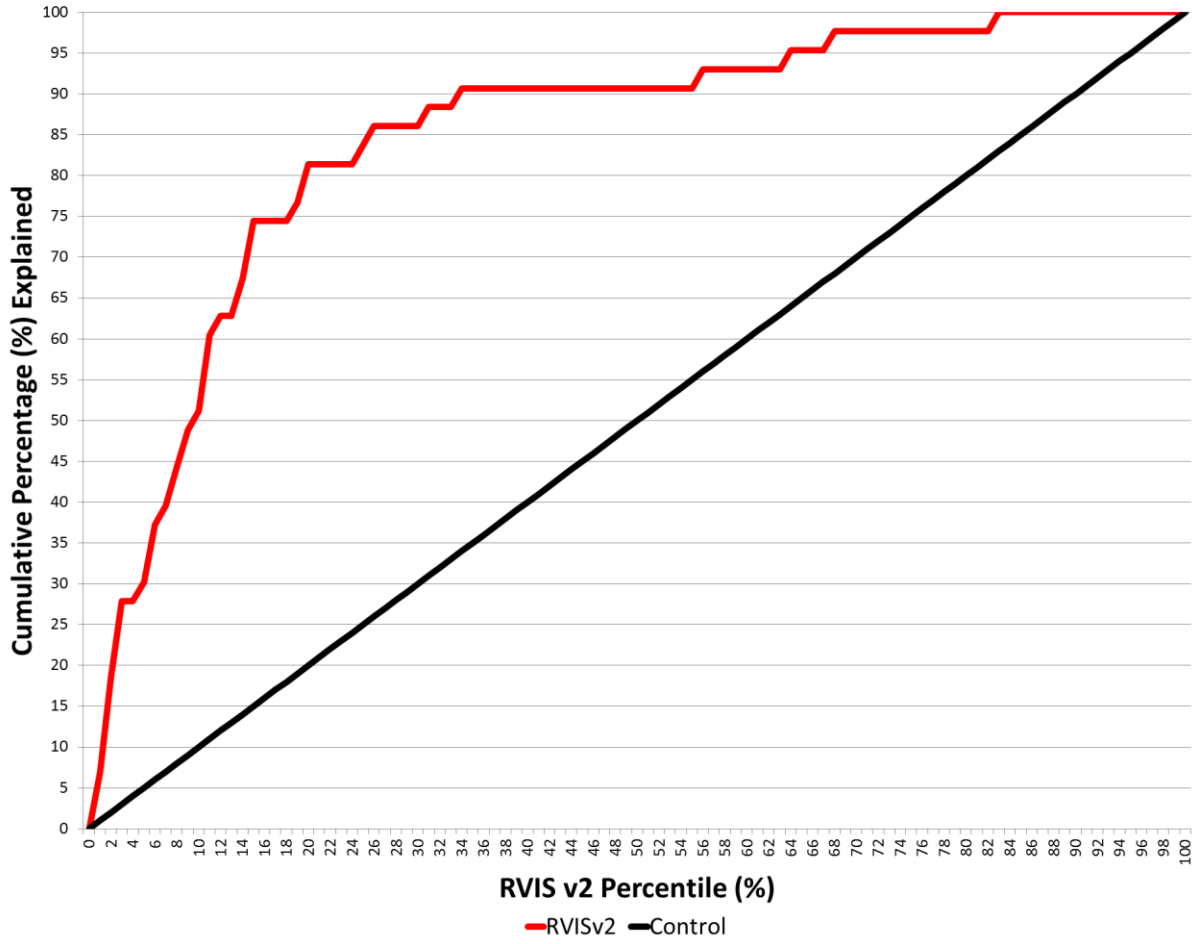
Supplementary Figure S3: Power curves for different control carrier frequencies.

Illustrating the number of cases required to achieve genome-wide significance under a two-sided Fisher's exact test ($\alpha = 2.5x10^{-6}$) with 80% power, assuming a constant cohort growth at the current 15%:85% (case:control) ratio. The estimated number of cases required to achieve genome-wide significance is represented along the y-axis. The different control carrier frequency scenarios are illustrated by coloured curves. **(A)** The case carrier frequency for a gene is represented along the x-axis. **(B)** The case-control Odds Ratio for a gene is plotted along the x-axis.



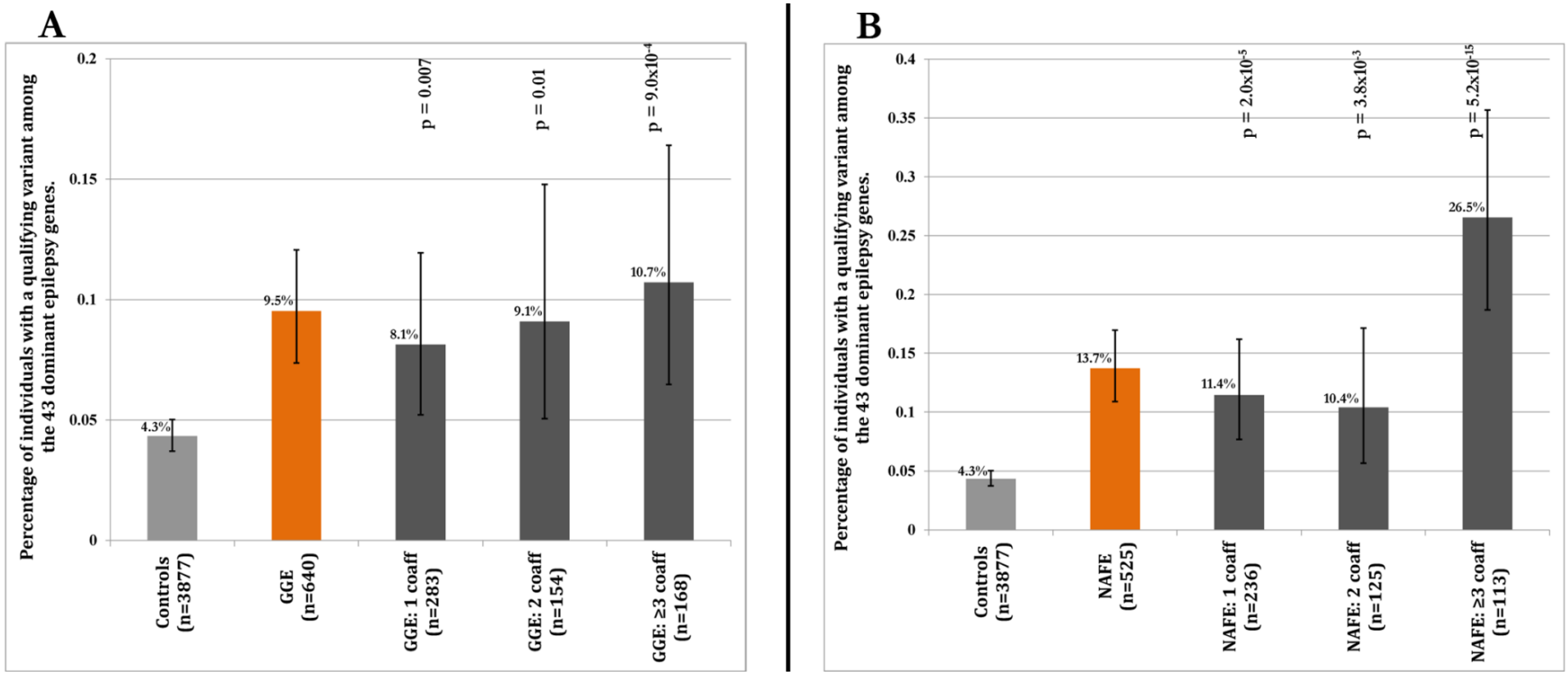
Supplementary Figure S4: Cumulative percentage (%) explained for the Residual Variation Intolerance Score (RVIS) percentile and the dominant epilepsy gene list (n=43 genes).

RVIS ExAC scores are available at http://igm.cumc.columbia.edu/GenicIntolerance/



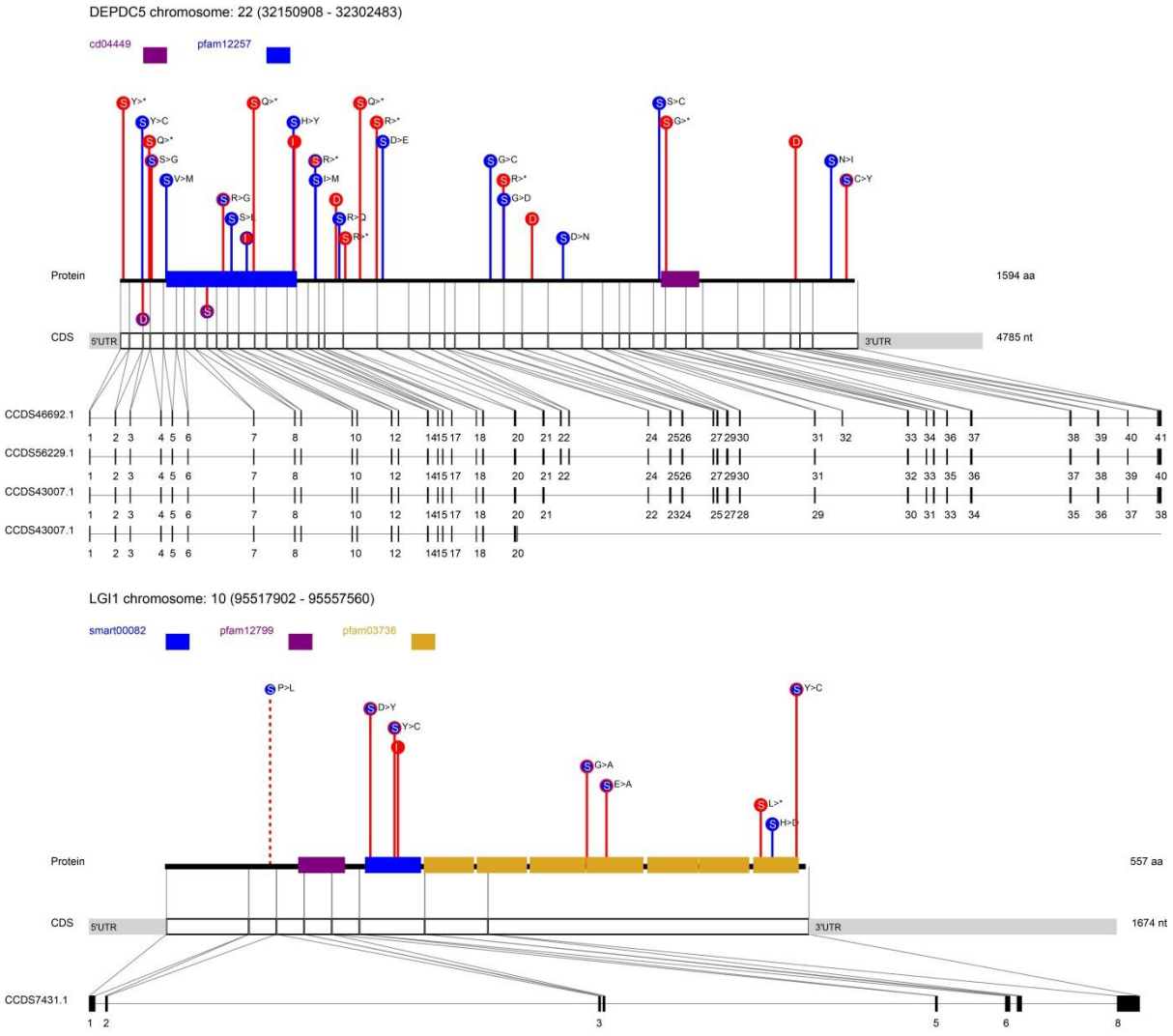
Supplementary Figure S5: Enrichment of epilepsy gene qualifying variants across index cases coming from families with one, two or greater than two additional affected family member(s).

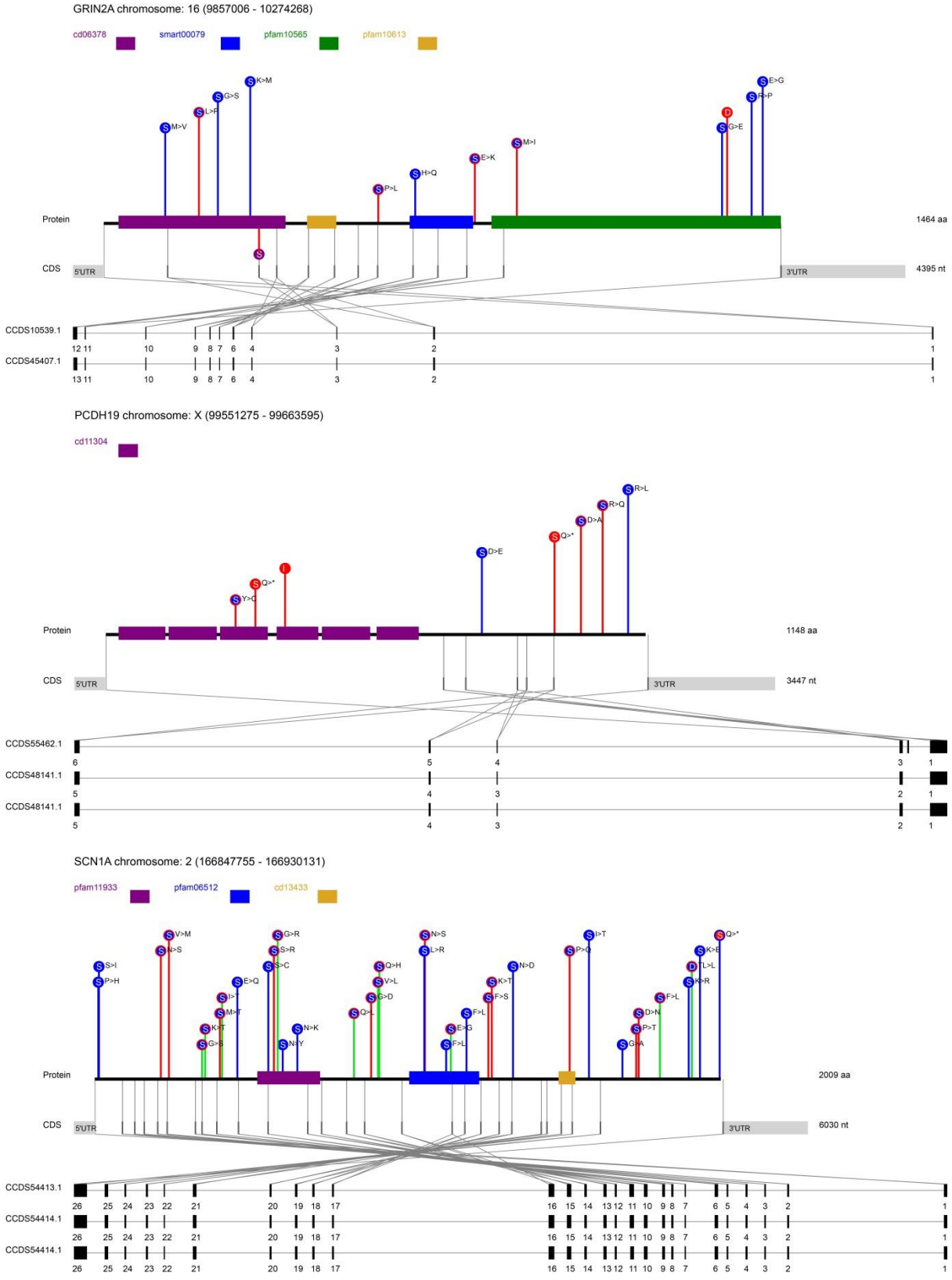
Plots present the percentage of individuals with at least one qualifying variant among the 43 dominant epilepsy genes, as per the primary collapsing analyses. **(A)** Presents the results of the familial GGE primary analysis comparing the IGM controls (light grey), to the familial GGE cases (orange), and subsequently the GGE cases stratified on the basis of how many family members of the index case are known/reported to have epilepsy (dark grey). This information was unavailable for 35 (5.5%) familial GGE index cases (omitted). **(B)** Presents the results of the familial NAFE primary analysis comparing the IGM controls (grey), to the familial NAFE cases (red), and subsequently the NAFE cases stratified on the basis of how many family members of the index case are known/reported to have epilepsy. This information was unavailable for 51 (9.7%) familial NAFE index cases (omitted). All p-values reflect Fisher's Exact two-tail tests comparing the rates among the case groups to the empirical control rate.



Supplementary Figure S6: Distribution of case and control qualifying variants for *DEPDC5, LGI1, GRIN2A, PCDH19,* and *SCN1A* from the NAFE with epilepsy family history analysis.

Loss-of-function variants are filled in red, and non-synonymous variants are filled in blue. Case variants are shown with red lines, control variants are shown with blue lines. Dotted lines indicate variant found in both case and controls. Variants reported below the protein line indicate canonical splice variants. For *SCN1A*, the GGE qualifying variants are also represented (green lines).

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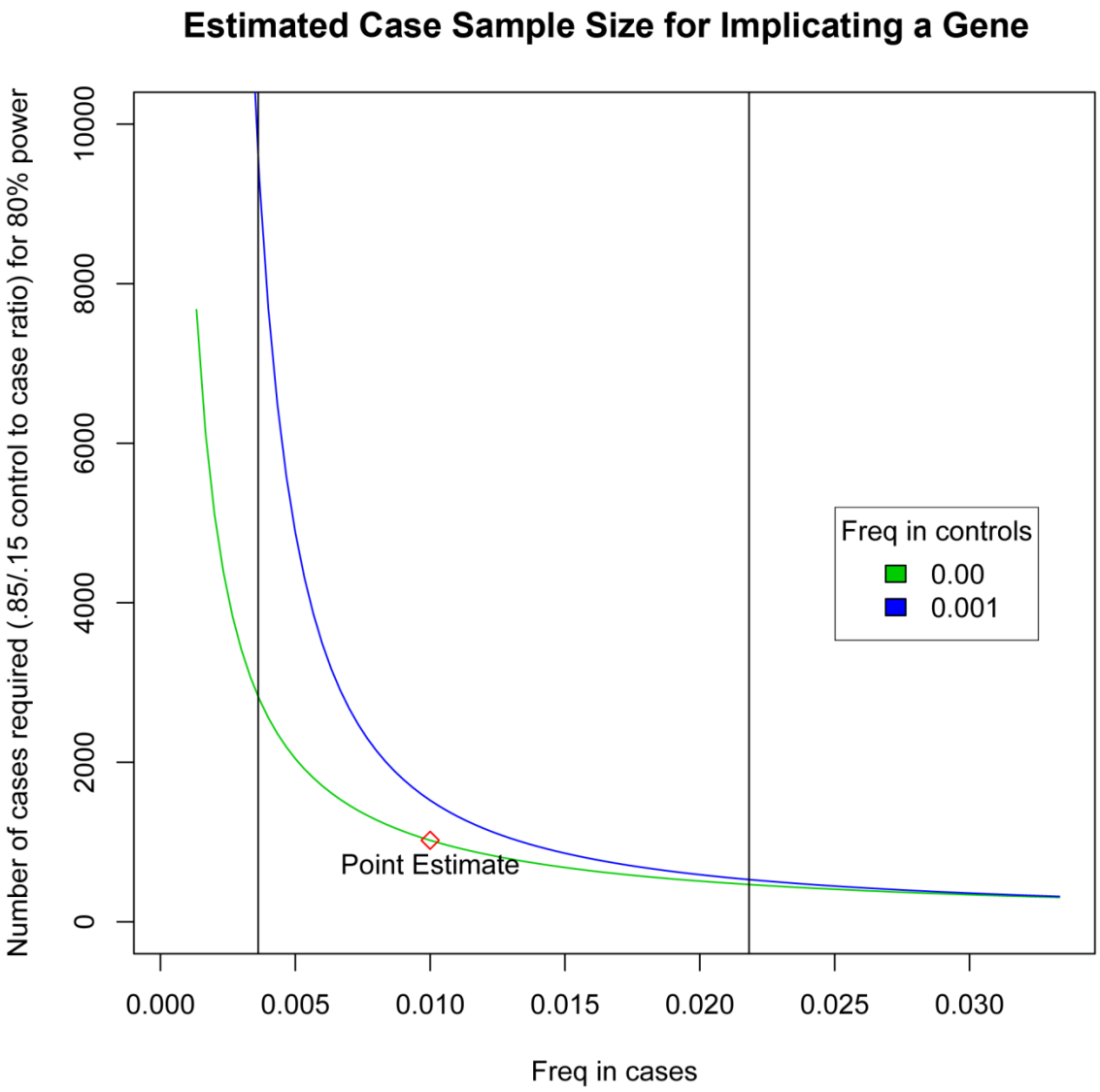
Protein
2009 aa
CDS
5'UTR
3'UTR
6030 nt
CCDS54413.1
CCDS54414.1
CCDS54414.1

Supplementary Figure S7: The 95% CI region for a gene that is currently observed among 1% of cases and 0% of controls.

