Omica Labs

PANEL OTORRINOLARINGOLOGÍA

Síndrome de Alport

COL4A3[1], COL4A4[1], COL4A5[1]

Ssíndrome branquio-oto-renal

EYA1[2], SIX1[2], SIX5[2], TFAP2A[3]

Pérdida de oído y sordera

ABHD12[4], ACTG1[5,6], ADGRV1[7], AIFM1[8], ALMS1[9], ATP6V1B1[10], BCS1L[11], BDP1[12], BSND[13], BTD [14], CABP2[15], CACNA1D[16], CCDC50[17], CD164[18], CDC14A[19], CDH23[20,21], CEACAM16[22], CEP78[23], CHD7[24], CIB2[25], CISD2 [26], CLDN14[27], CLPP[28], CLRN1[29], COCH[30], COL11A2[31,32], COL4A5[33], COL9A1[34], COL9A2[34], COL9A3[34], DIAPH1[35], DNMT1[36], DSPP[37], EDN3[38], EDNRB[39], EPS8[40], EPS8L2[41], EPSN[41], EPSRRB[42], EYA1[43], EYA4[44], FGF3[45], GATA3[46], GIPC3[47], GJB2[48], GJB3[48], GJB6[49], GPSM2[50], GRHL2[51], GRXCR1[52], GRXCR2[53], GSMDE[51], HGF[54], HOMER2[55], HSD17B4[56], ILDR1[57], KCNQ1[58], KCNQ4[59], LARS2[60], LHFPL5[61], LOXHD1[52], LRTOMT[62], MARVELD2[57], MIR96[63], MITF[64], MPZL2[65], MSRB3[40], MYH14[66], MYH9[67], MYO15A[68], MYO3A[69], MYO6[70], MYO7A[71], OSBPL2[72], OTOA[52], OTOF[73], OTOG[74], OTOGL[75], P2RX2[76], PAX3[77], PCDH15[78],PDZD7[79], PJVK[80], POU3F4[81], POY4F3[82], PRPS1[83],PTPRQ[84], RDX[85], RIPOR2[86], S1PR2[87], SERPINB6[88], SIX1[89], SLC17A8[90], SLC26A4[91], SLC52A2[92], SLC52A3[93], SLITRK6[94], SMPX[95], SOX10[96], STRC[97], SYNE4[98], TBC1D24[99], TCOF1[100], TECTA[101], TIMM8A[102], TMC1[103], TMIE[104], TMPRSS3[105], TPRN[106], TRIOBP[107], TUBB4B[108], USH1C[109], USH1G[110], USH2A[111], WFS1[112], WHRN[113]

Síndrome Pendred

FOXI1[114], KCNJ10[114], SLC26A4[114].

Síndrome Stickler

COL2A1[114], COL9A1[114], COL9A2[114], COL9A3[114], COL11A1[114], COL11A2[114].

Síndrome Usher

ADGRV1[115], CIB2[115], CDH23[115], CLRN1[115], MYO7A[115], PDZD7[115], PCDH15[115], USH1C[115], USH1G[115], USH2A[115], WHRN[115].

Síndrome Waardenburg
EDN3[116], EDNRB[116], MITF[116], PAX3[116], SNAI2[116], SOX10[116]

Síndrome Jervell and Lange-Nielsen
KCNQ1[116], KCNE1[116]

Anexo I- Bibliografía

1. Kashtan, C. E. Alport Syndrome. in *GeneReviews® [Internet]* (University of Washington, Seattle, 2019).
2. Smith, R. J. H. Branchiootorenal Spectrum Disorder. in *GeneReviews® [Internet]* (University of Washington, Seattle, 2018).
3. Reiber, J. *et al.* Additional clinical and molecular analyses of TFAP2A in patients with the branchio-oculo-facial syndrome. *Am. J. Med. Genet. A* **152A**, (2010).
4. Lerat, J. *et al.* A complex homozygous mutation in ABHD12 responsible for PHARC syndrome discovered with NGS and review of the literature. *J. Peripher. Nerv. Syst.* **22**, (2017).
5. Di Donato, N. *et al.* Update on the ACTG1-associated Baraitser-Winter cerebrofrontofacial syndrome. *Am. J. Med. Genet. A* **170**, (2016).
6. Wang, L. *et al.* Amino acid 118 in the Deafness Causing (DFNA20/26) ACTG1 gene is a Mutational Hot Spot. *Gene reports* **11**, (2018).

