

Genetic Predisposition to Sporadic Congenital Hearing Loss in a Pediatric Population

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Supplementary Information

Supplementary Figures S1-5

Supplementary Tables S1-8

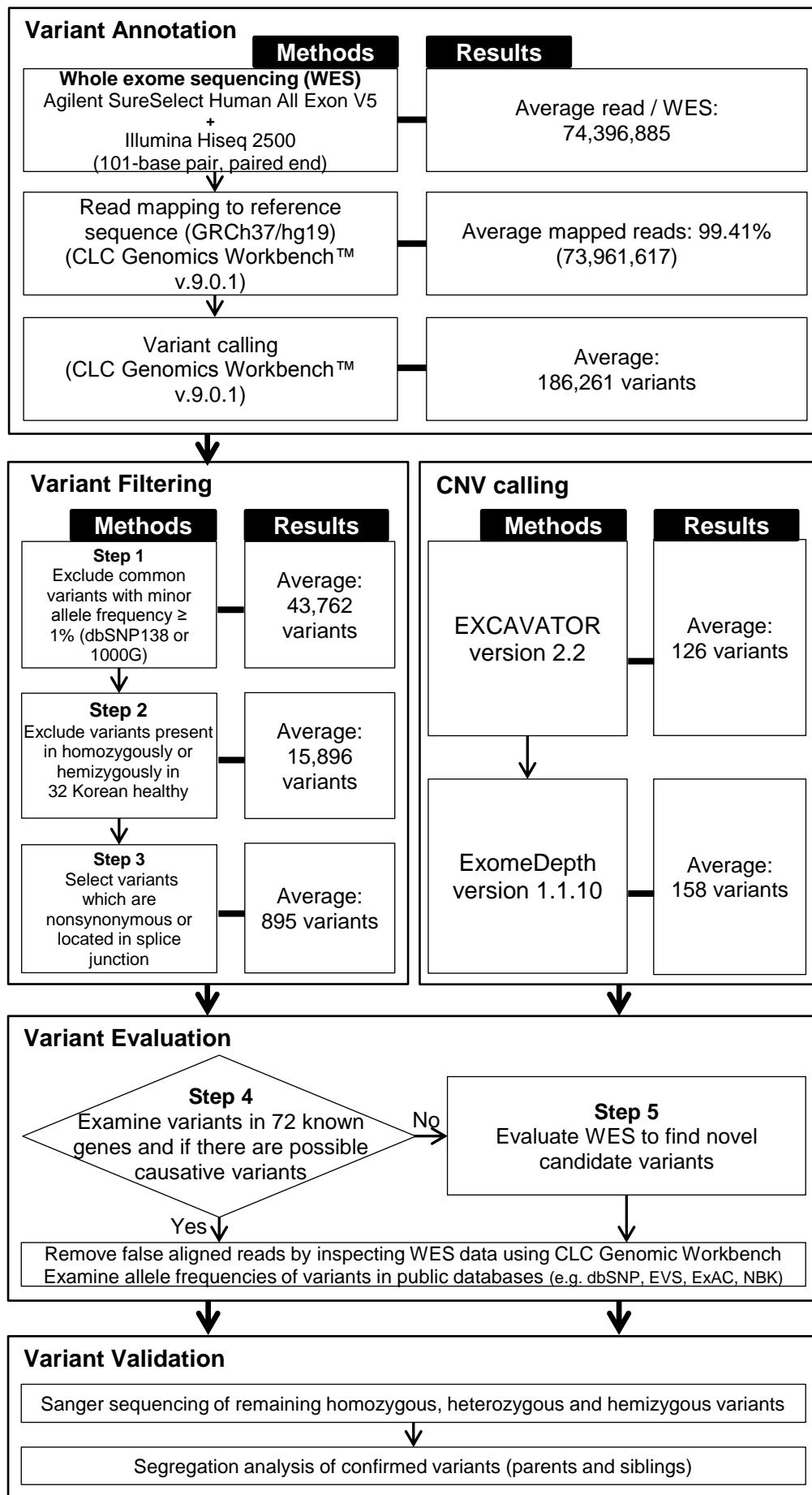
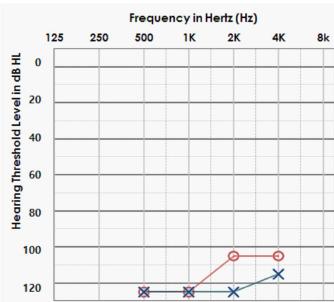
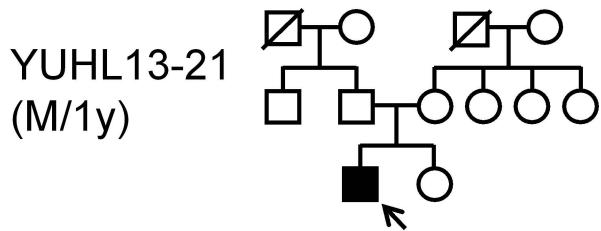
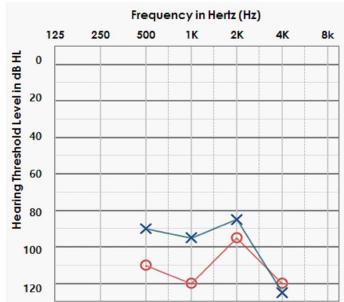
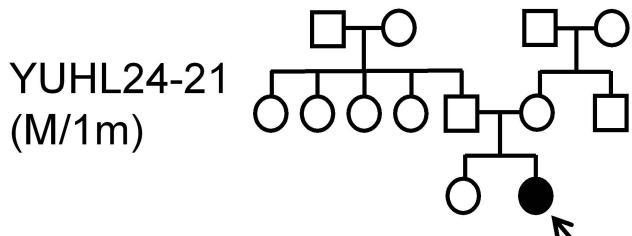
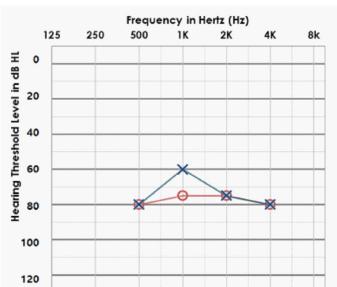
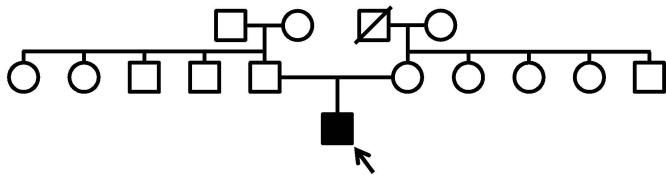
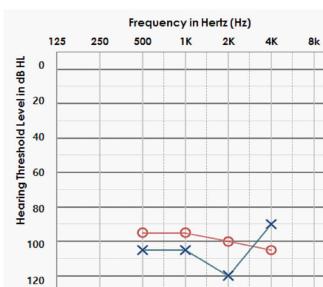
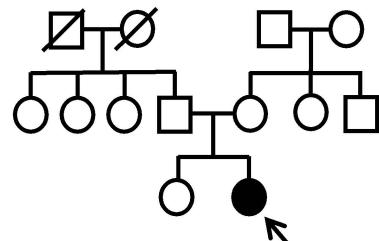