The plot illustrates the number of cases required to achieve genome-wide significance ($\alpha = 2.5x10^{-6}$) with 80% power, assuming a constant cohort growth at a 15%:85% (case:control) ratio. The axes include the qualifying variant carrier frequency (p1) for a gene among cases (X-axis) and the estimated number of cases required (Y-axis). Green line corresponds to the power curve (80%) for the lower CI bound (0%) for p0, and the blue line represents the power curve corresponding to upper CI bound (0.1%) for p0. The point estimate for a gene currently with 1% case and 0% control carrier frequency is marked with a red diamond, while the black vertical lines represent the 95% CI bounds for p1. The area enclosed by these four lines gives the 95% CI region for the number of cases needed to have at least 80% power to achieve genome-wide significance for a gene observed among the current data to have a case carrier frequency of 1% and control frequency of 0%.



Supplementary Figure S8: Cumulative sum of variation plot for site pruning using the familial GGE versus control coverage comparison analysis as the example.

The y-axis reflects the cumulative sum of variation explained as sites with the largest variation in coverage are pruned out (x-axis). Using the familial GGE versus control coverage comparison to illustrate this process, the green line represents the point at which we maximize the amount of study-wide variation explained (88.46%) while minimizing the percentage of the exome that is pruned out (8.94%). Identifying the exome site that occupies the 8.94% position translates back to a site that had 5.19% difference when comparing the familial GGE and control populations. Thus, the 8.94% of sites where there was a ≥5.19% difference in how many individuals from one group had adequate coverage compared to the other group were pruned out of the familial GGE versus controls collapsing analyses.

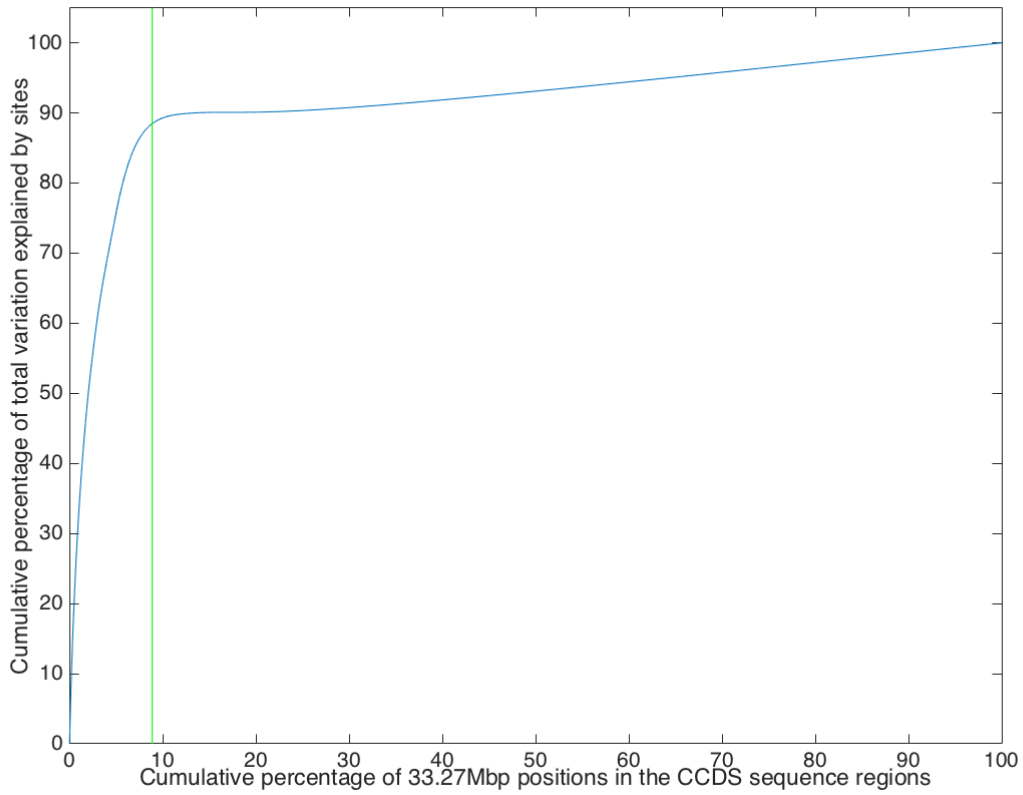


Table S1: Control cohort sources.

Ascertainment	Number of exomes	Percentage of controls
Non-disease healthy control	2166	55.87%
Amyotrophic Lateral Sclerosis (ALS)	896	23.11%
Pulmonary	334	8.61%
HIV	152	3.92%
Haemophilia	117	3.02%
Liver	74	1.91%
Urology	43	1.11%
Dementia	36	0.93%
Obsessive Compulsive Disorder (OCD)	33	0.85%
Various	26	0.67%
Total	**3877**	**100%**

The following individuals and/or groups contributed to control sample collection: D. Daskalakis; R Buckley; M.Hauser; J.Hoover-Fong, N. L. Sobreira and D. Valle; A. Poduri; T. Young and K. Whisenhunt; Z. Farfel, D. Lancet, and E. Pras; R. Gbadegesin and M. Winn; K. Schmader, S. McDonald, H. K. White and M. Yanamadala; R. Brown; S. H. Appel; E. Simpson; S. Halton, L. Lay; A. Holden; E. Behr; C. Moylan; A. M. Diehl and M. Abdelmalek; S. Palmer; G. Cavalleri; N. Delanty; G. Nestadt; D. Marchuk; V. Shashi; M. Carrington; R. Bedlack,; M. Harms; T. Miller; A. Pestronk; R. Bedlack; R. Brown; N. Shneider; S. Gibson; J. Ravits; A. Gilter; J. Glass; F. Baas; E. Simpson; and G. Rouleau; The ALS Sequencing Consortium; The Murdock Study Community Registry and Biorepository; the Carol Woods and Crosdaile Retirement Communities; Washington University Neuromuscular Genetics Project; the Utah Foundation for Biomedical Research; DUHS (Duke University Health System) Non-alcoholic Fatty Liver Disease Research Database and Specimen Repository, The Washington Heights, Inwood Columbia Aging Project. The collection of control samples and data was funded in part by: Biogen Idec.; Gilead Sciences, Inc.; New York-Presbyterian Hospital; The Columbia University College of Physicians and Surgeons; The Columbia University Medical Center; The Duke Chancellor's Discovery Program Research Fund 2014; Bill and Melinda Gates Foundation; The Stanley Institute for Cognitive Genomics at Cold Spring Harbor Laboratory; B57 SAIC-Fredrick Inc M11-074; The Ellison Medical Foundation New Scholar award AG-NS-0441-08; National Institute of Mental Health (K01MH098126, R01MH099216, R01MH097993); National Institute of Allergy and Infectious Diseases (1R56AI098588-01A1); National Human Genome Research Institute (U01HG007672); National Institute on Aging (R01AG037212, P01AG007232); National Institute of Neurological Disorders and Stroke (U01-NS077303, U01-NS053998); and National Institute of Allergy and Infectious Diseases Center (U19-AI067854, UM1-AI100645).

Table S2: Utilized case cohort recruitment sources.

Ascertainment	Recruiting Site	Number of exomes	Percentage of cases
GGE with family history	Epilepsy Phenome/Genome Project (EPGP) pairs	450	70.31%
	Melbourne (Austin Epilepsy Research Centre)	107	16.72%
	Swansea JME cohort	41	6.41%
	Epi4K Multiplex Families	30	4.69%
	Duke University recruitment	12	1.88%
	Total	**640**	**100.00%**
NAFE with family history	Epilepsy Phenome/Genome Project (EPGP) pairs	220	41.91%
	Duke University recruitment	91	17.33%
	Melbourne (Austin Epilepsy Research Centre)	79	15.05%
	Melbourne (Royal Melbourne Hospital - newly treated)	51	9.71%
	Epi4K Multiplex Families	34	6.48%
	The UK SANAD study of newly treated epilepsy	29	5.52%
	Ireland (Dublin) recruitment	21	4.00%
	Total	**525**	**100.00%**
Sporadic NAFE	The UK SANAD study of newly treated epilepsy	287	43.35%
	Duke University recruitment	129	19.49%
	Melbourne (Royal Melbourne Hospital - newly treated)	120	18.13%
	Melbourne (Austin Epilepsy Research Centre)	77	11.63%
	Ireland (Dublin) recruitment	49	7.40%
	Total	**662**	**100.00%**

Table S3: Homogeneous European genetic ancestry.

Screen	Familial GGE	Familial NAFE	Sporadic NAFE	Controls
Initial Available Cohort	815	677	717	8,354
Number with contamination >2% based on VerifyBamID	3	0	0	pre-screened
Number with gender discordance between clinically-reported and X:Y coverage ratios	2	1	1	pre-screened
Number with < 85% of CCDS r14 33.27M bases covered with at least 10-fold coverage	0	2	5	64
*Number where Cryptic Relatedness (KING and PLINK v1.07) tests identified unreported, yet seemingly related case/control samples.	2	5	3	52
Number of self-declared non-European ancestry	40	55	28	3,380
Subsequent number where EIGENSTRAT multinomial prediction for probability of European ancestry was p<0.50	92	59	10	772
Subsequent number who were outside of Principal Component ranges; PC1: [-0.008 to -0.003] and PC2: [-0.01 to 0.005] (Figure S1)	36	30	8	209
Final numbers	**640**	**525**	**662**	**3,877**
Percentage of samples of male gender	36.6%	45.5%	47.6%	54.7%
Agilent All Exon 50MB	0	0	0	96
Agilent All Exon 65MB	24	0	0	586
WGS	0	0	0	381
Nimblegen SeqCap	616	525	662	2,814

*EIGENSTRAT was run on the samples remaining after this filter was imposed (Figure S1).

Table S4: List of qualifying variants that overlap with earlier literature reports. Chromosomal coordinates based on NCBI Build37/hg19.

Epilepsy	Sample Name	Chromosomal coordinates (GRCh37/hg19)	HGNC	HGVS	Polyphen HumDiv	HGMD PubMed	Description
^GGE	epprnd31656wt1	chr1:g.43395596C>G	*SLC2A1*	NP_006507.2:p.Glu209Asp	0.918	23106342	same variant associated with early onset absence epilepsy
GGE	epifam30201bjk1	chr2:g.166848363A>G	*SCN1A*	NP_001159435.1:p.Phe1808Leu	0.996	12566275	same variant found in a child with a diagnosis of intractable childhood epilepsy with GTC
GGE	epprnd29825aog1	chr2:g.166848057AAGT>A	*SCN1A*	NP_001159435.1:p.Thr1909del	-	21248271	precise indel has been reported in a child with Severe Myoclonic Epilepsy of Infancy
GGE	epprnd30598xa1	chr5:g.161524846G>C	*GABRG2*	NP_944493.2:p.Arg177Pro	1	16550559	variant in the same codon previously found to segregate with familial febrile seizures
GGE	swjmem71	chr19:g.35524568C>G	*SCN1B*	NP_950238.1:p.Arg125Gly	0.965	19710327	recessive variant at the same site previously linked to myoclonic epilepsy of infancy
NAFE	epprnd33256asz1	chr1:g.154544222T>C	*CHRNB2*	NP_000739.1:p.Val308Ala	1	18456869	same variant has been associated with nocturnal frontal lobe epilepsy
#NAFE	epprnd37110axz1	chr2:g.166868689T>G	*SCN1A*	NP_001159435.1:p.Lys1270Thr	1	11756608	same variant associated with TLE and FS+
#NAFE	epprnd31416aqe1	chr10:g.95557034A>C	*LGI1*	NP_005088.1:p.Glu383Ala	0.999	11810107	same variant associated with epilepsy, partial, with auditory features
NAFE	epprnd32271atq1	chr10:g.95552601G>GC	*LGI1*	NP_005088.1:p.Glu205ArgfsTer9	-	11810107	pathogenic indel has been reported at or within 9 flanking bases of this indel start position
^NAFE	epprnd31182aqw1	chr16:g.10031815C>T	*GRIN2A*	NM_000833.4:c.1007+1G>A	-	23933818	same variant found to segregate in two independent families, ascertained for Autosomal Dominant Rolandic Epilepsy with Speech Dyspraxia and ECSWS, respectively.
NAFE	epprnd35451avm1	chr16:g.10031815C>T	*GRIN2A*	NM_000833.4:c.1007+1G>A	-	23933818	same variant found to segregate in two independent families, ascertained for Autosomal Dominant Rolandic Epilepsy with Speech Dyspraxia and ECSWS, respectively.
NAFE	epprnd30628aoq1	chr22:g.32210991C>T	*DEPDC5*	NP_001129501.1:p.Arg487Ter	-	23542697	same variant associated with Epilepsy, familial focal with variable foci
NAFE	epprnd39002bay1	chr22:g.32211195C>T	*DEPDC5*	NP_001129501.1:p.Arg555Ter	-	23542697	same variant associated with Epilepsy, familial focal with variable foci

NAFE	epprnd37551ayt1	chr22:g.32200196T>TC	*DEPDC5*	NP_001129501.1:p.Leu379IlefsTer6	-	20659151	pathogenic indel has been reported at or within 9 flanking bases of this indel start position
NAFE	epprnd21584apq1	chrX:g.99662647G>A	*PCDH19*	NP_001171809.1:p.Gln317Ter	-	22050978	same variant associated with Epilepsy and mental retardation limited to females
NAFE	epprnd33458ako1	chrX:g.99662772T>C	*PCDH19*	NP_001171809.1:p.Tyr275Cys	1	23334464	variant at the same site previously associated with Epilepsy and mental retardation in females
NAFE	epprnd31358aop1	chrX:g.99662458G>GGCCT	*PCDH19*	NP_001171809.1:p.Leu380ArgfsTer22	-	22267240	pathogenic indel has been reported at or within 9 flanking bases of this indel start position
sporadic NAFE	nlfebkvt10250	chr2:g.166866306G>A	*SCN1A*	NP_001159435.1:p.Leu1309Phe	0.997	20117752	same variant found in two sibling brothers with GEFS+
sporadic NAFE	dukeepi4312	chr10:g.95553026GC>G	*LGI1*	NP_005088.1:p.Ala253ValfsTer32	-	11978770	same indel variant associated with epilepsy, partial, with auditory features

These qualifying variants are based on the results from the Primary analysis where variants were required to be absent among EVS and ExAC control reference cohorts, and were found at a minor allele frequency <0.05% among the combined case and control IGM test cohorts. Only HGMD, ClinVar and OMIM (accessed June 2015) were adopted to find matches with existing disease literature. ^The variant was independently identified and reported after this family had been recruited into EPGP (variant not included in the test of enrichment with literature overlaps). [#]Subsequently determined that the individual belonged to a family that has been reported in literature (variant not included in the test of enrichment with literature overlaps).

Table S5: List of 43 established dominant human epilepsy genes.

AD = Autosomal Dominant, XLD = X-Linked Dominant

Dominant Epilepsy Genes	RVIS EVS (%)	RVIS ExAC (%)	Inheritance Mode	OMIM	Implicated with epileptic encephalopathies
SPTAN1	0.31	0.28	AD	http://www.omim.org/entry/182810	Yes
SCN8A	2.34	0.64	AD	http://www.omim.org/entry/600702	Yes
CHD2	2.37	0.92	AD	http://www.omim.org/entry/602119	Yes
SCN2A	1.77	1.05	AD	http://www.omim.org/entry/182390	Yes
GRIN2B	1.07	1.09	AD	http://www.omim.org/entry/138252	Yes
GRIN2A	3.89	1.17	AD	http://www.omim.org/entry/138253	Yes
SYNGAP1	6.23	1.36	AD	http://www.omim.org/entry/603384	Yes
KCNMA1	2.65	1.84	AD	http://www.omim.org/entry/600150	-
PRICKLE2	6.78	2.31	AD	http://www.omim.org/entry/608501	-
SCN1A	4.03	2.38	AD	http://www.omim.org/entry/182389	Yes
CDKL5	15.86	2.51	XLD	http://www.omim.org/entry/300203	Yes
KCNT1	1.62	2.81	AD	http://www.omim.org/entry/608167	Yes
GRIN1	6.72	4.67	AD	http://www.omim.org/entry/138249	Yes
PCDH19	10.43	5.33	XLD	http://www.omim.org/entry/300460	Yes
CHRNA4	1.79	5.57	AD	http://www.omim.org/entry/118504	-
KCNQ2	15.86	5.91	AD	http://www.omim.org/entry/602235	Yes
DEPDC5	6.62	6.73	AD	http://www.omim.org/entry/614191	-
KCNQ3	30.82	7.19	AD	http://www.omim.org/entry/602232	Yes
HCN1	13.33	7.87	AD	http://www.omim.org/entry/602780	Yes
CHRNA2	13.67	8.77	AD	http://www.omim.org/entry/118502	-
LGI1	14.40	8.78	AD	http://www.omim.org/entry/604619	-
SLC6A1	29.16	9.06	AD	http://www.omim.org/entry/137165	Yes
GNAO1	13.94	10.01	AD	http://www.omim.org/entry/139311	Yes
SLC2A1	7.66	10.41	AD	http://www.omim.org/entry/138140	Yes
GABRG2	25.15	10.52	AD	http://www.omim.org/entry/137164	Yes
KCNC1	15.62	10.88	AD	http://www.omim.org/entry/176258	Yes
DNM1	19.54	11.75	AD	http://www.omim.org/entry/602377	Yes
CHRNB2	14.97	13.14	AD	http://www.omim.org/entry/118507	-
KCNA2	25.15	13.35	AD	http://www.omim.org/entry/176262	Yes
HNRNPU	17.75	14.67	AD	http://www.omim.org/entry/602869	Yes
EEF1A2	15.62	14.82	AD	http://www.omim.org/entry/602959	Yes
STXBP1	14.97	14.90	AD	http://www.omim.org/entry/602926	Yes
MEF2C	58.00	18.97	AD	http://www.omim.org/entry/600662	Yes
GABRB3	22.36	19.82	AD	http://www.omim.org/entry/137192	Yes
GABRA1	24.00	19.82	AD	http://www.omim.org/entry/137160	Yes
SCN1B	83.25	24.12	AD	http://www.omim.org/entry/600235	-
SLC35A2	41.64	25.89	AD	http://www.omim.org/entry/314375	Yes
STX1B	41.25	30.28	AD	http://www.omim.org/entry/601485	Yes
KCNB1	50.34	33.14	AD	http://www.omim.org/entry/600397	Yes
PRRT2	81.38	55.22	AD	http://www.omim.org/entry/614386	-
SCN9A	73.63	63.31	AD	http://www.omim.org/entry/603415	-
SIK1	34.93	67.15	AD	http://www.omim.org/entry/605705	Yes
ALG13	8.37	82.54	XLD	http://www.omim.org/entry/300776	Yes

Table S6: Hypergeometric tests performed on the genome-wide ranks of the 43 known dominant epilepsy genes.

