Table S1: List of screening strategies for participating families

Family	Homozygosity mapping	Direct Sequencing*	Targeted capture	Exome sequencing
HLRB10	Yes	Yes	-	-
HLRB2	Yes	Yes	-	-
HLRB7	Yes	Yes	-	-
HLGM05	Yes	-	Yes	-
HLAI-20	-	-	Yes	-
HLGM16	-	-	Yes	-
HLAI-15	Yes	-	Yes	-
HLAI-21	Yes	-	Yes	-
HLAM01B	Yes	-	-	Yes
HLAM05	Yes	-	Yes	Yes
HLAM06	-	-	Yes	-
HLAM10	Yes	-	Yes	-
HLAM12A	-	-	Yes	Yes
HLAM12B	-	-	-	Yes
HLMI01	Yes	Yes	-	-
HLRB3	Yes	Yes	-	-
HLAI-06	Yes	-	-	Yes
HLAM07	-	-	Yes	Yes
HLAI-10	-	-	-	Yes
HLAI-25	-	-	Yes	-
HLAI-08	Yes	-	Yes	Yes
HLAM02	Yes	Yes	-	-
HLAI-27	-	-	Yes	-
PHLAI-01	Yes	Yes	-	-
HLAI-04	Yes	Yes	-	-
HLAI-14	Yes	Yes	-	-
HLAI-17	Yes	-	-	Yes
HLAI-13	-	-	Yes	-
HLAM08	Yes	-	Yes	-
HLM1	Yes	Yes	-	-
HLMI02	Yes	Yes	-	-
HLAI-09	Yes	-	Yes	-
HLGM14	-	-	Yes	-
HLAI-01	Yes	-	Yes	-
HLGM06	Yes	Yes	-	-
HLAI-07	Yes	-	Yes	-
HLAI-19	Yes	-	Yes	-
HLGM12	-	-	Yes	-
HLRB5	Yes	Yes	-	-
HLAM04	Yes	-	Yes	-
HLAM11	-	-	Yes	-
HLRB11	Yes	Yes	-	Yes
HLAI-24	Yes	-	Yes	Yes
HLGM24	-	-	Yes	-
HLAI-11	Yes	-	-	Yes
HLGM19	-	-	Yes	-
HLAI-26	-	-	Yes	-
HLMR3	Yes	-	-	Yes
HLAI-16	Yes	-	Yes	-
HLAI-18	Yes	-	Yes	-
HLGM15	Yes	Yes	-	-
HLAI-23	-	-	Yes	-

HLRB6	Yes	Yes	-	-
HLRB4	Yes	-	Yes	-
HLGM17	Yes	-	-	Yes
HLAI-05	Yes	-	-	Yes
USH-1	Yes	-	Yes	-
HLRB12	Yes	Yes	-	-
HLRB9	Yes	-	-	-
HLRB13	Yes	-	Yes	-
HLGM02	Yes	-	Yes	Yes
HLGM03	Yes	-	Yes	-
HLGM04	Yes	-	-	-
HLGM07	Yes	-	Yes	-
HLGM08	Yes	-	Yes	Yes
HLGM09	Yes	-	-	-
HLGM10	Yes	-	-	-
HLGM11	Yes	-	-	-
HLGM13	Yes	-	-	-
HLGM18	Yes	-	-	-
HLGM20	Yes	-	-	-
HLGM21	Yes	-	-	-
HLGM22	Yes	-	-	-
HLGM23	Yes	-	Yes	-
HLGM26	Yes	-	-	-
HLAI-03	Yes	-	-	Yes
HLAI-22	Yes	-	Yes	Yes
HLAM01A	Yes	-	-	Yes
HLAM03	Yes	-	Yes	Yes
IHT01A	Yes	-	-	-
IHT02	Yes	-	Yes	-
HLMR1	Yes	-	-	-
HLMR4	Yes	-	-	-

Note: *GJB2* was excluded for all families by Sanger sequencing samples from multiple affected individuals in each pedigree and therefore the nine families with *GJB2* variants are not included in the table. *The genes implicated by homozygosity mapping were sequenced using Sanger sequencing.