Figure S1. Variant filtering process for the identification of causative mutations.

a MYO15A (n = 2)**b CDH23 (n = 1)****c Unknown (n = 12)**

YUHL44-21(M/2y)

YUHL10-21
(M/4y)**Figure S2. Family pedigree and audiologic phenotype of families included in WES study.**

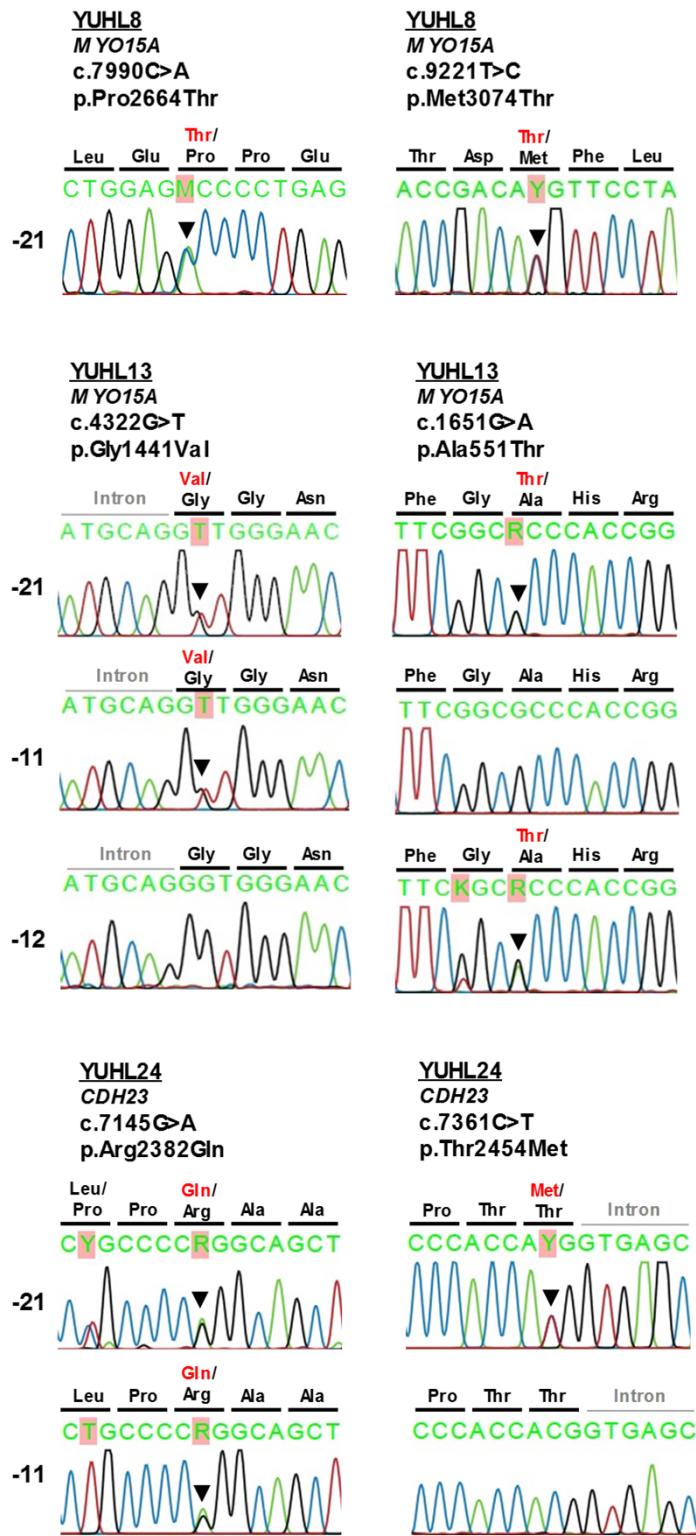


Figure S3. Sequencing traces of mutations detected in *MYO15A* and *CDH23*.