Primary analysis: GGE fam hx+			Primary analysis: NAFE fam hx+			Primary analysis: sporadic NAFE		
Rank	HGNC	**Hypergeom. p-value**	**Rank**	**HGNC**	**Hypergeom. p-value**	**Rank**	**HGNC**	**Hypergeom. p-value**
5	*KCNQ2*	0.01172	1	*DEPDC5*	0.00236	101	*EEF1A2*	0.21243
8	*GABRG2*	0.00015	2	*LGI1*	5.42E-06	152	*LGI1*	0.04979
11	*SCN1A*	1.98E-06	3	*PCDH19*	1.22E-08	546	*CHRNB2*	0.13693
57	*SCN1B*	9.62E-06	4	*SCN1A*	2.67E-11	990	*KCNMA1*	0.20299
71	*KCNA2*	6.61E-07	**5**	***GRIN2A***	**5.70E-14**	1349	*DNM1*	0.20933
114	*SLC6A1*	2.62E-07	245	*GABRB3*	2.21E-05	1745	*SPTAN1*	0.22456
151	***EEF1A2***	**5.78E-08**	246	*GABRA1*	1.58E-06	2054	*STX1B*	0.20401
434	*GABRA1*	6.68E-06	480	*SCN8A*	1.39E-05	2106	*ALG13*	0.11583
591	*SCN9A*	7.74E-06	1381	*CDKL5*	0.00425	2669	*DEPDC5*	0.16747
707	*KCNT1*	4.28E-06	1444	*HNRNPU*	0.00159	3221	*CHRNA2*	0.21625
828	*CHD2*	2.37E-06	1452	*SCN1B*	0.00041	3455	*KCNB1*	0.17652
1513	*GRIN2B*	0.00014	1691	*STX1B*	0.00039	3461	*KCNT1*	0.09964
2739	*DEPDC5*	0.00842	1810	*KCNA2*	0.00018	3662	*GABRG2*	0.07446
2740	*SPTAN1*	0.00303	2224	*GRIN2B*	0.00038	3791	*SCN9A*	0.04786
3088	*PCDH19*	0.00337	2511	*CHRNB2*	0.00039	4305	*KCNC1*	0.06267
3384	*GRIN1*	0.00307	2736	*KCNT1*	0.00029	4971	*PRRT2*	0.09906
3495	*LGI1*	0.00154	2750	*GRIN1*	0.00008	5271	*CHRNA4*	0.08690
3510	*HCN1*	0.00053	3614	*DNM1*	0.00076	5635	*GRIN2B*	0.08348
4408	*DNM1*	0.00308	3853	*SCN2A*	0.00056	6054	*GRIN2A*	0.08642
5020	*KCNC1*	0.00589	4260	*HCN1*	0.00071	6479	*SCN1A*	0.08956
5343	*SLC2A1*	0.00525	4361	*SCN9A*	0.00032	6807	*SCN8A*	0.08060
5377	*CHRNA4*	0.00225	4449	*SLC2A1*	0.00013	7540	*PCDH19*	0.12338
5645	*HNRNPU*	0.00170	5001	*CHD2*	0.00026	8398	*GRIN1*	0.20201
5652	*SCN8A*	0.00062	5450	*SYNGAP1*	0.00034	9069	*PRICKLE2*	0.25678
6452	*SYNGAP1*	0.00187	6830	*KCNC1*	0.00455	9286	*SYNGAP1*	0.21117
7362	*STXBP1*	0.00598	9040	*CHRNA2*	0.09909	9302	*SCN2A*	0.13615
7719	*STX1B*	0.00531	9722	*KCNB1*	0.13484	9908	*KCNQ3*	0.16610
7901	*ALG13*	0.00317	10292	*GABRG2*	0.15769	10051	*HCN1*	0.11941
8336	*MEF2C*	0.00323	10483	*PRICKLE2*	0.11886	10931	*CHD2*	0.19620
8952	*GABRB3*	0.00474	10635	*CHRNA4*	0.08238	11050	*SCN1B*	0.13826
8989	*SIK1*	0.00196	11779	*SPTAN1*	0.19038	11882	*SLC6A1*	0.21197
9380	*CDKL5*	0.00170	12165	*SLC6A1*	0.17881	12772	*SLC2A1*	0.32466
9556	*KCNQ3*	0.00087	13232	*STXBP1*	0.33158	13033	*STXBP1*	0.27636
10841	*CHRNA2*	0.00522	14697	*SLC35A2*	0.67737	13810	*CDKL5*	0.37484
10843	*CHRNB2*	0.00184	14729	*ALG13*	0.54479	14511	*SLC35A2*	0.46601
11493	*KCNB1*	0.00254	15001	*KCNMA1*	0.49016	15739	*KCNA2*	0.76484
12202	*PRICKLE2*	0.00382	15245	*EEF1A2*	0.42063	15866	*KCNQ2*	0.66956
12261	*SCN2A*	0.00129	15963	*KCNQ3*	0.54059	15887	*MEF2C*	0.50759
13468	*GRIN2A*	0.00549	15964	*KCNQ2*	0.35747	17101	*GNAO1*	0.86584
15187	*SLC35A2*	0.05388	15988	*MEF2C*	0.20075	17793	*GABRB3*	0.97656
15467	*KCNMA1*	0.03031	16295	*PRRT2*	0.14459	17830	*GABRA1*	0.92064
16621	*PRRT2*	0.09193	17145	*GNAO1*	0.25329	17912	*SIK1*	0.80418
17355	*GNAO1*	0.11263	17887	*SIK1*	0.41322	18326	*HNRNPU*	1.00000

Hypergeometric p-values were calculated using phyper from the R 'stats' package 3.2.2 on the basis of 43 known epilepsy genes and their corresponding rank among the Primary model results (Table S10, Table S11 and Table S12).

Table S7: Top Ranked Dominant Epilepsy Genes (n=43).

Shortlist of established epilepsy genes that achieved a Fisher's Exact uncorrected p-value <0.05 among the familial analyses - including the loss-of-function model.

Group	Collapsing Analysis	HGNC	Qual Case	Qual Case Freq (%)	Qual Ctrl	Qual Ctrl Freq (%)	Fisher's Exact P-value	OR [95% CI]
Familial NAFE (n=525)	LoF	*DEPDC5*	14	2.67	2	0.052	9.63E-12	53.1 [12.1 - 481.3]
	Primary	*DEPDC5*	15	2.86	14	0.361	1.82E-07	8.1 [3.6 - 18.3]
	Primary	*LGI1*	8	1.52	2	0.052	1.41E-06	29.9 [6.0 - 288.0]
	Primary	*PCDH19*	6	1.14	2	0.052	6.35E-05	22.4 [4.0 - 226.4]
	Primary	*SCN1A*	11	2.10	15	0.387	8.99E-05	5.5 [2.3 - 12.9]
	Primary	*GRIN2A*	7	1.33	7	0.181	0.0005	7.5 [2.2 - 25.1]
	LoF	*GRIN2A*	3	0.57	0	0	0.0017	>22.3 [3.1 - >1161]
	LoF	*PCDH19*	3	0.57	0	0	0.0017	>22.3 [3.1 - >1161]
	LoF	*KCNA2*	2	0.38	0	0	0.0142	>14.8 [1.4 - >869.5]
	LoF	*LGI1*	2	0.38	0	0	0.0142	>14.8 [1.4 - >869.5]
	Primary	*GABRB3*	2	0.38	1	0.026	0.0392	14.8 [0.8 - 869.3]
	Primary	*GABRA1*	2	0.38	1	0.026	0.0392	14.8 [0.8 - 869.3]
Familial GGE (n=640)	Primary	*KCNQ2*	4	0.62	0	0	0.0004	>24.3 [4.0 - >1192]
	Primary	*GABRG2*	5	0.78	2	0.052	0.0009	15.2 [2.5 - 160.2]
	Primary	*SCN1A*	10	1.56	15	0.387	0.0013	4.1 [1.6 - 9.8]
	Primary	*SCN1B*	3	0.47	1	0.026	0.0101	18.2 [1.5 - 952.7]
	Primary	*KCNA2*	3	0.47	1	0.026	0.0101	18.2 [1.5 - 952.7]
	Primary	*SLC6A1*	2	0.31	0	0	0.02	>12.1 [1.1 - >714]
	Primary	*EEF1A2*	2	0.31	0	0	0.02	>12.1 [1.1 - >714]

Table S8: Sanger Sequencing for preferential segregation among first degree relatives.

The preferential segregation among first degree relatives is calculated using a one-tail binomial p-value, where the *Ps* is defined at 0.5. *Six genes were eligible for testing based on meeting the minimal five affected first degree relatives required for the gene test to be able to achieve uncorrected p<0.05.

Group	Total qualifying variants available for Sanger validation	Unable to generate a clear Sanger trace	Sanger clearly illustrates absence of variant	Sanger clearly illustrates presence of variant (% samples)	Preferential segregation among 1st degree relatives
Index Cases from the collapsing analyses	135	3	4	128 (97.0%)	N/A
Affected first degree relatives (all 32 tested genes)	112	2	26	84 (76.4%)	**$1.3x10^{-8}$**
Affected first degree relatives (*SCN1A*)	18	1	2	15 (88.2%)	**0.00118**
Affected first degree relatives (*DEPDC5*)	11	0	0	11 (100%)	**0.00049**
Affected first degree relatives (*GRIN2A*)	7	0	0	7 (100%)	**0.00781**
Affected first degree relatives (*LGI1*)	7	0	1	6 (85.7%)	0.063
Affected first degree relatives (*COPB1*)	9	1	3	5 (62.5%)	0.856
Affected first degree relatives (*CACNA1B*)	8	0	3	5 (62.5%)	0.856
Affected first degree relatives (*ARNT2*)	4	0	3	1 (25.0%)	N/A*
Affected first degree relatives (*KCNA2*)	4	0	0	4 (100%)	N/A *
Affected first degree relatives (*PCDH19*)	4	0	0	4 (100%)	N/A *
Affected first degree relatives (*ATP1A3*)	3	0	1	2 (66.7%)	N/A *
Affected first degree relatives (*C5orf42*)	4	0	2	2 (50.0%)	N/A *
Affected first degree relatives (*GABRA1*)	3	0	0	3 (100%)	N/A *
Affected first degree relatives (*GABRG2*)	3	0	0	3 (100%)	N/A *
Affected first degree relatives (*GRIA4*)	4	0	2	2 (50.0%)	N/A *
Affected first degree relatives (*KEAP1*)	4	0	3	1 (25.0%)	N/A *
Affected first degree relatives (*TYRO3*)	3	0	3	0 (0%)	N/A *
Affected first degree relatives (*CDKL5*)	2	0	1	1 (50.0%)	N/A *
Affected first degree relatives (*KCNQ5*)	2	0	0	2 (100%)	N/A *
Affected first degree relatives (*SLC12A5*)	2	0	0	2 (100%)	N/A *
Affected first degree relatives (*CHRNB2*)	1	0	0	1 (100%)	N/A *
Affected first degree relatives (*EEF1A2*)	2	0	0	2 (100%)	N/A *
Affected first degree relatives (*FNIP1*)	1	0	1	0 (0%)	N/A *
Affected first degree relatives (*GABRB3*)	1	0	1	0 (0%)	N/A *
Affected first degree relatives (*KCNQ2*)	1	0	0	1 (100%)	N/A *
Affected first degree relatives (*SCN2A*)	1	0	0	1 (100%)	N/A *
Affected first degree relatives (*SCN8A*)	2	0	0	2 (100%)	N/A *
Affected first degree relatives (*SLC9A2*)	1	0	0	1 (100%)	N/A *

Table S9: Conditional analyses to compare relative contribution to epilepsy risk across rare allele frequencies.

Multivariate logistic regressions are presented for the three epilepsy cohort comparing the contribution of putatively damaging ultra-rare variation (Primary analysis) and putatively damaging variation up to 0.1% MAF across the 43 dominant epilepsy genes. *Ultra-rare variation is defined as variants with a MAF ≤0.05% among the combined test population of cases and controls and absent (MAF=0%) in both the EVS and ExAC reference cohorts. ExAC MAF (0 to 0.005%] variation is defined as variants with an ExAC MAF >0% and ≤0.005% among the ExAC global reference cohort and a MAF ≤0.05% among the combined test population of cases and controls. ExAC MAF (0.005% to 0.1%] variation is defined as variants with an ExAC and test population MAF >0.005% and ≤0.1%. Tests also corrected for the background rate of ultra-rare putatively neutral (synonymous) variants across the 43 dominant human epilepsy genes.

Study Group	Vectors	Number of observations among cases & controls	OR (95% CI)	Logistic Regression p-value
GGE with family history	Ultra-rare* variants	226	2.38 (1.74 – 3.22)	**2.8×10^{-8}**
	ExAC MAF (0 to 0.005%]	195	1.01 (0.65 – 1.49)	**0.97**
	ExAC MAF (0.005% to 0.1%]	157	0.76 (0.44 – 1.22)	**0.28**
	Neutral variants	225	0.91 (0.60 – 1.33)	**0.63**
NAFE with family history	Ultra-rare* variants	236	3.60 (2.67 – 4.81)	**1.4×10^{-17}**
	ExAC MAF (0 to 0.005%]	196	1.12 (0.72 – 1.69)	**0.60**
	ExAC MAF (0.005% to 0.1%]	157	0.92 (0.54 – 1.50)	**0.76**
	Neutral variants	220	0.96 (0.61 – 1.45)	**0.87**
Sporadic NAFE	Ultra-rare* variants	199	1.22 (0.82 – 1.76)	**0.30**
	ExAC MAF (0 to 0.005%]	206	1.30 (0.89 – 1.85)	**0.16**
	ExAC MAF (0.005% to 0.1%]	151	0.89 (0.54 – 1.40)	**0.63**
	Neutral variants	223	0.87 (0.57 – 1.27)	**0.48**

Table S10: Results for the analysis of 640 GGE cases with a family history of epilepsy and 3877 control exomes.

The top 300 ranked genes from the Primary model collapsing analysis. The exome-wide results can be accessed at http://epi4kdb.org/downloads/common-epilepsies/Table-S10.xlsx. A gender stratified Cochran-Mantel-Haenszel (CMH) test statistic is also available for the sex chromosomes (Table S13). Epi Gene: is among the 43 known dominant epilepsy genes; Qcase: number of cases carrying a qualifying variant; Qcase Freq: proportion of cases carrying a qualifying variant; Qctrl: number of controls carrying a qualifying variant; Qctrl Freq: proportion of controls carrying a qualifying variant; FET p-val: Fisher's exact two-tail p-value.

HGNC gene name	Epi Gene	**Familial GGE Qualifying variants: Primary analysis**					**Familial GGE Qualifying variants: LoF analysis**				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
CACNA1B	-	8	0.013	3	0.0008	**1.7E-5**	1	0.002	0	0.0000	**0.142**
KEAP1	-	5	0.008	0	0.0000	**5.6E-5**	2	0.003	1	0.0003	**0.055**
COPB1	-	7	0.011	4	0.0010	**2.2E-4**	2	0.003	0	0.0000	**0.020**
PHTF1	-	5	0.008	1	0.0003	**3.0E-4**	4	0.006	7	0.0018	**0.058**
KCNQ2	*Yes*	4	0.006	0	0.0000	**4.0E-4**	1	0.002	0	0.0000	**0.142**
SLC9A2	-	4	0.006	0	0.0000	**4.0E-4**	1	0.002	3	0.0008	**0.457**
ATP1A3	-	5	0.008	2	0.0005	**9.2E-4**	1	0.002	0	0.0000	**0.142**
GABRG2	*Yes*	5	0.008	2	0.0005	**9.2E-4**	0	0.000	0	0.0000	**1.000**
ZNF100	-	6	0.009	4	0.0010	**0.0010**	5	0.008	4	0.0010	**0.004**
CUX1	-	9	0.014	12	0.0031	**0.0013**	2	0.003	0	0.0000	**0.020**
SCN1A	*Yes*	10	0.016	15	0.0039	**0.0013**	0	0.000	1	0.0003	**1.000**
ARNT2	-	4	0.006	1	0.0003	**0.0018**	1	0.002	1	0.0003	**0.263**
RIOK2	-	4	0.006	1	0.0003	**0.0018**	2	0.003	2	0.0005	**0.099**
MBOAT1	-	4	0.006	1	0.0003	**0.0018**	0	0.000	2	0.0005	**1.000**
HSD17B4	-	4	0.006	1	0.0003	**0.0018**	1	0.002	0	0.0000	**0.142**
COL6A6	-	9	0.014	13	0.0034	**0.0019**	8	0.013	15	0.0039	**0.011**
MCM5	-	3	0.005	0	0.0000	**0.0028**	1	0.002	0	0.0000	**0.142**
EBI3	-	3	0.005	0	0.0000	**0.0028**	0	0.000	0	0.0000	**1.000**
MTMR3	-	3	0.005	0	0.0000	**0.0028**	0	0.000	0	0.0000	**1.000**
OR8K1	-	3	0.005	0	0.0000	**0.0028**	0	0.000	0	0.0000	**1.000**
PDIA3	-	3	0.005	0	0.0000	**0.0028**	0	0.000	0	0.0000	**1.000**
PMPCA	-	3	0.005	0	0.0000	**0.0028**	0	0.000	0	0.0000	**1.000**
GGPS1	-	3	0.005	0	0.0000	**0.0028**	1	0.002	1	0.0003	**0.263**
RTFDC1	-	3	0.005	0	0.0000	**0.0028**	1	0.002	0	0.0000	**0.142**
C19orf40	-	3	0.005	0	0.0000	**0.0028**	2	0.003	0	0.0000	**0.020**
FNDC7	-	6	0.009	6	0.0015	**0.0034**	1	0.002	5	0.0013	**0.600**
GRIA4	-	6	0.009	6	0.0015	**0.0034**	0	0.000	1	0.0003	**1.000**
KDM6B	-	5	0.008	4	0.0010	**0.0043**	1	0.002	0	0.0000	**0.142**
EVPL	-	5	0.008	4	0.0010	**0.0043**	2	0.003	1	0.0003	**0.055**
PIP5K1C	-	4	0.006	2	0.0005	**0.0047**	2	0.003	2	0.0005	**0.099**
ANKMY2	-	4	0.006	2	0.0005	**0.0047**	1	0.002	0	0.0000	**0.142**

HGNC gene name	Epi Gene	Familial GGE Qualifying variants: Primary analysis					Familial GGE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
ZNF536	-	4	0.006	2	0.0005	**0.0047**	0	0.000	0	0.0000	**1.000**
GIGYF1	-	4	0.006	2	0.0005	**0.0047**	0	0.000	0	0.0000	**1.000**
KCNQ5	-	4	0.006	2	0.0005	**0.0047**	1	0.002	0	0.0000	**0.142**
CSNK1E	-	4	0.006	2	0.0005	**0.0047**	1	0.002	0	0.0000	**0.142**
INTS2	-	4	0.006	2	0.0005	**0.0047**	2	0.003	1	0.0003	**0.055**
ESCO1	-	4	0.006	2	0.0005	**0.0047**	1	0.002	1	0.0003	**0.263**
VWCE	-	6	0.009	7	0.0018	**0.0056**	0	0.000	1	0.0003	**1.000**
PARD3B	-	5	0.008	5	0.0013	**0.0076**	1	0.002	0	0.0000	**0.142**
CEP44	-	5	0.008	5	0.0013	**0.0076**	2	0.003	1	0.0003	**0.055**
KIF18B	-	5	0.008	5	0.0013	**0.0076**	1	0.002	1	0.0003	**0.263**
GLDN	-	5	0.008	5	0.0013	**0.0076**	0	0.000	2	0.0005	**1.000**
ALDH1L1	-	5	0.008	5	0.0013	**0.0076**	2	0.003	6	0.0015	**0.317**
C6	-	6	0.009	8	0.0021	**0.0086**	3	0.005	4	0.0010	**0.064**
EXOC6	-	4	0.006	3	0.0008	**0.0098**	1	0.002	1	0.0003	**0.263**
TBCK	-	4	0.006	3	0.0008	**0.0098**	3	0.005	2	0.0005	**0.023**
MAD1L1	-	4	0.006	3	0.0008	**0.0098**	2	0.003	4	0.0010	**0.204**
WDR83	-	4	0.006	3	0.0008	**0.0098**	0	0.000	4	0.0010	**1.000**
PCDH12	-	4	0.006	3	0.0008	**0.0098**	1	0.002	3	0.0008	**0.457**
BRPF3	-	4	0.006	3	0.0008	**0.0098**	0	0.000	0	0.0000	**1.000**
CDH7	-	4	0.006	3	0.0008	**0.0098**	0	0.000	1	0.0003	**1.000**
MYLK4	-	4	0.006	3	0.0008	**0.0098**	0	0.000	2	0.0005	**1.000**
PRKCG	-	4	0.006	3	0.0008	**0.0098**	0	0.000	0	0.0000	**1.000**
DENND1C	-	4	0.006	3	0.0008	**0.0098**	0	0.000	3	0.0008	**1.000**
DRC1	-	4	0.006	3	0.0008	**0.0098**	2	0.003	9	0.0023	**0.662**
COL19A1	-	4	0.006	3	0.0008	**0.0098**	2	0.003	6	0.0015	**0.317**
SCN1B	*Yes*	3	0.005	1	0.0003	**0.0101**	0	0.000	0	0.0000	**1.000**
UNC50	-	3	0.005	1	0.0003	**0.0101**	0	0.000	0	0.0000	**1.000**
SOX13	-	3	0.005	1	0.0003	**0.0101**	1	0.002	0	0.0000	**0.142**
TESK2	-	3	0.005	1	0.0003	**0.0101**	1	0.002	3	0.0008	**0.457**
SRRM1	-	3	0.005	1	0.0003	**0.0101**	3	0.005	0	0.0000	**0.003**
UCP3	-	3	0.005	1	0.0003	**0.0101**	1	0.002	0	0.0000	**0.142**
GMCL1	-	3	0.005	1	0.0003	**0.0101**	0	0.000	1	0.0003	**1.000**
ZNF787	-	3	0.005	1	0.0003	**0.0101**	0	0.000	0	0.0000	**1.000**
ZNF583	-	3	0.005	1	0.0003	**0.0101**	0	0.000	1	0.0003	**1.000**
PNPLA1	-	3	0.005	1	0.0003	**0.0101**	1	0.002	0	0.0000	**0.142**
RTCA	-	3	0.005	1	0.0003	**0.0101**	1	0.002	1	0.0003	**0.263**
SAMD9L	-	3	0.005	1	0.0003	**0.0101**	2	0.003	4	0.0010	**0.204**
PRIM1	-	3	0.005	1	0.0003	**0.0101**	0	0.000	0	0.0000	**1.000**
KIAA1211L	-	3	0.005	1	0.0003	**0.0101**	1	0.002	0	0.0000	**0.142**
KCNA2	*Yes*	3	0.005	1	0.0003	**0.0101**	0	0.000	0	0.0000	**1.000**

