

Table S1 *POLD1* variants of uncertain significance pathogenicity predictions

Gene	Germline variants			Pathogenicity prediction tools												
	Nucleotide change	Amino acid change	Protein domain	EIGEN	EIGEN-PC	REVEL	PROVEAN	PRIMATEAI	CADD	DEOGEN	CHASM	UMD-PREDICTOR	PolyPhen-2 HDIV	PolyPhen2 HVAR	HOPE	
<i>POLD1</i>	c.2275G>A	p.Val759Ile	DNA polymerase family B	Pathogenic	Pathogenic	Benign	Neutral	Tolerated	Pathogenic	Tolerated	Benign	Polymorphism	Probably damaging	Probably damaging	(I) The mutant residue is bigger than the wild-type residue. (II) The mutated residue is located in a domain that is important for binding of other molecules. (III) The mutated residue is in contact with residues in another domain. It is possible that the mutation disturbs these contacts	
<i>POLD1</i>	c.353C>T	p.Ser118Phe	–	Benign	Benign	Benign	Damaging	Tolerated	16,21 (Benign)	Damaging	Benign	Probably pathogenic	Benign	Benign	(I) The mutant residue is bigger than the wild-type residue. (II) The mutant residue is more hydrophobic than the wild-type residue. (III) The wild-type residue is not conserved at this position	