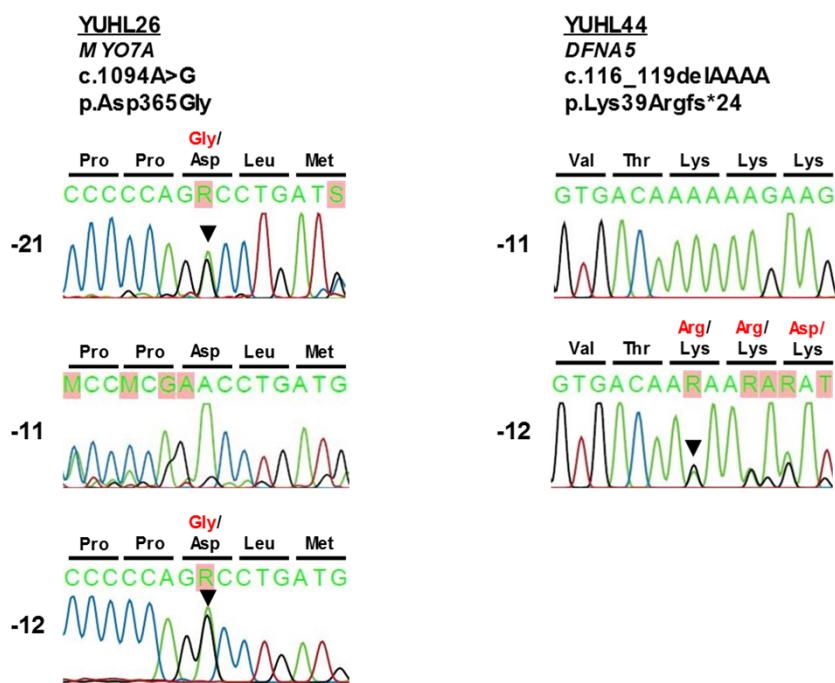


Figure S4. Sequencing traces of mutations detected in *MYO7A* and *DFNA5*.

a

YUHL10-21

chr6:30995156..30996641

**b**

YUHL25-21

chr6:30995156..30996641

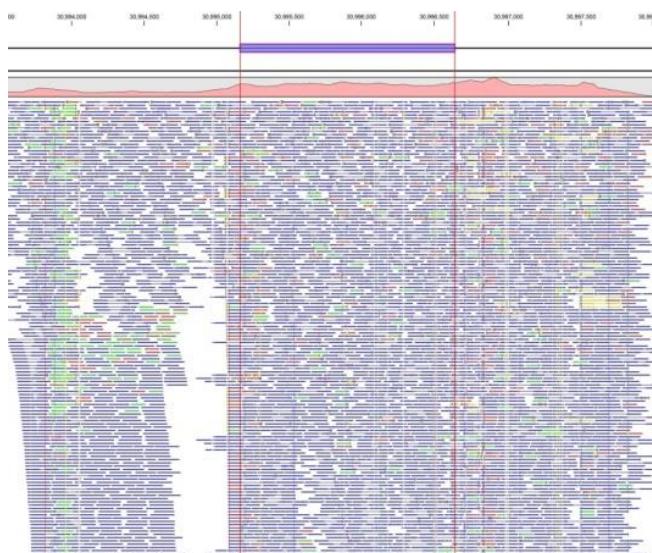
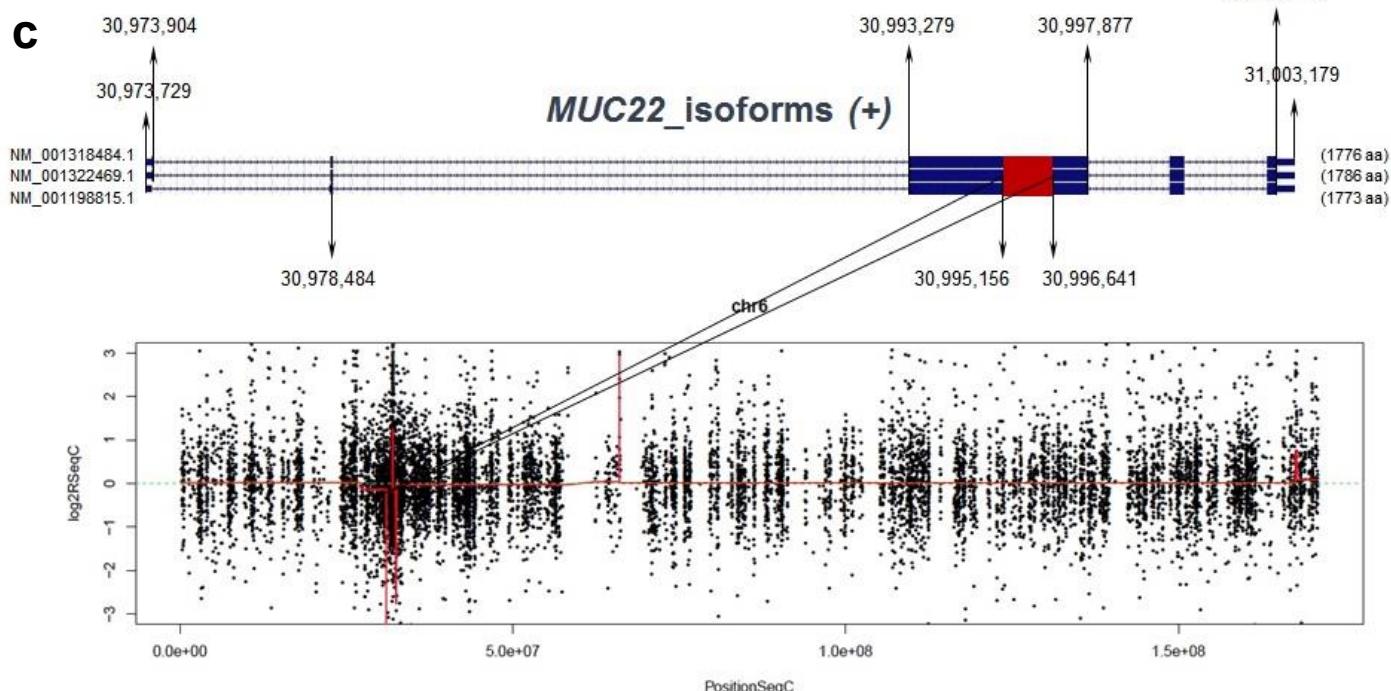
**c****Figure S5. Copy number variation.**