7. Yang, J., Huang, X. F., Tong, Y. & Jin, Z. B. Targeted exome sequencing identified two novel truncation mutations in GPR98 causing Usher syndrome. *Clin. Experiment. Ophthalmol.* **44**, (2016).
8. Sancho, P. *et al.* A newly distal hereditary motor neuropathy caused by a rare AIFM1 mutation. *Neurogenetics* **18**, (2017).
9. Taşkesen, M. *et al.* Novel Alu retrotransposon insertion leading to Alström syndrome. *Hum. Genet.* **131**, (2012).
10. Tian, C. *et al.* Hearing loss without overt metabolic acidosis in ATP6V1B1 deficient MRL mice, a new genetic model for non-syndromic deafness with enlarged vestibular aqueducts. *Hum. Mol. Genet.* **26**, (2017).
11. Falco, M. *et al.* Novel compound heterozygous mutations in BCS1L gene causing Bjornstad syndrome in two siblings. *Am. J. Med. Genet. A* **173**, (2017).
12. Girotto, G. *et al.* Linkage study and exome sequencing identify a BDP1 mutation associated with hereditary hearing loss. *PLoS One* **8**, (2013).
13. de Pablos, A. L. *et al.* Severe manifestation of Bartter syndrome Type IV caused by a novel insertion mutation in the BSND gene. *Clin. Nephrol.* **81**, (2014).
14. Hsu, R. H. *et al.* Genotypic and phenotypic correlations of biotinidase deficiency in the Chinese population. *Orphanet J. Rare Dis.* **14**, (2019).

15. Koohiyan, M. *et al.* A Novel Pathogenic Variant in the CABP2 Gene Causes Severe Nonsyndromic Hearing Loss in a Consanguineous Iranian Family. *Audiol. Neurootol.* **24**, (2019).
16. Satheesh, S. V. *et al.* Retrocochlear function of the peripheral deafness gene Cacna1d. *Hum. Mol. Genet.* **21**, (2012).
17. Tumane, R. G. *et al.* Expression of serum proteins in noise induced hearing loss workers of mining based industry. *J. Proteomics* **240**, (2021).
18. Oziębło, D. *et al.* Update on CD164 and LMX1A genes to strengthen their causative role in autosomal dominant hearing loss. *Hum. Genet.* **141**, (2022).
19. Imtiaz, A. *et al.* CDC14A phosphatase is essential for hearing and male fertility in mouse and human. *Hum. Mol. Genet.* **27**, (2018).
20. Zheng, Q. Y. *et al.* Digenic inheritance of deafness caused by mutations in genes encoding cadherin 23 and protocadherin 15 in mice and humans. *Hum. Mol. Genet.* **14**, (2005).
21. Miyagawa, M., Nishio, S. Y. & Usami, S. Prevalence and clinical features of hearing loss patients with CDH23 mutations: a large cohort study. *PLoS One* **7**, (2012).

22. Brownstein, Z. *et al.* Spectrum of genes for inherited hearing loss in the Israeli Jewish population, including the novel human deafness gene ATOH1. *Clin. Genet.* **98**, (2020).
23. Nikopoulos, K. *et al.* Mutations in CEP78 Cause Cone-Rod Dystrophy and Hearing Loss Associated with Primary-Cilia Defects. *Am. J. Hum. Genet.* **99**, (2016).
24. Lee, B. *et al.* Revealing the function of a novel splice-site mutation of CHD7 in CHARGE syndrome. *Gene* **576**, (2016).
25. Giese, A. P. J. *et al.* CIB2 interacts with TMC1 and TMC2 and is essential for mechanotransduction in auditory hair cells. *Nat. Commun.* **8**, (2017).
26. Gaines, C. H. *et al.* Behavioral characterization of a novel Cisd2 mutant mouse. *Behav. Brain Res.* **405**, (2021).
27. Shiraiwa, Y. *et al.* Measurements of ionic concentrations along with endocochlear potential in wild-type and claudin 14 knockout mice. *Auris Nasus Larynx* **45**, (2018).
28. Kremer, L. S. *et al.* Genetic diagnosis of Mendelian disorders via RNA sequencing. *Nat. Commun.* **8**, (2017).
29. Aller, E. *et al.* Mutation screening of USH3 gene (clarin-1) in Spanish patients with Usher syndrome: low prevalence and phenotypic variability. *Clin. Genet.* **66**, (2004).