Table S2: List of genes for targeted capture and massively parallel sequencing

Gene	Inheritance	Gene	Inheritance	Gene	Inheritance
ACTG1	Dominant	*OTOG*	Recessive	*SLITRK6*	Recessive
CCDC50	Dominant	*ELMOD3*	Recessive	*SUN1*	Recessive
CEACAM16	Dominant	*ESRRB*	Recessive	*SYNE4*	Recessive
CHD7	Dominant	*GIPC3*	Recessive	*VEZT*	Recessive
COCH	Dominant	*GJB6*	Recessive	*CDH23*	Recessive
COL11A1	Dominant	*GPR98*	Recessive	*CIB2*	Recessive
CRYM	Dominant	*GPSM2*	Recessive	*CLDN14*	Recessive
D1APH3	Dominant	*GRXCR1*	Recessive	*CLRN1*	Recessive
DFNA5	Dominant	*HGF*	Recessive	*COL4A4*	Recessive
DIABLO	Dominant	*ILDR1*	Recessive	*EPS8*	Recessive
DIAPH1	Dominant	*KARS*	Recessive	*ADCY1*	Recessive
DSPP	Dominant	*KCNQ1*	Recessive	*MYO6*	Recessive and dominant
EYA1	Dominant	*LOXHD1*	Recessive	*MYO7A*	Recessive and dominant
EYA4	Dominant	*LRTOMT*	Recessive	*TECTA*	Recessive and dominant
GRHL2	Dominant	*MARVELD2*	Recessive	*TMC1*	Recessive and dominant
KCNQ4	Dominant	*MSRB3*	Recessive	*WFS1*	Recessive and dominant
MIR96	Dominant	*MYO15A*	Recessive	*COL11A2*	Recessive and dominant
MYH14	Dominant	*MYO3A*	Recessive	*COL2A1*	Recessive and dominant
MYH9	Dominant	*OTOA*	Recessive	*COL4A3*	Recessive and dominant
MYO1A	Dominant	*OTOF*	Recessive	*ESPN*	Recessive and dominant
PAX3	Dominant	*PCDH15*	Recessive	*GJB2*	Recessive and dominant
POU4F3	Dominant	*PDZD7*	Recessive	*ABCA13*	Unknown
SEMA3E	Dominant	*PJVK*	Recessive	*COL4A5*	X-linked
SIX1	Dominant	*PTPRQ*	Recessive	*COL4A6*	X-linked
SIX5	Dominant	*RDX*	Recessive	*NDP*	X-linked
SLC17A8	Dominant	*SERPINB6*	Recessive	*PRPS1*	X-linked
SNAI2	Dominant	*STRC*	Recessive	*SMPX*	X-linked
SOX10	Dominant	*TMIE*	Recessive		
TCOF1	Dominant	*TMPRSS3*	Recessive		
TJP2	Dominant	*TPRN*	Recessive		
ATP2B2	Recessive	*TRIOBP*	Recessive		
BSND	Recessive	*USH1C*	Recessive		
COL9A1	Recessive	*USH1G*	Recessive		
DFNB59	Recessive	*USH2A*	Recessive		
EDN3	Recessive	*WHRN*	Recessive		
EDNRB	Recessive	*OTOGL*	Recessive		
ERCC6	Recessive	*PNPT1*	Recessive		
FGF3	Recessive	*S1PR2*	Recessive		
KCNE1	Recessive	*SLC26A4*	Recessive		
LHFPL5	Recessive	*SLC26A5*	Recessive		

Table S3: List of samples chosen for massively parallel sequencing and the implicated genes

