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.

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Clinical Diagnosis</th>
<th>Rs ID</th>
<th>Gene</th>
<th>Exon or Intron / Total no. exons</th>
<th>HGVSc</th>
<th>HGVSp</th>
<th>gnomAD allele frequency criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>385</td>
<td>NEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>534</td>
<td>cEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>967</td>
<td>NEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1289</td>
<td>NEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1421</td>
<td>NEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1464</td>
<td>NEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1542</td>
<td>NEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1681</td>
<td>NEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1717</td>
<td>NEDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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, VUS = variant of uncertain significance close to criteria for LP classification, 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.

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, VUS = variant of uncertain significance close to criteria for LP classification, 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.

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, VUS = variant of uncertain significance close to criteria for LP classification, 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.

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, VUS = variant of uncertain significance close to criteria for LP classification, 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.

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, VUS = variant of uncertain significance close to criteria for LP classification, 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.