30. Parzefall, T. *et al.* Identification of a rare COCH mutation by whole-exome sequencing : Implications for personalized therapeutic rehabilitation in an Austrian family with non-syndromic autosomal dominant late-onset hearing loss. *Wien. Klin. Wochenschr.* **130**, (2018).
31. El Naofal, M. *et al.* The genomic landscape of rare disorders in the Middle East. *Genome Med.* **15**, (2023).
32. Iwasa, Y. *et al.* Non-ocular Stickler syndrome with a novel mutation in COL11A2 diagnosed by massively parallel sequencing in Japanese hearing loss patients. *Ann. Otol. Rhinol. Laryngol.* **124 Suppl 1**, (2015).
33. Hashikami, K. *et al.* Establishment of X-linked Alport syndrome model mice with a Col4a5 R471X mutation. *Biochemistry and biophysics reports* **17**, (2018).
34. Nixon, T. R. W. *et al.* Homozygous Type IX collagen variants (COL9A1, COL9A2, and COL9A3) causing recessive Stickler syndrome-Expanding the phenotype. *Am. J. Med. Genet. A* **179**, (2019).
35. Neuhaus, C. *et al.* Extension of the clinical and molecular phenotype of DIAPH1-associated autosomal dominant hearing loss (DFNA1). *Clin. Genet.* **91**, (2017).
36. Winkelmann, J. *et al.* Mutations in DNMT1 cause autosomal dominant cerebellar ataxia, deafness and narcolepsy. *Hum. Mol. Genet.* **21**, (2012).

37. Lee, S. K. *et al.* A DSPP mutation causing dentinogenesis imperfecta and characterization of the mutational effect. *Biomed Res. Int.* **2013**, (2013).
38. Nasirnejad, S. F., Morovvati, S., Sabetghadam, M. M. & Entezari, M. Mutation detection and inhibitor risk in Iranian patients with Hemophilia A: Six novel mutations. *Clinical case reports* **8**, (2020).
39. Zaitoun, I. *et al.* Altered neuronal density and neurotransmitter expression in the ganglionated region of Ednrb null mice: implications for Hirschsprung's disease. *Neurogastroenterol. Motil.* **25**, (2013).
40. Richard, E. M. *et al.* Global genetic insight contributed by consanguineous Pakistani families segregating hearing loss. *Hum. Mutat.* **40**, (2019).
41. Wang, R., Han, S., Khan, A. & Zhang, X. Molecular Analysis of Twelve Pakistani Families with Nonsyndromic or Syndromic Hearing Loss. *Genet. Test. Mol. Biomarkers* **21**, (2017).
42. Ji, H., Lu, J., Wang, J., Li, H. & Lin, X. Combined examination of sequence and copy number variations in human deafness genes improves diagnosis for cases of genetic deafness. *BMC Ear Nose Throat Disord.* **14**, (2014).
43. Li, Y., Manaligod, J. M. & Weeks, D. L. EYA1 mutations associated with the branchio-oto-renal syndrome result in defective otic development in Xenopus laevis. *Biol. Cell* **102**, (2010).

44. Matsuzaki, S., Hosoya, M., Okano, H., Fujioka, M. & Ogawa, K. Expression pattern of EYA4 in the common marmoset (Callithrix jacchus) cochlea. *Neurosci. Lett.* **662**, (2018).
45. Urness, L. D. *et al.* Spatial and temporal inhibition of FGFR2b ligands reveals continuous requirements and novel targets in mouse inner ear morphogenesis. *Development* **145**, (2018).
46. Bardhan, T. *et al.* Gata3 is required for the functional maturation of inner hair cells and their innervation in the mouse cochlea. *J. Physiol.* **597**, (2019).
47. Rehman, A. U. *et al.* Mutations of GIPC3 cause nonsyndromic hearing loss DFNB72 but not DFNB81 that also maps to chromosome 19p. *Hum. Genet.* **130**, (2011).
48. Liu, X. Z. *et al.* Digenic inheritance of non-syndromic deafness caused by mutations at the gap junction proteins Cx26 and Cx31. *Hum. Genet.* **125**, (2009).
49. Yang, R. *et al.* A known mutation in GJB6 in a large Chinese family with hidrotic ectodermal dysplasia. *J. Eur. Acad. Dermatol. Venereol.* **30**, (2016).
50. Mauriac, S. A. *et al.* Defective Gpsm2/Gαi3 signalling disrupts stereocilia development and growth cone actin dynamics in Chudley-McCullough syndrome. *Nat. Commun.* **8**, (2017).

