Supplementary Table S1: Curation of patient variants using ACMG-based criteria via varsome.com

Variant	Evidence	Strength criteria	Curation
LARS2 c.1565C>A p.(Thr522Asn)	Combined evidence from ClinVar, UniProt and the literature, all indicating this as a pathogenic variant associated with gonadal dysgenesis and auditory dysfunction	PP5: Very Strong	1PVS+2PS+2PP = pathogenic
	The position is strongly conserved (phyloP100way = 7.54 is greater than 7.2) GnomAD exomes homozygous allele count = 0 is less than 2 for AD/AR	PM2: Strong	
	Pathogenic computational verdict based on 10 pathogenic predictions from DANN, DEOGEN2, EIGEN, FATHMM-MKL, LIST-S2, M-CAP, MVP, MutationAssessor, MutationTaster and SIFT vs 2 benign predictions from BayesDel_addAF and PrimateAI.	PPS: Supporting	
	Cosegregation with disease in multiple affected family members in a gene known to cause the disease	PP1: Supporting	
	Well-established in vitro or in vivo functional studies supportive of a damaging effect on the gene or gene product	PS3: Strong	
LARS2 c.1670A>G p.(Tyr557Cys)	The position is strongly conserved (phyloP100way = 8.9 is greater than 7.2). GnomAD exomes homozygous allele count = 0 is less than 2	PM2: Strong	2PS+2PP = pathogenic
	Pathogenic computational verdict based on 11 pathogenic predictions from BayesDel_addAF, DANN, DEOGEN2, EIGEN, FATHMM-MKL, LIST-S2, M-CAP, MVP, MutationAssessor, MutationTaster and SIFT vs 1 benign prediction from PrimateAI.	PP3: Supporting	
	Cosegregation with disease in multiple affected family members in a gene known to cause the disease	PP1: Supporting	
	*Well-established in vitro or in vivo functional studies supportive of a damaging effect on the gene or gene product	PS3: Strong	

*This criterion was only applied after functional studies were performed and escalated the variant from "likely pathogenic" to "pathogenic".