Whole Exome Sequencing
Gene package Hearing impairment, version 6, 30-9-2019

Technical information
DNA was enriched using Agilent SureSelect Clinical Research Exome V2 capture and paired-end sequenced on the Illumina platform (outsourced). The aim is to obtain 8.1 Giga base pairs per exome with a mapped fraction of 0.99. The average coverage of the exome is ~50x. Duplicate reads are excluded. Data are demultiplexed with bcl2fastq Conversion Software from Illumina. Reads are mapped to the genome using the BWA-MEM algorithm (reference: http://bio-bwa.sourceforge.net/). Variant detection is performed by the Genome Analysis Toolkit HaplotypeCaller (reference: http://www.broadinstitute.org/gatk/). The detected variants are filtered and annotated with Cartagenia software and classified with Alamut Visual. It is not excluded that pathogenic mutations are being missed using this technology. At this moment, there is not enough information about the sensitivity of this technique with respect to the detection of deletions and duplications of more than 5 nucleotides and of somatic mosaic mutations (all types of sequence changes).

Erasmus MC
University Medical Center Rotterdam

Dept. Clinical Genetics

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x	% covered >30x
ACTB	Baraitser-Winter syndrome 1, 243310?Dystonia, juvenile-onset, 607371	102630	192	100	100	100
ACTG1	Baraitser-Winter syndrome 2, 614583 Deafness 20/26, 604717	102560	188	100	100	100
ADCY1	?Deafness 44, 610154	103072	109	97	95	93
ADGRV1	?Febrile seizures, familial, 4, 604352 Usher syndrome, type 2C, 605472 Usher syndrome, type 2C, GPR98/PDZD7 digenic, 605472	602851	80	100	100	97
AIFM1	Combined oxidative phosphorylation deficiency 6, 300816 Cowchock syndrome, 310490 Deafness 5, 300614	300169	55	100	96	82
ATP1A3	Alternating hemiplegia of childhood 2, 614820 CAPOS syndrome, 601338 Dystonia-12, 128235	182350	144	100	100	100
ATP2B2	{Deafness 12, modifier of}, 601386	108733	139	100	100	100
ATP6V1B1	Renal tubular acidosis with deafness, 267300	192132	136	100	100	100
BCS1L	Bjornstad syndrome, 262000 GRACILE syndrome, 603358 Leigh syndrome, 256000 Mitochondrial complex III deficiency, nuclear type 1, 124000	603647	170	100	100	100
BDP1	?Deafness 112, 618257	607012	60	99	96	85

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BSND	Bartter syndrome, type 4a, 602522 Sensorineural deafness with mild renal dysfunction, 602522	606412	115	100	100	100
CABP2	Deafness 93, 614899	607314	94	100	100	96
CACNA1D	Primary aldosteronism, seizures, and neurologic abnormalities, 615474 Sinoatrial node dysfunction and deafness, 614896	114206	102	100	100	98
CCDC50	?Deafness 44, 607453	611051	73	100	100	98
CD164	?Deafness 66, 616969	603356	71	100	100	93
CDC14A	Deafness 32, with or without immotile sperm, 608653	603504	79	100	100	94
CDH23	Deafness 12, 601386 {Pituitary adenoma 5, multiple types}, 617540 Usher syndrome, type 1D, 601067 Usher syndrome, type 1D/F digenic, 601067	605516	135	100	100	100
CEACAM16	Deafness 4B, 614614 Deafness 113, 618410	614591	94	100	100	100
CEP78	Cone-rod dystrophy and hearing loss, 617236	617110	69	100	100	94
CIB2	Deafness 48, 609439 Usher syndrome, type IJ, 614869	605564	195	100	100	100
CLDN14	Deafness 29, 614035	605608	66	100	98	91
CLIC5	?Deafness 103, 616042	607293	76	100	100	100
CLPP	Perrault syndrome 3, 614129	601119	125	100	100	100
CLRN1	Retinitis pigmentosa 61, 614180 Usher syndrome, type 3A, 276902	606397	83	100	100	97
COA8	Mitochondrial complex IV deficiency, 220110	616003	No coverage data			
COCH	Deafness 9, 601369 ?Deafness 110, 618094	603196	71	98	95	93
COL11A1	?Deafness 37, 618533 Fibrochondrogenesis 1, 228520 {Lumbar disc herniation, susceptibility to}, 603932 Marshall syndrome, 154780 Stickler syndrome, type II, 604841	120280	62	100	99	93
COL11A2	Deafness 13, 601868 Deafness 53, 609706 Fibrochondrogenesis 2, 614524 Otospondylomegaepiphyseal dysplasia, 184840 Otospondylomegaepiphyseal dysplasia, 215150	120290	110	100	100	100