HGNC gene name	Epi Gene	**Familial GGE Qualifying variants: Primary analysis**					**Familial GGE Qualifying variants: LoF analysis**				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
SNAP47	-	3	0.005	1	0.0003	**0.0101**	1	0.002	0	0.0000	**0.142**
MTNR1B	-	3	0.005	1	0.0003	**0.0101**	0	0.000	1	0.0003	**1.000**
PIGN	-	3	0.005	1	0.0003	**0.0101**	1	0.002	1	0.0003	**0.263**
KIF25	-	3	0.005	1	0.0003	**0.0101**	1	0.002	0	0.0000	**0.142**
MAK16	-	3	0.005	1	0.0003	**0.0101**	0	0.000	1	0.0003	**1.000**
XPO7	-	3	0.005	1	0.0003	**0.0101**	0	0.000	0	0.0000	**1.000**
MYO10	-	10	0.016	22	0.0057	**0.0104**	0	0.000	3	0.0008	**1.000**
TANC2	-	7	0.011	12	0.0031	**0.0119**	0	0.000	1	0.0003	**1.000**
ATP8B1	-	5	0.008	6	0.0015	**0.0124**	1	0.002	2	0.0005	**0.368**
TMEM260	-	5	0.008	6	0.0015	**0.0124**	1	0.002	2	0.0005	**0.368**
CILP	-	5	0.008	6	0.0015	**0.0124**	0	0.000	4	0.0010	**1.000**
OTUD7B	-	5	0.008	6	0.0015	**0.0124**	1	0.002	1	0.0003	**0.263**
CNGA3	-	5	0.008	6	0.0015	**0.0124**	1	0.002	3	0.0008	**0.457**
SOGA1	-	6	0.009	9	0.0023	**0.0127**	0	0.000	0	0.0000	**1.000**
FAT4	-	12	0.019	30	0.0077	**0.0128**	1	0.002	5	0.0013	**0.600**
SLC6A17	-	4	0.006	4	0.0010	**0.0174**	0	0.000	1	0.0003	**1.000**
SLC46A2	-	4	0.006	4	0.0010	**0.0174**	2	0.003	2	0.0005	**0.099**
PMM1	-	4	0.006	4	0.0010	**0.0174**	0	0.000	2	0.0005	**1.000**
IFT81	-	4	0.006	4	0.0010	**0.0174**	2	0.003	4	0.0010	**0.204**
PLCB2	-	4	0.006	4	0.0010	**0.0174**	1	0.002	1	0.0003	**0.263**
PZP	-	4	0.006	4	0.0010	**0.0174**	2	0.003	12	0.0031	**1.000**
FAM81B	-	4	0.006	4	0.0010	**0.0174**	0	0.000	0	0.0000	**1.000**
CSGALNACT1	-	4	0.006	4	0.0010	**0.0174**	1	0.002	1	0.0003	**0.263**
HEXIM2	-	4	0.006	4	0.0010	**0.0174**	1	0.002	1	0.0003	**0.263**
RPS6KC1	-	4	0.006	4	0.0010	**0.0174**	3	0.005	2	0.0005	**0.023**
SPATA13	-	6	0.009	10	0.0026	**0.0179**	0	0.000	1	0.0003	**1.000**
GAK	-	6	0.009	10	0.0026	**0.0179**	0	0.000	1	0.0003	**1.000**
ATXN1	-	6	0.009	10	0.0026	**0.0179**	0	0.000	0	0.0000	**1.000**
TEX14	-	5	0.008	7	0.0018	**0.0188**	3	0.005	12	0.0031	**0.460**
MTOR	-	5	0.008	7	0.0018	**0.0188**	0	0.000	1	0.0003	**1.000**
NFASC	-	5	0.008	7	0.0018	**0.0188**	0	0.000	3	0.0008	**1.000**
COMP	-	5	0.008	7	0.0018	**0.0188**	1	0.002	6	0.0015	**1.000**
F8	-	2	0.003	54	0.0139	**0.0189**	0	0.000	24	0.0062	**0.039**
GALR1	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
NELFB	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
PLEKHB2	-	2	0.003	0	0.0000	**0.02**	2	0.003	4	0.0010	**0.204**
OR10J1	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
RPL12	-	2	0.003	0	0.0000	**0.02**	1	0.002	2	0.0005	**0.368**
CNPY2	-	2	0.003	0	0.0000	**0.02**	1	0.002	1	0.0003	**0.263**
PABPN1	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**

HGNC gene name	Epi Gene	Familial GGE Qualifying variants: Primary analysis					Familial GGE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
HIST1H4G	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
OR13C5	-	2	0.003	0	0.0000	**0.02**	1	0.002	1	0.0003	**0.263**
SLC6A1	*Yes*	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
LACTB	-	2	0.003	0	0.0000	**0.02**	2	0.003	0	0.0000	**0.020**
BCL2L2-PABPN1	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
C11orf74	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
CCNG2	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
IFT57	-	2	0.003	0	0.0000	**0.02**	1	0.002	1	0.0003	**0.263**
CRX	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
TSTD2	-	2	0.003	0	0.0000	**0.02**	1	0.002	5	0.0013	**0.600**
RPS19BP1	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
DDX59	-	2	0.003	0	0.0000	**0.02**	0	0.000	2	0.0005	**1.000**
PUSL1	-	2	0.003	0	0.0000	**0.02**	1	0.002	5	0.0013	**0.600**
OR5M1	-	2	0.003	0	0.0000	**0.02**	0	0.000	2	0.0005	**1.000**
IFNAR2	-	2	0.003	0	0.0000	**0.02**	2	0.003	0	0.0000	**0.020**
ESRRG	-	2	0.003	0	0.0000	**0.02**	2	0.003	0	0.0000	**0.020**
MRPS23	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
APMAP	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
FHIT	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
SLMO1	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
FOXD4L1	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
HLA-DQA2	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
FAM83E	-	2	0.003	0	0.0000	**0.02**	0	0.000	2	0.0005	**1.000**
FIP1L1	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
PTRF	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
SAMD12	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
OR5B21	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
LYZL4	-	2	0.003	0	0.0000	**0.02**	0	0.000	1	0.0003	**1.000**
CHCHD6	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
GDAP2	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
TMEM19	-	2	0.003	0	0.0000	**0.02**	0	0.000	6	0.0015	**1.000**
ALG14	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
ZDHHC22	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
GPKOW	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
FGFRL1	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
EIF2B3	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
BEST1	-	2	0.003	0	0.0000	**0.02**	1	0.002	5	0.0013	**0.600**
SV2C	-	2	0.003	0	0.0000	**0.02**	1	0.002	1	0.0003	**0.263**
BRMS1L	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
EEF1A2	*Yes*	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**

HGNC gene name	Epi Gene	Familial GGE Qualifying variants: Primary analysis					Familial GGE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
UTP11L	-	2	0.003	0	0.0000	**0.02**	2	0.003	1	0.0003	**0.055**
ACSL4	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
KLK7	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
KLK1	-	2	0.003	0	0.0000	**0.02**	0	0.000	3	0.0008	**1.000**
SAP30L	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
NSMCE2	-	2	0.003	0	0.0000	**0.02**	0	0.000	2	0.0005	**1.000**
RORB	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
USF1	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
PHF19	-	2	0.003	0	0.0000	**0.02**	0	0.000	1	0.0003	**1.000**
GSX1	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
KRT86	-	2	0.003	0	0.0000	**0.02**	0	0.000	1	0.0003	**1.000**
PPP4R4	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
DPRX	-	2	0.003	0	0.0000	**0.02**	1	0.002	4	0.0010	**0.534**
STK3	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
PPAPDC3	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
DUSP14	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
PLXDC1	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
GPR149	-	2	0.003	0	0.0000	**0.02**	0	0.000	1	0.0003	**1.000**
C22orf31	-	2	0.003	0	0.0000	**0.02**	1	0.002	1	0.0003	**0.263**
TRAF3	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
EFNB1	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
FAM174A	-	2	0.003	0	0.0000	**0.02**	0	0.000	2	0.0005	**1.000**
EPCAM	-	2	0.003	0	0.0000	**0.02**	2	0.003	0	0.0000	**0.020**
IQSEC2	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
PCDHGA2	-	2	0.003	0	0.0000	**0.02**	0	0.000	3	0.0008	**1.000**
TRMT1L	-	2	0.003	0	0.0000	**0.02**	1	0.002	0	0.0000	**0.142**
RABGEF1	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
PDE12	-	2	0.003	0	0.0000	**0.02**	1	0.002	1	0.0003	**0.263**
AIRE	-	2	0.003	0	0.0000	**0.02**	0	0.000	0	0.0000	**1.000**
TFPI2	-	2	0.003	0	0.0000	**0.02**	1	0.002	1	0.0003	**0.263**
KIAA1109	-	7	0.011	14	0.0036	**0.0213**	0	0.000	5	0.0013	**1.000**
DMXL2	-	7	0.011	14	0.0036	**0.0213**	0	0.000	0	0.0000	**1.000**
MGRN1	-	3	0.005	2	0.0005	**0.0227**	1	0.002	0	0.0000	**0.142**
SUPT16H	-	3	0.005	2	0.0005	**0.0227**	0	0.000	0	0.0000	**1.000**
HP	-	3	0.005	2	0.0005	**0.0227**	1	0.002	1	0.0003	**0.263**
PLEKHM3	-	3	0.005	2	0.0005	**0.0227**	2	0.003	0	0.0000	**0.020**
CREB3	-	3	0.005	2	0.0005	**0.0227**	3	0.005	2	0.0005	**0.023**
XXYLT1	-	3	0.005	2	0.0005	**0.0227**	1	0.002	1	0.0003	**0.263**
SLC32A1	-	3	0.005	2	0.0005	**0.0227**	0	0.000	0	0.0000	**1.000**
APEH	-	3	0.005	2	0.0005	**0.0227**	1	0.002	3	0.0008	**0.457**

HGNC gene name	Epi Gene	Familial GGE Qualifying variants: Primary analysis					Familial GGE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
DDX55	-	3	0.005	2	0.0005	**0.0227**	0	0.000	7	0.0018	**0.603**
ZNF529	-	3	0.005	2	0.0005	**0.0227**	0	0.000	7	0.0018	**0.603**
GJB4	-	3	0.005	2	0.0005	**0.0227**	1	0.002	0	0.0000	**0.142**
ZNF417	-	3	0.005	2	0.0005	**0.0227**	1	0.002	1	0.0003	**0.263**
SLC35B2	-	3	0.005	2	0.0005	**0.0227**	1	0.002	1	0.0003	**0.263**
PLA2G4D	-	3	0.005	2	0.0005	**0.0227**	1	0.002	5	0.0013	**0.600**
ZNF251	-	3	0.005	2	0.0005	**0.0227**	1	0.002	2	0.0005	**0.368**
MFSD7	-	3	0.005	2	0.0005	**0.0227**	1	0.002	4	0.0010	**0.534**
ORC4	-	3	0.005	2	0.0005	**0.0227**	0	0.000	1	0.0003	**1.000**
ZFC3H1	-	3	0.005	2	0.0005	**0.0227**	0	0.000	1	0.0003	**1.000**
CELA3A	-	3	0.005	2	0.0005	**0.0227**	0	0.000	6	0.0015	**1.000**
RPTN	-	3	0.005	2	0.0005	**0.0227**	2	0.003	5	0.0013	**0.260**
SRPX	-	3	0.005	2	0.0005	**0.0227**	1	0.002	0	0.0000	**0.142**
CLTC	-	3	0.005	2	0.0005	**0.0227**	0	0.000	0	0.0000	**1.000**
EPS8	-	3	0.005	2	0.0005	**0.0227**	1	0.002	1	0.0003	**0.263**
TOB1	-	3	0.005	2	0.0005	**0.0227**	1	0.002	0	0.0000	**0.142**
RGS4	-	3	0.005	2	0.0005	**0.0227**	2	0.003	2	0.0005	**0.099**
PDCL2	-	3	0.005	2	0.0005	**0.0227**	3	0.005	0	0.0000	**0.003**
ALKBH1	-	3	0.005	2	0.0005	**0.0227**	2	0.003	2	0.0005	**0.099**
SLC2A12	-	3	0.005	2	0.0005	**0.0227**	0	0.000	1	0.0003	**1.000**
ZC3H3	-	6	0.009	11	0.0028	**0.0244**	0	0.000	1	0.0003	**1.000**
MSH2	-	6	0.009	11	0.0028	**0.0244**	0	0.000	0	0.0000	**1.000**
LRBA	-	0	0.000	27	0.0070	**0.0254**	0	0.000	5	0.0013	**1.000**
MYO18A	-	0	0.000	28	0.0072	**0.0258**	0	0.000	4	0.0010	**1.000**
TNNI3K	-	5	0.008	8	0.0021	**0.0271**	1	0.002	13	0.0034	**0.708**
CHPF2	-	5	0.008	8	0.0021	**0.0271**	3	0.005	3	0.0008	**0.041**
LIPE	-	5	0.008	8	0.0021	**0.0271**	3	0.005	1	0.0003	**0.010**
LRIG3	-	5	0.008	8	0.0021	**0.0271**	1	0.002	6	0.0015	**1.000**
PLIN4	-	5	0.008	8	0.0021	**0.0271**	0	0.000	3	0.0008	**1.000**
OSBPL2	-	4	0.006	5	0.0013	**0.0279**	0	0.000	0	0.0000	**1.000**
TRMT6	-	4	0.006	5	0.0013	**0.0279**	1	0.002	2	0.0005	**0.368**
VPS41	-	4	0.006	5	0.0013	**0.0279**	1	0.002	4	0.0010	**0.534**
SLC27A6	-	4	0.006	5	0.0013	**0.0279**	2	0.003	1	0.0003	**0.055**
EWSR1	-	4	0.006	5	0.0013	**0.0279**	0	0.000	1	0.0003	**1.000**
ZNF25	-	4	0.006	5	0.0013	**0.0279**	0	0.000	3	0.0008	**1.000**
ZNF695	-	4	0.006	5	0.0013	**0.0279**	1	0.002	3	0.0008	**0.457**
METTL22	-	4	0.006	5	0.0013	**0.0279**	3	0.005	4	0.0010	**0.064**
FGFR1	-	4	0.006	5	0.0013	**0.0279**	0	0.000	0	0.0000	**1.000**
CHL1	-	4	0.006	5	0.0013	**0.0279**	0	0.000	2	0.0005	**1.000**
TMC6	-	4	0.006	5	0.0013	**0.0279**	0	0.000	1	0.0003	**1.000**

HGNC gene name	Epi Gene	Familial GGE Qualifying variants: Primary analysis					Familial GGE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
LEPR	-	4	0.006	5	0.0013	**0.0279**	0	0.000	1	0.0003	**1.000**
CREBZF	-	4	0.006	5	0.0013	**0.0279**	0	0.000	0	0.0000	**1.000**
ABI3BP	-	4	0.006	5	0.0013	**0.0279**	1	0.002	1	0.0003	**0.263**
ESCO2	-	4	0.006	5	0.0013	**0.0279**	1	0.002	4	0.0010	**0.534**
ANK3	-	10	0.016	26	0.0067	**0.0282**	0	0.000	0	0.0000	**1.000**
ARAP2	-	6	0.009	12	0.0031	**0.0324**	4	0.006	6	0.0015	**0.041**
ANKRD12	-	7	0.011	16	0.0041	**0.0349**	3	0.005	2	0.0005	**0.023**
LTBP2	-	5	0.008	9	0.0023	**0.0374**	1	0.002	1	0.0003	**0.263**
STAB1	-	11	0.017	30	0.0077	**0.0383**	1	0.002	13	0.0034	**0.708**
PARP8	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
MON1B	-	3	0.005	3	0.0008	**0.0406**	0	0.000	1	0.0003	**1.000**
GANAB	-	3	0.005	3	0.0008	**0.0406**	1	0.002	0	0.0000	**0.142**
SLC4A4	-	3	0.005	3	0.0008	**0.0406**	0	0.000	1	0.0003	**1.000**
LRRTM3	-	3	0.005	3	0.0008	**0.0406**	0	0.000	1	0.0003	**1.000**
KY	-	3	0.005	3	0.0008	**0.0406**	0	0.000	1	0.0003	**1.000**
EPHB4	-	3	0.005	3	0.0008	**0.0406**	1	0.002	0	0.0000	**0.142**
IRF7	-	3	0.005	3	0.0008	**0.0406**	0	0.000	2	0.0005	**1.000**
ABCG4	-	3	0.005	3	0.0008	**0.0406**	2	0.003	0	0.0000	**0.020**
VNN2	-	3	0.005	3	0.0008	**0.0406**	2	0.003	3	0.0008	**0.150**
APC2	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
SNTB1	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
TGFBR3	-	3	0.005	3	0.0008	**0.0406**	2	0.003	0	0.0000	**0.020**
CEP76	-	3	0.005	3	0.0008	**0.0406**	1	0.002	0	0.0000	**0.142**
CEP89	-	3	0.005	3	0.0008	**0.0406**	0	0.000	4	0.0010	**1.000**
TYRO3	-	3	0.005	3	0.0008	**0.0406**	0	0.000	1	0.0003	**1.000**
SMPD3	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
CWC27	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
EHD3	-	3	0.005	3	0.0008	**0.0406**	0	0.000	1	0.0003	**1.000**
CD68	-	3	0.005	3	0.0008	**0.0406**	2	0.003	1	0.0003	**0.055**
FBXL13	-	3	0.005	3	0.0008	**0.0406**	2	0.003	2	0.0005	**0.099**
FBXL22	-	3	0.005	3	0.0008	**0.0406**	1	0.002	0	0.0000	**0.142**
ZNF419	-	3	0.005	3	0.0008	**0.0406**	2	0.003	2	0.0005	**0.099**
MN1	-	3	0.005	3	0.0008	**0.0406**	0	0.000	1	0.0003	**1.000**
ZNF285	-	3	0.005	3	0.0008	**0.0406**	2	0.003	5	0.0013	**0.260**
ADAT2	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
KDM4A	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
ANAPC1	-	3	0.005	3	0.0008	**0.0406**	1	0.002	1	0.0003	**0.263**
SLC26A10	-	3	0.005	3	0.0008	**0.0406**	1	0.002	1	0.0003	**0.263**
PGAP2	-	3	0.005	3	0.0008	**0.0406**	0	0.000	5	0.0013	**1.000**
GRIK4	-	3	0.005	3	0.0008	**0.0406**	1	0.002	1	0.0003	**0.263**