Family	Samples	Target Capture	Exome	Gene ID	Locus Heterogeneity
HLGM05	1	Yes	-	*SLC26A4*	-
HLAI-20	1	Yes	-	*SLC26A4*	-
HLGM16	1	Yes	-	*SLC26A4*	-
HLAM01B	1	-	Yes	*SLC26A4*	Yes
HLAM06	1	Yes	-	*SLC26A4*	-
HLAM10	1	Yes	-	*SLC26A4*	-
HLAM12A	1	-	Yes	*SLC26A4*	Yes
HLAM05	1	Yes	Yes	*MYO15A*	-
HLAI-06	3	-	Yes	*MYO15A*	-
HLAM07	1	Yes	-	*MYO15A*	-
HLAI-10	3	-	Yes	*MYO15A*	-
HLAI-25	1	Yes	-	*MYO15A*	-
HLAI-08	1	Yes	-	-	-
HLAI-27	1	Yes	-	*TMC1*	-
HLAI-17	3	-	Yes	-	-
HLAI-13	1	Yes	-	*TMPRSS3*	-
HLAM08	1	Yes	-	*TMPRSS3*	-
HLAI-09	1	-	Yes	*OTOF*	-
HLGM14	1	Yes	-	*OTOF*	-
HLAI-01	1	-	Yes	*OTOF*	-
HLAI-07	1	Yes	-	-	-
HLAI-19	1	-	Yes	*MYO7A*	-
HLGM12	1	Yes	-	*MYO7A*	-
HLAM04	1	Yes	-	*CLDN14*	-
HLAM11	1	Yes	-	*CLDN14*	-
HLGM24	1	Yes	-	*CDH23*	-
HLAI-11	1	-	Yes	*GIPC3*	-
HLGM19	1	Yes	-	*TECTA*	-
HLAI-26	1	Yes	-	*TRIOBP*	-
HLMR3	1	-	Yes	*ESPN*	Yes
HLAI-16	1	-	Yes	*MYO6*	-
HLAI-18	1	Yes	-	*HGF*	Yes
HLAI-23	1	Yes	-	*BSND*	-
HLRB4	1	Yes	-	*PTPRQ*	-
HLGM17	1	-	Yes	*MET*	-
HLAI-05	1	-	Yes	*GRXCR2*	Yes
USH-1	1	Yes	-	*USH1C*	-
HLRB11	1	-	-	-	-
HLRB13	1	Yes	-	-	-

HLGM02	2	Yes	Yes	-	-
HLGM03	1	Yes	-	-	-
HLGM07	1	Yes	-	-	-
HLGM08	3	Yes	Yes	-	-
HLGM23	1	Yes	-	-	-
HLAI-03	1	-	Yes	-	-
HLAI-22	3	Yes	Yes	-	-
HLAI-24	1	Yes	Yes	-	-
HLAM01A	1	-	Yes	-	-
HLAM03	3	-	Yes	-	-
HLAM12B	2	-	Yes	-	Yes
IHT02	1	Yes	-	-	-

Table S4: References for the identified mutations

Gene	Family ID	Variant	Reference PMID
SLC26A4	HLRB10	c.170C>A:p.(Ser57X)	12676893
NM_000441.1	HLRB2	c.716T>A:p.(Val239Asp)	12676893
	HLRB7	c.716T>A:p.(Val239Asp)	12676893
	HLGM05	c.716T>A:p.(Val239Asp)	12676893
	HLAI-20	c.716T>A:p.(Val239Asp)	12676893
	HLGM16	c.965dupA:p.N322KfsX8	18813951
	HLAI-15	c.1337A>G:p.(Gln446Arg)	10700480
	HLAI-21	c.1337A>G:p.(Gln446Arg)	10700480
	HLAM01B	c.1337A>G:p.(Gln446Arg)	10700480
	HLAM06	c.1337A>G:p.(Gln446Arg)	10700480
	HLAM10	c.1337A>G:p.(Gln446Arg)	10700480
	HLAM12A	c.1667A>G:p.(Tyr556Cys)	9618167
	HLAM12B	c.1667A>G:p.(Tyr556Cys)	9618167
GJB2	HLAI-02	c.71G>A:p.(Trp24X)	9139825
NM_004004.5	HLAI-12	c.71G>A:p.(Trp24X)	9139825
	HLGM25	c.71G>A:p.(Trp24X)	9139825
	HLMS16	c.71G>A:p.(Trp24X)	9139825
	HLMS34	c.71G>A:p.(Trp24X)	9139825
	HLRB1	c.231G>A:p.(Trp77X)	9139825
	HLRB8	c.71G>A/c.231G>A p.(Trp24X)/p.(Trp77X)	9139825
	HLAM09	c.71G>A/c.231G>A p.(Trp24X)/p.(Trp77X)	9139825
	HLMR2	c.358_360 del: p.(Glu120del)	15967879
MYO15A	HLRB3	c.1185dupC: p.(Glu396ArgfsX36)*	22245518
NM_016239.3	HLAM05	c.1657delC:p.(Arg553GlyfsX76)	This report
	HLAI-06	c.2456C>A:p.(Ser819X)	This report
	HLAM07	c.3866+1G>A	17546645
	HLAI-10	c.6589C>T:p.(Gln2197X)	27375115
	HLAI-25	c.8158G>A:p.(Asp2720Asn)	This report
TMC1	HLAM02	c.100C>T:p.(Arg34X)	11850618
NM_138691.1	HLAI-27	c.596A>T:p.(Asn199Ile)*	26879195
	PHLAI-01	c.1166G>A:p.(Arg389Gln)	18985073
	HLAI-04	c.1404+1G>T*	26879195
	HLAI-14	c.1788C>A:p.(Ser596Arg)*	26879195
TMPRSS3	HLAI-13	c.208delC:p.(His70ThrfsX19)	11907649
NM_00024022.2	HLAM08	c.1219T>C:p.(Cys407Arg)	11424922
	HLM1	c.323–6 G>A:p.(Val108AlafsX132)	11137999
	HLMI02	c.323–6 G>A:p.Val108AlafsX132)	11137999
OTOF	HLAI-09	c.2965_2967del:p.(Phe989del)	This report
NM_194248.2	HLGM14	c.3289-1G>T	This report
	HLAI-01	c.4805G>T:p.(Gly1602Val)	This report
MYO7A	HLAI-19	c.1183C>T:p.(Arg395Cys)	This report
NM_000260.3	HLGM12	c.6354G>C:p.(Lys2118Asn)	This report
CLDN14	HLRB5	c.254T>A:p.(Val85Asp)	11163249
NM_144492.2	HLAM04	c.254T>A: p.(Val85Asp)	11163249
	HLAM11	c.254T>A: p.(Val85Asp)	11163249
CDH23	HLGM24	c.7814A>G:p.(Asn2605Ser)	This report
NM_022124.5			
GIPC3	HLAI-11	c.662C>T:p.(Thr221Ile)	21660509
NM_133261.2			