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COL2A1	Achondrogenesis, type II or hypochondrogenesis, 200610 Avascular necrosis of the femoral head, 608805 Czech dysplasia, 609162 Epiphyseal dysplasia, multiple, with myopia and deafness, 132450 Kniest dysplasia, 156550 Legg-Calve-Perthes disease, 150600 Osteoarthritis with mild chondrodysplasia, 604864 Platyspondylic skeletal dysplasia, Torrance type, 151210 SED congenita, 183900 SMED Strudwick type, 184250 Spondyloepiphyseal dysplasia, Stanescu type, 616583 Spondyloperipheral dysplasia, 271700 Stickler sydrome, type I, nonsyndromic ocular, 609508 Stickler syndrome, type I, 108300 Vitreoretinopathy with phalangeal epiphyseal dysplasia	120140	97	100	100	99
COL4A3	Alport syndrome 2, 203780 Alport syndrome 3, 104200 Hematuria, benign familial, 141200	120070	63	100	97	90
COL4A4	Alport syndrome 2, 203780 Hematuria, familial benign, 141200	120131	70	100	100	96
COL4A5	Alport syndrome 1, 301050	303630	42	100	88	67
COL4A6	?Deafness 6, 300914	303631	62	100	98	90
COL9A1	?Epiphyseal dysplasia, multiple, 6, 614135 Stickler syndrome, type IV, 614134	120210	65	100	99	91
COL9A2	Epiphyseal dysplasia, multiple, 2, 600204 ?Stickler syndrome, type V, 614284	120260	100	100	99	96
CRYM	Deafness 40, 616357	123740	76	100	100	99
DCDC2	?Deafness 66, 610212 Nephronophthisis 19, 616217 Sclerosing cholangitis, neonatal, 617394	605755	96	100	100	97
DIABLO	Deafness 64, 614152	605219	105	100	100	99
DIAPH1	Deafness 1, 124900 Seizures, cortical blindness, microcephaly syndrome, 616632	602121	84	100	99	93
DIAPH3	Auditory neuropathy, 1, 609129	614567	61	100	99	93
DMXL2	?Deafness 71, 617605 ?Polyendocrine-polyneuropathy syndrome, 616113	612186	67	100	99	93