51. Hosoya, M., Fujioka, M., Ogawa, K. & Okano, H. Distinct Expression Patterns Of Causative Genes Responsible For Hereditary Progressive Hearing Loss In Non-Human Primate Cochlea. *Sci. Rep.* **6**, (2016).
52. Sloan-Heggen, C. M. *et al.* Comprehensive genetic testing in the clinical evaluation of 1119 patients with hearing loss. *Hum. Genet.* **135**, (2016).
53. Wu, D. *et al.* Clinical and genetic study of 12 Chinese Han families with nonsyndromic deafness. *Molecular genetics & genomic medicine* **8**, (2020).
54. Mei, X. *et al.* Next-Generation Sequencing Identifies Pathogenic Variants in HGF, POU3F4, TECTA, and MYO7A in Consanguineous Pakistani Deaf Families. *Neural Plast.* **2021**, (2021).
55. Lu, X. *et al.* Whole exome sequencing identified a second pathogenic variant in HOMER2 for autosomal dominant non-syndromic deafness. *Clin. Genet.* **94**, (2018).
56. Chen, K. *et al.* A homozygous missense variant in HSD17B4 identified in a consanguineous Chinese Han family with type II Perrault syndrome. *BMC Med. Genet.* **18**, (2017).
57. Yan, D. *et al.* Spectrum of DNA variants for non-syndromic deafness in a large cohort from multiple continents. *Hum. Genet.* **135**, (2016).

58. Uysal, F. *et al.* 'Homozygous, and compound heterozygous mutation in 3 Turkish family with Jervell and Lange-Nielsen syndrome: case reports'. *BMC Med. Genet.* **18**, (2017).

59. Huang, B. *et al.* A novel pore-region mutation, c.887G > A (p.G296D) in KCNQ4, causing hearing loss in a Chinese family with autosomal dominant non-syndromic deafness 2. *BMC Med. Genet.* **18**, (2017).

60. Kosaki, R., Horikawa, R., Fujii, E. & Kosaki, K. Biallelic mutations in LARS2 can cause Perrault syndrome type 2 with neurologic symptoms. *Am. J. Med. Genet. A* **176**, (2018).

61. Komara, M., John, A., Suleiman, J., Ali, B. R. & Al-Gazali, L. Clinical and molecular delineation of dysequilibrium syndrome type 2 and profound sensorineural hearing loss in an inbred Arab family. *Am. J. Med. Genet. A* **170A**, (2016).

62. Tlili, A. *et al.* Localization of a novel autosomal recessive non-syndromic hearing impairment locus DFNB63 to chromosome 11q13.3-q13.4. *Ann. Hum. Genet.* **71**, (2007).

63. Weston *et al.* A mouse model of miR-96, miR-182 and miR-183 misexpression implicates miRNAs in cochlear cell fate and homeostasis. *Sci. Rep.* **8**, (2018).

64. Sun, J. *et al.* Functional analysis of a nonstop mutation in MITF gene identified in a patient with Waardenburg syndrome type 2. *J. Hum. Genet.* **62**, (2017).
65. Amalou, G. *et al.* A homozygous MPZL2 deletion is associated with non syndromic hearing loss in a moroccan family. *Int. J. Pediatr. Otorhinolaryngol.* **140**, (2021).
66. Song, M. H. *et al.* Genetic Inheritance of Late-Onset, Down-Sloping Hearing Loss and Its Implications for Auditory Rehabilitation. *Ear Hear.* **41**, (2020).
67. Dantas, V. G. *et al.* c.G2114A MYH9 mutation (DFNA17) causes non-syndromic autosomal dominant hearing loss in a Brazilian family. *Genet. Mol. Biol.* **37**, (2014).
68. Rehman, A. U. *et al.* Mutational Spectrum of MYO15A and the Molecular Mechanisms of DFNB3 Human Deafness. *Hum. Mutat.* **37**, (2016).
69. Qu, R. *et al.* Identification of a novel homozygous mutation in MYO3A in a Chinese family with DFNB30 non-syndromic hearing impairment. *Int. J. Pediatr. Otorhinolaryngol.* **84**, (2016).
70. Wong, E. Y., Xu, C. Y., Brahmachary, M. & Xu, P. X. A Novel ENU-Induced Mutation in Myo6 Causes Vestibular Dysfunction and Deafness. *PLoS One* **11**, (2016).