HGNC gene name	Epi Gene	Familial GGE Qualifying variants: Primary analysis					Familial GGE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
APOL1	-	3	0.005	3	0.0008	**0.0406**	1	0.002	4	0.0010	**0.534**
SYTL4	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
ASAP1	-	3	0.005	3	0.0008	**0.0406**	0	0.000	1	0.0003	**1.000**
ESF1	-	3	0.005	3	0.0008	**0.0406**	0	0.000	3	0.0008	**1.000**
MAN2B2	-	3	0.005	3	0.0008	**0.0406**	0	0.000	2	0.0005	**1.000**
PROM2	-	3	0.005	3	0.0008	**0.0406**	0	0.000	4	0.0010	**1.000**
ALPI	-	3	0.005	3	0.0008	**0.0406**	2	0.003	2	0.0005	**0.099**
SIPA1	-	3	0.005	3	0.0008	**0.0406**	1	0.002	0	0.0000	**0.142**
CPB1	-	3	0.005	3	0.0008	**0.0406**	2	0.003	2	0.0005	**0.099**
RGS3	-	3	0.005	3	0.0008	**0.0406**	3	0.005	5	0.0013	**0.092**
OTUD4	-	3	0.005	3	0.0008	**0.0406**	0	0.000	0	0.0000	**1.000**
KLF17	-	3	0.005	3	0.0008	**0.0406**	0	0.000	3	0.0008	**1.000**
EML6	-	11	0.017	31	0.0080	**0.041**	0	0.000	4	0.0010	**1.000**
AFG3L2	-	4	0.006	6	0.0015	**0.0414**	1	0.002	2	0.0005	**0.368**
MED1	-	4	0.006	6	0.0015	**0.0414**	0	0.000	0	0.0000	**1.000**
EXOC7	-	4	0.006	6	0.0015	**0.0414**	1	0.002	2	0.0005	**0.368**
CD163	-	4	0.006	6	0.0015	**0.0414**	0	0.000	0	0.0000	**1.000**
ILVBL	-	4	0.006	6	0.0015	**0.0414**	2	0.003	1	0.0003	**0.055**
WDR96	-	4	0.006	6	0.0015	**0.0414**	2	0.003	6	0.0015	**0.317**
INSC	-	4	0.006	6	0.0015	**0.0414**	2	0.003	3	0.0008	**0.150**
ACSS2	-	4	0.006	6	0.0015	**0.0414**	2	0.003	1	0.0003	**0.055**
FAM171A1	-	4	0.006	6	0.0015	**0.0414**	0	0.000	1	0.0003	**1.000**
ARID4B	-	4	0.006	6	0.0015	**0.0414**	0	0.000	0	0.0000	**1.000**
USP6	-	4	0.006	6	0.0015	**0.0414**	1	0.002	7	0.0018	**1.000**
SMCHD1	-	4	0.006	6	0.0015	**0.0414**	0	0.000	0	0.0000	**1.000**
DUSP27	-	4	0.006	6	0.0015	**0.0414**	2	0.003	7	0.0018	**0.372**
LRIF1	-	4	0.006	6	0.0015	**0.0414**	0	0.000	1	0.0003	**1.000**
AMT	-	4	0.006	6	0.0015	**0.0414**	1	0.002	0	0.0000	**0.142**
POLR3E	-	4	0.006	6	0.0015	**0.0414**	1	0.002	2	0.0005	**0.368**

Table S11: Results for the analysis of 525 NAFE cases with a family history of epilepsy and 3877 control exomes.

The top 300 ranked genes from the Primary model collapsing analysis. The full exome-wide results can be accessed at http://epi4kdb.org/downloads/common-epilepsies/Table-S11.xlsx. A gender stratified Cochran-Mantel-Haenszel (CMH) test statistic is also available for the sex chromosomes (Table S13). Epi Gene: is among the 43 known dominant epilepsy genes; Qcase: number of cases carrying a qualifying variant; Qcase Freq: proportion of cases carrying a qualifying variant; Qctrl: number of controls carrying a qualifying variant; Qctrl Freq: proportion of controls carrying a qualifying variant; FET p-val: Fisher's exact two-tail p-value.

HGNC gene name	Epi Gene	**Familial NAFE Qualifying variants: Primary analysis**					**Familial NAFE Qualifying variants: LoF analysis**				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
DEPDC5	*Yes*	15	0.029	14	0.0036	**1.8E-7**	14	0.027	2	0.0005	**9.6E-12**
LGI1	*Yes*	8	0.015	2	0.0005	**1.4E-6**	2	0.004	0	0.0000	**0.014**
PCDH19	*Yes*	6	0.011	2	0.0005	**6.4E-5**	3	0.006	0	0.0000	**0.002**
SCN1A	*Yes*	11	0.021	15	0.0039	**9.0E-5**	0	0.000	1	0.0003	**1.000**
GRIN2A	*Yes*	7	0.013	7	0.0018	**5.3E-4**	3	0.006	0	0.0000	**0.002**
TYRO3	-	5	0.010	3	0.0008	**9.7E-4**	0	0.000	1	0.0003	**1.000**
LMAN1L	-	5	0.010	3	0.0008	**9.7E-4**	3	0.006	4	0.0010	**0.041**
PKHD1	-	10	0.019	19	0.0049	**0.0013**	1	0.002	8	0.0021	**1.000**
ATP8B1	-	6	0.011	6	0.0015	**0.0014**	2	0.004	2	0.0005	**0.072**
PCDHB6	-	6	0.011	6	0.0015	**0.0014**	0	0.000	3	0.0008	**1.000**
MAGEA6	-	3	0.006	0	0.0000	**0.0017**	1	0.002	1	0.0003	**0.224**
PSMC4	-	3	0.006	0	0.0000	**0.0017**	2	0.004	0	0.0000	**0.014**
OR4N5	-	3	0.006	0	0.0000	**0.0017**	1	0.002	0	0.0000	**0.119**
OR4K13	-	3	0.006	0	0.0000	**0.0017**	0	0.000	0	0.0000	**1.000**
SLC9A2	-	3	0.006	0	0.0000	**0.0017**	2	0.004	3	0.0008	**0.111**
SLC8A2	-	3	0.006	0	0.0000	**0.0017**	0	0.000	0	0.0000	**1.000**
CCDC14	-	5	0.010	4	0.0010	**0.002**	4	0.008	5	0.0013	**0.015**
ZNF804A	-	4	0.008	2	0.0005	**0.0025**	0	0.000	0	0.0000	**1.000**
BZRAP1	-	5	0.010	5	0.0013	**0.0036**	0	0.000	1	0.0003	**1.000**
SLC44A4	-	5	0.010	5	0.0013	**0.0036**	2	0.004	6	0.0015	**0.246**
SATL1	-	5	0.010	5	0.0013	**0.0036**	1	0.002	3	0.0008	**0.398**
FNIP1	-	5	0.010	5	0.0013	**0.0036**	1	0.002	1	0.0003	**0.224**
FRMD3	-	4	0.008	3	0.0008	**0.0052**	1	0.002	0	0.0000	**0.119**
SLC12A5	-	4	0.008	3	0.0008	**0.0052**	2	0.004	0	0.0000	**0.014**
CCDC11	-	4	0.008	3	0.0008	**0.0052**	3	0.006	7	0.0018	**0.107**
DRC1	-	4	0.008	3	0.0008	**0.0052**	2	0.004	9	0.0023	**0.631**
PCLO	-	13	0.025	36	0.0093	**0.0057**	1	0.002	0	0.0000	**0.119**
TSHR	-	5	0.010	6	0.0015	**0.0059**	0	0.000	4	0.0010	**1.000**
OR10Z1	-	3	0.006	1	0.0003	**0.0062**	0	0.000	0	0.0000	**1.000**
OR6A2	-	3	0.006	1	0.0003	**0.0062**	0	0.000	1	0.0003	**1.000**

HGNC gene name	Epi Gene	Familial NAFE Qualifying variants: Primary analysis					Familial NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
SULT1C3	-	3	0.006	1	0.0003	**0.0062**	0	0.000	4	0.0010	**1.000**
ZNF606	-	3	0.006	1	0.0003	**0.0062**	1	0.002	0	0.0000	**0.119**
ZNF692	-	3	0.006	1	0.0003	**0.0062**	2	0.004	1	0.0003	**0.039**
EHD4	-	3	0.006	1	0.0003	**0.0062**	0	0.000	0	0.0000	**1.000**
CCR3	-	3	0.006	1	0.0003	**0.0062**	0	0.000	0	0.0000	**1.000**
SAMD9L	-	3	0.006	1	0.0003	**0.0062**	5	0.010	4	0.0010	**0.002**
ZNF497	-	3	0.006	1	0.0003	**0.0062**	1	0.002	0	0.0000	**0.119**
PDSS1	-	3	0.006	1	0.0003	**0.0062**	1	0.002	0	0.0000	**0.119**
SLC43A3	-	3	0.006	1	0.0003	**0.0062**	1	0.002	0	0.0000	**0.119**
MPG	-	3	0.006	1	0.0003	**0.0062**	2	0.004	2	0.0005	**0.072**
CYP4V2	-	3	0.006	1	0.0003	**0.0062**	3	0.006	1	0.0003	**0.006**
CCDC15	-	3	0.006	1	0.0003	**0.0062**	2	0.004	2	0.0005	**0.072**
OR7A10	-	3	0.006	1	0.0003	**0.0062**	0	0.000	1	0.0003	**1.000**
ZSWIM3	-	3	0.006	1	0.0003	**0.0062**	0	0.000	0	0.0000	**1.000**
BNIP1	-	3	0.006	1	0.0003	**0.0062**	1	0.002	3	0.0008	**0.398**
C5orf42	-	6	0.011	10	0.0026	**0.0078**	4	0.008	2	0.0005	**0.003**
WDR78	-	4	0.008	4	0.0010	**0.0094**	2	0.004	12	0.0031	**0.680**
SEC31A	-	4	0.008	4	0.0010	**0.0094**	0	0.000	0	0.0000	**1.000**
SYNE3	-	4	0.008	4	0.0010	**0.0094**	0	0.000	1	0.0003	**1.000**
PGS1	-	4	0.008	4	0.0010	**0.0094**	1	0.002	2	0.0005	**0.317**
BCLAF1	-	4	0.008	4	0.0010	**0.0094**	0	0.000	0	0.0000	**1.000**
ADCY10	-	6	0.011	11	0.0028	**0.0109**	2	0.004	7	0.0018	**0.293**
F8	-	1	0.002	54	0.0139	**0.0117**	0	0.000	24	0.0062	**0.105**
RALGPS1	-	3	0.006	2	0.0005	**0.014**	1	0.002	0	0.0000	**0.119**
OR2T4	-	3	0.006	2	0.0005	**0.014**	0	0.000	0	0.0000	**1.000**
ZC2HC1A	-	3	0.006	2	0.0005	**0.014**	1	0.002	0	0.0000	**0.119**
BVES	-	3	0.006	2	0.0005	**0.014**	1	0.002	0	0.0000	**0.119**
MPPE1	-	3	0.006	2	0.0005	**0.014**	2	0.004	0	0.0000	**0.014**
HPN	-	3	0.006	2	0.0005	**0.014**	1	0.002	0	0.0000	**0.119**
POC1B-GALNT4	-	3	0.006	2	0.0005	**0.014**	1	0.002	3	0.0008	**0.398**
VPS52	-	3	0.006	2	0.0005	**0.014**	0	0.000	0	0.0000	**1.000**
IL2RB	-	3	0.006	2	0.0005	**0.014**	0	0.000	1	0.0003	**1.000**
WDR93	-	3	0.006	2	0.0005	**0.014**	2	0.004	6	0.0015	**0.246**
KCNJ10	-	3	0.006	2	0.0005	**0.014**	1	0.002	0	0.0000	**0.119**
PLA2G4D	-	3	0.006	2	0.0005	**0.014**	0	0.000	2	0.0005	**1.000**
ZNF213	-	3	0.006	2	0.0005	**0.014**	0	0.000	1	0.0003	**1.000**
GALNT4	-	3	0.006	2	0.0005	**0.014**	0	0.000	3	0.0008	**1.000**
GIGYF1	-	3	0.006	2	0.0005	**0.014**	0	0.000	0	0.0000	**1.000**
FAM222B	-	3	0.006	2	0.0005	**0.014**	1	0.002	1	0.0003	**0.224**

HGNC gene name	Epi Gene	Familial NAFE Qualifying variants: Primary analysis					Familial NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
ST6GALNAC1	-	3	0.006	2	0.0005	**0.014**	4	0.008	3	0.0008	**0.005**
SNX5	-	3	0.006	2	0.0005	**0.014**	0	0.000	1	0.0003	**1.000**
ZFC3H1	-	3	0.006	2	0.0005	**0.014**	0	0.000	1	0.0003	**1.000**
FAM166A	-	3	0.006	2	0.0005	**0.014**	0	0.000	8	0.0021	**0.607**
C17orf80	-	3	0.006	2	0.0005	**0.014**	1	0.002	2	0.0005	**0.317**
AAAS	-	3	0.006	2	0.0005	**0.014**	2	0.004	1	0.0003	**0.039**
ZFP69	-	3	0.006	2	0.0005	**0.014**	1	0.002	0	0.0000	**0.119**
AGT	-	3	0.006	2	0.0005	**0.014**	0	0.000	0	0.0000	**1.000**
NRXN2	-	3	0.006	2	0.0005	**0.014**	0	0.000	0	0.0000	**1.000**
MAOA	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
SH2D7	-	2	0.004	0	0.0000	**0.0142**	1	0.002	1	0.0003	**0.224**
MBL2	-	2	0.004	0	0.0000	**0.0142**	0	0.000	1	0.0003	**1.000**
OSBPL8	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
APRT	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
SOX10	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
RNF41	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
RPP40	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
CHST2	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
VSIG2	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
SERGEF	-	2	0.004	0	0.0000	**0.0142**	1	0.002	5	0.0013	**0.534**
IFNAR2	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
RRP9	-	2	0.004	0	0.0000	**0.0142**	0	0.000	1	0.0003	**1.000**
IL18BP	-	2	0.004	0	0.0000	**0.0142**	0	0.000	2	0.0005	**1.000**
TMEM207	-	2	0.004	0	0.0000	**0.0142**	1	0.002	0	0.0000	**0.119**
TOMM40	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
TTLL10	-	2	0.004	0	0.0000	**0.0142**	0	0.000	1	0.0003	**1.000**
SPINT4	-	2	0.004	0	0.0000	**0.0142**	2	0.004	0	0.0000	**0.014**
CD70	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
GDAP2	-	2	0.004	0	0.0000	**0.0142**	2	0.004	0	0.0000	**0.014**
TTLL1	-	2	0.004	0	0.0000	**0.0142**	0	0.000	2	0.0005	**1.000**
CARF	-	2	0.004	0	0.0000	**0.0142**	1	0.002	0	0.0000	**0.119**
CBR4	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
CACNG6	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
SLC25A22	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
WNT7A	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
NDUFAF4	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
TSKU	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
PRKCD	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
MT1M	-	2	0.004	0	0.0000	**0.0142**	1	0.002	0	0.0000	**0.119**
TSN	-	2	0.004	0	0.0000	**0.0142**	1	0.002	0	0.0000	**0.119**

HGNC gene name	Epi Gene	Familial NAFE Qualifying variants: Primary analysis					Familial NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
C9orf173	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
GPATCH8	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
COG1	-	2	0.004	0	0.0000	**0.0142**	1	0.002	1	0.0003	**0.224**
TRAM2	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
CADM1	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
TRIM36	-	2	0.004	0	0.0000	**0.0142**	1	0.002	0	0.0000	**0.119**
TRIM65	-	2	0.004	0	0.0000	**0.0142**	0	0.000	1	0.0003	**1.000**
C1orf74	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
C19orf45	-	2	0.004	0	0.0000	**0.0142**	1	0.002	2	0.0005	**0.317**
C1orf68	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
C1orf27	-	2	0.004	0	0.0000	**0.0142**	0	0.000	0	0.0000	**1.000**
ANXA9	-	2	0.004	0	0.0000	**0.0142**	1	0.002	1	0.0003	**0.224**
NAT9	-	2	0.004	0	0.0000	**0.0142**	0	0.000	3	0.0008	**1.000**
ZDBF2	-	6	0.011	12	0.0031	**0.0147**	2	0.004	3	0.0008	**0.111**
SEMA5A	-	4	0.008	5	0.0013	**0.0154**	2	0.004	0	0.0000	**0.014**
CPSF3L	-	4	0.008	5	0.0013	**0.0154**	2	0.004	9	0.0023	**0.631**
ZNF518B	-	4	0.008	5	0.0013	**0.0154**	2	0.004	1	0.0003	**0.039**
TUBGCP2	-	4	0.008	5	0.0013	**0.0154**	1	0.002	5	0.0013	**0.534**
CHADL	-	4	0.008	5	0.0013	**0.0154**	2	0.004	2	0.0005	**0.072**
ZSWIM6	-	4	0.008	5	0.0013	**0.0154**	0	0.000	0	0.0000	**1.000**
SPG11	-	7	0.013	18	0.0046	**0.0232**	1	0.002	16	0.0041	**0.712**
SPECC1	-	4	0.008	6	0.0015	**0.0233**	2	0.004	1	0.0003	**0.039**
CDH26	-	4	0.008	6	0.0015	**0.0233**	3	0.006	14	0.0036	**0.446**
CNTN5	-	4	0.008	6	0.0015	**0.0233**	0	0.000	1	0.0003	**1.000**
TTC7A	-	4	0.008	6	0.0015	**0.0233**	1	0.002	4	0.0010	**0.470**
APOBR	-	4	0.008	6	0.0015	**0.0233**	2	0.004	0	0.0000	**0.014**
SLC28A1	-	4	0.008	6	0.0015	**0.0233**	1	0.002	5	0.0013	**0.534**
DSC2	-	4	0.008	6	0.0015	**0.0233**	2	0.004	4	0.0010	**0.154**
ACAD10	-	3	0.006	3	0.0008	**0.0256**	2	0.004	5	0.0013	**0.199**
PYGO2	-	3	0.006	3	0.0008	**0.0256**	0	0.000	1	0.0003	**1.000**
SNTB1	-	3	0.006	3	0.0008	**0.0256**	2	0.004	0	0.0000	**0.014**
TBCK	-	3	0.006	3	0.0008	**0.0256**	0	0.000	2	0.0005	**1.000**
EVI2B	-	3	0.006	3	0.0008	**0.0256**	0	0.000	0	0.0000	**1.000**
MAP1B	-	3	0.006	3	0.0008	**0.0256**	0	0.000	1	0.0003	**1.000**
MTHFSD	-	3	0.006	3	0.0008	**0.0256**	2	0.004	2	0.0005	**0.072**
OIT3	-	3	0.006	3	0.0008	**0.0256**	0	0.000	2	0.0005	**1.000**
CTNNA2	-	3	0.006	3	0.0008	**0.0256**	0	0.000	0	0.0000	**1.000**
GPR87	-	3	0.006	3	0.0008	**0.0256**	1	0.002	2	0.0005	**0.317**
TMEM209	-	3	0.006	3	0.0008	**0.0256**	0	0.000	2	0.0005	**1.000**
SHCBP1L	-	3	0.006	3	0.0008	**0.0256**	0	0.000	2	0.0005	**1.000**