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DSPP	Deafness 39, with dentinogenesis, 605594 Dentin dysplasia, type II, 125420 Dentinogenesis imperfecta, Shields type II, 125490 Dentinogenesis imperfecta, Shields type III, 125500	125485	43	95	70	55
EDN3	Central hypoventilation syndrome, congenital, 209880 {Hirschsprung disease, susceptibility to, 4}, 613712 Waardenburg syndrome, type 4B, 613265	131242	90	100	100	98
EDNRB	ABCD syndrome, 600501 {Hirschsprung disease, susceptibility to, 2}, 600155 Waardenburg syndrome, type 4A, 277580	131244	96	100	100	100
ELMOD3	?Deafness 88, 615429	615427	96	100	100	97
EPS8	?Deafness 102, 615974	600206	68	100	100	94
EPS8L2	Deafness autosomal recessive 106, 617637	614988	132	100	97	95
ERAL1	Perrault syndrome 6, 617565	607435	132	100	100	100
ESPN	Deafness 36, 609006 Deafness, neurosensory, without vestibular involvement, 609006	606351	101	97	88	81
ESRP1	?Deafness 109, 618013	612959	67	100	98	93
ESRRB	Deafness 35, 608565	602167	142	100	100	100
EXOSC2	Short stature, hearing loss, retinitis pigmentosa, and distinctive facies, 617763	602238	69	100	100	97
EYA1	Anterior segment anomalies with or without cataract, 602588 Branchiootic syndrome 1, 602588 Branchiootorenal syndrome 1, with or without cataracts, 113650 ?Otofaciocervical syndrome, 166780	601653	86	100	100	98
EYA4	?Cardiomyopathy, dilated, 1J, 605362 Deafness 10, 601316	603550	62	100	100	94
FGF3	Deafness, congenital with inner ear agenesis, microtia, and microdontia, 610706	164950	122	100	100	100
FOXF2	No OMIM phenotype	603250	109	95	91	89
FOXI1	Enlarged vestibular aqueduct, 600791	601093	161	100	100	100
GAB1	?Deafness 26, 605428	604439	72	100	99	97
GATA3	Hypoparathyroidism, sensorineural deafness, and renal dysplasia, 146255	131320	203	100	100	100
GIPC3	Deafness 15, 601869	608792	115	100	95	93
GJB2	Bart-Pumphrey syndrome, 149200 Deafness 3A, 601544 Deafness 1A, 220290 Hystrix-like ichthyosis with deafness, 602540 Keratitis-ichthyosis-deafness syndrome, 148210 Keratoderma, palmoplantar, with deafness, 148350 Vohwinkel syndrome, 124500	121011	150	100	100	100

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x	% covered >30x
GJB3	Deafness 2B, 612644 Deafness, with peripheral neuropathy Deafness Deafness, digenic, GJB2/GJB3, 220290 Erythrokeratodermia variabilis et progressiva 1, 133200	603324	182	100	100	100
GJB6	Deafness 3B, 612643 Deafness 1B, 612645 Deafness, digenic GJB2/GJB6, 220290 Ectodermal dysplasia 2, Clouston type, 129500	604418	75	100	100	99
GPSM2	Chudley-McCullough syndrome, 604213	609245	93	100	100	96
GRAP	Deafness 114, 618456	604330	52	68	68	65
GREB1L	Renal hypodysplasia/aplasia 3, 617805	617782	72	100	98	93
GRHL2	Corneal dystrophy, posterior polymorphous, 4, 618031 Deafness 28, 608641 Ectodermal dysplasia/short stature syndrome, 616029	608576	81	100	100	99
GRXCR1	Deafness 25, 613285	613283	100	100	100	99
GRXCR2	?Deafness 101, 615837	615762	109	100	100	100
GSDME	Deafness 5, 600994	608798	94	100	100	100
HARS1	Charcot-Marie-Tooth disease, axonal, type 2W, 616625 Usher syndrome type 3B, 614504	142810	104	100	100	99
HARS2	?Perrault syndrome 2, 614926	600783	76	100	100	99
HGF	Deafness 39, 608265	142409	73	100	100	96
HOMER2	?Deafness 68, 616707	604799	121	99	98	98
HSD17B4	D-bifunctional protein deficiency, 261515 Perrault syndrome 1, 233400	601860	62	100	98	93
IFNLR1	No OMIM phenotype	607404	92	100	97	95
ILDR1	Deafness 42, 609646	609739	95	100	100	97
KARS1	?Charcot-Marie-Tooth disease, recessive intermediate, B, 613641 Deafness 89, 613916	601421	126	100	100	97
KCNE1	Jervell and Lange-Nielsen syndrome 2, 612347 Long QT syndrome 5, 613695	176261	252	100	100	100
KCNJ10	Enlarged vestibular aqueduct, digenic, 600791 SESAME syndrome, 612780	602208	171	100	100	100
KCNQ1	Atrial fibrillation, familial, 3, 607554 Jervell and Lange-Nielsen syndrome, 220400 Long QT syndrome 1, 192500 {Long QT syndrome 1, acquired, susceptibility to}, 192500 Short QT syndrome 2, 609621	607542	160	97	94	93
KCNQ4	Deafness 2A, 600101	603537	147	98	95	91

