Diagnostic Yield of Targeted Hearing Loss Gene Panel Sequencing
in a Large German Cohort with a Balanced Age Distribution
from a Single Diagnostic Center: An Eight-Year Study

Supplemental Digital Content 4.
Table including all Genetic Variants of Genetically Diagnosed Patients Undergoing Targeted Gene Analysis (in alphabetical order).

ID	Gene transcript	Variant 1 (protein change 1)	Variant type	Variant 2 (protein change 2)	Variant type	Zyg	Clin Var	DVD	ACMG/ AMP	ACMG/AMP rules applied	Seg
25	*ACTG1* NM_001199954.1	c.721G>A (p.(Glu241Lys))	Missense	-		Het	LP	P	LP	PS1_Strong, PM2_Moderate, PP3_Supporting	ND
39	*CDH23* NM_022124.5	c.3215C>A (p.(Ala1072Asp))	Missense	c.3215C>A (p.(Ala1072Asp))	Missense	Hom	US	P	LP; LP	PS1_Supporting, PM2_Moderate, PM3_Supporting, PP3_Supporting; PS1_Supporting, PM2_Moderate, PM3_Supporting, PP3_Supporting	ND
286	*COCH* NM_001347720.1	c.346C>T (p.(Pro116Ser))	Missense	-		Het	P	P	LP	PS1_Strong, PM2_Moderate, PP3_Supporting	ND
262*	*COL11A1* NM_080629.2	c.652-1G>C (p.?)	Splice acceptor	-		Het	LP	LP	LP	PS2_Supporting, PS3_Supporting, PM2_Moderate; PP1_Supporting, PP3_Supporting	Yes
58	*COL11A1* NM_080629.2	c.2644C>T (p.(Arg882Trp))	Missense	-		Het	NL	US	LP	PM2_Moderate, PP3_Strong	ND
67	*COL11A1* NM_080630.3	c.2930G>C (p.(Gly977Ala))	Missense	-		Het	NL	NL	LP	PM1_Moderate, PM2_Moderate, PP3_Strong	ND
273	*COL11A1* NM_080629.2	c.4338+2T>C (p.?)	Splice donor	-		Het	LP	NL	LP	PS2_Supporting, PS3_Supporting, PM2_Moderate, PP1_Supporting, PP3_Supporting	Yes

56	*COL2A1* NM_001844.4	c.1364C>T (p.(Thr455Met))	Missense & splice region	-		Het	NL	P	LP	PP1_Moderate, PP3_Strong, BS2_Strong	Yes
255	*COL4A3* NM_080630.3	c.4421T>C (p.(Leu474Pro))	Missense	-		Het	C	P	LP	PS1_Strong, PM2_Moderate, PP3_Supporting	ND
270	*COL4A3* NM_000091.3	c.4421T>C (p.(Leu474Pro)	Missense	-		Het	C	P	LP	PS1_Strong, PM2_Moderate, PP3_Supporting	ND
32	*COL4A3* NM_000091.3	c.4882T>G (p.(Ser1628Ala))	Missense	-		Het	US	US	P	PM2_Moderate, PP1_Strong, PP4_Strong	Yes
214	*COL4A5* NM_033380.2	c.4706G>A (p.(Arg1569Gln))	Missense & splice region	-		Hemi	P	P	LP	PVS1_Strong, PM2_Moderate, PP4_Moderate	ND
230	*COL9A2* NM_001852.3	c.1510C>T (p.(Arg540*))	Stop gained	c.1510C>T (p.(Arg540*))	Stop gained	Hom	NL, NL	US, US	LP; LP	PVS1_Strong, PM2_Moderate; PVS1_Strong, PM2_Moderate	ND
279	*DIAPH1* NM_005219.4	c.3268dup (p.(Met1090Asnfs*13))	Frameshift	-		Het	LP	LP	LP	PVS1_Strong, PM2_Moderate	ND
277	*DIAPH3* NM_001042517.1	c.2266-2A>G (p.?)	Splice acceptor	-		Het	US	US	LP	PVS1_Strong, PM2_Moderate	ND
127	*EDNRB* NM_001201397.1	c.18T>A (p.(Cys6*))	Stop gained	-		Het	NL[#]	US	LP	PVS1_Strong, PM2_Moderate, PP4_Supporting	ND
247	*EDNRB* NM_000115.4	c.878dup (p.(Tyr293*))	Nonsense	-		Het	LP	NL	LP	PVS1_Strong, PM2_Moderate	ND
120	*EYA4* NM_001301013.1	c.1481dup (p.(Glu496Argfs*4))	Frameshift	-		Het	NL	NL	LP	PVS1_Strong, PM2_Moderate	ND
224	*GATA3* NM_001002295.1	c.153dup (p.(Asn52*))	Nonsense	-		Het	NL	NL	LP	PVS1_Strong, PM2_Moderate	ND