TECTA NM_005422.2	HLGM19	c.64+2T>C	This report
TRIOBP NM_001039141.2	HLAI-26	c.2968C>T:p.(Arg990X)	This report
ESPN NM_031475.2	HLMR3	c.2019dupG:p.(Leu674AlafsX72)	This report
MYO6 NM_004999.3	HLAI-16	c.1729_1741del:p.(Phe577IlefsX28)	This report
HGF NM_000601.4	HLAI-18	c.482+1986_1988delTGA	19576567
DFNB59 NM_001042702.3	HLGM15	c.1028G>C:p.(Cys343Ser)*	22617256
BSND NM_057176.2	HLAI-23	c.35 T>C:p.(Ile12Thr)	19646679
TPRN NM_001128228.1	HLRB6	c.42_52del11:p.(Gly15AlafsX150)	20170899
PTPRQ NM_001145026.1	HLRB4	c.189delC:p.(Glu65LysfsX95)	This report
MET NM_000245.2	HLGM17	c.2521T>G:p.(Phe841Val)*	25941349
GRXCR2 NM_001080516.1	HLAI-05	c.714dupT:p.(Gly239TrpfsX74)*	24619944
USH1C NM_005709.3	USH-1	c. 605dupC:p.(Gly203TrpfsX47)	This report
USH1G NM_173477.4	HLRB12	c.163_164+13del15:p.(Gly55GlyfsX56)*	20811388

*These variants were first identified segregating with hearing loss in members of families in this cohort and were reported previously by us. PMID; PubMed-Indexed for MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed).

