Variant	Prediction on protein	Inheritance	Segregation	Phenotype	Method	Comments
Pathogenic or likely pathogenic variants						
c.-84-1G>C	p.?	sporadic	de novo	WS4 or PCWH (learning delay, hypotonia at birth; short segment HSCR)	Sanger	
c.44_62del	p.(Val15Alafs*11)	?	ND	WS4	Sanger	Sun, *Sci Rep* 2016;6:35499
c.61del	p.(Arg21Alafs*11)	sporadic	parents not carriers	PCW + olfactory bulbs agenesis	Sanger	
c.89C>A	p.(Ser30*)	familial	cosegregates	PCWH in index case and mother, isolated SNHL in sister	Sanger	Cassatella, *Eur J Endocrinol* 2018;178:377
c.236T>G	p.(Val79Gly)	familial	de novo in father	PCWH (index case : demyelinating neuropathy, SNHL ; son : peripheral neuropathy + HSCR + depigmentation, hearing is said to be normal)	Sanger	
c.255G>A	p.(Trp85*)	sporadic	de novo	WS4 (long segment HSCR)	Sanger	Sun, *Sci Rep 2016;*6:35498
c.325A>T	p.(Asn109Tyr)	sporadic	de novo	WS2 + anosmia	Sanger	
c.331T>C	p.(Phe111Leu)	sporadic	ND	WS2 or PCW (motor delay and ID), anosmia and hypoplastic olfactory bulbs	Sanger	Liu, *Int J Pediatr Otorhinolaryngol 2019;*130:109806
c.333C>A	p.(Phe111Leu)	sporadic	parents not carriers	WS2	NGS panel	
c.335T>C	p.(Met112Thr)	sporadic	de novo	WS2 + vestibular areflexia	NGS panel	
c.335T>C	p.(Met112Thr)	familial	de novo in mother	WS4 in 2 index case brothers (short segment HSCR), WS2 in mother	Sanger	
c.335_336del	p.(Met112Serfs*21)	sporadic	parents not carriers	WS2 + vestibular areflexia	Sanger	
c.338T>C	p.(Val113Ala)	familial	cosegregates	WS4 in 2 index case brothers , one has a possible hypogonadism; a third brother has SNHL; father has WS2	NGS panel	
c.341G>A	p.(Trp114*)	sporadic	parents not carriers	WS4	NGS panel	
c.342G>A	p.(Trp114*)	familial	?	WS2	sanger	
c.342G>T	p.(Trp114Cys)	sporadic	de novo	WS2 + mild hypotonia	sanger	
c.355C>G	p.(Arg119Gly)	sporadic	parents not carriers	WS2	Sanger	
c.356_357del	p.(Arg119Glnfs*14)	sporadic	parents not carriers	WS2 or PCW, hyperpigmentation of hands	Sanger	