315[$]	*GJB2* NM_004004.5	c.-23+1G>A (p.?)	Splice donor	c.-23+1G>A (p.?)	Splice donor	Hom	P, P	P, P	P; P	PVS1_Strong, PS3_Strong, PP3_Supporting; PVS1_Strong, PS3_Strong, PP3_Supporting	ND
290	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.35del (p.(Gly12Valfs*2))	Frameshift	Hom	P, P,	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS3_Strong	ND
296[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.35del (p.(Gly12Valfs*2))	Frameshift	Hom	P, P	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS3_Strong	ND
297[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.35del (p.(Gly12Valfs*2))	Frameshift	Hom	P, P	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS3_Strong	ND
298[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.35del (p.(Gly12Valfs*2))	Frameshift	Hom	P, P	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS3_Strong	ND
304[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.139G>T (p.(Glu47*))	Stop gained	Comp het	P, P	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS1_Strong, PM2_Moderate, PM3_Moderate, PM5_Moderate	ND
305[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.313_326del (p.(Lys105Glyfs*5))	Frameshift	Comp het	P, P	P, P	P; LP	PVS1_Strong, PS3_Strong; PVS1_Strong, PM2_Moderate, PM3_Moderate	Yes
306[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.269T>C (p.(Leu90Pro))	Missense	Comp het	P, P	P, P	P; P	PVS1_Strong, PS3_Strong; PS1_Strong, PM2_Moderate, PM3_Supporting, PM5_Moderate, PP3_Supporting	ND

307[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.139G>T (p.(Glu47*))	Stop gained	Comp het	P, P	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS1_Strong, PM2_Moderate, PM3_Moderate, PM5_Moderate	Yes
308[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.35del (p.(Gly12Valfs*2))	Frameshift	Hom	P, P,	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS3_Strong	ND
309[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.35del (p.(Gly12Valfs*2))	Frameshift	Hom	P, P,	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS3_Strong	Yes
310[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.35del (p.(Gly12Valfs*2))	Frameshift	Hom	P, P,	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS3_Strong	ND
311[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.313_326del (p.(Lys105Glyfs*5))	Frameshift	Comp het	P, P	P, P	P; LP	PVS1_Strong, PS3_Strong; PVS1_Strong, PM2_Moderate, PM3_Moderate	ND
314[$]	*GJB2* NM_004004.5	c.35del (p.(Gly12Valfs*2))	Frameshift	c.35del (p.(Gly12Valfs*2))	Frameshift	Hom	P, P,	P, P	P; P	PVS1_Strong, PS3_Strong; PVS1_Strong, PS3_Strong	ND
90	*GJB2* NM_004004.5	c.71G>A (p.(Trp24*))	Stop gained	c.71G>A (p.(Trp24*))	Stop gained	Hom	P, P	P, P	P; P	PVS1_Strong, PS3_Moderate, PM2_Moderate, PM3_Moderate; PVS1_Strong, PS3_Moderate, PM2_Moderate, PM3_Moderate	ND
302[$]	*GJB2* NM_004004.5	c.71G>A (p.(Trp24*))	Stop gained	c.71G>A (p.(Trp24*))	Stop gained	Hom	P, P	P, P	P; P	PVS1_Strong, PS3_Moderate, PM2_Moderate, PP1_Supporting; PVS1_Strong, PS3_Moderate, PM2_Moderate, PP1_Supporting	Yes