Table S1. Primer sequences for Sanger's sequencing of *SLC26A4* and *GJB2*

SLC26A4	Ex1-1	sense	5'-CCCCTGCGTGGCAGCC-3'
		anti-sense	5'-GTCTTCCCAACCGATCCTATC-3'
	Ex1-2	sense	5'-TGCAGGAGGGTAGGATTCTTT-3'
		anti-sense	5'-TGTGGGCATCTCAGGGCGAA-3'
	Ex2-1	sense	5'-CTCCCTCCTCGCTGCC-3'
		anti-sense	5'-GCCGCGACACCATGTAGCT-3'
	Ex2-2	sense	5'-GCCGCAGCTCCCCGAGTA-3'
		anti-sense	5'-GCTCCGCTTCTCTACGC-3'
	Ex3	sense	5'-TTGGTTGTGACTGAGATTGGATTG-3'
		anti-sense	5'-GGAGACCAGAACTCTCAATCTG-3'
	Ex4-1	sense	5'-TGAATGTAATCACTTGATGTGC-3'
		anti-sense	5'-AACATGAGCAAATATAATTGTAAAATATAC-3'
	Ex4-2	sense	5'-TATCCTGACATACTTATCTTGGAA-3'
		anti-sense	5'-AACATGAGCAAATATAATTGTAAAATATAC-3'
	Ex5-1	sense	5'-TGATTAATAACTGATTAATTGTTAGAGAC-3'
		anti-sense	5'-TATCATAGTAGTATTAAATACAGTTCATT-3'
	Ex5-2	sense	5'-CGAACACTTCTCGTATCCAGCA-3'
		anti-sense	5'-TACATCCATCTATTTACTTGTAAGTTC-3'
	Ex6	sense	5'-AAACATTTAATTTCTTCCTTTCTTATC-3'
		anti-sense	5'-CCCTGGAGCAAGAACACAC-3'
	Ex7	sense	5'-AGCAGCAGGAAGTATATAAAATTATTTTC-3'
		anti-sense	5'-TGCTGAACTTCTAACTACATATTCTAC-3'
	Ex8	sense	5'-ATTATTAACCAATGGAGTTTAAACATC-3'
		anti-sense	5'-TATTAGTACTAAGAGGAACACCAC-3'
	Ex9-1	sense	5'-GTCATCTCACAGCATTTCAC-3'
		anti-sense	5'-TGCAGCCAGCATCTCCGAGAA-3'
	Ex9-2	sense	5'-CTGAACCTCACACCTGTGAGCT-3'
		anti-sense	5'-TTCCAGCCCTATAAAACCAGTTC-3'
	Ex10	sense	5'-ATCGTTGTCATCCAGTCTTCC-3'
		anti-sense	5'-ATGGATATCATAAGGCTGTTGTTCC-3'

