Supplementary Table 16. Rare germline variants (CADD> 15) in genes previously published as abnormally expressed in skin fibroblasts from cEDS patients (Ref 30), list of genes in supplementary methods.

Patient ID	Clinical Diagnosis	Rs ID	CADD DANN	Current Gene annotation	Gene	Exon or Intron / Total no. exons	HGVSc	HGVSp	gnomAD allele frequency	ACMG classification (See footnote) criteria
395	hEDS	–	22.5 0.998	a)	DTL	14/15	ENST00000366 c.1993G>A	ENSP00000355 p.Ala665Thr	0.0001178	
534	cEDS	–	29.4 0.999	a)	POSTN	9/23	ENST00000379 c.1160T>C	ENSP00000369 p.Leu387Pro	0	
967	hEDS	rs755934955	25.7 0.999	a)	EDIL3	9/11	ENST00000296 c.994G>A	ENSP00000296 p.Asp332Asn	0.00002033	
1289	hEDS	–	27.5 0.998	c)	KIF4A	8/31	ENST00000374 c.836A>G	ENSP00000363 p.Asp279Gly	0	VUS PM2 PP3 (Supp)
1421	hEDS	rs768395830	28.3 0.998	c)	CSPP1	12/29	ENST00000262 c.1576A>G	ENSP00000262 p.Asn526Asp	0.000008126	VUS PM2
1464	hEDS	rs142868256	23.5 0.985	c)	C3	37/41	ENST00000245 c.4535G>A	ENSP00000245 p.Arg1512His	0.0001178	VUS PM2 PP5 BP6
1642	hEDS	–	23.3 0.995	a)	POSTN	7/23	ENST00000379 c.766A>T	ENSP00000369 p.Thr256Ser	0	
1681	hEDS	rs142868256	23.5 0.985	c)	C3	37/41	ENST00000245 c.4535G>A	ENSP00000245 p.Arg1512His	0.0001178	VUS PM2 PM5 BP6
1717	hEDS	rs759948962	24.4 0.998	c)	C3	9/41	ENST00000245 c.910C>T	ENSP00000245 p.Arg304Trp	0.000004067	VUS PM2
1717	hEDS	rs141915646	26.7 0.998	a)	MKI67	8/15	ENST00000368 c.1513C>T	ENSP00000357 p.Arg505Cys	0.00003249	

Current gene annotation:
a) Germline variants in this gene not currently associated with Mendelian disorder
b) Germline variants in this gene associated with disorder of bone metabolism or skeletal dysplasia
c) Germline variants in this gene associated with non-EDS / HTAD phenotype

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

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.