**A novel homozygous synonymous variant further expands the phenotypic spectrum of *POLR3A-*related pathologies**

**Supporting Information**

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| --- | --- | --- | --- |
| **Chromosome** | **Start** | **End** | **Size** |
| [16](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr16:18854588-52439376) | 18854613 | 52439351 | 33584739 |
| [8](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr8:61376476-84184857) | 61376501 | 84184832 | 22808332 |
| [4](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr4:86103231-97840774) | 86103256 | 97840749 | 11737494 |
| [10](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr10:77184807-86438177) | 77184832 | 86438152 | 9253321 |
| [4](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr4:76382443-84631754) | 76382468 | 84631729 | 8249262 |
| [9](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr9:74685264-79391715) | 74685289 | 79391690 | 4706402 |
| [6](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr6:95586711-98905421) | 95586736 | 98905396 | 3318661 |
| [17](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr17:17276142-19705664) | 17276167 | 19705639 | 2429473 |
| [17](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr17:72122769-74230831) | 72122794 | 74230806 | 2108013 |
| [10](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr10:49735950-51698312) | 49735975 | 51698287 | 1962313 |
| [17](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr17:80248240-81512468) | 80248265 | 81512443 | 1264179 |
| [1](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr1:179341279-180274414) | 179341304 | 180274389 | 933086 |
| [10](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr10:45648485-46292016) | 45648510 | 46291991 | 643482 |
| [22](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr22:29094135-29570353) | 29094160 | 29570328 | 476169 |
| [1](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr1:169594904-170024350) | 169594929 | 170024325 | 429397 |
| [10](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr10:17771383-18140720) | 17771408 | 18140695 | 369288 |
| [1](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr1:19092897-19385470) | 19092922 | 19385445 | 292524 |
| [19](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr19:49436437-49686586) | 49436462 | 49686561 | 250100 |
| [22](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr22:31530732-31758514) | 31530757 | 31758489 | 227733 |

**Supporting Table 1.** Regions of homozygosity (ROH) from the WES data of the affected individual are shown. Altogether ROH span ~105Mb (Megabases) of her exome. Note that *POLR3A* is located within the fourth largest ROH spanning ~9.25Mb (red).

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Chr** | **Start** | **End** | **Gene** | **cDNA** | **amino acid** | **gnomAD** | **Proband** | **Sister** |
| [4](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr4:78926507-78926557) | 78926532 | 78926532 | *PAQR3* | c.691C>T | p.Pro231Ser | 0/14/251392 | homozygous | heterozygous |
| [4](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr4:83300979-83301029) | 83301004 | 83301004 | *HPSE* | c.1428T>G | p.Asp476Glu | 1/214/281078 | homozygous | homozygous |
| [10](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr10:77984180-77984230) | 77984205 | 77984205 | *POLR3A* | c.3336G>A | p.Glu1112= | not identified | homozygous | wt |
| [16](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr16:20348452-20348502) | 20348477 | 20348477 | *UMOD* | c.824A>G | p.Asn275Ser | 0/4/277452 | homozygous | heterozygous |
| [16](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr16:23557209-23557259) | 23557234 | 23557234 | *EARS2* | c.110T>C | p.Val37Ala | not identified | homozygous | homozygous |
| [17](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr17:81251201-81251251) | 81251226 | 81251226 | *SLC38A10* | c.2332G>A | p.Ala778Thr | 0/51/257818 | homozygous | homozygous |
| [17](http://genome-euro.ucsc.edu/cgi-bin/hgTracks?org=Human&db=hg38&position=chr17:81251250-81251302) | 81251275 | 81251277 | *SLC38A10* | c.2283dup | p.His762Thrfs\*10 | not identified | homozygous | homozygous |

**Supporting Table 2.** List of rare homozygous variants within ROH and results of segregation analyses utilizing DNA sample of the unaffected sister.