GJB2	Ex11	sense	5'-GAGAAGGACGAATCCTTTCATAG-3'
		anti-sense	5'-AATCGGTATGCAGAGAACAGG-3'
	Ex12	sense	5'-TTCCCTGAATAACACAGCCTCTC-3'
		anti-sense	5'-GAAGCATATAAGAACCAAATCTTATTTC-3'
	Ex13	sense	5'-ACATTAATATAATTCTTTCATTTCTATTTTTCC-3'
		anti-sense	5'-AGTGTGTTGTTCTGTTATAGGAAATC-3'
	Ex14	sense	5'-CGGCTGTTCCAAAAAAATCTTGAC-3'
		anti-sense	5'-CCAAGTCCAGCAAATGTCTCAC-3'
	Ex15	sense	5'-TTGAAATTATTAATCCCAGACAATTTC-3'
		anti-sense	5'-TCTCAAAAGAGGTTAGAAAACAAATTTC-3'
	Ex16	sense	5'-CATTAAAGTAACCTGACATTATTCC-3'
		anti-sense	5'-TAAGGGGGAAAAGAAAGATGTCATC-3'
	Ex17-1	sense	5'-AAATCTTGACAATTAAAGTTGACAGTG-3'
		anti-sense	5'-GGAACGTTCACTTGACTGGAAG-3'
	Ex17-2	sense	5'-ATAGAGATTCAAGTGGATTGAACTC-3'
		anti-sense	5'-CAAATGTATAATTCAAGAAAACCAGAAC-3'
	Ex18	sense	5'-AGGTTGTTAATTGTTACAAACTCTCC-3'
		anti-sense	5'-AAGGGCTTACGGGAAAGTCTTAC-3'
	Ex19-1	sense	5'-ACTAACAAAACATTGTGTCTTCTTTG-3'
		anti-sense	5'-TAGAAAAGATACATCTGTAGAAAGGTTG-3'
	Ex19-2	sense	5'-ACTAACAAAACATTGTGTCTTCTTTG-3'
		anti-sense	5'-CCGTCAAAAAGAATGTGTCCTTCT-3'
	Ex20	sense	5'-TGCTATTCTATTCTACCCGTGTT-3'
		anti-sense	5'-ACTCTAATTATTCAAAATGTAATTCAAATATTTC-3'
	Ex21	sense	5'-TTCAGTTGTATCAACACTTGTCC-3'
		anti-sense	5'-CATTGAGGAAGTTGTCTTGTATTTC-3'
	Ex2-1	sense	5'-TGGTGTTGCTCAGGAAGAG-3'
		anti-sense	5'-TTGTGTAGGTCCACCAACAGG-3'
	Ex2-2	sense	5'-GCCTACCGGAGACATGAGAA-3'
		anti-sense	5'-GGCCTACAGGGGTTCAAAT-3'

Table S2. Filtering process for variants from normal reference sequence (VRS) following whole exome sequencing (WES) in YUHL.

Individual	Total sequence reads	Matched Reads (percentage of reads)	Total number of variants detected	^a dbSNP138 (MAF<1%)	^b Variants filtered by 32 control	^c Nonsynonymous and splice variants	% c / a	Located within splice site	Deletion or Insertion	Stop codon gained or lost	Missense
YUHL8-21	56,886,008	56,772,683 (99.80%)	179,970	49,441	16,540	1,035	2.09%	76	46	12	901
YUHL10-21	58,952,558	58,843,748 (99.82%)	175,270	46,130	15,338	996	2.16%	66	31	11	888
YUHL13-21	88,416,680	88,248,060 (99.81%)	206,699	53,182	17,689	762	1.43%	44	38	15	665
YUHL14-21	66,659,216	66,531,054 (99.81%)	194,398	52,428	17,883	909	1.73%	55	37	9	808
YUHL20-21	71,029,998	70,889,041 (99.80%)	190,036	51,104	17,041	891	1.74%	70	37	8	776
YUHL21-21	78,198,704	77,247,208 (98.78%)	194,277	53,546	22,538	874	1.63%	38	55	17	764
YUHL24-21	85,635,052	85,401,914 (99.73%)	191,531	38,741	9,997	565	1.46%	38	30	8	489
YUHL25-21	108,081,258	107,763,230 (99.71%)	195,767	39,273	15,217	898	2.29%	54	77	16	751
YUHL26-21	96,145,100	95,832,419 (99.67%)	200,817	41,451	16,802	912	2.20%	74	64	5	769
YUHL36-21	96,689,608	94,539,588 (97.78%)	194,569	39,346	15,327	910	2.31%	61	73	17	759
YUHL40-21	58,508,176	58,080,725 (99.27%)	163,533	34,035	12,587	910	2.67%	67	65	13	765
YUHL43-21	50,266,852	49,975,337 (99.42%)	164,309	34,646	16,010	1,040	3.00%	95	92	11	842
YUHL44-21	51,690,290	51,376,008 (99.39%)	170,215	35,587	13,677	929	2.61%	82	63	17	767
Mean value / ^d SD	74,396,885 / 19,167,152	73,961,617 (99.41%)	186,261 / 14,076	43,762 / 7,450	15,896 / 2,967	895 / 122	2.04%	63 / 17	54 / 20	12 / 4	765 / 103

^aVariants which are not common dbSNP138 (MAF<1%)

^bVariants which are not shared by 32 control of healthy individuals.

^cVariants which are located in nonsynonymous and splice site

^dStandard deviation

Table S3. 72 known NSHL genes examined in this study.

