**Table S4.** Summary of positive molecular results (children and adults (patient 62 and 63)). AD = autosomal dominant, AR= autosomal recessive, HL= hearing loss, LDS= Loeys-Dietz Syndrome, L.P. = Likely Pathogenic, MIM= Mendelian Inheritance in Man, N.A.= not applicable, p= protein, P.=Pathogenic, Pt.=Patient, rs= Reference SNP, XL = X-linked.

| Gene ID | Molecular Results | Rs Number | ACMG classification | Transmission type | Phenotype (Phenotype MIM number) | Syndromic | Inheritance | Pt. |
|---|---|---|---|---|---|---|---|---|
| *COL4A5* | heterozygous c.1525G>C, p.(Gly509Arg) | N.A. | L.P. (class IV) | XL | Alport syndrome, 1 X-linked (MIM: 301050) | Yes potentially | *De novo* | *1* |
| *USH1G* | homozygous c.1373A>T, p.(Asp458Val) | rs397517925 | L.P. (class IV) | AR | Usher syndrome, 1G (MIM: 606943) | Yes | Inherited in trans | *2* |
| *GJB2* | compound heterozygous for c.35delG, p.(Gly12Valfs*2) ; heterozygous c.101T>C, p.(Met34Thr) | rs80338939, rs35887622 | P. (class V)/P. (class V) | AR | Deafness, autosomal recessive 1A (MIM: 220290) | No | Inherited in trans | *3* |
| *GJB2* | compound heterozygous c.35del, p.(Gly12Valfs*2) ; c.139G>T, p.(Glu47*) | rs80338939, rs104894398 | P. (class V)/P. (class V) | AR | Deafness, autosomal recessive 1A (MIM: 220290) | No | Inherited in trans | *8* |
| *GJB2* | heterozygous c. 223C>T, p.(Arg75Trp) | rs104894402 | P. (class V) | AD | Keratoderma, palmoplantar, with deafness (MIM: 148350) | Yes | *De novo* | *20* |
| *SIX1* | heterozygous c.386A>C, p.(Tyr129Ser) | rs104894478 | P. (class V) | AD | Branchiootic syndrome, 3 (MIM: 608389) ; Deafness, autosomal dominant 23 (MIM:605192) | Yes | *De novo* | *4* |

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|---|---|---|---|---|---|---|---|---|
| *LARS2* | compound heterozygous c.457A>C, p.(Asn153His); c.1565C>A, p.(Thr522Asn) | rs786205560, rs199589947 | L.P. (class IV) / P. (class V) | AR | Perrault syndrome, 4 (MIM: 615300) | Yes ovarian failure diagnosed after molecular diagnosis | Inherited in trans | *5* |
| *ILDR1* | homozygous c.942C>A, p.(Cys314*) | rs752714222 | P. (class V) | AR | Deafness, autosomal recessive 42 (MIM: 609646) | No | Inherited in trans | *6* |
| *ACTG1* | heterozygous c.440G>A, p.(Arg147His) | N.A. | L.P. (class IV) | AD | Deafness, autosomal dominant 20/26 (MIM: 604717) | No | *De novo* | *7* |
| *ACTG1* | heterozygous c.826G>A, p.(Glu276Lys) | N.A. | L.P. (class IV) | AD | Deafness, autosomal dominant 20/26 (MIM: 604717) | No | *De novo* | *16* |
| *ACTG1* | heterozygous c.830C>T p.(Thr277Ile) | N.A. | P. (class V) | AD | Deafness, autosomal dominant progressive 20/26 (MIM: 604717), Baraitser-Winter syndrome (MIM: 614853) | Yes potentially | *De novo* | *30* |
| *GATA3* | heterozygous c.778+1G>A, p.(?) | N.A. | P. (class V) | AD | Hypoparathyroidism, sensorineural deafness, and renal dysplasia (MIM: 146255) | Yes | *De novo* | *9* |
| *GATA3* | heterozygous c.431delG, p.(Gly144Alafs*51) | rs1588377948 | P. (class V) | AD | Hypoparathyroidism, sensorineural deafness, and renal dysplasia (MIM: 146255) | Yes | *De novo* | *19* |
| *SLC17A8* | heterozygous c.634C>A, p.(Pro212Thr) | N.A. | L.P. (class IV) | AD | Deafness, autosomal dominant 25 (MIM: 605583) | No | Inherited from mother without HL | *10* |
| *LOXHD1* | homozygous c.3061+1G>A, p.(?) | rs537227442 | P. (class V) | AR | Deafness, autosomal recessive 77 (MIM: 613079) | No | Inherited one variant from mother/father N.A. | *11* |

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|---|---|---|---|---|---|---|---|---|
| *OTOA* | Compound heterozygous for a gene conversion between *OTOA* gene and *OTOAP1* pseudogene; deletion of *OTOA* | N.A. | P. (class V) | AR | Deafness, autosomal recessive 22 (MIM: 607039) | No | Inherited in trans | *17* |
| *WFS1* | heterozygous c.2051C>T, p.(Ala684Val) | rs387906930 | P. (class V) | AD | Wolfram-like syndrome, autosomal dominant (MIM: 614296) | Yes optic atrophy discovered after molecular diagnosis | *De novo* | *18* |
| *STRC* | compound heterozygous *CKMT1B, STRC, CATSPER2* deletion ; c.4917_4918delACinsCT, p.(Leu1640Phe) in *STRC* | N.A./ rs727503441 | P.(class V)/ V.U.S (class III) | AR | Deafness, autosomal recessive 16 (MIM: 603720) | No | Inherited in trans | *12* |
| *STRC* | compound heterozygous *CKMT1B, STRC* deletion; *CKMT1B, STRC, CATSPER2* deletion | N.A. | P. (class V)/P. (class V) | AR | Deafness, autosomal recessive 16 (MIM: 603720) | No | Inherited in trans | *13* |