312*[$]	*GJB2* NM_004004.5	c.71G>A (p.(Trp24*))	Stop gained	c.71G>A (p.(Trp24*))	Stop gained	Hom	P, P	P, P	P; P	PVS1_Strong, PS3_Moderate, PM2_Moderate, PM3_Moderate; PVS1_Strong, PS3_Moderate, PM2_Moderate, PM3_Moderate	Yes
294[$]	*GJB2* NM_004004.5	c.109G>A (p.(Val37Ile))	Missense	c.109G>A (p.(Val37Ile))	Missense	Hom	P, P	P, P	P; P	PS1_Very strong, PM3_Supporting, PM5_Moderate, PP3_Supporting; PS1_Very strong, PM3_Supporting, PM5_Moderate, PP3_Supporting	ND
287	*GJB2* NM_004004.5	c.269T>C (p.(Leu90Pro))	Missense	c.269T>C (p.(Leu90Pro))	Missense	Hom	P, P	P, P	P; P	PS1_Strong, PM2_Moderate, PM3_Supporting, PM5_Moderate, PP3_Supporting; PS1_Strong, PM2_Moderate, PM3_Supporting, PM5_Moderate, PP3_Supporting	ND
211	*KCNQ4* NM_004700.3	c.1251del (p.(Cys418Alafs*78))	Frameshift	-		Het	NL	NL	LP	PVS1_Strong, PM2_Moderate	ND
115*	*LOXHD1* NM_144612.6	c.1904T>C (p.(Leu635Pro))	Missense	c.2314A>T (p.(Ile772Phe))	Missense	Comp het	NL, NL	LP, LP	LP; LP	PM2_Supporting, PM5_Moderate, PP1_Moderate, PP3_Supporting; PM2_Moderate, PM3_Moderate, PP1_Moderate, PP3_Supporting	Yes
59	*LOXHD1* NM_144612.6	c.3061+1G>A (p.?)	Splice donor	c.5144del (p.(Asn1715Thrfs*4))	Frameshift	Comp het	P, NL	US, US	LP; LP	PVS1_Strong, PM2_Moderate; PVS1_Strong, PM2_Moderate	ND

89	*LOXHD1* NM_144612.6	c.5721T>A (p.(Tyr1907*))	Nonsense	c.5721T>A (p.(Tyr1907*))	Nonsense	Hom	NL, NL	US, US	LP; LP	PVS1_Strong, PM2_Moderate, BP4_Supporting; PVS1_Strong, PM2_Moderate, BP4_Supporting	ND
246	*MANBA* NM_005908.3	c.1236G>A (p.(Trp412*))	Stop gained	c.1236G>A (p.(Trp412*))	Stop gained	Hom	LP, LP	LP, LP	LP; LP	PVS1_Strong, PM2_Moderate; PVS1_Strong, PM2_Moderate	ND
257	*MARVELD2* NM_001038603.2	c.880_890del (p.(Phe294Argfs*17))	Frameshift	c.1331+2T>C (p.?)	Splice donor	Comp het	LP, LP	LP, P	LP; LP	PVS1_Strong, PM2_Moderate, PM3_Supporting; PVS1_Strong, PM2_Moderate, PM3_Supporting	Yes
259	*MITF* NM_001354604.1	c.1180-2A>G (p.?)	Splice acceptor	-		Het	LP	LP	LP	PVS1_Strong, PM2_Moderate	ND
23	*MYO15A* NM_016239.3	c.1137del (p.(Tyr380Metfs*64))	Frameshift	c.8183G>A (p.(Arg2728His))	Missense	Comp het	P, LP	P, P	P; P	PVS1_Very strong, PS1_Strong, PM2_Supporting, PP1_Supporting; PS1_Strong, PM2_Moderate, PM3_Moderate, PP3_Supporting	ND
140	*MYO15A* NM_016239.3	c.1137del (p.(Tyr380Metfs*64))	Frameshift	c.2677C>T (p.(Arg893*))	Stop gained	Comp het	P, NL	P, US	P; LP	PVS1_Very strong, PS1_Strong, PM2_Supporting, PM3_Moderate, PP1_Supporting; PVS1_Strong, PM2_Moderate, PM3_Moderate, PP1_Supporting	Yes
289*	*MYO15A* NM_016239.3	c.4351G>A (p.(Asp1451Asn))	Missense	c.4351G>A (p.(Asp1451Asn))	Missense	Hom	P, P	P, P	P; P	PS1_Very strong, PM2_Moderate, PM3_Supporting, PP1_Supporting, PP3_Supporting; PS1_Very strong, PM2_Moderate, PM3_Supporting, PP1_Supporting, PP3_Supporting	Yes

