Supplementary Figures and Tables

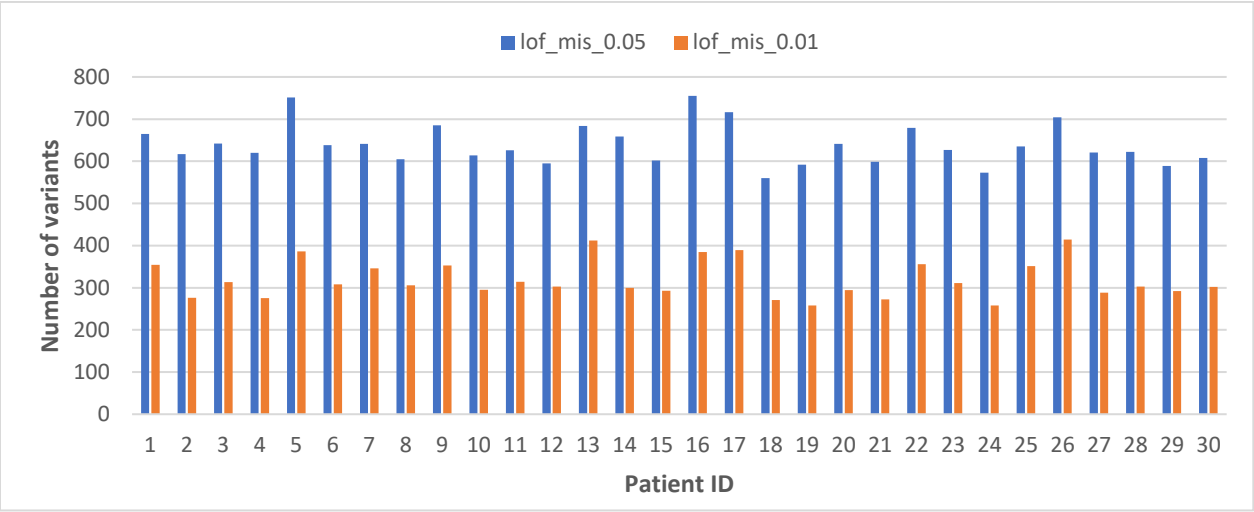
Supplementary Figure 1: Aggregate variant counts for the epilepsy cohort. A plot of aggregate variant counts, where **A** displays single nucleotide variants and indels (at 1% and 5% frequency), and **B** displays rare exonic copy number variants (also at 1% and 5% frequency). LoF, loss-of-function; mis, missense.

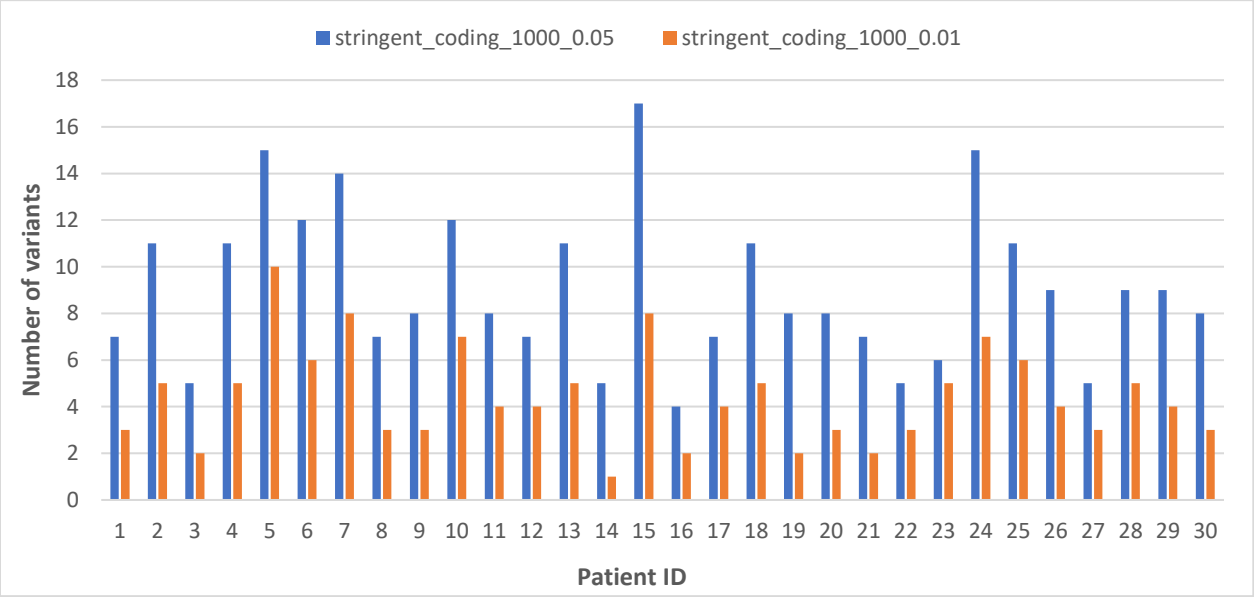
Supplementary Figure 2: A scatterplot depicting a principal component analysis of the epilepsy cohort. This scatterplot depicts the top two principal components (PCs) from a principal component analysis, where 1000 Genome Project samples were used as reference population groups to generate ancestry clusters for each patient with epilepsy. *Abbreviations*: European (EUR), American (AMR), African (AFR), East Asian (EAS) and South Asian (SAS).