Table S5: Pathogenic variants and their allele frequencies

Locus/Gene	Variant	dbSNP	Frequency	Reference PMID
DFNB4/*SLC26A4*	c.170C>A:p.(Ser57X)	*rs111033200*	0.000008236	12676893
NM_000441.1	c.716T>A:p.(Val239Asp)	*rs111033256*	0.0002389	12676893
	c.1337A>G:p.(Gln446Arg)	*rs768471577*	0.00008259	10700480
	c.1667A>G:p.(Tyr556Cys)	*rs763006761*	0.00002487	9618167
DFNB1/*GJB2*	c.71G>A:p.(Trp24X)	*rs104894396*	0.0005767	9139825
NM_004004.5	c.231G>A:p.(Trp77X)	*rs80338944*	0.0001483	9139825
	c.358_360 del: p.(Glu120del)	*rs80338947*	0.00006589	10544226
DFNB3/MYO15A	c.1657delC:p.(Arg553GlyfsX76)*	*rs750651809*	0.00000864	This report
NM_016239.3	c.3866+1G>A	*rs374742590*	0.000083	17546645
DFNB7/*TMC1*	c.100C>T:p.(Arg34X)	*rs121908073*	0.00005242	11850618
NM_138691.1	c.596A>T:p.(Asn199Ile)*	*rs141523206*	0.000008237	26879195
	c.1166G>A:p.(Arg389Gln)	*rs772640673*	0.00001648	18616530
DFNB8/*TMPRSS3*	c.208delC:p.(His70ThrfsX19)	*rs727503493*	0.0004412	11907649
NM_00024022 .2	c.1219T>C:p.(Cys407Arg)	*rs773780151*	0.00004954	11424922
DFNB29/*CLDN14*	c.254T>A:p.(Val85Asp)	*rs74315437*	0.000008385	11163249
NM_144492.2				
DFNB12/*USH1D*/*CDH23*	c.7814A>G:p.(Asn2605Ser) *	*rs780917129*	0.00005447	This report
NM_022124.5				
DFNB15/*72*/*95*/*GIPC3*	c.662C>T:p.(Thr221Ile)	*rs761543680*	0.00004152	21660509
NM_133261.2				
DFNB59/*DFNB59*	c.1028G>C:p.(Cys343Ser)*	*rs569088856*	0.00003315	22617256
NM_001042702.3				
DFNB73/BSND	c.35 T>C:p.(Ile12Thr)	*rs121908144*	0.00002473	19646679
NM_057176.2				
DFNB84/*PTPRQ*	c.189delC:p.(Glu65LysfsX95)*	*rs773511370*	0.00005612	This report
NM_001145026.1				

All allele frequencies are reported from exome aggregation consortium ExAC, (http://exac.broadinstitute.org/), except *MYO15A* c.3866+1G>A, which comes from the NHLBI Exome Sequencing Project database (http://evs.gs.washington.edu/EVS/). dbSNP, database of single nucleotide polymorphsims (http://www.ncbi.nlm.nih.gov/snp/); HL, hearing loss; References to the first description of the mutation in literature describing association with hearing loss are provided as PMID; PubMed-Indexed for MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed). *Previously not known to cause hearing loss; co-segregation with HL phenotype demonstrated in participating families of this cohort.

