SUPPLEMENTRAY TABLE 2. Deleterious Prediction of *CDH23* Variants with the Packages in a Standard Clinical WES Protocol.

Gene	Variation	Domain	Nucleotide	Protein	Polyphen-2	SIFT	PROVEAN	Mutation Taster	SNAP2	FATHMM	SNPs and GO	PhD-SNP	Summary
CDH23	1	EC10	c.3262G > A	p.Val1088Met	Probably damaging (0.983)	Damaging (0.002)	Neutral (-1.46)	Disease causing (0.9999963209)	Effect (41;71%)	Tolerated (0.04)	Neutral (RI = 4)	Disease (RI = 5)	Uncertain
	2	EC19	c.6049G > A	p.Glu2017Ser	Probably damaging (1)	Damaging (0.005)	Deleterious (-3.82)	Disease causing (1)	Effect (49;71%)	Tolerated (-0.67)	Neutral (RI = 8)	Disease (RI = 0)	Pathogenic
	3	EC21	c.6911G > A	p.Arg2304Gln	Benign (0.062)	Tolerated (0.107)	Neutral (0.14)	Disease causing (0.9898613192)	Neutral (-16;57%)	Tolerated (0.71)	Neutral (RI = 7)	Neutral (RI = 6)	Uncertain

WES, whole-exome sequencing; EC, extracellular; *CDH23*, cadherin-related 23; SNP, single nucleotide polymorphism.

SUPPLEMENTRAY TABLE 3. The Secondary Structures of *CDH23* EC Domains.

Gene	Domain	Sample	Alpha helix	Extended strand	Beta turn	Random coil
CDH23	EC10	Wild-type	8.00%	37.00%	8.00%	47.00%
		c.3262G > A p.Val1088Met	3.00%*	39.00%	10.00%	48.00%
	EC19	Wild-type	5.83%	43.69%	9.71%	40.78%
		c.6049G > A p.Glu2017Ser	5.83%	43.69%	9.71%	40.78%
	EC21	Wild-type	13.27%	37.76%	16.33%	32.65%
		c.6911G > A p.Arg2304Gln	7.14%*	42.86%	15.31%	34.69%
	EC10-EC21	Wild-type	5.20%	38.39%	4.19%	52.22%
		c.3262G > A, p.Val1088Met c.6911 G > A, p.Arg2304Gln	5.20%	37.51%	3.31%	53.99%

*The asterisk meant evident changes of the *CDH23* EC domains in secondary structures.
EC, extracellular; *CDH23*, cadherin-related 23.

SUPPLEMENTRAY TABLE 4. The Structural Stability of *CDH23* Variants Predicted by I-Mutant2.0, DUET, and Maestro Web.

		I-Mutant v2.0		DUET		Maestro Web	
Gene	Variation	DDG	Stability	ΔΔG	Stability	ΔΔG	Stability
CDH23	p.Val1088Met*	-2.74	Decrease	-0.952	Destabilizing	1.831	Destabilizing
	p.Glu2017Ser*	-1.87	Decrease	-1.78	Destabilizing	1.84	Destabilizing
	p.Arg2304Gln	-0.7	Decrease	0.066	Stabilizing	-0.101	Stabilizing

CDH23, cadherin-related 23.