

Genomic position	*cDNA position (NM_022454.4)	Protein position	Variant effect	Diagnosis	Reference	Sex	Age at diagnosis (years)	Exon	CADD	REVEL	ACMG classification	VF (gnomAD)
8:55370742	c.44A>C	p.Gln15Pro	Missense	IPAH/HPAH	Montani et al., 2022	M	53	1	25.5	0.616	VUS	0.00000504
8:55370769	c.72_76del	p.Met24fsTer52	Frameshift	IPAH/HPAH	Zhu et al., 2018	M	3	1	.	.	LP	.
8:55370862	c.164C>T	p.Pro55Leu	Missense	IPAH/HPAH	Gräf et al., 2018	unk	unk	1	22.9	0.196	LB	0.0000043
8:55370897	c.199C>G	p.Arg67Gly	Missense	IPAH/HPAH	Montani et al., 2022	F	12	1	26.5	0.738	VUS	0.0000319
8:55370906	c.208C>T	p.Arg70Trp	Missense	IPAH/HPAH	Montani et al., 2022	F	35	1	32.0	0.961	VUS	.
8:55370907	c.209G>A	p.Arg70Gln	Missense	IPAH/HPAH	Hiraide et al., 2018	F M	51 25	1	32.0	0.969	VUS	.
8:55370907	c.209G>T	p.Arg70Leu	Missense	IPAH/HPAH	This study	M	11 months	1	32.0	0.988	VUS	.
8:55370916	c.218A>C	p.Asn73Thr	Missense	IPAH/HPAH	This study	M	6	1	26.7	0.855	VUS	.
8:55370924 8:55370924	c.226A>G c.226A>G	p.Met76Val p.Met76Val	Missense Missense	APAH-CHD APAH-CHD	Zhu et al., 2018 Zhu et al., 2019	F F	3 3	1	27.4	0.967	VUS	.
8:55370942	c.244G>T	p.Glu82Ter	Nonsense	APAH-CHD	This study	M	.	1	40.0	.	LP	.
8:54458415	c.277C>A	p.Leu93Met	Missense	APAH-portopulmonar	Zhu et al., 2019	F	57	1	24.1	0.634	VUS	.
8:55370982	c.284A>G	p.Asn95Ser	Missense	APAH-CHD	Zhu et al., 2018	M	1	1	26.3	0.925	VUS	.
8:55370985	c.287C>A	p.Ala96Asp	Missense	IPAH/HPAH	Montani et al., 2022	F	21	1	29.8	0.937	VUS	.
8:55371010	c.307+5G>C	NA	Splicing	IPAH/HPAH	Gräf et al., 2018	unk	unk		29.8	.	LP	.
8:55370729	c.317G>T	p.Trp106Leu	Missense	IPAH/HPAH	Zhu et al., 2018	F	32	2	32	0.90	VUS	.
8:55371632	c.322G>T	p.Ala108Ser	Missense	APAH-CHD	Hiraide et al., 2018	F	2	2	24.1	0.632	LB	.
8:55371653	c.344del	p.Arg115fsTer29	Frameshift	APAH-CHD	Zhu et al., 2018	F	14	2	.	.	LP	.
8:54459111	c.361G>A	p.Ala121Thr	Missense	IPAH/HPAH	Wang et al., 2019	unk	unk	2	29.9	0.975	VUS	.
8:54459112	c.365_366del	p.Glu122AlafsTer39	Frameshift	IPAH/HPAH	Zhu et al., 2019	F	7	2	.	.	LP	.
8:54459129	c.379C>T	p.Gln127Ter	Nonsense	IPAH/HPAH	Wang et al., 2021	F	7	2	39.0	.	P	.
8:55371698	c.388C>T	p.Gln130Ter	Nonsense	APAH-CHD	Zhu et al., 2018	M	34	2	39.0	.	LP	.
8:54459142 8:54459142 8:54459142	c.392A>G c.392A>G c.392A>G	p.Asp131Gly p.Asp131Gly p.Asp131Gly	Missense Missense Missense	APAH-CHD IPAH/HPAH APAH-CHD	Zhu et al., 2019 Zhu et al., 2019 Zhu et al., 2018	F F F	31 40 38	2	28.9	0.890	VUS	.
8:55371704 8:55371704	c.394C>G c.394C>G	p.His132Asp p.His132Asp	Missense Missense	IPAH/HPAH IPAH/HPAH	Gräf et al., 2018 Montani et al., 2022	unk M	unk 16	2	27.0	0.808	VUS	.