#	Gene symbol	Gene Name	Accession #	MIM-phenotype #	Mode	Coding Exons
1	<i>ACTG1</i>	actin gamma 1	NM_001199954	102560	AD	6
2	<i>ADCY1</i>	adenylyl cyclase 1	NM_021116	103072	AR	20
3	<i>BSND</i>	barttin CLCNK type accessory beta subunit	NM_057176	606412	AR	4
4	<i>CCDC50</i>	coiled-coil domain containing 50	NM_178335	611051	AD	12
5	<i>CDH23</i>	cadherin related 23	NM_022124	605516	AR	68
6	<i>CEACAM16</i>	carcinoembryonic antigen related cell adhesion molecule 16	NM_001039213	614591	AD	7
7	<i>CIB2</i>	calcium and integrin binding family member 2	NM_006383	605564	AR	6
8	<i>CLDN14</i>	claudin 14	NM_144492	605608	AR	3
9	<i>COCH</i>	cochlin	NM_004086	603196	AD	12
10	<i>COL11A2</i>	collagen type XI alpha 2 chain	NM_080680	120290	AD	66
11	<i>DFNA5</i>	DFNA5, deafness associated tumor suppressor	NM_004403	608798	AD	10
12	<i>DFNB59</i>	deafness, autosomal recessive 59	NM_001042702	610219	AR	7
13	<i>DIABLO</i>	diablo IAP-binding mitochondrial protein	NM_019887	605219	AD	7
14	<i>DIAPH1</i>	diaphanous related formin 1	NM_001314007	602121	AD	29
15	<i>ELMOD3</i>	ELMO domain containing 3	NM_001135021	615427	AR	15
16	<i>EPS8</i>	epidermal growth factor receptor pathway substrate 8	NM_004447	600206	AR	21
17	<i>ESPN</i>	espin	NM_031475	606351	AR	13
18	<i>ESRRB</i>	estrogen related receptor beta	NM_004452	602167	AR	11
19	<i>EYA4</i>	EYA transcriptional coactivator and phosphatase 4	NM_004100	603550	AD	20
20	<i>FAM65B</i>	family with sequence similarity 65 member B	NM_014722	611410	AR	23

21	<i>GIPC3</i>	GIPC PDZ domain containing family member 3	NM_133261	608792	AR	6
22	<i>GJB2</i>	gap junction protein beta 2	NM_004004	121011	AD	2
23	<i>GPSM2</i>	G-protein signaling modulator 2	NM_001321039	609245	AR	16
24	<i>GRHL2</i>	grainyhead like transcription factor 2	NM_024915	608576	AD	16
25	<i>GRXCR1</i>	glutaredoxin and cysteine rich domain containing 1	NM_001080476	613283	AR	4
26	<i>GRXCR2</i>	glutaredoxin and cysteine rich domain containing 2	NM_001080516	615762	AR	3
27	<i>HGF</i>	hepatocyte growth factor	NM_000601	142409	AR	18
28	<i>HOMER2</i>	homer scaffolding protein 2	NM_199330	604799	AD	9
29	<i>ILDR1</i>	immunoglobulin like domain containing receptor 1	NM_001199799	609739	AR	8
30	<i>KARS</i>	lysyl-tRNA synthetase	NM_001130089	601421	AR	15
31	<i>KCNQ4</i>	potassium voltage-gated channel subfamily Q member 4	NM_004700	603537	AD	14
32	<i>LHFPL5</i>	lipoma HMGIC fusion partner-like 5	NM_182548	609427	AR	4
33	<i>LOXHD1</i>	lipoxygenase homology domains 1	NM_144612	613072	AR	40
34	<i>LRTOMT</i>	leucine rich transmembrane and O-methyltransferase domain containing	NM_001145309	612414	AR	9
35	<i>MARVELD2</i>	MARVEL domain containing 2	NM_001038603	610572	AR	7
36	<i>MET</i>	MET proto-oncogene, receptor tyrosine kinase	NM_001127500	164860	AR	21
37	<i>MIR96</i>	microRNA 96	NR_029512	611606	AD	1
38	<i>MSRB3</i>	methionine sulfoxide reductase B3	NM_001193460	613719	AR	8
39	<i>MYH14</i>	myosin heavy chain 14	NM_001145809	608568	AD	43
40	<i>MYH9</i>	myosin heavy chain 9	NM_002473	160775	AD	41
41	<i>MYO15A</i>	myosin XVA	NM_016239	602666	AR	65
42	<i>MYO3A</i>	myosin IIIA	NM_017433	606808	AR	35

43	<i>MYO6</i>	myosin VI	NM_004999	600970	AD	35
44	<i>MYO7A</i>	myosin VIIA	NM_000260	276903	AD	49
45	<i>OSBPL2</i>	oxysterol binding protein like 2	NM_144498	606731	AD	14
46	<i>OTOA</i>	otoancorin	NM_144672	607038	AR	28
47	<i>OTOF</i>	otoferlin	NM_194248	603681	AR	47
48	<i>OTOG</i>	otogelin	NM_001292063	604487	AR	56
49	<i>OTOGL</i>	otogelin like	NM_173591	614925	AR	58
50	<i>P2RX2</i>	purinergic receptor P2X 2	NM_174873	600844	AD	12
51	<i>PCDH15</i>	protocadherin related 15	NM_001142769	605514	AR	36
52	<i>POU3F4</i>	POU class 3 homeobox 4	NM_000307	300039	XR	1
53	<i>POU4F3</i>	POU class 4 homeobox 3	NM_002700	602460	AD	2
54	<i>PRPS1</i>	phosphoribosyl pyrophosphate synthetase 1	NM_002764	311850	XR	7
55	<i>RDX</i>	radixin	NM_001260492	179410	AR	16
56	<i>S1PR2</i>	sphingosine-1-phosphate receptor 2	NM_004230	605111	AR	2
57	<i>SERPINB6</i>	serpin family B member 6	NM_001195291	173321	AR	8
58	<i>SLC26A4</i>	solute carrier family 26 member 4	NM_000441	605646	AR	21
59	<i>SMPX</i>	small muscle protein, X-linked	NR_045617	300226	XR	6
60	<i>STRC</i>	stereocilin	NM_153700	606440	AR	29
61	<i>SYNE4</i>	spectrin repeat containing nuclear envelope family member 4	NM_001039876	615535	AR	8
62	<i>TBC1D24</i>	TBC1 domain family member 24	NM_001199107	613577	AR	8
63	<i>TECTA</i>	tectorin alpha	NM_005422	602574	AD	23
64	<i>TMC1</i>	transmembrane channel like 1	NM_138691	606706	AD	24
65	<i>TMIE</i>	transmembrane inner ear	NM_147196	607237	AR	4