HGNC gene name	Epi Gene	Familial NAFE Qualifying variants: Primary analysis					Familial NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
NOX5	-	3	0.006	3	0.0008	**0.0256**	3	0.006	8	0.0021	**0.135**
SHCBP1	-	3	0.006	3	0.0008	**0.0256**	2	0.004	0	0.0000	**0.014**
PUS7	-	3	0.006	3	0.0008	**0.0256**	1	0.002	0	0.0000	**0.119**
ZNF486	-	3	0.006	3	0.0008	**0.0256**	2	0.004	3	0.0008	**0.111**
FAM213A	-	3	0.006	3	0.0008	**0.0256**	1	0.002	1	0.0003	**0.224**
SLFN12L	-	3	0.006	3	0.0008	**0.0256**	2	0.004	6	0.0015	**0.246**
MET	-	3	0.006	3	0.0008	**0.0256**	0	0.000	1	0.0003	**1.000**
CASQ2	-	3	0.006	3	0.0008	**0.0256**	0	0.000	1	0.0003	**1.000**
TPTE2	-	3	0.006	3	0.0008	**0.0256**	1	0.002	6	0.0015	**0.589**
ITPRIPL2	-	3	0.006	3	0.0008	**0.0256**	1	0.002	1	0.0003	**0.224**
GFOD2	-	3	0.006	3	0.0008	**0.0256**	0	0.000	1	0.0003	**1.000**
C10orf90	-	3	0.006	3	0.0008	**0.0256**	1	0.002	2	0.0005	**0.317**
RGS14	-	3	0.006	3	0.0008	**0.0256**	1	0.002	2	0.0005	**0.317**
RLBP1	-	3	0.006	3	0.0008	**0.0256**	0	0.000	0	0.0000	**1.000**
FCRL5	-	3	0.006	3	0.0008	**0.0256**	1	0.002	0	0.0000	**0.119**
PKHD1L1	-	0	0.000	33	0.0085	**0.0275**	1	0.002	29	0.0075	**0.251**
DLC1	-	6	0.011	15	0.0039	**0.0316**	0	0.000	0	0.0000	**1.000**
ABCC4	-	4	0.008	7	0.0018	**0.0332**	3	0.006	12	0.0031	**0.411**
INADL	-	4	0.008	7	0.0018	**0.0332**	2	0.004	4	0.0010	**0.154**
TEX14	-	4	0.008	7	0.0018	**0.0332**	3	0.006	12	0.0031	**0.411**
NOC4L	-	4	0.008	7	0.0018	**0.0332**	0	0.000	1	0.0003	**1.000**
TCHH	-	5	0.010	11	0.0028	**0.0337**	2	0.004	15	0.0039	**1.000**
LRRD1	-	5	0.010	11	0.0028	**0.0337**	0	0.000	7	0.0018	**1.000**
KIAA1731	-	9	0.017	29	0.0075	**0.0389**	4	0.008	8	0.0021	**0.045**
OR2D3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
ADCK2	-	2	0.004	1	0.0003	**0.0392**	1	0.002	1	0.0003	**0.224**
PARD6A	-	2	0.004	1	0.0003	**0.0392**	1	0.002	1	0.0003	**0.224**
ECHDC3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	2	0.0005	**1.000**
MAPKAPK3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
PATE1	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
SRD5A3	-	2	0.004	1	0.0003	**0.0392**	1	0.002	7	0.0018	**1.000**
OR13H1	-	2	0.004	1	0.0003	**0.0392**	1	0.002	1	0.0003	**0.224**
RBM48	-	2	0.004	1	0.0003	**0.0392**	1	0.002	2	0.0005	**0.317**
RTDR1	-	2	0.004	1	0.0003	**0.0392**	0	0.000	4	0.0010	**1.000**
PSMG4	-	2	0.004	1	0.0003	**0.0392**	1	0.002	1	0.0003	**0.224**
C11orf80	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
HOXC9	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
IFNAR1	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
ZNF784	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
DCTN4	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**

HGNC gene name	Epi Gene	Familial NAFE Qualifying variants: Primary analysis					Familial NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
SRPK3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
DAZL	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
FURIN	-	2	0.004	1	0.0003	**0.0392**	1	0.002	0	0.0000	**0.119**
ETV3L	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
HIST1H2AD	-	2	0.004	1	0.0003	**0.0392**	1	0.002	3	0.0008	**0.398**
GMPPB	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
GPC4	-	2	0.004	1	0.0003	**0.0392**	1	0.002	0	0.0000	**0.119**
DCPS	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
DGAT2L6	-	2	0.004	1	0.0003	**0.0392**	0	0.000	2	0.0005	**1.000**
LAMP3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
NACC2	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
ZZZ3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
CDNF	-	2	0.004	1	0.0003	**0.0392**	1	0.002	1	0.0003	**0.224**
SESN3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
PRDM14	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
FAM96B	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
DAPK2	-	2	0.004	1	0.0003	**0.0392**	1	0.002	5	0.0013	**0.534**
TMEM119	-	2	0.004	1	0.0003	**0.0392**	2	0.004	0	0.0000	**0.014**
SLC20A1	-	2	0.004	1	0.0003	**0.0392**	1	0.002	0	0.0000	**0.119**
UBXN11	-	2	0.004	1	0.0003	**0.0392**	1	0.002	2	0.0005	**0.317**
SLC35C1	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
ZDHHC19	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
TRIM7	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
DCP1B	-	2	0.004	1	0.0003	**0.0392**	0	0.000	3	0.0008	**1.000**
EPSTI1	-	2	0.004	1	0.0003	**0.0392**	1	0.002	9	0.0023	**1.000**
GJA10	-	2	0.004	1	0.0003	**0.0392**	1	0.002	2	0.0005	**0.317**
SLC25A23	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
FAM118B	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
MFAP5	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
DSCR3	-	2	0.004	1	0.0003	**0.0392**	1	0.002	1	0.0003	**0.224**
DIO3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
IARS2	-	2	0.004	1	0.0003	**0.0392**	0	0.000	2	0.0005	**1.000**
IMMP2L	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
TGIF2	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
ZDHHC2	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
FBXW11	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
TIMM21	-	2	0.004	1	0.0003	**0.0392**	1	0.002	4	0.0010	**0.470**
CHI3L2	-	2	0.004	1	0.0003	**0.0392**	2	0.004	2	0.0005	**0.072**
HKDC1	-	2	0.004	1	0.0003	**0.0392**	1	0.002	2	0.0005	**0.317**
TRMU	-	2	0.004	1	0.0003	**0.0392**	1	0.002	2	0.0005	**0.317**

HGNC gene name	Epi Gene	Familial NAFE Qualifying variants: Primary analysis					Familial NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
SP7	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
EPC1	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
ZMYND15	-	2	0.004	1	0.0003	**0.0392**	0	0.000	2	0.0005	**1.000**
NCSTN	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
GRPR	-	2	0.004	1	0.0003	**0.0392**	1	0.002	0	0.0000	**0.119**
PPAPDC3	-	2	0.004	1	0.0003	**0.0392**	1	0.002	0	0.0000	**0.119**
AMTN	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
OR8B12	-	2	0.004	1	0.0003	**0.0392**	1	0.002	0	0.0000	**0.119**
AVPR1A	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
C22orf42	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
ALG5	-	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
COX7A2L	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
LMNB1	-	2	0.004	1	0.0003	**0.0392**	0	0.000	2	0.0005	**1.000**
ADA	-	2	0.004	1	0.0003	**0.0392**	1	0.002	1	0.0003	**0.224**
JAKMIP1	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
GABRB3	*Yes*	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
GABRA1	*Yes*	2	0.004	1	0.0003	**0.0392**	0	0.000	1	0.0003	**1.000**
GABRA3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
GUCY1A2	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
NUP35	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
DNAJA1	-	2	0.004	1	0.0003	**0.0392**	1	0.002	0	0.0000	**0.119**
PHACTR3	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
PDCL	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
C1RL	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
C19orf26	-	2	0.004	1	0.0003	**0.0392**	0	0.000	0	0.0000	**1.000**
C1orf168	-	2	0.004	1	0.0003	**0.0392**	1	0.002	3	0.0008	**0.398**
FAM9B	-	2	0.004	1	0.0003	**0.0392**	2	0.004	1	0.0003	**0.039**
PARP1	-	3	0.006	4	0.0010	**0.0408**	2	0.004	1	0.0003	**0.039**
ZFP69B	-	3	0.006	4	0.0010	**0.0408**	1	0.002	3	0.0008	**0.398**
TET1	-	3	0.006	4	0.0010	**0.0408**	1	0.002	0	0.0000	**0.119**
GPI	-	3	0.006	4	0.0010	**0.0408**	0	0.000	0	0.0000	**1.000**
CD209	-	3	0.006	4	0.0010	**0.0408**	1	0.002	1	0.0003	**0.224**
USP45	-	3	0.006	4	0.0010	**0.0408**	3	0.006	6	0.0015	**0.082**
MIB1	-	3	0.006	4	0.0010	**0.0408**	2	0.004	12	0.0031	**0.680**
MAPK6	-	3	0.006	4	0.0010	**0.0408**	0	0.000	0	0.0000	**1.000**
HELQ	-	3	0.006	4	0.0010	**0.0408**	1	0.002	3	0.0008	**0.398**
DDX52	-	3	0.006	4	0.0010	**0.0408**	0	0.000	11	0.0028	**0.382**
ATP13A2	-	3	0.006	4	0.0010	**0.0408**	0	0.000	5	0.0013	**1.000**
ZNF559	-	3	0.006	4	0.0010	**0.0408**	3	0.006	6	0.0015	**0.082**
NFATC3	-	3	0.006	4	0.0010	**0.0408**	0	0.000	0	0.0000	**1.000**

HGNC gene name	Epi Gene	Familial NAFE Qualifying variants: Primary analysis					Familial NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
ZNF644	-	3	0.006	4	0.0010	**0.0408**	0	0.000	0	0.0000	**1.000**
GLYCTK	-	3	0.006	4	0.0010	**0.0408**	0	0.000	1	0.0003	**1.000**
CD99	-	3	0.006	4	0.0010	**0.0408**	0	0.000	0	0.0000	**1.000**
C1QTNF1	-	3	0.006	4	0.0010	**0.0408**	2	0.004	4	0.0010	**0.154**
PIBF1	-	3	0.006	4	0.0010	**0.0408**	2	0.004	3	0.0008	**0.111**
SLC16A4	-	3	0.006	4	0.0010	**0.0408**	0	0.000	1	0.0003	**1.000**
ENO3	-	3	0.006	4	0.0010	**0.0408**	2	0.004	8	0.0021	**0.339**
MYLK3	-	3	0.006	4	0.0010	**0.0408**	0	0.000	3	0.0008	**1.000**
COL22A1	-	3	0.006	4	0.0010	**0.0408**	2	0.004	7	0.0018	**0.293**
SCYL1	-	3	0.006	4	0.0010	**0.0408**	2	0.004	3	0.0008	**0.111**
PROM2	-	3	0.006	4	0.0010	**0.0408**	1	0.002	4	0.0010	**0.470**
RBP4	-	3	0.006	4	0.0010	**0.0408**	1	0.002	1	0.0003	**0.224**
FAM194A	-	3	0.006	4	0.0010	**0.0408**	0	0.000	15	0.0039	**0.242**
PIGQ	-	3	0.006	4	0.0010	**0.0408**	0	0.000	5	0.0013	**1.000**
RBL2	-	3	0.006	4	0.0010	**0.0408**	0	0.000	1	0.0003	**1.000**
CRIM1	-	3	0.006	4	0.0010	**0.0408**	0	0.000	0	0.0000	**1.000**
STAP1	-	3	0.006	4	0.0010	**0.0408**	2	0.004	1	0.0003	**0.039**
URB1	-	7	0.013	21	0.0054	**0.0417**	2	0.004	3	0.0008	**0.111**
KIAA1107	-	5	0.010	12	0.0031	**0.0433**	1	0.002	1	0.0003	**0.224**
ABCC10	-	5	0.010	12	0.0031	**0.0433**	1	0.002	3	0.0008	**0.398**
OGDHL	-	4	0.008	8	0.0021	**0.0453**	1	0.002	1	0.0003	**0.224**
NIM1	-	4	0.008	8	0.0021	**0.0453**	0	0.000	1	0.0003	**1.000**
PCDHA3	-	4	0.008	8	0.0021	**0.0453**	3	0.006	3	0.0008	**0.026**
SETBP1	-	4	0.008	8	0.0021	**0.0453**	1	0.002	2	0.0005	**0.317**
TSPEAR	-	4	0.008	8	0.0021	**0.0453**	2	0.004	14	0.0036	**1.000**
ZNF197	-	4	0.008	8	0.0021	**0.0453**	0	0.000	4	0.0010	**1.000**
BEAN1	-	4	0.008	8	0.0021	**0.0453**	0	0.000	1	0.0003	**1.000**
LMO7	-	6	0.011	17	0.0044	**0.0479**	1	0.002	11	0.0028	**1.000**
TAF1C	-	5	0.010	13	0.0034	**0.0542**	1	0.002	3	0.0008	**0.398**
FASN	-	5	0.010	13	0.0034	**0.0542**	0	0.000	1	0.0003	**1.000**
KIAA0100	-	6	0.011	18	0.0046	**0.0577**	1	0.002	3	0.0008	**0.398**

Table S12: Results for the analysis of 662 sporadic NAFE cases and 3877 control exomes.

The top 300 ranked genes from the Primary model collapsing analysis. The full exome-wide results can be accessed at http://epi4kdb.org/downloads/common-epilepsies/Table-S12.xlsx. A gender stratified Cochran-Mantel-Haenszel (CMH) test statistic is also available for the sex chromosomes (Table S13). Epi Gene: is among the 43 known dominant epilepsy genes; Qcase: number of cases carrying a qualifying variant; Qcase Freq: proportion of cases carrying a qualifying variant; Qctrl: number of controls carrying a qualifying variant; Qctrl Freq: proportion of controls carrying a qualifying variant; FET p-val: Fisher's exact two-tail p-value.

HGNC gene name	Epi Gene	**Sporadic NAFE Qualifying variants: Primary analysis**					**Sporadic NAFE Qualifying variants: LoF analysis**				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
PAXIP1	-	5	0.008	0	0.0000	**6.5E-5**	1	0.002	0	0.0000	**0.146**
LDB3	-	8	0.012	6	0.0015	**2.6E-4**	2	0.003	1	0.0003	**0.058**
GPAM	-	6	0.009	3	0.0008	**5.3E-4**	0	0.000	0	0.0000	**1.000**
CTNNBL1	-	4	0.006	1	0.0003	**0.0020**	0	0.000	0	0.0000	**1.000**
CEP89	-	5	0.008	3	0.0008	**0.0025**	1	0.002	4	0.0010	**0.546**
ARHGAP12	-	5	0.008	3	0.0008	**0.0025**	0	0.000	0	0.0000	**1.000**
LIPE	-	7	0.011	8	0.0021	**0.0030**	3	0.005	1	0.0003	**0.011**
VMO1	-	3	0.005	0	0.0000	**0.0031**	1	0.002	1	0.0003	**0.271**
EDA2R	-	3	0.005	0	0.0000	**0.0031**	0	0.000	0	0.0000	**1.000**
RTP3	-	3	0.005	0	0.0000	**0.0031**	2	0.003	0	0.0000	**0.021**
KLHDC8B	-	3	0.005	0	0.0000	**0.0031**	0	0.000	0	0.0000	**1.000**
FAM174A	-	3	0.005	0	0.0000	**0.0031**	1	0.002	2	0.0005	**0.377**
PMPCA	-	3	0.005	0	0.0000	**0.0031**	0	0.000	0	0.0000	**1.000**
F8	-	1	0.002	54	0.0139	**0.0032**	0	0.000	24	0.0062	**0.039**
PNPT1	-	5	0.008	4	0.0010	**0.0049**	0	0.000	2	0.0005	**1.000**
NFATC3	-	5	0.008	4	0.0010	**0.0049**	1	0.002	0	0.0000	**0.146**
FBXO25	-	4	0.006	2	0.0005	**0.0053**	2	0.003	1	0.0003	**0.058**
SLC10A1	-	4	0.006	2	0.0005	**0.0053**	0	0.000	5	0.0013	**1.000**
FSTL1	-	4	0.006	2	0.0005	**0.0053**	0	0.000	2	0.0005	**1.000**
ST14	-	4	0.006	2	0.0005	**0.0053**	0	0.000	0	0.0000	**1.000**
PFDN2	-	4	0.006	2	0.0005	**0.0053**	0	0.000	0	0.0000	**1.000**
KIAA0753	-	6	0.009	7	0.0018	**0.0065**	3	0.005	8	0.0021	**0.209**
PDE4DIP	-	8	0.012	13	0.0034	**0.0069**	3	0.005	3	0.0008	**0.044**
ABCA4	-	7	0.011	10	0.0026	**0.007**	2	0.003	3	0.0008	**0.157**
C5orf42	-	7	0.011	10	0.0026	**0.007**	3	0.005	2	0.0005	**0.025**
PCNXL2	-	8	0.012	14	0.0036	**0.0095**	3	0.005	5	0.0013	**0.098**
SMARCA2	-	6	0.009	8	0.0021	**0.0099**	0	0.000	1	0.0003	**1.000**
NCKAP5	-	7	0.011	11	0.0028	**0.01**	0	0.000	1	0.0003	**1.000**
OR1K1	-	4	0.006	3	0.0008	**0.0109**	3	0.005	4	0.0010	**0.069**
PCDHB3	-	4	0.006	3	0.0008	**0.0109**	4	0.006	2	0.0005	**0.005**
RCBTB2	-	4	0.006	3	0.0008	**0.0109**	1	0.002	2	0.0005	**0.377**

HGNC gene name	Epi Gene	Sporadic NAFE Qualifying variants: Primary analysis					Sporadic NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
TAOK3	-	4	0.006	3	0.0008	**0.0109**	0	0.000	0	0.0000	**1.000**
GPR87	-	4	0.006	3	0.0008	**0.0109**	1	0.002	2	0.0005	**0.377**
SRCAP	-	4	0.006	3	0.0008	**0.0109**	0	0.000	0	0.0000	**1.000**
PAPOLG	-	4	0.006	3	0.0008	**0.0109**	1	0.002	0	0.0000	**0.146**
HEPACAM2	-	4	0.006	3	0.0008	**0.0109**	3	0.005	3	0.0008	**0.044**
ATAD3B	-	4	0.006	3	0.0008	**0.0109**	2	0.003	3	0.0008	**0.157**
SCYL2	-	4	0.006	3	0.0008	**0.0109**	0	0.000	1	0.0003	**1.000**
DNAH14	-	4	0.006	3	0.0008	**0.0109**	0	0.000	1	0.0003	**1.000**
TATDN2	-	4	0.006	3	0.0008	**0.0109**	1	0.002	0	0.0000	**0.146**
ATP6V0D2	-	3	0.005	1	0.0003	**0.011**	0	0.000	6	0.0015	**0.602**
MINA	-	3	0.005	1	0.0003	**0.011**	1	0.002	2	0.0005	**0.377**
PMM2	-	3	0.005	1	0.0003	**0.011**	2	0.003	4	0.0010	**0.214**
HRH1	-	3	0.005	1	0.0003	**0.011**	0	0.000	0	0.0000	**1.000**
DET1	-	3	0.005	1	0.0003	**0.011**	0	0.000	0	0.0000	**1.000**
CCDC64B	-	3	0.005	1	0.0003	**0.011**	1	0.002	0	0.0000	**0.146**
FAM49A	-	3	0.005	1	0.0003	**0.011**	1	0.002	1	0.0003	**0.271**
PAK4	-	3	0.005	1	0.0003	**0.011**	1	0.002	0	0.0000	**0.146**
R3HDM2	-	3	0.005	1	0.0003	**0.011**	0	0.000	0	0.0000	**1.000**
HKDC1	-	3	0.005	1	0.0003	**0.011**	0	0.000	2	0.0005	**1.000**
CLK2	-	3	0.005	1	0.0003	**0.011**	0	0.000	0	0.0000	**1.000**
STK39	-	3	0.005	1	0.0003	**0.011**	0	0.000	0	0.0000	**1.000**
ZCCHC4	-	3	0.005	1	0.0003	**0.011**	1	0.002	7	0.0018	**1.000**
C1RL	-	3	0.005	1	0.0003	**0.011**	0	0.000	0	0.0000	**1.000**
OR52L1	-	3	0.005	1	0.0003	**0.011**	0	0.000	2	0.0005	**1.000**
OR52N5	-	3	0.005	1	0.0003	**0.011**	1	0.002	0	0.0000	**0.146**
C1orf94	-	3	0.005	1	0.0003	**0.011**	0	0.000	0	0.0000	**1.000**
CABS1	-	3	0.005	1	0.0003	**0.011**	0	0.000	0	0.0000	**1.000**
PPP6R2	-	5	0.008	6	0.0015	**0.014**	0	0.000	2	0.0005	**1.000**
CNGA3	-	5	0.008	6	0.0015	**0.014**	1	0.002	3	0.0008	**0.468**
RUFY1	-	6	0.009	9	0.0023	**0.0146**	3	0.005	4	0.0010	**0.069**
NPC1L1	-	6	0.009	9	0.0023	**0.0146**	2	0.003	8	0.0021	**0.647**
ST8SIA6	-	4	0.006	4	0.0010	**0.0193**	0	0.000	0	0.0000	**1.000**
TCHP	-	4	0.006	4	0.0010	**0.0193**	2	0.003	7	0.0018	**0.628**
MCM7	-	4	0.006	4	0.0010	**0.0193**	0	0.000	8	0.0021	**0.613**
SZT2	-	4	0.006	4	0.0010	**0.0193**	2	0.003	5	0.0013	**0.272**
DGKE	-	4	0.006	4	0.0010	**0.0193**	0	0.000	6	0.0015	**0.602**
L3MBTL1	-	4	0.006	4	0.0010	**0.0193**	2	0.003	1	0.0003	**0.058**
ADAM19	-	4	0.006	4	0.0010	**0.0193**	0	0.000	2	0.0005	**1.000**
SH2D3C	-	4	0.006	4	0.0010	**0.0193**	0	0.000	2	0.0005	**1.000**
PFKP	-	5	0.008	7	0.0018	**0.0212**	2	0.003	3	0.0008	**0.157**

