GRHL3	*List of variants detected in affected subjects*												
	(GRCh38/hg38)			***NM_198174.2***	***NP_937817.3***								
chr	***chr pos start***	***chr pos end***	***Change type***	***HGVS_Transcript consequence***	***HGVS_Protein consequence***	***Variant effect***	***Domains - Amino acids***	***Variant class***	***Phenotype***	***Reference***	***PMID***	***Allele freq gnomAD***	***comments***
1	24331456		INS	c.48dupC	p.Asp16Aspfs*10	frame-shift		Patho.Var	NTD	Lemay *et al* (2017)	28276201	Not Found	Consanguineous family: homozygous 1child (CLP+NTD+ scoliosis), homozygous 2nd child (NTD+ scoliosis), parents carriers
1	24336483	24336493	DEL	c.268_278del11	p.Tyr90Hisfs*4	frame-shift		Patho.Var	VWS2	Peyrard-Janvid *et al* (2014)	24360809	Not Found	Dominant negative -in an israeli family V-III, compound heterozygous
1	24336685	24336685	DEL	c.470delC	p.Gly158Alaf*r55	frame-shift		Patho.Var	nsCP	Eshete *et al* (2017)	28886269	Not Found	Strongly hypomorphic or null/parent carrier (African cohort)
1	24336712		SUB	c.497C>A	p.Pro166His	missense		VUS	nsCP	Eshete *et al* (2017)	28886269	Not Found	Modestly hypomorphic/parent carrier (African cohort)
1	24337687		SUB	c.738C>T	p.Gly246fs*10	frame-shift	DBD 230-423	Patho.Var	nsCP	Mangold *et al* (2016)	27018475	Not Found	De novo
1	24337790		SUB	c.840+1G>T	p.?	splice-site (donor)	DBD 230-423	Patho.Var	nsCP	Mangold *et al* (2016)	27018475	Not Found	De novo
1	24338044		SUB	c.893G>A	p.Arg298His	missense	DBD 230-423	Patho.Var	VWS2	Peyrard-Janvid *et al* (2014)	24360809	0.02447	Family also carries IRF6 c.239A>G.
1	24338067	24338068	INS	c.916dupC	p.Arg306Profs*11	frame-shift	DBD 230-423	Patho.Var	nsCP	Mangold *et al* (2016)	27018475	Not Found	Complete co-segregation
1	24339686	24339687	INS	c.971_972insGT	p.Phe324Leufs*22	frame-shift	DBD 230-423	Patho.Var	VWS2	Peyrard-Janvid *et al* (2014)	24360809	Not Found	Dominant negative
1	24339764		SUB	c.1047+2T>C	p.Ala318Glyfs*26	frame-shift	DBD 230-423	Patho.Var	NTD	Lemay *et al* (2017)	28276201	Not Found	Sporadic spina bifida: alternative splicing causes skipping exon 8
1	24342238		SUB	c.1171C>T	p.Arg391Cys	missense	DBD 230-423	Patho.Var	VWS2 or nsCP or NTD	Peyrard-Janvid *et al* (2014)	24360809	0.004096	Identified in this study as nsCP germline mutations in 2 families CLP-398 and CLP-986 and in other studies as de novo VWS2 and as de novo NTD
1	24342716		SUB	c.1229A>G	p.Asp410Gly	missense	DBD 230-423	VUS	nsCP	Eshete *et al* (2017)	28886269	0.004061	Strongly hypomorphic or null, parent carrier (African cohort)
1	24342769		SUB	c.1282A>C	p.Ser428Arg	missense		VUS	nsCP	Eshete *et al* (2017)	28886269	Not Found	Dominant negative, parent N/A (African cohort)
1	24342774	24342774	DEL	c.1285+2delT	p.?	splice-site (donor)		Patho.Var	nsCP	Mangold *et al* (2016)	27018475	Not Found	Complete co-segregation
1	24342967		SUB	c.1361C>T	p.Thr454Met	missense		Assoc. Var	nsCP	Leslie *et al* (2016)	27018472	0.02312	Disease-associated polymorphism with additional supporting functional evidence- retains 40% of its activity
1	24343026		SUB	c.1419+1G>T	p.?	splice-site (donor)		Patho.Var	VWS2	Peyrard-Janvid *et al* (2014)	24360809	Not Found	Dominant negative
1	24347483		SUB	c.1559G>A	p.Arg520Gln	missense	DD 493-602	Patho.Var	VWS2	Peyrard-Janvid *et al* (2014)	24360809	0.004061	Dominant negative
1	24347487	24347490	DEL	c.1563_1566delGGAG	p.Glu522Leufs*10	frame-shift	DD 493-602	Patho.Var	VWS2	Peyrard-Janvid *et al* (2014)	24360809	Not Found	Dominant negative
1	24347500	24347500	DEL	c.1576delG	p.Val526Cysfs*7	frame-shift	DD 493-602	Patho.Var	VWS2	Peyrard-Janvid *et al* (2014)	24360809	Not Found	Dominant negative
1	24347510		SUB	c.1586C>T	p.Ala529Val	missense	DD 493-602	Patho.Var	NTD	Lemay *et al* (2017)	28276201	0.06493	Sporadic spina bifida: reduced activation of target genes in a luciferase reprorter assay
1	24350089		SUB	c.1661A>G	p.Asn554Ser	missense	DD 493-602	Patho.Var	VWS2	Peyrard-Janvid *et al* (2014)	24360809	0.004065	Dominant negative -in an israeli family V-III, compound heterozygous
1	24350105		SUB	c.1677C>A	p.Tyr559*	stop_gained	DD 493-602	Patho.Var	nsCP	Eshete *et al* (2017)	28886269	Not Found	Modestly hypomorphic/parent carrier (African cohort)

Legend:

Variant class

Patho.Var: Pathogenic Variant	All LoF and missense either neomutation, co-segregagting in >=2,or funct validated as deleterious	
VUS: Variant of unknown significance	Rare >0.5% gnomAD	
Assoc.Var: Associated Variant	>1% gnomAD frequent variant but losses some of it's activity compared to wild-type	

Domains -Amino acids

DBD	DNA-binding domain (230-423)
DD	dimerisation (493-602)

Associated disorders

NTD	Neural Tube Defects
VWS2	Van der Woude syndrome 2
nsCP	Non-syndromic cleft palate