66	<i>TMPRSS3</i>	transmembrane protease, serine 3	NM_024022	605511	AR	13
67	<i>TPRN</i>	taperin	NM_001128228	613354	AR	4
68	<i>TRIOBP</i>	TRIO and F-actin binding protein	NM_001039141	609761	AR	24
69	<i>TSPEAR</i>	thrombospondin type laminin G domain and EAR repeats	NM_001272037	612920	AR	13
70	<i>USH1C</i>	USH1 protein network component harmonin	NM_153676	605242	AR	27
71	<i>WFS1</i>	wolframin ER transmembrane glycoprotein	NM_001145853	606201	AD	8
72	<i>WHRN</i>	whirlin	NM_001083885	607928	AR	12

Table S5. Variants in autosomal dominant NSHL genes detected by WES in this study

Gene Symbol	Individual	Sex	Age of onset	Nucleotide change ^a	Amino acid change	Exon (zygosity, segregation)	Amino acid sequence conservation ^b	Frequencies in the dbSNP database ^c	Frequencies in the ExAC database ^d	Frequencies in the NBK database ^e	PP2 ^f	MT ^g	PROVEAN ^h	SIFT ⁱ
MYO7A	YUHL 26-21	Fm	8 yr	c.1094A>G	p.Asp365Gly	11 (het, M)	<i>D. rerio</i>	ND	ND	ND	Bn (0.341)	DC (0.999)	Del (-3.39)	Tol (0.307)
DFNA5	YUHL 44-21	MI	2 yr	c.116_119del AAAA	p.Lys39Argfs*24	2 (het, M)	NA	rs773853744 (MAF: -=0.00003/4)	ND	ND	NA	DC (1.000)	NA	NA

Abbreviations are as follows: Bn, benign; Dam, damaging; DC, disease causing; Del, deleterious; F, heterozygous mutation identified in father; Fm, female; het, heterozygous in affected individual; M, heterozygous mutation identified in mother; MAF, minor allele frequency; MI, male; NA, not applicable; ND, no data or DNA available; Neu, neutral; PD, probably damaging; PM, Polymorphism; PP2, PolyPhen-2 prediction score Humvar; PROVEAN, Protein Variation Effect Analyzer; SIFT, Sorting Intolerant from Tolerant; SNP, single nucleotide polymorphism; Tol, tolerant; yr, years.

^acDNA mutations are numbered according to human cDNA reference sequence NM_000260.3 (*MYO7A*), NM_004403.2 (*DFNA5*); +1 corresponds to the A of ATG translation initiation codon. ^bAmino acid residue is continually conserved throughout evolution including the species as indicated. ^cdbSNP database (<http://www.ncbi.nlm.nih.gov/SNP>). ^dExAC browser (<http://exac.broadinstitute.org/>). ^eNational Biobank of Korea, the Centers for Disease Control and Prevention. ^fPolyPhen-2 prediction score HumVar ranges from 0 to 1.0; 0 = benign, 1.0 = probably damaging (<http://genetics.bwh.harvard.edu/pph2/>).

^gMutation taster (<http://www.mutationtaster.org/>). ^hPROVEAN (<http://provean.jcvi.org/index.php>). ⁱSIFT (<http://sift.jcvi.org/>).

Table S6. Heterozygous variants in autosomal recessive NSHL genes detected by WES in this study

Individual	Gene Symbol	Sex	Age of onset	Nucleotide change ^a	Amino acid change	Exon	Amino acid sequence conservation ^b	Frequencies in the dbSNP database ^c	Frequencies in the ExAC database ^d	Frequencies in the NBK database ^e	PP2 ^f	MT ^g	PROVEAN ^h	SIFT
YUHL 13-21	<i>LOXHD1</i>	Ml	1 yr	c.3185C>T	p.Ser1062Leu	20	<i>D. rerio</i>	ND	ND	ND	PD (0.993)	DC (0.672)	Del (-4.43)	Dam (0.004)
	<i>GIPC3</i>	Ml	1 yr	c.58C>T	p.Pro20Ser	1	<i>M. musculus</i>	ND	ND	ND	Bn (0.003)	DC (0.945)	Neu (-0.21)	Tol (0.249)
YUHL 20-21	<i>LOXHD1</i>	Ml	2 yr	c.1810-2A>T	NA	13 (intron)	ND	ND	ND	A:0.00125945	NA	DC (1.000)	NA	NA
	<i>GRXCR2</i>	Ml	2 yr	c.88C>T	p.Arg30*	1	ND	ND	ND	ND	NA	DC (1.000)	NA	NA
YUHL 14-21	<i>PCDH15</i>	Fm	5 yr	c.4703A>G	p.Lys1568Arg	35	<i>X. tropicalis</i>	rs774523472 (C=0.00002/3)	3/120774 (no hom)	ND	Bn (0.149)	PM (0.956)	Neu (-0.18)	Dam (0.023)
YUHL 26-21	<i>MYO3A</i>	Fm	8 yr	c.2902G>A	p.Val968Ile	26	<i>D. rerio</i>	rs747578242 (A=0.000008/1)	1/121398 (no hom)	ND	PD (0.971)	DC (0.999)	Neu (-0.82)	Dam (0.045)
YUHL 36-21	<i>TSPEAR</i>	Fm	4 yr	c.1144A>G	p.Lys382Glu	7	<i>D. rerio</i>	rs782103811 (C=0.000008/1)	1/121366 (no hom)	C:0.00251889	Bn (0.225)	PM (0.908)	Neu (-1.10)	Tol (0.297)
YUHL 44-21	<i>KARS</i>	Ml	2 yr	c.1450T>G	p.Cys484Gly	12	<i>D. rerio</i>	rs772704062 (C=0.000008/1)	1/121136 (no hom)	ND	PD (0.989)	DC (0.999)	Del (-9.11)	Dam (0.01)
	<i>FAM65B</i>	Ml	2 yr	c.3176G>A	p.Arg1059His	23	<i>M. musculus</i>	rs753906236 (T=0.00009/2)	2/21828 (no hom)	ND	Bn (0.023)	DC (0.992)	Neu (-0.85)	Tol (0.1)