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KITLG	Deafness 69, unilateral or asymmetric, 616697 Hyperpigmentation with or without hypopigmentation, 145250 [Skin/hair/eye pigmentation 7, blond/brown hair], 611664	184745	78	100	100	97
LARS2	?Hydrops, lactic acidosis, and sideroblastic anemia, 617021 Perrault syndrome 4, 615300	604544	79	100	100	99
LHFPL5	Deafness 67, 610265	609427	175	100	100	100
LMX1A	No OMIM phenotype	600298	81	100	100	99
LOXHD1	Deafness 77, 613079	613072	118	100	100	99
LRTOMT	Deafness 63, 611451	612414	111	100	100	100
MARVELD2	Deafness 49, 610153	610572	92	100	100	97
MCM2	?Deafness 70, 616968	116945	122	100	100	100
MET	?Deafness 97, 616705 Hepatocellular carcinoma, childhood type, somatic, 114550 {Osteofibrous dysplasia, susceptibility to}, 607278 Renal cell carcinoma, papillary, 1, familial and somatic, 605074	164860	64	100	100	96
MIR96	Deafness 50, 613074	611606	No coverage data			
MITF	COMMAD syndrome, 617306 {Melanoma, cutaneous malignant, susceptibility to, 8}, 614456 Tietz albinism-deafness syndrome, 103500 Waardenburg syndrome, type 2A, 193510 Waardenburg syndrome/ocular albinism, digenic, 103470	156845	87	100	100	99
MPZL2	Deafness 111, 618145	604873	64	100	100	98
MSRB3	Deafness 74, 613718	613719	72	100	100	93
MYH14	Deafness 4A, 600652 ?Peripheral neuropathy, myopathy, hoarseness, and hearing loss, 614369	608568	114	100	99	97
MYH9	Deafness 17, 603622 Macrothrombocytopenia and granulocyte inclusions with or without nephritis or sensorineural hearing loss, 155100	160775	125	100	100	99
MYO15A	Deafness 3, 600316	602666	134	100	99	98
MYO3A	Deafness 30, 607101	606808	73	100	99	95
MYO6	Deafness 22, 606346 Deafness 22, with hypertrophic cardiomyopathy, 606346 Deafness 37, 607821	600970	82	100	99	94
MYO7A	Deafness 11, 601317 Deafness 2, 600060 Usher syndrome, type 1B, 276900	276903	109	100	100	99
NARS2	Combined oxidative phosphorylation deficiency 24, 616239 ?Deafness 94, 618434	612803	55	99	97	92

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NLRP3	CINCA syndrome, 607115 Deafness 34, with or without inflammation, 617772 Familial cold inflammatory syndrome 1, 120100 Keratoendothelitis fugax hereditaria, 148200 Muckle-Wells syndrome, 191900	606416	125	100	100	100
OPA1	Behr syndrome, 210000 {Glaucoma, normal tension, susceptibility to}, 606657 ?Mitochondrial DNA depletion syndrome 14 (encephalocardiomyopathic type), 616896 Optic atrophy 1, 165500 Optic atrophy plus syndrome, 125250	605290	59	100	98	89
OSBPL2	Deafness 67, 616340	606731	102	100	100	100
OTOA	Deafness 22, 607039	607038	78	77	74	72
OTOF	Auditory neuropathy, 1, 601071 Deafness 9, 601071	603681	113	100	100	100
OTOG	Deafness 18B, 614945	604487	121	100	100	99
OTOGL	Deafness 84B, 614944	614925	76	100	100	95
P2RX2	Deafness 41, 608224	600844	136	100	100	99
PAX3	Craniofacial-deafness-hand syndrome, 122880 Rhabdomyosarcoma 2, alveolar, 268220 Waardenburg syndrome, type 1, 193500 Waardenburg syndrome, type 3, 148820	606597	104	100	100	100
PCDH15	Deafness 23, 609533 Usher syndrome, type 1D/F digenic, 601067 Usher syndrome, type 1F, 602083	605514	72	100	100	95
PDE1C	?Deafness 74, 618140	602987	63	100	97	90
PDZD7	Deafness 57, 618003 {Retinal disease in Usher syndrome type IIA, modifier of}, 276901 Usher syndrome, type IIC, GPR98/PDZD7 digenic, 605472	612971	84	100	100	99
PET100	Mitochondrial complex IV deficiency, 220110	614770	85	92	66	66
PEX1	Heimler syndrome 1, 234580 Peroxisome biogenesis disorder 1A (Zellweger), 214100 Peroxisome biogenesis disorder 1B (NALD/IRD), 601539	602136	62	100	99	94
PEX26	Peroxisome biogenesis disorder 7A (Zellweger), 614872 Peroxisome biogenesis disorder 7B, 614873	608666	118	100	100	100
PEX6	Heimler syndrome 2, 616617 Peroxisome biogenesis disorder 4A (Zellweger), 614862 Peroxisome biogenesis disorder 4B, 614863	601498	107	100	99	95
PJVK	Deafness 59, 610220	610219	93	100	100	99

