Supplementary Table 8. Rare variants, (CADD> 15), in genes associated with familial intracranial aneurysm and loci associated with an increased risk of intracranial aneurysm in genome wide association studies (23, 24).

Patient ID	Clinical Diagnosis	Gene NM	Protein	CADD	gnomAD allele frequency	Exon or intron number / total number of exons	ClinVar ID (classification)	Rs ID	ACMG classification (See footnote)	Intracranial Aneurysm	Other vascular Involvement
34	HDCT	TMEM132B NM_052907.3 c.767G>A	p.Arg256Gln	23.3	0.000104	2/9	–	rs377588294	VUS PM2	–	–
54	hEDS	DNAH9 NM_001372.4 c.11678C>T	p.Ser3893Leu	24	0	61/69	–	rs761550523	VUS PM2	+	+
65	hEDS	ANGPTL6 NM_031917.2 c.1208G>A	p.Arg403Gln Fibrinogen like	28.7	0	5/6	–	–	VUS PM2	FHx ICA	–
65	hEDS	HSPG2 NM_005529.7 c.2633G>A	p.Arg878His	26.2	0.000236	21/97	875716 (VUS)	rs149479865	VUS PM2	ICA + FHx ICA	–
70, 884	hEDS	ARHGEF17 NM_014786.4 c.5651G>C	p.Cys1884Ser	22.6	0.000127	19/21	–	rs199726713	VUS PM2	–	–
79	HDCT	DNAH9 NM_001372.4 c.5644G>A	p.Asp1882Asn	31	0.0000398	27/69	–	rs371105048	VUS PM2	–	Aneurysm, NOS
99	HDCT	ARHGEF17 NM_014786.4 c.626G>A	p.Arg209His	28.1	0	1/21	–	–	VUS PM2 BP4 (Supp)	–	carotid dissection
100	hEDS	STARD13 NM_178006.4 c.2888C>A	p.Pro963His	28.2	0	12/14	–	rs1261673521	VUS PM2	+	–
422, 423	HDCT	ADAMTS15 NM_139055.3 c.263T>A	p.Leu88His	17.1	0	1/8	–	–	VUS PM2	–	FHx sudden death
453	HDCT	RNF213 NM_001256071.3 c.9178T>A	p.Phe3060Ile	23.3	0	29/68	–	–	VUS PM2	–	carotid dissection
755	hEDS	TMEM132B NM_052907.3 c.1862C>A	p.Thr621Asn	25.4	0.0000121	7/9	875716 (VUS)	rs776596875	VUS PM2 BP4 (Supp)	–	–
777	HDCT	ARHGEF11 NM_198236.3 c.1019C>T	p.Pro340Leu	22.7	0.00000796	12/14	–	rs1391083996	VUS PM2	ICA	–
1002, 1003	cEDS	RNF213 NM_001256071.3 c.1669G>T	p.Glu557Ter	35	0.00000398	9/68	–	rs755262916	VUS PM2	–	–
1424	hEDS	THSD1 NM_018676.4 c.1858C>T	p.Pro620Ser	22.7	0.00000398	5/5	–	rs1188780320	VUS PM2 BP4 (Supp)	FHx (SDR)	–
1665	hEDS	RNF213 NM_001256071.3 c.12496G>A	p.Asp4166Asn	25.9	0.00033	47/68	–	rs148157068	VUS PM2, BP2	–	–

ACMG criteria as per Richards *et al.* (9): P = pathogenic, LP = likely pathogenic, VUS/LP = variant of uncertain significance close to criteria for LP classification, VUS = variant of uncertain significance, LB = likely benign, B = benign. Individual criteria ((9), Table 3)

VUS* are defined here as including VUS that according to ACGS criteria are "hot", "warm" or "tepid" Variants of Uncertain Significance (Figure 6 of https://www.acgs.uk.com/media/11631/uk-practice-guidelines-for-variant-classification-v4-01-2020.pdf).

Segregation analysis, re-evaluation for specific phenotypic features and/or further functional analysis may enable variant reclassification, using ACMG criteria.