99	*MYO15A* NM_016239.3	c.9620G>T (p.(Arg3207Arg))	Missense	c.9620G>T (p.(Arg3207Arg))	Missense	Hom	LP, LP	NL, NL	LP; LP	PM2_Moderate, PM3_Supporting, PM5_Strong, PP3_Suporting; PM2_Moderate, PM3_Supporting, PM5_Strong, PP3_Supporting	ND
181	*MYO6* NM_004999.3	c.866_869del (p.(Lys289Argfs*17))	Frameshift	-		Het	NL[#]	P	LP	PVS1_Strong, PM2_Moderate	ND
68	*MYO6* NM_004999.3	c.2397C>A (p.(Cys799*))	Nonsense	-		Het	NL	NL	LP	PVS1_Strong, PM2_Moderate	ND
112	*MYO7A* NM_000260.3	c.1211G>A (p.(Gly404Glu))	Missense	-		Het	NL[#]	NL	LP	PM2_Strong, PP1_Moderate, PP3_Supporting	Yes
299[$]	*OTOF* NM_194248.2	c.2719C>T (p.(Gln907*))	Nonsense	c.5203C>T (p.(Arg1735Trp))	Missense	Comp het	NL[#]	NL	LP; LP	PVS1_Strong, PM2_Moderate, PM3_Moderate; PS1_Strong, PM2_Moderate, PM5_Moderate, PP3_Supporting	Yes
51	*PAX3* NM_181459.3	c.167G>T (p.(Arg56Leu))	Frameshift	-		Het	P	P	LP	PS1_Moderate, PM2_Moderate, PM5_Moderate, PP3_Supporting	ND
172	*POU4F3* NM_002700.2	c.545C>G (p.(Ser182*))	Nonsense	-		Het	NL	NL	LP	PVS1_Strong, PM2_Moderate	ND
74	*SLC26A4* NM_000441.1	c.703C>T (p.(Gln235*))	Nonsense	c.1280C>A (p.(Ser427Tyr))	Missense	Comp het	NL, NL	NL, NL	P; LP	PVS1_Strong, PM2_Moderate, PM3_Supporting, PP4_Supporting; PM2_Moderate, PM3_Supporting, PP3_Supporting, PP4_Supporting	ND
278	*SLC26A4* NM_000441.1	c.707T>C (p.(Leu236Pro))	Missense	c.2145G>T (p.(Lys715Asn))	Missense	Comp het	P, LP	P, P	LP; LP	PS1_Strong, PM2_Supporting, PM5_Moderate, PP3_Supporting; PS1_Strong, PM2_Supporting, BP4_Supporting	ND

300[$]	*SLC26A4* NM_000441.1	c.918+1G>T (p.?)	Splice donor	c.1001+1G>A (p.?)	Splice donor	Comp het	LP, P	LP, P	P; P	PVS1_Strong, PS1_Strong, PM2_Moderate, PP4_Supporting; PVS1_Strong, PS1_Strong, PM2_Supporting, PM3_Moderate, PP4_Supporting	ND
65	*SLC26A4* NM_000441.1	c.1001+1G>A (p.?)	Splice donor	c.2219G>T (p.(Gly740Val))	Missense	Comp het	P, US	P, P	P; LP	PVS1_Strong, PM2_Supporting, PM3_Moderate, PP4_Supporting; PM2_Supporting, PM3_Moderate, PP4_Supporting	ND
41	*SMPX* NM_014332.2	c.140del (p.(Pro47Leufs*34))	Frameshift	-		Hemi	NL	NL	LP	PVS1_Strong, PM2_Moderate	ND
88	*SOX10* NM_006941.3	c.570C>A (p.(Cys190*))	Stop gained	-		Het	NL	P	P	PVS1_Strong, PM2_Moderate, PP4_Supporting	ND
86	*STRC* NM_153700.2	c.(?_3499)_ (4993_?)del	Partial deletion	c.(?_3499)_ (4993_?)del	Partial deletion	Hom	P, P	NL, NL	P; P	N/A	ND
250	*TECTA* NM_005422.2	c.2359del (p.(Glu787LysfsX4))	Frameshift	-		Het	LP	LP	LP	PVS1_Strong, PM2_Moderate	ND
206	*TECTA* NM_005422.2	c.2785del (p.(Val929Trpfs*2))	Frameshift	c.2367G>A (p.(Lys789=))	Synonymous	Comp het	NL, NL	NL, NL	LP; LP	PVS1_Strong, PM2_Moderate; PVS1_Strong, PM2_Moderate	ND
202	*TFAP2A* NM_003220.2	c.9G>A (p.(Trp3*))	Nonsense	-		Het	NL	NL	LP	PVS1_Strong, PM2_Moderate	ND
265	*TMIE* NM_147196.2	c.250C>T (p.(Arg84Trp))	Missense	c.250C>T (p.(Arg84Trp))	Missense	Hom	P, P	P, P	LP; LP	PS1_Moderate, PM2_Moderate, PM5_Moderate, PP3_Supporting; PS1_Moderate, PM2_Moderate, PM5_Moderate, PP3_Supporting	Yes
83*	*TMPRSS3* NM_024022.2	c.208del (p.(His70Thrfs*19))	Frameshift & splice region	c.413C>A (p.(Ala138Glu))	Missense	Comp het	P, P	P, P	LP; LP	PVS1_Strong, PM2_Supporting, PM5_Moderate; PS1_Strong, PM2_Moderate, PP3_Supporting	ND