HGNC gene name	Epi Gene	Sporadic NAFE Qualifying variants: Primary analysis					Sporadic NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
RALGPS2	-	2	0.003	0	0.0000	**0.0212**	2	0.003	2	0.0005	**0.104**
ST8SIA4	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
PPIB	-	2	0.003	0	0.0000	**0.0212**	1	0.002	1	0.0003	**0.271**
SDHAF2	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
ARHGEF5	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
PTPN6	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
SLC22A18	-	2	0.003	0	0.0000	**0.0212**	1	0.002	3	0.0008	**0.468**
ADH1B	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
SNRPA	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
IL21R	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
TAAR8	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
UAP1L1	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
TSTD1	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
WDR18	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
DCLRE1B	-	2	0.003	0	0.0000	**0.0212**	2	0.003	0	0.0000	**0.021**
FOXD4L1	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
ANXA13	-	2	0.003	0	0.0000	**0.0212**	0	0.000	5	0.0013	**1.000**
PSENEN	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
CD58	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
VWA1	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
THAP1	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
GNPDA2	-	2	0.003	0	0.0000	**0.0212**	1	0.002	1	0.0003	**0.271**
TTLL1	-	2	0.003	0	0.0000	**0.0212**	0	0.000	2	0.0005	**1.000**
TMEM173	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
ANGPT1	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
MPHOSPH6	-	2	0.003	0	0.0000	**0.0212**	2	0.003	0	0.0000	**0.021**
TRIT1	-	2	0.003	0	0.0000	**0.0212**	1	0.002	6	0.0015	**1.000**
SV2C	-	2	0.003	0	0.0000	**0.0212**	0	0.000	1	0.0003	**1.000**
ARHGEF25	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
EEF1A2	*Yes*	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
CES2	-	2	0.003	0	0.0000	**0.0212**	1	0.002	4	0.0010	**0.546**
TMEM184C	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
C2CD4C	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
C3orf36	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
KCNF1	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
SEC13	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
EMC7	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
ADORA1	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
AGGF1	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
CCDC89	-	2	0.003	0	0.0000	**0.0212**	0	0.000	3	0.0008	**1.000**

HGNC gene name	Epi Gene	Sporadic NAFE Qualifying variants: Primary analysis					Sporadic NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
C16orf46	-	2	0.003	0	0.0000	**0.0212**	0	0.000	1	0.0003	**1.000**
RGS19	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
GPR149	-	2	0.003	0	0.0000	**0.0212**	0	0.000	1	0.0003	**1.000**
TRMT10C	-	2	0.003	0	0.0000	**0.0212**	1	0.002	1	0.0003	**0.271**
GSK3B	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
RGMA	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
GGPS1	-	2	0.003	0	0.0000	**0.0212**	1	0.002	1	0.0003	**0.271**
GABRA5	-	2	0.003	0	0.0000	**0.0212**	1	0.002	0	0.0000	**0.146**
SRSF12	-	2	0.003	0	0.0000	**0.0212**	0	0.000	2	0.0005	**1.000**
C5orf38	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
PCDHGA2	-	2	0.003	0	0.0000	**0.0212**	0	0.000	3	0.0008	**1.000**
C5orf45	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
TRMT1L	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
C1orf64	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
C1orf112	-	2	0.003	0	0.0000	**0.0212**	0	0.000	1	0.0003	**1.000**
GAP43	-	2	0.003	0	0.0000	**0.0212**	0	0.000	0	0.0000	**1.000**
HERC1	-	1	0.002	40	0.0103	**0.0237**	0	0.000	1	0.0003	**1.000**
SLC3A1	-	3	0.005	2	0.0005	**0.0246**	2	0.003	4	0.0010	**0.214**
RBM12	-	3	0.005	2	0.0005	**0.0246**	1	0.002	1	0.0003	**0.271**
ZNF791	-	3	0.005	2	0.0005	**0.0246**	1	0.002	2	0.0005	**0.377**
STXBP4	-	3	0.005	2	0.0005	**0.0246**	1	0.002	2	0.0005	**0.377**
ZNF878	-	3	0.005	2	0.0005	**0.0246**	1	0.002	4	0.0010	**0.546**
KCNIP2	-	3	0.005	2	0.0005	**0.0246**	0	0.000	1	0.0003	**1.000**
ZNF679	-	3	0.005	2	0.0005	**0.0246**	2	0.003	4	0.0010	**0.214**
ATP11A	-	3	0.005	2	0.0005	**0.0246**	2	0.003	1	0.0003	**0.058**
FMO3	-	3	0.005	2	0.0005	**0.0246**	1	0.002	4	0.0010	**0.546**
PCYOX1	-	3	0.005	2	0.0005	**0.0246**	2	0.003	3	0.0008	**0.157**
FAM212B	-	3	0.005	2	0.0005	**0.0246**	1	0.002	1	0.0003	**0.271**
KDM4E	-	3	0.005	2	0.0005	**0.0246**	1	0.002	0	0.0000	**0.146**
PAQR7	-	3	0.005	2	0.0005	**0.0246**	1	0.002	1	0.0003	**0.271**
ZFP36L2	-	3	0.005	2	0.0005	**0.0246**	0	0.000	1	0.0003	**1.000**
EML4	-	3	0.005	2	0.0005	**0.0246**	1	0.002	1	0.0003	**0.271**
NEUROD6	-	3	0.005	2	0.0005	**0.0246**	0	0.000	0	0.0000	**1.000**
SPAG16	-	3	0.005	2	0.0005	**0.0246**	1	0.002	3	0.0008	**0.468**
CAPN11	-	3	0.005	2	0.0005	**0.0246**	1	0.002	1	0.0003	**0.271**
CRELD1	-	3	0.005	2	0.0005	**0.0246**	2	0.003	4	0.0010	**0.214**
DOK2	-	3	0.005	2	0.0005	**0.0246**	1	0.002	2	0.0005	**0.377**
C9orf84	-	3	0.005	2	0.0005	**0.0246**	2	0.003	0	0.0000	**0.021**
ITGB5	-	3	0.005	2	0.0005	**0.0246**	3	0.005	1	0.0003	**0.011**
CGRRF1	-	3	0.005	2	0.0005	**0.0246**	0	0.000	0	0.0000	**1.000**

HGNC gene name	Epi Gene	Sporadic NAFE Qualifying variants: Primary analysis					Sporadic NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
LGI1	*Yes*	3	0.005	2	0.0005	**0.0246**	2	0.003	0	0.0000	**0.021**
DNAI1	-	3	0.005	2	0.0005	**0.0246**	0	0.000	8	0.0021	**0.613**
AZGP1	-	3	0.005	2	0.0005	**0.0246**	1	0.002	0	0.0000	**0.146**
C7orf72	-	3	0.005	2	0.0005	**0.0246**	0	0.000	0	0.0000	**1.000**
FGFR1OP	-	3	0.005	2	0.0005	**0.0246**	3	0.005	0	0.0000	**0.003**
SPNS2	-	3	0.005	2	0.0005	**0.0246**	0	0.000	0	0.0000	**1.000**
ACOT6	-	3	0.005	2	0.0005	**0.0246**	0	0.000	0	0.0000	**1.000**
PPARGC1A	-	3	0.005	2	0.0005	**0.0246**	1	0.002	0	0.0000	**0.146**
RSBN1	-	3	0.005	2	0.0005	**0.0246**	0	0.000	0	0.0000	**1.000**
NRXN2	-	3	0.005	2	0.0005	**0.0246**	0	0.000	0	0.0000	**1.000**
PMS2	-	5	0.008	8	0.0021	**0.0304**	1	0.002	3	0.0008	**0.468**
ZNF74	-	5	0.008	8	0.0021	**0.0304**	1	0.002	4	0.0010	**0.546**
TBP	-	5	0.008	8	0.0021	**0.0304**	0	0.000	0	0.0000	**1.000**
SYNPO2L	-	5	0.008	8	0.0021	**0.0304**	3	0.005	3	0.0008	**0.044**
TRAPPC10	-	4	0.006	5	0.0013	**0.0307**	0	0.000	1	0.0003	**1.000**
TDRD1	-	4	0.006	5	0.0013	**0.0307**	1	0.002	2	0.0005	**0.377**
SLC2A3	-	4	0.006	5	0.0013	**0.0307**	1	0.002	1	0.0003	**0.271**
KIAA1199	-	4	0.006	5	0.0013	**0.0307**	1	0.002	0	0.0000	**0.146**
LTA4H	-	4	0.006	5	0.0013	**0.0307**	1	0.002	1	0.0003	**0.271**
DHX35	-	4	0.006	5	0.0013	**0.0307**	2	0.003	5	0.0013	**0.272**
C6orf132	-	4	0.006	5	0.0013	**0.0307**	0	0.000	0	0.0000	**1.000**
GNPTG	-	4	0.006	5	0.0013	**0.0307**	3	0.005	0	0.0000	**0.003**
C1orf228	-	4	0.006	5	0.0013	**0.0307**	0	0.000	2	0.0005	**1.000**
ASXL1	-	4	0.006	5	0.0013	**0.0307**	1	0.002	3	0.0008	**0.468**
TRMT44	-	4	0.006	5	0.0013	**0.0307**	2	0.003	10	0.0026	**0.691**
FANCI	-	4	0.006	5	0.0013	**0.0307**	0	0.000	5	0.0013	**1.000**
LRP1B	-	9	0.014	22	0.0057	**0.0359**	0	0.000	1	0.0003	**1.000**
ROBO1	-	6	0.009	12	0.0031	**0.0368**	2	0.003	1	0.0003	**0.058**
PTPN13	-	0	0.000	24	0.0062	**0.0392**	0	0.000	6	0.0015	**0.602**
TRPC4	-	5	0.008	9	0.0023	**0.0418**	0	0.000	0	0.0000	**1.000**
CENPF	-	5	0.008	9	0.0023	**0.0418**	2	0.003	13	0.0034	**1.000**
RNPC3	-	5	0.008	9	0.0023	**0.0418**	1	0.002	1	0.0003	**0.271**
ATP12A	-	5	0.008	9	0.0023	**0.0418**	0	0.000	0	0.0000	**1.000**
IGSF9	-	5	0.008	9	0.0023	**0.0418**	3	0.005	2	0.0005	**0.025**
ACAD10	-	3	0.005	3	0.0008	**0.0439**	2	0.003	5	0.0013	**0.272**
GRN	-	3	0.005	3	0.0008	**0.0439**	0	0.000	1	0.0003	**1.000**
RNF222	-	3	0.005	3	0.0008	**0.0439**	0	0.000	1	0.0003	**1.000**
GGT6	-	3	0.005	3	0.0008	**0.0439**	0	0.000	1	0.0003	**1.000**
USP47	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
SPATS2	-	3	0.005	3	0.0008	**0.0439**	0	0.000	1	0.0003	**1.000**

HGNC gene name	Epi Gene	Sporadic NAFE Qualifying variants: Primary analysis					Sporadic NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
PUS10	-	3	0.005	3	0.0008	**0.0439**	0	0.000	2	0.0005	**1.000**
FBXO24	-	3	0.005	3	0.0008	**0.0439**	0	0.000	1	0.0003	**1.000**
CTNNA2	-	3	0.005	3	0.0008	**0.0439**	0	0.000	0	0.0000	**1.000**
ZNF879	-	3	0.005	3	0.0008	**0.0439**	2	0.003	0	0.0000	**0.021**
TSHZ2	-	3	0.005	3	0.0008	**0.0439**	0	0.000	0	0.0000	**1.000**
FGL2	-	3	0.005	3	0.0008	**0.0439**	0	0.000	0	0.0000	**1.000**
FGL1	-	3	0.005	3	0.0008	**0.0439**	1	0.002	3	0.0008	**0.468**
RASAL3	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
RNF103	-	3	0.005	3	0.0008	**0.0439**	1	0.002	0	0.0000	**0.146**
KATNAL2	-	3	0.005	3	0.0008	**0.0439**	1	0.002	4	0.0010	**0.546**
KPRP	-	3	0.005	3	0.0008	**0.0439**	1	0.002	3	0.0008	**0.468**
ADARB1	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
FAM222A	-	3	0.005	3	0.0008	**0.0439**	0	0.000	0	0.0000	**1.000**
YIPF1	-	3	0.005	3	0.0008	**0.0439**	0	0.000	2	0.0005	**1.000**
CRTAM	-	3	0.005	3	0.0008	**0.0439**	1	0.002	2	0.0005	**0.377**
FBLIM1	-	3	0.005	3	0.0008	**0.0439**	0	0.000	0	0.0000	**1.000**
AFF1	-	3	0.005	3	0.0008	**0.0439**	0	0.000	0	0.0000	**1.000**
RTN4IP1	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
ESF1	-	3	0.005	3	0.0008	**0.0439**	0	0.000	3	0.0008	**1.000**
ABI3	-	3	0.005	3	0.0008	**0.0439**	0	0.000	1	0.0003	**1.000**
CLK1	-	3	0.005	3	0.0008	**0.0439**	1	0.002	2	0.0005	**0.377**
HAS1	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
FAM196A	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
SCTR	-	3	0.005	3	0.0008	**0.0439**	0	0.000	1	0.0003	**1.000**
TLR9	-	3	0.005	3	0.0008	**0.0439**	2	0.003	1	0.0003	**0.058**
CCDC169-SOHLH2	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
SHC3	-	3	0.005	3	0.0008	**0.0439**	2	0.003	0	0.0000	**0.021**
KLF10	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
TCHHL1	-	3	0.005	3	0.0008	**0.0439**	2	0.003	1	0.0003	**0.058**
TCF19	-	3	0.005	3	0.0008	**0.0439**	2	0.003	3	0.0008	**0.157**
PRKAA1	-	3	0.005	3	0.0008	**0.0439**	1	0.002	1	0.0003	**0.271**
PBXIP1	-	3	0.005	3	0.0008	**0.0439**	0	0.000	3	0.0008	**1.000**
XRN2	-	3	0.005	3	0.0008	**0.0439**	0	0.000	0	0.0000	**1.000**
DCAF17	-	3	0.005	3	0.0008	**0.0439**	0	0.000	0	0.0000	**1.000**
CPNE5	-	3	0.005	3	0.0008	**0.0439**	0	0.000	1	0.0003	**1.000**
HGS	-	4	0.006	6	0.0015	**0.0455**	0	0.000	3	0.0008	**1.000**
ZRANB3	-	4	0.006	6	0.0015	**0.0455**	3	0.005	2	0.0005	**0.025**
BCAS1	-	4	0.006	6	0.0015	**0.0455**	0	0.000	1	0.0003	**1.000**
ATHL1	-	4	0.006	6	0.0015	**0.0455**	0	0.000	8	0.0021	**0.613**

HGNC gene name	Epi Gene	Sporadic NAFE Qualifying variants: Primary analysis					Sporadic NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
GTSE1	-	4	0.006	6	0.0015	**0.0455**	0	0.000	2	0.0005	**1.000**
ALDH7A1	-	4	0.006	6	0.0015	**0.0455**	1	0.002	2	0.0005	**0.377**
ITGA8	-	4	0.006	6	0.0015	**0.0455**	0	0.000	1	0.0003	**1.000**
TSC22D1	-	4	0.006	6	0.0015	**0.0455**	1	0.002	0	0.0000	**0.146**
GPR156	-	4	0.006	6	0.0015	**0.0455**	1	0.002	4	0.0010	**0.546**
FRMD4B	-	4	0.006	6	0.0015	**0.0455**	0	0.000	1	0.0003	**1.000**
NCOR2	-	4	0.006	6	0.0015	**0.0455**	0	0.000	0	0.0000	**1.000**
PADI1	-	4	0.006	6	0.0015	**0.0455**	4	0.006	9	0.0023	**0.109**
SEMA4B	-	5	0.008	10	0.0026	**0.0554**	0	0.000	1	0.0003	**1.000**
SPATA17	-	2	0.003	1	0.0003	**0.0576**	0	0.000	2	0.0005	**1.000**
ACADM	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
C5AR1	-	2	0.003	1	0.0003	**0.0576**	0	0.000	1	0.0003	**1.000**
STEAP2	-	2	0.003	1	0.0003	**0.0576**	1	0.002	13	0.0034	**0.708**
CAMK2B	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
PSKH2	-	2	0.003	1	0.0003	**0.0576**	0	0.000	3	0.0008	**1.000**
ARNT2	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
SLC30A8	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
ARL5B	-	2	0.003	1	0.0003	**0.0576**	0	0.000	1	0.0003	**1.000**
MAPKAPK3	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
PTRHD1	-	2	0.003	1	0.0003	**0.0576**	2	0.003	0	0.0000	**0.021**
SRCRB4D	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
SLC6A18	-	2	0.003	1	0.0003	**0.0576**	0	0.000	4	0.0010	**1.000**
RNF220	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
OR1D2	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
OR13H1	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
PSMB3	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
CYB5D1	-	2	0.003	1	0.0003	**0.0576**	2	0.003	4	0.0010	**0.214**
EGFL6	-	2	0.003	1	0.0003	**0.0576**	2	0.003	0	0.0000	**0.021**
NECAB1	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
CA9	-	2	0.003	1	0.0003	**0.0576**	0	0.000	8	0.0021	**0.613**
CAMKV	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
C11orf57	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
MGME1	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
A1BG	-	2	0.003	1	0.0003	**0.0576**	2	0.003	3	0.0008	**0.157**
HOXC8	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
HOXB7	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
SOHLH2	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
ART5	-	2	0.003	1	0.0003	**0.0576**	1	0.002	4	0.0010	**0.546**
CHST4	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
SERTAD3	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**

HGNC gene name	Epi Gene	Sporadic NAFE Qualifying variants: Primary analysis					Sporadic NAFE Qualifying variants: LoF analysis				
		Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**	Qcase	Qcase Freq	Qctrl	Qctrl Freq	**FET *p*-val**
UHMK1	-	2	0.003	1	0.0003	**0.0576**	0	0.000	1	0.0003	**1.000**
PRTFDC1	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
TMEM38B	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
C4orf29	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
TMEM201	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
PRDX6	-	2	0.003	1	0.0003	**0.0576**	2	0.003	4	0.0010	**0.214**
COL4A3BP	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
MOSPD2	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
MAPK15	-	2	0.003	1	0.0003	**0.0576**	2	0.003	8	0.0021	**0.647**
ZNF563	-	2	0.003	1	0.0003	**0.0576**	1	0.002	5	0.0013	**1.000**
FURIN	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
ZNF19	-	2	0.003	1	0.0003	**0.0576**	0	0.000	1	0.0003	**1.000**
OR9Q2	-	2	0.003	1	0.0003	**0.0576**	0	0.000	1	0.0003	**1.000**
IPCEF1	-	2	0.003	1	0.0003	**0.0576**	0	0.000	1	0.0003	**1.000**
C10orf128	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
RIPK1	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
RNF145	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
EHD4	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
SAMD13	-	2	0.003	1	0.0003	**0.0576**	1	0.002	2	0.0005	**0.377**
TMED8	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
CCR3	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
CD63	-	2	0.003	1	0.0003	**0.0576**	1	0.002	0	0.0000	**0.146**
ZNF496	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**
ZNF461	-	2	0.003	1	0.0003	**0.0576**	0	0.000	7	0.0018	**0.603**
CDNF	-	2	0.003	1	0.0003	**0.0576**	2	0.003	1	0.0003	**0.058**
ZNF420	-	2	0.003	1	0.0003	**0.0576**	2	0.003	1	0.0003	**0.058**
CDH5	-	2	0.003	1	0.0003	**0.0576**	1	0.002	8	0.0021	**1.000**
DAPK2	-	2	0.003	1	0.0003	**0.0576**	1	0.002	5	0.0013	**1.000**
CPPED1	-	2	0.003	1	0.0003	**0.0576**	1	0.002	1	0.0003	**0.271**
CDH20	-	2	0.003	1	0.0003	**0.0576**	0	0.000	0	0.0000	**1.000**

Table S13: Summary of the sex chromosome gender stratified gene tests.