71. Yu, I. M. *et al.* Myosin 7 and its adaptors link cadherins to actin. *Nat. Commun.* **8**, (2017).
72. Yao, J. *et al.* OSBPL2-disrupted pigs recapitulate dual features of human hearing loss and hypercholesterolaemia. *J. Genet. Genomics* **46**, (2019).
73. Iwasa, Y. I. *et al.* Detailed clinical features and genotype-phenotype correlation in an OTOF-related hearing loss cohort in Japan. *Hum. Genet.* **141**, (2022).
74. Roberts, R., Elsner, J. & Bagnall, M. W. Delayed Otolith Development Does Not Impair Vestibular Circuit Formation in Zebrafish. *J. Assoc. Res. Otolaryngol.* **18**, (2017).
75. Barake, R., Abou-Rizk, S., Nemer, G. & Bassim, M. The OTOGL p.Arg925* Variant is Associated with Moderate Hearing Loss in a Syrian Nonconsanguineous Family. *Genet. Test. Mol. Biomarkers* **21**, (2017).
76. Azizi, M. R., Mohammadi, A. J. & Ghanbari, F. Identification of a Novel Stop Loss Mutation in P2RX2 Gene in an Iranian Family with Autosomal Nonsyndromic Hearing Loss. *Iran. Biomed. J.* **25**, (2021).
77. Choi, E. Y., Choi, W. & Lee, C. S. A novel PAX3 mutation in a Korean patient with Waardenburg syndrome type 1 and unilateral branch retinal vein and artery occlusion: a case report. *BMC Ophthalmol.* **18**, (2018).

78. Bolz, H. *et al.* Mutation of CDH23, encoding a new member of the cadherin gene family, causes Usher syndrome type 1D. *Nat. Genet.* **27**, (2001).
79. Booth, K. T. *et al.* PDZD7 and hearing loss: More than just a modifier. *Am. J. Med. Genet. A* **167A**, (2015).
80. Salime, S. *et al.* Homozygous mutations in PJVK and MYO15A genes associated with non-syndromic hearing loss in Moroccan families. *Int. J. Pediatr. Otorhinolaryngol.* **101**, (2017).
81. Pollak, A. *et al.* Novel and De Novo Mutations Extend Association of POU3F4 with Distinct Clinical and Radiological Phenotype of Hearing Loss. *PLoS One* **11**, (2016).
82. Gao, X. *et al.* A Missense Mutation in POU4F3 Causes Midfrequency Hearing Loss in a Chinese ADNSHL Family. *Biomed Res. Int.* **2018**, (2018).
83. Kim, S. Y. *et al.* Functional characterization of a novel loss-of-function mutation of PRPS1 related to early-onset progressive nonsyndromic hearing loss in Koreans (DFNX1): Potential implications on future therapeutic intervention. *J. Gene Med.* **18**, (2016).
84. Eisenberger, T. *et al.* A C-terminal nonsense mutation links PTPRQ with autosomal-dominant hearing loss, DFNA73. *Genet. Med.* **20**, (2018).

85. Bademci, G. *et al.* Comprehensive analysis via exome sequencing uncovers genetic etiology in autosomal recessive nonsyndromic deafness in a large multiethnic cohort. *Genet. Med.* **18**, (2016).
86. Zhao, B., Wu, Z. & Müller, U. Murine Fam65b forms ring-like structures at the base of stereocilia critical for mechanosensory hair cell function. *Elife* **5**, (2016).
87. Santos-Cortez, R. L. *et al.* Autosomal-Recessive Hearing Impairment Due to Rare Missense Variants within S1PR2. *Am. J. Hum. Genet.* **98**, (2016).
88. Tan, J., Prakash, Kaiserman, D. & Bird, P. I. Absence of SERPINB6A causes sensorineural hearing loss with multiple histopathologies in the mouse inner ear. *Am. J. Pathol.* **183**, (2013).
89. Unzaki, A. *et al.* Clinically diverse phenotypes and genotypes of patients with branchio-oto-renal syndrome. *J. Hum. Genet.* **63**, (2018).
90. Van Heurck, R. *et al.* Benefits of Exome Sequencing in Children with Suspected Isolated Hearing Loss. *Genes* **12**, (2021).
91. Hosoya, M., Fujioka, M., Kobayashi, R., Okano, H. & Ogawa, K. Overlapping expression of anion exchangers in the cochlea of a non-human primate suggests functional compensation. *Neurosci. Res.* **110**, (2016).
92. Gudbjartsson, D. F. *et al.* Large-scale whole-genome sequencing of the Icelandic population. *Nat. Genet.* **47**, (2015).

93. Manole, A. *et al.* Clinical, pathological and functional characterization of riboflavin-responsive neuropathy. *Brain* **140**, (2017).