288	*TMPRSS3* NM_024022.2	c.316C>T (p.(Arg106Cys))	Missense	c.413C>A (p.(Ala138Glu))	Missense	Comp het	LP, P	P, P	LP; LP	PS1_Strong, PM2_Supporting, PP3_Supporting; PS1_Strong, PM1_Moderate, PP3_Supporting	ND
55	*TMPRSS3* NM_024022.2	c.413C>A (p.(Ala138Glu))	Missense	c.965C>A (p.(Pro322His))	Missense	Comp het	P, NL	P, NL	LP; LP	PS1_Strong, PM2_Moderate, PP3_Supporting; PM2_Moderate, PM3_Moderate, PP3_Moderate	ND
271	*USH2A* NM_206933.2	c.5118G>A (p.(Trp1706*))	Stop gained	c.5118G>A (p.(Trp1706*))	Stop gained	Hom	P, P	P, P	LP; LP	PVS1_Strong, PM2_Moderate; PVS1_Strong, PM2_Moderate	ND
276	*USH2A* NM_206933.2	c.5776+1G>A (p.?)	Splice donor	c.5776+1G>A (p.?)	Splice donor	Hom	P, P	P, P	P; P	PVS1_Strong, PS1_Strong, PM2_Moderate, PM3_Supporting; PVS1_Strong, PS1_Strong, PM2_Moderate, PP3_Supporting	ND
197	*WFS1* NM_001145853.1	c.1316T>G (p.(Phe439Cys))	Missense	-		Het	LP	P	LP	PS1_Strong, PM1_Moderate, PP3_Supporting	ND
252*	*WFS1* NM_006005.3	c.1371G>T (p.(Arg457Ser))	Missense	-		Het	C	P	LP	PS1_Strong, PM2_Moderate, PM5_Moderate, PP3_Supporting	Yes
243	*WFS1* NM_006005.3	c.2020G>A (p.(Gly674Arg))	Missense	-		Het	C	P	LP	PS1_Strong, PM5_Moderate, PP3_Supporting	ND
148	*WFS1* NM_006005.3	c.2054G>A (p.(Arg685His))	Missense	-		Het	US	US	LP	PS1_Strong, PM2_Moderate, PM5_Moderate, PP3_Supporting	ND

Abbreviations (in alphabetical order):
ACMG/AMP, American College of Medical Genetics and Genomics and the Association for Molecular Pathology; B, benign; C, conflicting interpretations of pathogenicity; Comp het, compound heterozygous; D, deleterious; DC, disease causing; Del, deletion; DVD, deafness variation database; Het, heterozygous; Hom, homozygous; LB, likely benign; LP, likely pathogenic; MT, MutationTaster; N/A, not applicable; ND, not determined; NL, not listed; P, pathogenic; PP2, PolyPhen-2; Seg, segregation testing; T,

tolerated; US, uncertain significance; Zyg, zygosity.

A question mark represents uncertainty about compound heterozygosity.
* Index patient of a family; other family members are omitted from this table.
[#] Variant is not listed in ClinVar but linked to dbSNP. The variant type is named after the DVD (Azaiez et al. 2018) or according to VarSome.com (Kopanos et al. 2019) for variants that were not listed in the DVD.
[$] Causal variants derived from single-gene analysis.

REFERENCES

Azaiez, H., Booth, K. T., Ephraim, S. S., et al. (2018). Genomic Landscape and Mutational Signatures of Deafness-Associated Genes. *Am J Hum Genet, 103*, 484-497.

Kopanos, C., Tsiolkas, V., Kouris, A., et al. (2019). VarSome: The human genomic variant search engine. *Bioinformatics, 35*, 1978–1980.