Supplementary Figure 3: Detection and validation of *DIP2B* CGG tandem repeat expansion. This schematic shows the design, and the original uncropped blot from a Southern blotting experiment for the targeted TR in *DIP2B* in the following individuals: patient 4, their mother (4A) and father (4B). This blot also includes unrelated samples: Family A (37543, father; 37544, mother; 37542; child), Family B (52194, father; 52196, mother; 52195, proband) and Family C (52444, child). Numbers in brackets refer to the number of CGG repeat units detected.

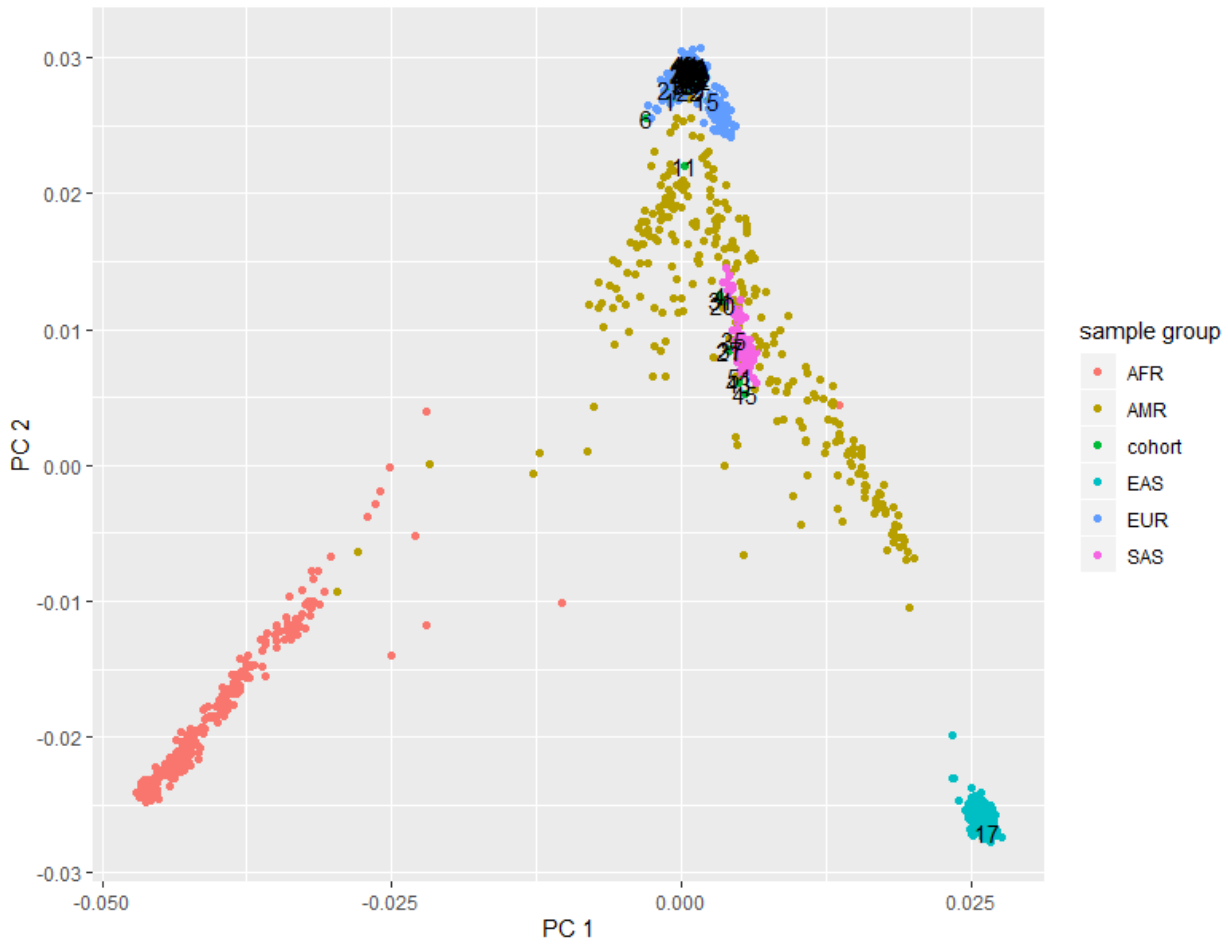
Supplementary Table 1: Summary of epilepsy cohort genome sequencing metrics. A and B refer to patient's mother and father, respectively. There are two pairs of identical twins (Patients 8 & 12; Patients 29 & 30). The read depth coverage for 13 individuals is NA as pipeline statistics were not generated for this batch. Abbreviations: CNV, copy number variant; SNV, single nucleotide variant.