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PNPT1	Combined oxidative phosphorylation deficiency 13, 614932 Deafness 70, 614934	610316	57	100	97	83
POU3F4	Deafness 2, 304400	300039	120	100	100	100
POU4F3	Deafness 15, 602459	602460	247	100	100	100
PPIP5K2	Deafness 100, 618422	611648	48	99	93	80
PRKCB	No OMIM phenotype	176970	73	100	100	99
PRPS1	Arts syndrome, 301835 Charcot-Marie-Tooth disease recessive, 5, 311070 Deafness 1, 304500 Gout, PRPS-related, 300661 Phosphoribosylpyrophosphate synthetase superactivity, 300661	311850	50	100	99	90
PTPRQ	Deafness 73, 617663 Deafness 84A, 613391	603317	80	100	99	95
RAI1	Smith-Magenis syndrome, 182290	607642	187	100	100	100
RDX	Deafness 24, 611022	179410	54	100	93	76
RIPOR2	?Deafness 104, 616515	611410	77	100	100	97
ROR1	?Deafness 108, 617654	602336	87	97	96	96
S1PR2	Deafness 68, 610419	605111	153	100	100	100
SERPINB6	?Deafness 91, 613453	173321	85	100	100	98
SIX1	Branchiootic syndrome 3, 608389 Deafness 23, 605192	601205	119	100	100	100
SIX5	Branchiootorenal syndrome 2, 610896	600963	75	100	95	85
SLC17A8	Deafness 25, 605583	607557	66	100	100	99
SLC22A4	{Rheumatoid arthritis, susceptibility to}, 180300	604190	103	100	100	96
SLC26A4	Deafness 4, with enlarged vestibular aqueduct, 600791 Pendred syndrome, 274600	605646	68	100	100	94
SLC26A5	?Deafness 61, 613865	604943	61	100	100	96
SLC29A3	Histiocytosis-lymphadenopathy plus syndrome, 602782	612373	152	100	99	99
SLC33A1	Congenital cataracts, hearing loss, and neurodegeneration, 614482 Spastic paraplegia 42, 612539	603690	68	100	98	86
SLC44A4	?Deafness 72, 617606	606107	94	100	100	100
SLC52A2	Brown-Vialetto-Van Laere syndrome 2, 614707	607882	173	100	100	100
SLITRK6	Deafness and myopia, 221200	609681	75	100	100	99
SMPX	Deafness 4, 300066	300226	51	100	100	83
SNAI2	Piebaldism, 172800 Waardenburg syndrome, type 2D, 608890	602150	66	100	100	100
SOX10	PCWH syndrome, 609136 Waardenburg syndrome, type 2E, with or without neurologic involvement, 611584 Waardenburg syndrome, type 4C, 613266	602229	72	100	97	89