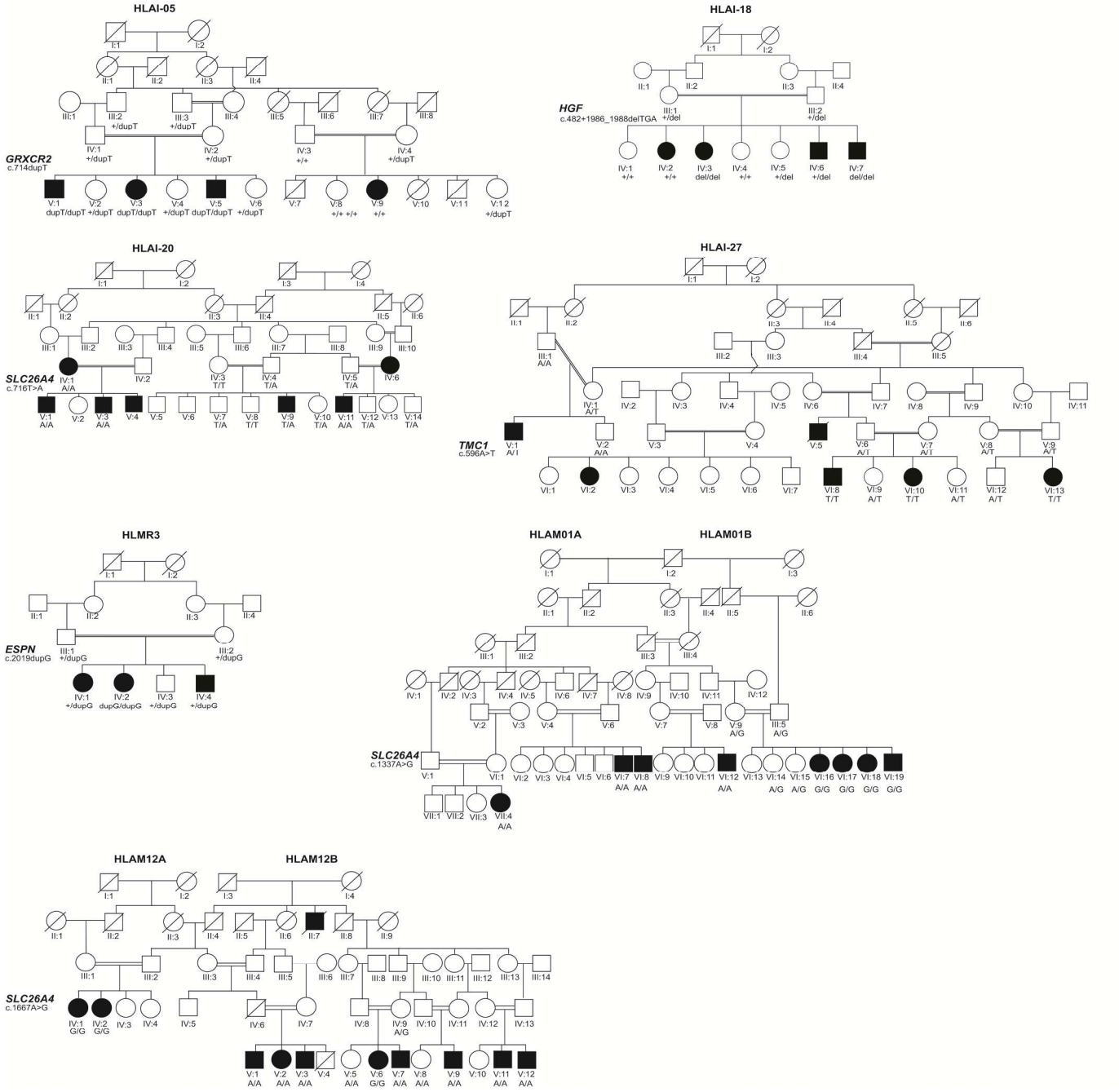

Fig. S1. Pedigrees of families exhibiting genetic heterogeneity. Genotypes are shown for variants in respective genes for all participants

RESULTS

Novel variants and hearing loss

Novel variants of ***MYO15A*** (OMIM 602666) contributed to hearing loss in four families. Three of these mutations create premature stop codons within exon 2 (1) (Table 1) and are predicted to result only in the loss of isoform 1 of *MYO15A* (2). A new missense mutation in exon 44, c.8158G>A, p.D2720N was identified in family HLAI-25. A previously observed variant causing profound deafness in Pakistan changed the evolutionary conserved p.Asp2720 (Fig. 2) to histidine (3).

Novel pathogenic variants in ***OTOF*** (OMIM 603681) were identified in three families segregating moderate or severe hearing loss. These included an in-frame deletion, a missense mutation and a splice site variant. The in-frame deletion is predicted to remove a conserved amino acid (Fig. 2) while p.(Gly1602Val) substitutes an evolutionary conserved glycine with a valine (Fig. 2). The splice site mutation, c.3989-1G>T is predicted to cause skipping of exon 27 which will delete 40 codons and remove 40 residues in-frame from the mature protein.

We identified two novel variants, c.1183C>T, p.(Arg395Cys) and c.6354G>C, p.(Lys2118Asn) in ***MYO7A*** (OMIM 276903) which are substitutions of conserved residues of myosin 7A (Fig. 2). The mutations co-segregated with severe hearing loss which was progressive for HLAI-19. The p.(Arg395Cys) affects the same residue that is mutated to histidine and is associated with moderate or severe to profound hearing loss in an Iranian family (4). The affected individuals who were homozygous for p.(Arg395Cys) in Pakistani family HLAI-19 had no manifestations of retinitis pigmentosa even at the age of 45 years. However, in the second decade of life one

affected member of family HLGM12 segregating a p.(Lys2118Asn) allele reported night vision loss, and thus this mutation is associated with Usher syndrome type 1B (OMIM 276900).

A family with predominantly moderate or severe hearing loss had a novel homozygous missense mutation c.7949A>G, p.(Asn2655Ser) which affects a conserved residue in CDH23 (Fig. 2). ***CDH23*** (OMIM 605516) variants cause severe to profound deafness with few exceptions. In some individuals with compound heterozygous mutations, hearing loss was moderate to severe (5) and two individuals homozygous for the p.(Phe1888Ser) allele of *CDH23* had normal hearing at low frequencies (6).

