Variant		Variant type	Heterozygous/homozygous status	Number of patients	*De novo*	ACMG classification	ACMG criteria
SNVs							
NM_005359.6:c.430_431del	p.(Ser144Argfs*7)	Frameshift mutation	Heterozygous	1 patient	*De novo*	Pathogenic	PVS1 Very Strong, PP5 Strong, PM2 Supporting
NM_005359.6:c.593del	p.(Pro198Glnfs*4)	Frameshift mutation	Heterozygous	3 patients from 1 family	-	Likely pathogenic	PVS1 Very Strong, PM2 Supporting
NM_005359.6:c.1052A>T	p.(Asp351Val)	Missense	Heterozygous	1 patient	-	Likely pathogenic	PM5 Strong, PS3 Strong, PM2 Supporting
NM_005359.6:c.1052A>G	p.(Asp351Gly)	Missense	Heterozygous	1 patient	-	Likely pathogenic	PM5 Strong, PS3 Strong, PM2 Supporting
NM_005359.6:c.1074dup	p.(Gly359Argfs*19)	Frameshift mutation	Heterozygous	2 patients from 1 family	-	Likely pathogenic	PVS1 Very Strong, PM2 Supporting

NM_005359.6:c.1081C>T	p.(Arg361Cys)	Missense	Heterozygous	3 patients from 3 families	*De novo* in one patient	Likely pathogenic	PM5 Strong, PS3 Strong, PM2 Supporting
NM_005359.6:c.1245_1248del	p.(Asp415Glufs*20)	Frameshift mutation	Heterozygous	19 patients from 5 families	-	Pathogenic	PVS1 Very Strong, PP5 Very Strong, PM2 Supporting
CNVs							
GRCh38(chr18):g.(?_51029975)_(51078357_?)del		Gene deletion (MLPA)	Heterozygous	2 patients from 1 family		Pathogenic	
Arr[GRCh37] 18q21.1q21.2(47887141_51431815)x1		Gene deletion (CMA)	Heterozygous	1 patient	*De novo*	Pathogenic	

Supplementary Table 1: Identified *SMAD4* variants. SNVs and the deletion detected with MLPA ((Multiplex Ligation-dependent Probe Amplification) follow HGVS recommendations, using NM_005359.6. The deletion detected with CMA (Chromosomal microarray) follows ISCN nomenclature.