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SPATA5	Epilepsy, hearing loss, and mental retardation syndrome, 616577	613940	68	100	100	97
STRC	Deafness 16, 603720	606440	66	53	48	46
SYNE4	Deafness 76, 615540	615535	107	100	100	100
TBC1D24	DOORS syndrome, 220500 Deafness 86, 614617 Deafness 65, 616044 Epilepsy, rolandic, with proxysmal exercise-induce dystonia and writer's cramp, 608105 Epileptic encephalopathy, early infantile, 16, 615338 Myoclonic epilepsy, infantile, familial, 605021	613577	158	100	100	100
TECTA	Deafness 8/12, 601543 Deafness 21, 603629	602574	123	100	100	98
TIMM8A	Mohr-Tranebjaerg syndrome, 304700	300356	138	100	100	100
TJP2	Cholestasis, progressive familial intrahepatic 4, 615878 Hypercholanemia, familial, 607748	607709	83	100	100	99
TMC1	Deafness 36, 606705 Deafness 7, 600974	606706	61	100	100	94
TMEM132E	?Deafness 99, 618481	616178	117	100	99	96
TMIE	Deafness 6, 600971	607237	85	100	100	99
TMPRSS3	Deafness 8/10, 601072	605511	74	100	100	99
TMTC2	No OMIM phenotype	615856	79	100	100	98
TNC	Deafness 56, 615629	187380	110	100	100	98
TPRN	Deafness 79, 613307	613354	94	92	86	79
TRIOBP	Deafness 28, 609823	609761	182	100	99	97
TSPEAR	?Deafness 98, 614861 Ectodermal dysplasia 14, hair/tooth type with or without hypohidrosis, 618180	612920	105	100	100	100
TWNK	Mitochondrial DNA depletion syndrome 7 (hepatocerebral type), 271245 Perrault syndrome 5, 616138 Progressive external ophthalmoplegia with mitochondrial DNA deletions 3, 609286	606075	145	100	100	100
TYR	Albinism, oculocutaneous, type IA, 203100 Albinism, oculocutaneous, type IB, 606952 {Melanoma, cutaneous malignant, susceptibility to, 8}, 601800 [Skin/hair/eye pigmentation 3, blue/green eyes], 601800 [Skin/hair/eye pigmentation 3, light/dark/freckling skin], 601800 Waardenburg syndrome/albinism, digenic, 103470	606933	83	100	100	98
USH1C	Deafness 18A, 602092 Usher syndrome, type 1C, 276904	605242	80	100	98	92
USH1G	Usher syndrome, type 1G, 606943	607696	180	100	100	100
USH2A	Retinitis pigmentosa 39, 613809 Usher syndrome, type 2A, 276901	608400	82	100	100	98

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WBP2	Deafness 107, 617639	606962	60	100	96	89
WFS1	?Cataract 41, 116400 Deafness 6/14/38, 600965 {Diabetes mellitus, noninsulin-dependent, association with}, 125853 Wolfram syndrome 1, 222300 Wolfram-like syndrome, 614296	606201	196	100	100	100
WHRN	Deafness 31, 607084 Usher syndrome, type 2D, 611383	607928	119	100	100	100
YAP1	Coloboma, ocular, with or without hearing impairment, cleft lip/palate, and/or mental retardation, 120433	606608	73	100	99	94

- Gene symbols according HGCN
- OMIM release used: 8-9-2019
- "No OMIM phenotypes" indicates a gene without a current OMIM association
- OMIM phenotypes between "[ ]", indicate "nondiseases," mainly genetic variations that lead to apparently abnormal laboratory test values
- OMIM phenotypes between "{}", indicate risk factors
- OMIM phenotypes with a question mark, "?", before the disease name indicates an unconfirmed or possibly spurious mapping
- The statistics above are based on a set of 100 samples
- Median depth is the median of the mean sequence depth over the protein coding exons (±10bp flanking introns) of the longest transcript
- % Covered 10x , 20x and 30 x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 10x, 20x or 30x