c.364C>G	p.(Leu122Val)	sporadic	de novo	WS2	Sanger	
c.380del	p.(Pro127Argfs*19)	familial	ND	WS2	Sanger	Was initially suspected of having WS1 due to unexplained dystopia canthorum in the index case only)
c.383dup	p.(His128Glnfs*6)	sporadic	parents not carriers	PCW	Sanger	
c.403A>G	p.(Ser135Gly)	sporadic	ND	WS2 + KS	Sanger	Marcos, *J Clin Endocrinol Metab* 2014;99:E213 Gach, *Mol Cell Endocrinol* 2020;517:110968
c.415G>C	p.(Gly139Arg)	sporadic	de novo	WS2	Sanger	Not expected: sent for WS1 (due to inherited hpertelorism)
c.416_426del	p.(Gly139Glufs*7)	familial	cosegregates	PCWH/PCW in the 2 index cases, father has WS2	Sanger	
c.424T>C	p.(Trp142Arg)	sporadic	de novo	WS2 + olfactory bulbs agenesis	Sanger	Initially sent for WS1
c.428+2T>G	p.?	sporadic	ND	WS2 (+ dysmorphy and developmental delay suspectedly due to another cause)	NGS panel	Pingault, *Hum Mutat* 2010;31:391
c.467_469del	p.(Glu156del)	Sporadic	ND	SNHL (asymmetric) + KS + hyperpigmentation	NGS panel	Initially sent for CHARGE syndrome
c.475del	p.(Arg159Glyfs*127)	Sporadic	parents not carriers	WS2	Sanger	
c.476G>C	p.(Arg159Pro)	familial	cosegregates	WS4 without hearing loss (short segment HSCR) , father has WS2	Sanger	
c.580G>T	p.(Glu194*)	sporadic	parents not carriers	WS2	NGS panel	
c.667del	p.(Met223Cysfs*63)	sporadic	parents not carriers	WS4, aortic coarctation	Sanger	
c.725dup	p.(Thr243Asnfs*38)	sporadic	parents not carriers	WS4 (short segment HSCR)	NGS panel	
c.773_774delinsA	p.(Arg258Glnfs*28)	sporadic	ND	PCWH with extent depigmentation (short segment HSCR)	Sanger	
c.865del	p.(Met289Trpfs*22)	sporadic	ND	WS4	Sanger	Hogan, *Pediatr Gastroenterol Hepatol Nutr* 2019;22 :488
c.897del	p.(Gln299Hisfs*12)	sporadic	ND	PCWH (short segment HSCR)	NGS panel	
c.900C>A	p.(Tyr300*)	sporadic	ND	PCWH, severe	Sanger	
c.1091_1092delinsT	p.(Gln364Leufs*138)	parents not carriers	parents not carriers	WS2	NGS panel	
c.1095del	p.(Pro367Hisfs*135)	Sporadic	parents not carriers	WS2	NGS panel	Sun, *Sci Rep* 2016 *;*,6:35499

c.1160_1179dup	p.(Ser394Thrfs*115)	Sporadic	ND	WS4 (short segment HSCR)	Sanger	
c.1169C>G	p.(Ser390*)	familial	cosegregates	WS4 or PCWH (developmental delay but MRI is said to be normal) in twin brothers, a sister has HSCR and motor delay, father has SNHL and HSCR; no depigmentation reported in the whole family	Sanger	Somashekar, *Clin Genet* 2019;95:398
c.1302_1314del	p.(Leu435Serfs*63)	sporadic	parents not carriers	WS2	Sanger	
c.1399T>C	p.(*467Glnext*86)	sporadic	parents not carriers	PCWH, severe	Sanger	
c.1399T>C	p.(*467Glnext*86)	sporadic	ND	PCWH	Sanger	
Genic rearrangements and copy number variations						
c.698-351_1227del	p.?	sporadic	parents not carriers	SNHL, anosmia	NGS panel	Initially sent for CHARGE syndrome (due to association with inter-ventricular communication)
dele5 (hg19:chr22;g38367276_38371138del		sporadic	ND	WS4 (short segment HSCR)	QM-PSF, MLPA	
Full gene deletion, 1,6Mb including about 50 genes		familial	mocaicism in asymptomatic parent	WS4 (hypotonia with central abnormalities different from PCWH, possibly due to contiguous gene syndrome?), sister has small depigmentations and light hypotonia	QM-PSF, MLPA and array-CGH	
Full gene deletion		sporadic	parents not carriers	WS2	QM-PSF, MLPA	
Full gene deletion		sporadic	parents not carriers	WS2	QM-PSF, MLPA	
Triplication 1Mb, about 30 genes from GGA1 to CBY (hg19:chr22;g38004181-38009846_39053183-39057638del)		sporadic	de novo	Atypical WS with hypo and hyperpigmentation, bilateral deafness, hypotonia, polymalformation. Severe. Girl, no sex reversal.	QM-PSF, MLPA and array-CGH	

Variants of unknown significance awaiting for larger familial segregation						
c.356G>T	p.(Arg119Leu)	familial	familial; inherited from affected mother, a complement of clinical investigation and familial segregation has been asked for	WS2	NGS panel	
c.374A>C	p.(Gln125Pro)	familial	ND	WS2	anger	Not expected: sent for WS1

Supplemental table 1: Unpublished cases with heterozygous *SOX10* variants of interest collected in our laboratory over the last years. When a mutation is already reported in an independent case, the reference is indicated in the comments column. p.? indicates that the consequence on the protein is difficult to predict. The other variants are newly described. ND : not determined. ID: intellectual deficiency. QM-PSF: Quantitative Multiplex PCR of Short Fluorescent Fragments. MLPA: Multiplex Ligation-dependent Probe Amplification.