A gender stratified Cochran-Mantel-Haenszel (CMH) test statistic was performed to supplement the sex chromosome gene tests. We report the top 100 ranked sex chromosome genes across the various epilepsy groups and the corresponding collapsing analysis model. The full sex chromosome results can be accessed at http://epi4kdb.org/downloads/common-epilepsies/Table-S13.xlsx. Qcase: number of cases carrying a qualifying variant; UQcase: number of cases not carrying a qualifying variant; Qcase Freq: proportion of cases carrying a qualifying variant; Qctrl: number of controls carrying a qualifying variant; UQctrl: number of control not carrying a qualifying variant; Qctrl Freq: proportion of controls carrying a qualifying variant; Fem: Female; CMH: Cochran-Mantel-Haenszel test; Source FET p-val: corresponding Fisher's exact two-tail p-value among Tables S10 – S12; fam: familial; spor = sporadic; Com: common; MAF: minor allele frequency.

Collapsing Analysis Model	HGNC gene name	Male Qcase	Male UQcase	Male Qcase Freq	Male Qctrl	Male UQctrl	Male Qctrl Freq	Fem Qcase	Fem UQcase	Fem Qcase Freq	Fem Qctrl	Fem UQctrl	Fem Qctrl Freq	CMH Exact p-val	Source FET p-val
fam NAFE - Primary Model	*PCDH19*	1	238	0.004	2	2119	0.0009	5	281	0.017	0	1756	0.0000	8.2E-5	6.4E-5
fam NAFE - Primary Model	*MAGEA6*	1	238	0.004	0	2121	0.0000	2	284	0.007	0	1756	0.0000	0.002	0.002
fam GGE - Com (0.1% MAF)	*DGAT2L6*	3	231	0.013	2	2119	0.0009	4	402	0.010	5	1751	0.0028	0.003	0.002
fam NAFE - LoF Model	*PCDH19*	0	239	0.000	0	2121	0.0000	3	283	0.010	0	1756	0.0000	0.003	0.002
spor NAFE - Primary Model	*EDA2R*	0	315	0.000	0	2121	0.0000	3	344	0.009	0	1756	0.0000	0.004	0.003
spor NAFE - Com (0.1% MAF)	*ACTRT1*	2	313	0.006	1	2120	0.0005	3	344	0.009	3	1753	0.0017	0.006	0.005
fam GGE - LoF Model	*KCNE1L*	0	234	0.000	0	2121	0.0000	3	403	0.007	0	1756	0.0000	0.007	0.003
fam NAFE - Primary Model	*SATL1*	0	239	0.000	0	2121	0.0000	5	281	0.017	5	1751	0.0028	0.007	0.004
spor NAFE - Primary Model	*F8*	1	314	0.003	49	2072	0.0231	0	347	0.000	5	1751	0.0028	0.008	0.003
fam GGE - LoF Model	*ASMTL*	2	232	0.009	5	2116	0.0024	3	403	0.007	1	1755	0.0006	0.008	0.012
fam GGE - Com (0.1% MAF)	*DRP2*	2	232	0.009	7	2114	0.0033	5	401	0.012	4	1752	0.0023	0.009	0.009
fam GGE - Com (0.1% MAF)	*F8*	0	234	0.000	58	2063	0.0273	2	404	0.005	14	1742	0.0080	0.009	0.002
fam NAFE - Com (0.1% MAF)	*PCDH19*	1	238	0.004	5	2116	0.0024	5	281	0.017	5	1751	0.0028	0.010	0.008
spor NAFE - Com (0.1% MAF)	*F8*	1	314	0.003	59	2062	0.0278	2	345	0.006	14	1742	0.0080	0.010	0.005
spor NAFE - Com (0.1% MAF)	*NHS*	0	315	0.000	14	2107	0.0066	0	347	0.000	18	1738	0.0103	0.010	0.017
fam NAFE - Com (0.1% MAF)	*ZCCHC5*	1	238	0.004	2	2119	0.0009	3	283	0.010	2	1754	0.0011	0.011	0.009
fam NAFE - Primary Model	*MAOA*	1	238	0.004	0	2121	0.0000	1	285	0.003	0	1756	0.0000	0.014	0.014

Collapsing Analysis Model	HGNC gene name	Male Qcase	Male UQcase	Male Qcase Freq	Male Qctrl	Male UQctrl	Male Qctrl Freq	Fem Qcase	Fem UQcase	Fem Qcase Freq	Fem Qctrl	Fem UQctrl	Fem Qctrl Freq	CMH Exact p-val	Source FET p-val
spor NAFE - LoF Model	*DCX*	2	313	0.006	0	2121	0.0000	0	347	0.000	0	1756	0.0000	0.017	0.021
fam GGE - Com (0.1% MAF)	*TAF1*	3	231	0.013	3	2118	0.0014	3	403	0.007	6	1750	0.0034	0.017	0.013
fam GGE - Com (0.1% MAF)	*PLXNB3*	1	233	0.004	6	2115	0.0028	6	400	0.015	6	1750	0.0034	0.018	0.012
fam GGE - Com (0.1% MAF)	*EFNB1*	1	233	0.004	0	2121	0.0000	1	405	0.002	0	1756	0.0000	0.019	0.020
fam GGE - Com (0.1% MAF)	*HMGB3*	1	233	0.004	0	2121	0.0000	1	405	0.002	0	1756	0.0000	0.019	0.020
fam GGE - Com (0.1% MAF)	*NR0B1*	1	233	0.004	0	2121	0.0000	1	405	0.002	0	1756	0.0000	0.019	0.020
fam GGE - Primary Model	*ACSL4*	1	233	0.004	0	2121	0.0000	1	405	0.002	0	1756	0.0000	0.019	0.020
fam GGE - LoF Model	*CNGA2*	1	233	0.004	0	2121	0.0000	1	405	0.002	0	1756	0.0000	0.019	0.020
fam GGE - Primary Model	*EFNB1*	1	233	0.004	0	2121	0.0000	1	405	0.002	0	1756	0.0000	0.019	0.020
fam NAFE - Com (0.1% MAF)	*DMD*	0	239	0.000	31	2090	0.0146	3	283	0.010	43	1713	0.0245	0.021	0.031
spor NAFE - LoF Model	*EGFL6*	1	314	0.003	0	2121	0.0000	1	346	0.003	0	1756	0.0000	0.021	0.021
spor NAFE - Com (0.1% MAF)	*EDA2R*	0	315	0.000	3	2118	0.0014	4	343	0.012	1	1755	0.0006	0.022	0.019
fam GGE - Com (0.1% MAF)	*KCNE1L*	0	234	0.000	0	2121	0.0000	3	403	0.007	1	1755	0.0006	0.023	0.010
spor NAFE - Com (0.1% MAF)	*PSMD10*	0	315	0.000	2	2119	0.0009	4	343	0.012	2	1754	0.0011	0.024	0.019
fam GGE - Com (0.1% MAF)	*TKTL1*	1	233	0.004	4	2117	0.0019	3	403	0.007	1	1755	0.0006	0.025	0.028
fam GGE - Com (0.1% MAF)	*ATG4A*	3	231	0.013	3	2118	0.0014	3	403	0.007	7	1749	0.0040	0.026	0.018
fam NAFE - Primary Model	*F8*	0	239	0.000	49	2072	0.0231	1	285	0.003	5	1751	0.0028	0.026	0.012
spor NAFE - Com (0.1% MAF)	*GLOD5*	2	313	0.006	0	2121	0.0000	1	346	0.003	2	1754	0.0011	0.027	0.025
fam GGE - Com (0.1% MAF)	*PLXNA3*	6	228	0.026	19	2102	0.0090	8	398	0.020	20	1736	0.0114	0.027	0.016
fam NAFE - Com (0.1% MAF)	*IL2RG*	2	237	0.008	1	2120	0.0005	0	286	0.000	0	1756	0.0000	0.029	0.039
fam NAFE - Com (0.1% MAF)	*SASH3*	2	237	0.008	1	2120	0.0005	2	284	0.007	5	1751	0.0028	0.030	0.023
fam NAFE - Com (0.1% MAF)	*MAGEA6*	1	238	0.004	1	2120	0.0005	2	284	0.007	2	1754	0.0011	0.030	0.026
spor NAFE - Com (0.1% MAF)	*BEX5*	0	315	0.000	1	2120	0.0005	3	344	0.009	1	1755	0.0006	0.030	0.025
spor NAFE - Com (0.1% MAF)	*USP9Y*	3	312	0.010	3	2118	0.0014	0	347	0.000	0	1756	0.0000	0.032	0.044
fam GGE - Com (0.1% MAF)	*ASB12*	2	232	0.009	5	2116	0.0024	4	402	0.010	6	1750	0.0034	0.032	0.024

Collapsing Analysis Model	HGNC gene name	Male Qcase	Male UQcase	Male Qcase Freq	Male Qctrl	Male UQctrl	Male Qctrl Freq	Fem Qcase	Fem UQcase	Fem Qcase Freq	Fem Qctrl	Fem UQctrl	Fem Qctrl Freq	CMH Exact p-val	Source FET p-val
fam NAFE - Com (0.1% MAF)	*DRP2*	2	237	0.008	7	2114	0.0033	3	283	0.010	4	1752	0.0023	0.032	0.034
fam GGE - Com (0.1% MAF)	*ARMCX6*	1	233	0.004	5	2116	0.0024	3	403	0.007	1	1755	0.0006	0.034	0.041
fam GGE - Com (0.1% MAF)	*ARL13A*	0	234	0.000	0	2121	0.0000	2	404	0.005	0	1756	0.0000	0.035	0.020
fam GGE - Com (0.1% MAF)	*DUSP21*	0	234	0.000	0	2121	0.0000	2	404	0.005	0	1756	0.0000	0.035	0.020
fam GGE - Com (0.1% MAF)	*IQSEC2*	0	234	0.000	0	2121	0.0000	2	404	0.005	0	1756	0.0000	0.035	0.020
fam GGE - LoF Model	*DUSP21*	0	234	0.000	0	2121	0.0000	2	404	0.005	0	1756	0.0000	0.035	0.020
fam GGE - Primary Model	*GPKOW*	0	234	0.000	0	2121	0.0000	2	404	0.005	0	1756	0.0000	0.035	0.020
fam GGE - Primary Model	*IQSEC2*	0	234	0.000	0	2121	0.0000	2	404	0.005	0	1756	0.0000	0.035	0.020
fam NAFE - LoF Model	*CENPI*	1	238	0.004	1	2120	0.0005	1	285	0.003	0	1756	0.0000	0.036	0.039
fam NAFE - Primary Model	*FAM9B*	1	238	0.004	1	2120	0.0005	1	285	0.003	0	1756	0.0000	0.036	0.039
fam NAFE - LoF Model	*FAM9B*	1	238	0.004	1	2120	0.0005	1	285	0.003	0	1756	0.0000	0.036	0.039
fam NAFE - Primary Model	*GPC4*	1	238	0.004	1	2120	0.0005	1	285	0.003	0	1756	0.0000	0.036	0.039
fam NAFE - Com (0.1% MAF)	*MAOA*	1	238	0.004	1	2120	0.0005	1	285	0.003	0	1756	0.0000	0.036	0.039
fam NAFE - Primary Model	*SRPK3*	1	238	0.004	1	2120	0.0005	1	285	0.003	0	1756	0.0000	0.036	0.039
fam GGE - Primary Model	*SRPX*	1	233	0.004	0	2121	0.0000	2	404	0.005	2	1754	0.0011	0.037	0.023
fam NAFE - Primary Model	*CD99*	2	237	0.008	2	2119	0.0009	1	285	0.003	2	1754	0.0011	0.039	0.041
fam NAFE - Com (0.1% MAF)	*CD99*	2	237	0.008	2	2119	0.0009	1	285	0.003	2	1754	0.0011	0.039	0.041
fam NAFE - Com (0.1% MAF)	*ASB11*	0	239	0.000	3	2118	0.0014	4	282	0.014	4	1752	0.0023	0.043	0.033
fam NAFE - Com (0.1% MAF)	*MAOB*	1	238	0.004	2	2119	0.0009	3	283	0.010	5	1751	0.0028	0.043	0.033
fam GGE - Primary Model	*ATG4A*	1	233	0.004	1	2120	0.0005	1	405	0.002	0	1756	0.0000	0.043	0.055
fam GGE - Primary Model	*ZNF185*	1	233	0.004	1	2120	0.0005	1	405	0.002	0	1756	0.0000	0.043	0.055
fam NAFE - Com (0.1% MAF)	*CITED1*	0	239	0.000	1	2120	0.0005	2	284	0.007	0	1756	0.0000	0.044	0.039
fam NAFE - Primary Model	*DGAT2L6*	0	239	0.000	1	2120	0.0005	2	284	0.007	0	1756	0.0000	0.044	0.039
fam NAFE - Primary Model	*GRPR*	1	238	0.004	0	2121	0.0000	1	285	0.003	1	1755	0.0006	0.044	0.039
fam NAFE - Primary Model	*OR13H1*	1	238	0.004	0	2121	0.0000	1	285	0.003	1	1755	0.0006	0.044	0.039

Collapsing Analysis Model	HGNC gene name	Male Qcase	Male UQcase	Male Qcase Freq	Male Qctrl	Male UQctrl	Male Qctrl Freq	Fem Qcase	Fem UQcase	Fem Qcase Freq	Fem Qctrl	Fem UQctrl	Fem Qctrl Freq	CMH Exact p-val	Source FET p-val
fam NAFE - Com (0.1% MAF)	*DACH2*	4	235	0.017	2	2119	0.0009	0	286	0.000	6	1750	0.0034	0.047	0.045
spor NAFE - Com (0.1% MAF)	*BMX*	1	314	0.003	1	2120	0.0005	2	345	0.006	2	1754	0.0011	0.050	0.044
fam GGE - LoF Model	*IL3RA*	4	230	0.017	8	2113	0.0038	1	405	0.002	4	1752	0.0023	0.051	0.081
fam GGE - Com (0.1% MAF)	*MCF2*	1	233	0.004	1	2120	0.0005	2	404	0.005	2	1754	0.0011	0.053	0.041
fam GGE - Com (0.1% MAF)	*PPEF1*	0	234	0.000	2	2119	0.0009	3	403	0.007	1	1755	0.0006	0.053	0.041
fam NAFE - Primary Model	*GABRA3*	0	239	0.000	0	2121	0.0000	2	284	0.007	1	1755	0.0006	0.053	0.039
fam NAFE - Com (0.1% MAF)	*GABRA3*	0	239	0.000	0	2121	0.0000	2	284	0.007	1	1755	0.0006	0.053	0.039
fam NAFE - Com (0.1% MAF)	*MAGEC1*	1	238	0.004	5	2116	0.0024	4	282	0.014	7	1749	0.0040	0.053	0.043
spor NAFE - LoF Model	*CHDC2*	1	314	0.003	1	2120	0.0005	1	346	0.003	0	1756	0.0000	0.054	0.058
spor NAFE - Com (0.1% MAF)	*LRCH2*	0	315	0.000	3	2118	0.0014	4	343	0.012	3	1753	0.0017	0.054	0.046
spor NAFE - Com (0.1% MAF)	*ARMCX1*	1	314	0.003	0	2121	0.0000	2	345	0.006	3	1753	0.0017	0.055	0.044
fam NAFE - Com (0.1% MAF)	*FAM9C*	0	239	0.000	1	2120	0.0005	3	283	0.010	3	1753	0.0017	0.056	0.041
fam GGE - Com (0.1% MAF)	*SYTL4*	1	233	0.004	0	2121	0.0000	3	403	0.007	5	1751	0.0028	0.058	0.028
fam NAFE - Com (0.1% MAF)	*F8*	0	239	0.000	58	2063	0.0273	3	283	0.010	14	1742	0.0080	0.059	0.030
spor NAFE - Com (0.1% MAF)	*SRPX*	0	315	0.000	5	2116	0.0024	0	347	0.000	15	1741	0.0085	0.059	0.102
fam NAFE - Com (0.1% MAF)	*PIR*	0	239	0.000	0	2121	0.0000	3	283	0.010	4	1752	0.0023	0.062	0.041
spor NAFE - Primary Model	*EGFL6*	1	314	0.003	0	2121	0.0000	1	346	0.003	1	1755	0.0006	0.063	0.058
spor NAFE - Primary Model	*MOSPD2*	0	315	0.000	1	2120	0.0005	2	345	0.006	0	1756	0.0000	0.063	0.058
spor NAFE - Primary Model	*TNMD*	1	314	0.003	0	2121	0.0000	1	346	0.003	1	1755	0.0006	0.063	0.058
fam NAFE - Primary Model	*FAM47A*	1	238	0.004	2	2119	0.0009	1	285	0.003	0	1756	0.0000	0.063	0.072
fam NAFE - Com (0.1% MAF)	*FAM9B*	1	238	0.004	2	2119	0.0009	1	285	0.003	0	1756	0.0000	0.063	0.072
spor NAFE - LoF Model	*F8*	0	315	0.000	24	2097	0.0113	0	347	0.000	0	1756	0.0000	0.063	0.039
fam GGE - Com (0.1% MAF)	*ENOX2*	2	232	0.009	3	2118	0.0014	2	404	0.005	4	1752	0.0023	0.064	0.058
fam GGE - Primary Model	*ACRC*	1	233	0.004	0	2121	0.0000	1	405	0.002	1	1755	0.0006	0.066	0.055
fam GGE - Primary Model	*SSX3*	0	234	0.000	1	2120	0.0005	2	404	0.005	0	1756	0.0000	0.066	0.055

Collapsing Analysis Model	HGNC gene name	Male Qcase	Male UQcase	Male Qcase Freq	Male Qctrl	Male UQctrl	Male Qctrl Freq	Fem Qcase	Fem UQcase	Fem Qcase Freq	Fem Qctrl	Fem UQctrl	Fem Qctrl Freq	CMH Exact p-val	Source FET p-val
fam GGE - Primary Model	*STS*	1	233	0.004	0	2121	0.0000	1	405	0.002	1	1755	0.0006	0.066	0.055
fam GGE - Com (0.1% MAF)	*LAGE3*	0	234	0.000	1	2120	0.0005	2	404	0.005	0	1756	0.0000	0.066	0.055
fam GGE - Com (0.1% MAF)	*SLC25A14*	0	234	0.000	1	2120	0.0005	2	404	0.005	0	1756	0.0000	0.066	0.055
spor NAFE - Com (0.1% MAF)	*CCNB3*	1	314	0.003	4	2117	0.0019	4	343	0.012	6	1750	0.0034	0.066	0.055
fam NAFE - Primary Model	*DACH2*	3	236	0.013	0	2121	0.0000	0	286	0.000	5	1751	0.0028	0.068	0.060
fam NAFE - Primary Model	*CSF2RA*	0	239	0.000	15	2106	0.0071	0	286	0.000	13	1743	0.0074	0.070	0.070
spor NAFE - Com (0.1% MAF)	*ZNF182*	2	313	0.006	2	2119	0.0009	2	345	0.006	5	1751	0.0028	0.072	0.063
spor NAFE - LoF Model	*DMD*	0	315	0.000	0	2121	0.0000	2	345	0.006	1	1755	0.0006	0.073	0.058

Table S14: Gene lists used for gene-list enrichment analyses.

The full gene lists used in this study can be accessed at http://epi4kdb.org/downloads/common-epilepsies/Table-S14.xlsx.

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