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|---|---|---|---|---|---|---|---|---|
| *STRC* | compound heterozygous c.4425G>C, p.(Trp1475Cys) in *STRC* and *CKMT1B, STRC, CATSPER2* deletion | rs727503443/ N.A. | L.P. (class IV)/ P. (class V) | AR | Deafness, autosomal recessive 16 (MIM: 603720) | No | Inherited in trans | *14* |
| *STRC ; CKMT1B ; CATSPER2* | homozygous deletion of *CKMT1B, STRC, CATSPER2* | N.A. | P. (class V)/P. (class V) | AR | Deafness and male infertility (MIM: 611102) | Yes potentially | Inherited in trans | *15* |
| *STRC* | compound heterozygous c.4837G>T, p.(Glu1613*)in *STRC* and *CKMT1B, STRC*, (and maybe *CATSPER2* ) deletion | rs769443188/ N.A. | P. (class V)/P. (class V) | AR | Deafness, autosomal recessive 16 (MIM: 603720) | No | Inherited in trans | *22* |
| *POU4F3; OPA1* | heterozygous c.502del, p.(Ala168Profs* 36) in *POU4F3;* heterozygous c.1118C>G, p.(Ser373Cys) in *OPA1* | rs766631025/ N.A. | P. (class V)/ L.P. (class IV) | AD | Deafness, autosomal dominant 15 (MIM: 602459); Optic atrophy plus syndrome (MIM: 125250). | Yes potentially | POU4F3 Inherited from father with HL/OPA1 *de novo* | *21* |
| *COL11A1* | heterozygous deletion | N.A. | P. (class V) | AD | Deafness, autosmal dominant 37 (MIM 618533) Stickler Syndrome II (MIM: 604841) / Marshall syndrome (MIM: 154780) | Yes potentially | Inherited from mother with HL | *23* |

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|---|---|---|---|---|---|---|---|---|
| *COL11A1* | heterozygous deletion splicing site *COL11A1*, (c.4519-2Adel,p.(?)) | N.A. | L.P. (class IV) | AD | Deafness, autosmal dominant 37 (MIM 618533) Stickler Syndrome II (MIM: 604841) / Marshall syndrome (MIM: 154780) | Yes potentially | Inherited from mother without HL | *26* |
| *COL11A1; SMAD3* | heterozygous c.4547G>T, p.(Gly1516Val) in *COL11A1;* heterozygous c.3G>A (p.Met1?) in *SMAD3* | rs1553193910 /N.A. | P. (class V)/ L.P. (class IV) | AD | Deafness, autosmal dominant 37 (MIM 618533) Stickler Syndrome II (MIM: 604841) / Marshall syndrome (MIM: 154780); Loeys-Dietz syndrome (MIM:613795) | Yes for Stickler syndrome/ potentially for LDS | SMAD3 inherited from affected mother/COLL1A1 *de novo* | *24* |
| *TRIOBP* | homozygous c.3214dup, p.(Arg1072Profs*12) | N.A. | P. (class V) | AR | Deafness, autosomal recessive 28 (MIM: 609823) | No | N.A. | *25* |
| *TMPRSS3* | compound heterozygous c.400A>T (p.LYS134*); c.646C>T (p.Arg216Cys) | N.A /N.A. | P. (class V)/P. (class V) | AR | Deafness, autosomal recessive 8 (MIM: 601072) | No | Inherited in trans | *27* |
| *TMPRSS3* | compound heterozygous c.916G>A p.(Ala306Thr); c.749delT p.(Leu250Argfs*25) | rs181949335/ N.A | P. (class V)/P. (class V) | AR | Deafness, autosomal recessive 8 (MIM: 601072) | No | Inherited in trans | *29* |
| *COL4A3* | heterozygous c.4826G>A, p.(Arg1609Gln) | rs1380878336 | L.P. (class IV) | AD | Alport syndrome, 3 autosomal dominant (MIM: 104200) | Yes potentially | Inherited from father with HL and no sign of | *28* |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | altered kidney function | |
| *MarvelD2* | homozygous c.1331+2T>C p.(?) | rs762352115 | P. (class V) | AR | Deafness, autosmal recessive 49 (MIM: 610153) | No | Inherited in trans | *31* |
| *MYO15A* | homozygous c.6046+1G>A, p.(?) | rs201978571 | P. (class V) | AR | Deafness, autosomal recessive 3 (MIM: 600316) | No | Inherited in trans | *32* |
| *NF2* | heterozygous c.1579 G>T, p.(Glu527*) | rs74315505 | P. (class V) | AD | Neurofirbomatose type 2 (MIM: 101000) | Yes | N.A. | *62* |
| *COCH* | heterozygous c.341T>C , p.(Leu114Pro) | N.A. | P. (class V) | AD | Deafness, autsomal dominant 9 (MIM: 601369) | No | N.A. | *63* |