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8:55371707	c.397C>T	p.Pro133Ser	Missense	IPAH/HPAH	Gräf et al., 2018	unk	unk	2	28.6	0.927	VUS	.
8:55371707	c.397C>G	p.Pro133Ala	Missense	IPAH/HPAH	Hiraide et al., 2018	F	33	2	26.9	0.930	VUS	.
8:55371708	c.398C>T	p.Pro133Leu	Missense	APAH-CHD	Zhu et al., 2018	M	5	2	31.0	0.908	VUS	.
8:54459158	c.408G>C	p.Lys136Asn	Missense	IPAH/HPAH	Wang et al., 2019	unk	unk	2	25.1	0.878	VUS	.
8:55371721	c.411C>G	p.Tyr137Ter	Nonsense	IPAH/HPAH	Gräf et al., 2018	unk	unk	2	38.0	.	P	.
8:55371723	c.413G>C	p.Arg138Pro	Missense	IPAH/HPAH	Montani et al., 2022	M	8	2	31.0	0.872	VUS	.
8:55371723	c.413G>C	p.Arg138Pro	Missense	IPAH/HPAH	Montani et al., 2022	M	2					
8:55371726	c.416C>T	p.Pro139Leu	Missense	IPAH/HPAH	Montani et al., 2022	F	36	2	29.9	0.793	VUS	.
8:54459168	c.418C>T	p.Arg140Trp	Missense	IPAH/HPAH	Zhu et al., 2019	F	5	2	32.0	0.684	VUS	.
8:54459168	c.418C>T	p.Arg140Trp	Missense	IPAH/HPAH	Montani et al., 2022	M	10					
8:55371729	c.419G>C	p.Arg140Pro	Missense	IPAH/HPAH	Gräf et al., 2018	unk	unk	2	31.0	0.847	VUS	.
8:55371729	c.419G>C	p.Arg140Pro	Missense	IPAH/HPAH	Montani et al., 2022	F	18					
8:55371732	c.422G>A	p.Arg141Gln	Missense	IPAH/HPAH	Montani et al., 2022	M	26	2	32.0	0.870	VUS	.
8:55371732	c.422G>A	p.Arg141Gln	Missense	IPAH/HPAH	Montani et al., 2022	F	13					
8:55371732	c.422G>T	p.Arg141Leu	Missense	IPAH/HPAH	Montani et al., 2022	F	10	2	31.0	0.901	VUS	.
8:55371750	c.440G>A	p.Arg147Gln	Missense	IPAH/HPAH	Montani et al., 2022	F	13	2	29.0	0.661	VUS	.
8:55371799	c.489G>C	p.Gln163His	Missense	APAH-CTD	This study	F	34	2	15.6	0.313	B	0.0000189
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	APAH-CHD	Zhu et al., 2018	M	7 (months)					
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	APAH-CHD	Zhu et al., 2018	F	3					
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	IPAH/HPAH	Zhu et al., 2018	F	5					
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	IPAH/HPAH	This study	M	54					
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	IPAH/HPAH	This study	F	2	2	.	.	P	.
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	IPAH/HPAH	Gräf et al., 2018	unk	unk					
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	IPAH/HPAH	Zhu et al., 2019	F	5					
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	IPAH/HPAH	Montani et al., 2022	F	6					
8:55371798	c.499_520del	p.Leu167TrpfsTer213	Frameshift	IPAH/HPAH	Montani et al., 2022	M	32					
8:55371920	c.610C>T	p.Arg204Cys	Missense	IPAH/HPAH	Montani et al., 2022	F	24	2	29.1	0.634	LB	.
8:55371974	c.664C>A	p.Pro222Ala	Missense	APAH-CHD	Zhu et al., 2018	M	9	2	27.6	0.648	VUS	.
8:54459442	c.693delC	p.Asp233fsTer154	Frameshift	IPAH/HPAH	Wang et al., 2019	unk	unk	2	.	.	LP	.
8:55372028	c.718C>G	p.Pro240Ala	Missense	IPAH/HPAH	Montani et al., 2022	M	27	2	15.0	0.230	LB	.

8:54459532	c.788delC	p.Pro263ArgfsTer124	Frameshift	APAH-TX	Zhu et al., 2019	M	31	2	.	.	LP	.
8:54459532 8:54459532	c.788dupC c.788dupC	p.Glu264GlyfsTer101 p.Glu264GlyfsTer101	Frameshift Frameshift	IPAH/HPAH IPAH/HPAH	This study Montani et al., 2022	M F	11 3	2	.	.	LP	.
8:55372122	c.817dupC	p.Arg273ProfsTer92	Frameshift	IPAH/HPAH	Gräf et al., 2018	unk	unk	2	.	.	LP	.
8:54459567	c.818dupG	p.Leu274ThrfsTer91	Frameshift	IPAH/HPAH	Wang et al., 2019	unk	unk	2	.	.	LP	.
8:55372392	c.1082C>A	p.Thr361Lys	Missense	IPAH/HPAH	Gräf et al., 2018	unk	unk	2	26.3	0.474	LB	.
8:55372446	c.1136A>T	p.Tyr379Phe	Missense	IPAH/HPAH	Gräf et al., 2018	unk	unk	2	22.6	0.292	LB	0.00000796
8:54459940	c.1190C>T	p.Ser397Leu	Missense	IPAH/HPAH	Zhu et al., 2019	F	66	2	32.0	0.801	VUS	0.00000398
8:55372512	c.1203delC	p.Asp401fsTer53	Frameshift	APAH-CHD	Zhu et al., 2018	F	30	2	.	.	LP	.
8:54459973	c.1224delC	p.Cys409AlafsTer45	Frameshift	IPAH/HPAH	Zhu et al., 2019	M	19	2	.	.	LP	.

Supplementary Table S1. Summary of *SOX17* variants described by the literature and this study. Sex: M: Male; F: female; unk: unknown; VF: variant frequency. CADD (v1.6); ACMG classification: P (pathogenic); LP (likely pathogenic); VUS (variant of unknown significance); LB (likely benign); B (benign).