Abbreviations are as follows: Bn, benign; Dam, damaging; DC, disease causing; Del, deleterious; F, heterozygous mutation identified in father; Fm, female; het, heterozygous in affected individual; M, heterozygous mutation identified in mother; MAF, minor allele frequency; Ml, male; mo, month; NA, not applicable; ND, no data or DNA available; Neu, neutral; PD, probably damaging; PM, Polymorphism; PP2, PolyPhen-2 prediction score Humvar; PROVEAN, Protein Variation Effect Analyzer; SIFT, Sorting Intolerant from Tolerant; SNP, single nucleotide polymorphism; Tol, tolerant; yr, years.

^acDNA mutations are numbered according to human cDNA reference sequence NM_144612.6 (*LOXHD1*), NM_133261.2 (*GIPC3*), NM_001142763.1 (*PCDH15*), NM_001080516.1 (*GRXCR2*), NM_017433.4 (*MYO3A*), NM_144991.2 (*TSPEAR*), NM_001130089.1 (*KARS*), NM_014722.3 (*FAM65B*); +1 corresponds to the A of ATG translation initiation codon. ^bAmino acid residue is continually conserved throughout evolution including the species as indicated. ^cdbSNP database (<http://www.ncbi.nlm.nih.gov/SNP>). ^dExAC browser (<http://exac.broadinstitute.org/>). ^eNational Biobank of Korea, the Centers for Disease Control and Prevention. ^fPolyPhen-2 prediction score HumVar ranges from 0 to 1.0; 0 = benign, 1.0 = probably damaging (<http://genetics.bwh.harvard.edu/pph2/>). ^gMutation taster (<http://www.mutationtaster.org/>). ^hPROVEAN (<http://provean.jcvi.org/index.php>). ⁱSIFT (<http://sift.jcvi.org/>).

YUHL 44-21	Hemi	SSX3	chrX:48213531T>C	NM_021014.3	c.185-2A>G		50	50			No	No	No	PM (0.989)	No	No	No	
	De novo	CAND2	chr3:12858190G>A	NM_001162499.1	c.1759G>A	p.Val587Met	22	49	V	V	No	No	No	DC (0.999)	Probably Damaging (0.997)	Del (-2.88)	Dam (0)	No
	De novo	DOPEY2	chr21:37653848G>C	NM_005128.3	c.6099G>C	p.Gln2033His	34	76	Q	Q	No	No	No	DC (0.999)	Probably Damaging (0.998)	Del (-2.8)	Dam (0.008)	No
	De novo	ADAMTSL3	chr15:84506875C>G	NM_207517.2	c.635C>G	p.Ala212Gly	17	40	A	A	No	No	No	DC (0.999)	Probably Damaging (0.994)	Del (-2.8)	Dam (0)	No
	De novo	SWI5	chr9:131050954A>G	NM_001040011.1	c.667A>G	p.Lys223Glu	21	36	K		No	No	No	DC (0.961)	Probably Damaging (0.975)	Del (-2.8)	Dam (0.012)	No
	De novo	CEND1	chr11:788449T>C	NM_016564.3	c.128A>G	p.Glu43Gly	6	16	D	D	No	No	No	DC (0.819)	Possibly Damaging (0.466)	Del (-4.83)	Dam (0.005)	No

Table S8. Number of copy number variation detected by EXCAVATOR and ExomeDepth

#	Family ID	EXCAVATOR		ExomeDepth	
		CNV	biallelic deletions	CNV	biallelic deletions
1	YUHL8	111	4	168	3
2	YUHL10	138	5	185	8
3	YUHL13	142	9	185	8
4	YUHL14	99	5	181	7
5	YUHL20	144	3	184	10
6	YUHL21	95	2	113	1
7	YUHL24	112	10	148	5
8	YUHL25	132	8	121	5
9	YUHL26	121	9	190	9
10	YUHL36	112	5	176	9
11	YUHL40	148	12	151	10
12	YUHL43	139	9	114	5
13	YUHL44	144	6	135	6
Average		125.92	6.69	157.77	6.62