94. van Beeck Calkoen, E. A. *et al.* The etiological evaluation of sensorineural hearing loss in children. *Eur. J. Pediatr.* **178**, (2019).

95. Niu, Z. *et al.* A novel frameshift mutation of SMPX causes a rare form of X-linked nonsyndromic hearing loss in a Chinese family. *PLoS One* **12**, (2017).

96. Ma, J. *et al.* Waardenburg syndrome type II in a Chinese patient caused by a novel nonsense mutation in the SOX10 gene. *Int. J. Pediatr. Otorhinolaryngol.* **85**, (2016).

97. Sagong, B., Baek, J. I., Bok, J., Lee, K. Y. & Kim, U. K. Identification of a nonsense mutation in the STRC gene in a Korean family with moderate hearing loss. *Int. J. Pediatr. Otorhinolaryngol.* **80**, (2016).

98. Masterson, J., Yıldırım, B., Gökkaya, E., Tokgöz, Y. S. & Tekin, M. A Novel Variant in SYNE4 Confirms its Causative Role in Sensorineural Hearing Loss. *Balkan Med. J.* **35**, (2018).

99. Balestrini, S. *et al.* TBC1D24 genotype-phenotype correlation: Epilepsies and other neurologic features. *Neurology* **87**, (2016).

100. Fan, X. *et al.* TCOF1 pathogenic variants identified by Whole-exome sequencing in Chinese Treacher Collins syndrome families and hearing rehabilitation effect. *Orphanet J. Rare Dis.* **14**, (2019).

101. Asgharzade, S. *et al.* A novel TECTA mutation causes ARNSHL. *Int. J. Pediatr. Otorhinolaryngol.* **92**, (2017).

102. Ha, A. D. *et al.* The phenotypic spectrum of dystonia in Mohr-Tranebjaerg syndrome. *Mov. Disord.* **27**, (2012).

103. Nishio, S. Y. & Usami, S. I. Prevalence and clinical features of autosomal dominant and recessive TMC1-associated hearing loss. *Hum. Genet.* **141**, (2022).

104. Zhao, B. *et al.* TMIE is an essential component of the mechanotransduction machinery of cochlear hair cells. *Neuron* **84**, (2014).

105. Gao, X. *et al.* Identification of TMPRSS3 as a Significant Contributor to Autosomal Recessive Hearing Loss in the Chinese Population. *Neural Plast.* **2017**, (2017).

106. Chen, M. *et al.* Progressive hearing loss and degeneration of hair cell stereocilia in taperin gene knockout mice. *Biochem. Biophys. Res. Commun.* **479**, (2016).

107. Riazuddin, S. *et al.* Mutations in TRIOBP, which encodes a putative cytoskeletal-organizing protein, are associated with nonsyndromic recessive deafness. *Am. J. Hum. Genet.* **78**, (2006).

108. Luscan, R. *et al.* Mutations in TUBB4B Cause a Distinctive Sensorineural Disease. *Am. J. Hum. Genet.* **101**, (2017).

109. Ouyang, X. M. *et al.* Mutations in the alternatively spliced exons of USH1C cause non-syndromic recessive deafness. *Hum. Genet.* **111**, (2002).

110. Bashir, R., Fatima, A. & Naz, S. A frameshift mutation in SANS results in atypical Usher syndrome. *Clin. Genet.* **78**, (2010).

111. van Wijk, E. *et al.* Identification of 51 novel exons of the Usher syndrome type 2A (USH2A) gene that encode multiple conserved functional domains and that are mutated in patients with Usher syndrome type II. *Am. J. Hum. Genet.* **74**, (2004).

112. Kobayashi, M. *et al.* WFS1 mutation screening in a large series of Japanese hearing loss patients: Massively parallel DNA sequencing-based analysis. *PLoS One* **13**, (2018).

113. Tlili, A. *et al.* Identification of a novel frameshift mutation in the DFNB31/WHRN gene in a Tunisian consanguineous family with hereditary non-syndromic recessive hearing loss. *Hum. Mutat.* **25**, (2005).

114. Pique, L. M. *et al.* Mutation analysis of the SLC26A4, FOXI1 and KCNJ10 genes in individuals with congenital hearing loss. *PeerJ* **2**, (2014).

115. Orphanet: Usher syndrome. https://www.orpha.net/en/disease/detail/886.

116. Huang, S. *et al.* Genetic insights, disease mechanisms, and biological therapeutics for Waardenburg syndrome. *Gene Ther.* **29**, 479–497 (2021).