Supplementary Figure 1

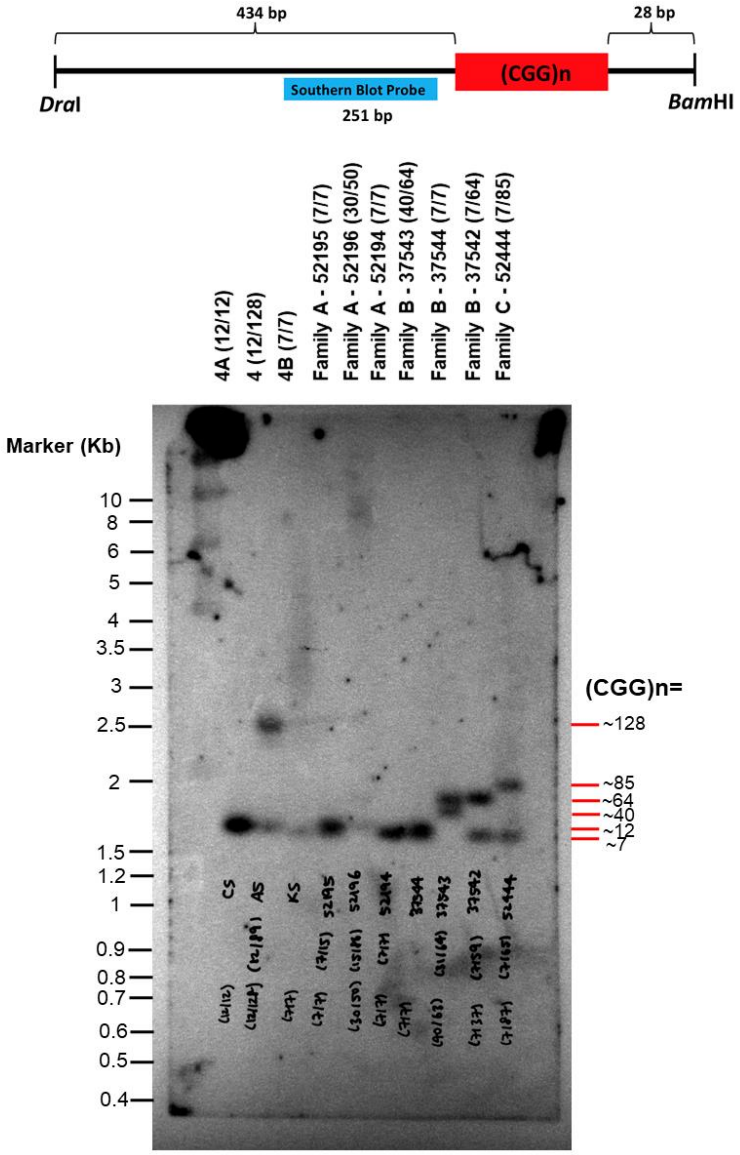




Supplementary Figure 2



Supplementary Figure 3



Supplementary Table 1

Patient ID	Read Depth	Total indels and SNVs	Rare indels and SNVs	Total CNVs	Rare CNVs
1	NA	4,660,660	354	728	3
2	NA	4,595,059	276	702	5
3	33.44	4,653,896	313	669	2
4	39.83	4,609,674	275	748	5
5	NA	4,726,032	386	705	10
6	NA	4,483,231	308	742	6
7	38.77	4,585,502	346	641	8
8	39.91	4,624,131	306	713	3
9	NA	4,737,791	353	744	3
10	NA	4,573,916	295	718	7
12	39.17	4,510,526	303	705	4
13	NA	4,621,644	412	735	5
14	37.58	4,579,400	300	713	1
15	NA	4,606,247	293	717	8
16	39.84	4,492,503	385	676	2
17	39.5	4,722,290	389	715	4
18	NA	4,603,571	271	721	5
19	NA	4,616,483	258	691	2
20	38.87	4,602,984	294	707	3
21	NA	4,630,089	272	710	2
22	37.32	4,605,899	356	726	3
23	37.67	4,610,403	311	711	5
24	NA	4,595,027	258	756	7
25	NA	4,602,002	351	784	6
26	36.27	4,783,882	414	736	3
27	35.22	4,647,210	288	688	5
28	37.01	4,569,228	303	680	3
29	33.62	4,456,544	292	680	4
30	33.95	4,592,096	302	701	4
3A	35.7	4,620,791	279	692	3
3B	37.02	4,602,556	304	677	4
4A	36.65	4,305,260	243	711	5
4B	37.01	4,292,983	226	664	4
7A	37.25	4,316,670	270	745	6
7B	36.73	4,269,226	249	717	7

8A	35.28	4,280,359	227	711	4
8B	36.73	4,312,714	240	700	1
16A	37.26	4,331,967	287	702	2
16B	37.48	4,259,967	324	675	6
17A	36.43	4,278,024	265	684	5
17B	36.57	4,380,674	350	693	3
20A	36.66	4,291,188	239	706	1
20B	38.25	4,281,869	229	691	3
22A	38.83	4,670,279	306	727	3
22B	37.82	4,634,087	338	711	2
26A	35.2	4,787,307	450	714	8
26B	35.56	4,726,878	421	698	1
27A	35.65	4,667,391	300	668	6
27B	35.02	4,602,762	296	715	3
28A	37.67	4,315,131	243	663	3
28B	36.8	4,338,375	282	682	1