The pathogenic variants c.2968C>T,p.(Arg990X), c.2019dupG,p.(Leu674AlafsX72), c.1729_1741del,p.(Phe577IlefsX28) of *TRIOBP* (OMIM 609761), *ESPN* (OMIM 606351), and *MYO6* (OMIM 600970) respectively, link these genes for the first time as cause of moderate to severe hearing loss. All three variants are predicted to be null alleles and previous recessive mutations of these genes have been associated with profound deafness (7-9).

Novel mutations were identified in *TECTA* (OMIM 602574) c.64+2T>C, *PTPRQ* (OMIM 603317) c.189delC,p.(Glu65LysfsX95) and *USH1C* (OMIM 605242) c. 605dupC,p.(Gly203TrpfsX47). The variant of *TECTA* is located in the first intron and is therefore likely to result in loss of gene transcription due to failure of recognition of the first exon, or altered frame due to retention of intron or use of cryptic splice sites (10, 11). Both variants in *PTPRQ* and *USH1C* are frameshifting and are expected to lead to null alleles via nonsense mediated decay of the transcripts.

Novel variants of *DFNB59* (OMIM 610219), *USH1G* (OMIM 607696) and *TMC1* (OMIM 606706) were previously described by us (12-14).

Known variants and hearing loss

Two mutant alleles (p.(Trp24X) and p.(Trp77X) of ***GJB2*** (OMIM 121011) accounted for hearing loss in eight families in this cohort (15) while the affected individuals in the ninth family were homozygous for another variant p.(Glu120del). The p.(Trp24X) and p.(Trp77X) variants have been reported to cause profound deafness in hundreds of individuals of South Asian descent (16-19). However, the p.(Glu120del) variant was reported as a compound heterozygous mutation in one individual (20) and is annotated as a variant of unknown significance in the Human Gene Mutation Database (HGMD, http://www.hgmd.cf.ac.uk/, accessed June 2016).

We identified two known variants in ***MYO15A***. The variant c.3866+1G>A at the donor splice site of exon 5 observed in family HLAM07 in this study was previously reported in two families from Pakistan with profound deafness (3, 19). We observed a nonsense mutation c.6589 C>T, p.Q2197X in exon 31 of *MYO15A* in family HLAI-10 which has four affected members. One individual in this family has a severe hearing loss (PTA 83 dB HL). This mutation has also been observed in two families from Pakistan (21), however audiometric data was not available for comparison.

We found three known variants in ***TMPRSS3*** (OMIM 605511). In family HLAI-13 segregating a frameshift mutation c.208delC, p.(His70ThrfsX19) and in family HLAM08 segregating a missense p.(Cys407Arg) variant affecting TMPRSS3, a moderate to severe hearing loss was

observed in most affected members. This is in contrast to the profound deafness manifested by the affected individuals due to homozygosity of these same alleles as reported in other studies (22-24). In addition, the hearing loss in two families HLM1 and HLMI02 was due to a cryptic acceptor splice site variant (25) of *TMPRSS3* in intron 4 (Table 1). In family HLM1, a similar childhood onset hearing loss, progressing to profound deafness by the second decade of life was present as that reported in another family with the same mutation (25), while in family HLMI02 hearing loss was of childhood onset (3-4 years) and the degree was moderate or severe at the age of 22 years.

We identified one missense variant of ***CLDN14*** (OMIM 605608) which caused the phenotype in three families. Our audiometric findings for family HLRB5 (26) and two other families (Table 1) demonstrated that hearing loss can vary in severity due to *CLDN14* mutations, an observation supported by other studies (27, 28).

In two affected individuals with progressive and moderate to severe hearing loss of family HLAI-18, we found a variant of ***HGF*** (OMIM 142409) which segregated with progressive and severe hearing loss (73 dB HL). This same variant was previously reported to cause profound deafness in other affected individuals from Pakistan (29).

The known variants of *GIPC3* (OMIM 608792) and *BSND* (OMIM 606412) were identified in two families (Table 1) which segregated with similar progressive or moderate to severe phenotype as manifested by other families with the identical mutations (30, 31).

The progressive, moderate to severe hearing loss of family HLRB6 with a known *TPRN* (OMIM 613354) variant was previously described by us (32).

Supplementary References

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