Whole Exome Sequencing
Gene package Hearing impairment, version 3, 1-7-2017

Technical information
After DNA was enriched using Agilent Sureselect Clinical Research Exome (CRE) Capture, samples were run on the Illumina Hiseq platform. The aim is to obtain 50 million total reads per exome with a mapped fraction >0.98. The average coverage of the exome is ~50x. Data are demultiplexed by Illumina software bcl2fastq. Reads are mapped to the genome using BWA (reference: http://bio-bwa.sourceforge.net/). Variant detection is performed by Genome Analysis Toolkit (reference: http://www.broadinstitute.org/gatk/). Analysis is performed in Cartagenia using The Variant Calling File (VCF) followed by filtering. 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
ACTB	Baraitser-Winter syndrome 1, 243310 ?Dystonia, juvenile-onset, 607371	102630	77	100	100
ACTG1	Baraitser-Winter syndrome 2, 614583 Deafness 20/26, 604717	102560	104	100	100
ADCY1	?Deafness 44, 610154	103072	55	95	89
ADGRV1	?Febrile seizures, familial, 4, 604352 Usher syndrome, type 2C, 605472 Usher syndrome, type 2C, GPR98/PDZD7 digenic, 605472	602851	79	100	99
AIFM1	Combined oxidative phosphorylation deficiency 6, 300816 Cowchock syndrome, 310490 Deafness 5, 300614	300169	55	100	94
APOPT1	Mitochondrial complex IV deficiency, 220110	616003	35	97	80
ATP1A2	Alternating hemiplegia of childhood, 104290 Migraine, familial basilar, 602481 Migraine, familial hemiplegic, 2, 602481	182340	109	100	100
ATP6V1B1	Renal tubular acidosis with deafness, 267300	192132	115	100	100
BCS1L	Bjornstad syndrome, 262000 GRACILE syndrome, 603358 Leigh syndrome, 256000 Mitochondrial complex III deficiency, nuclear type 1, 124000	603647	114	100	100
BDP1	No OMIM phenotype	607012	43	88	72

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
BSND	Bartter syndrome, type 4a, 602522 Sensorineural deafness with mild renal dysfunction, 602522	606412	104	100	100
CABP2	Deafness 93, 614899	607314	58	100	95
CACNA1D	Primary aldosteronism, seizures, and neurologic abnormalities, 615474 Sinoatrial node dysfunction and deafness, 614896	114206	95	100	99
CC2D2A	COACH syndrome, 216360 Joubert syndrome 9, 612285 Meckel syndrome 6, 612284	612013	82	100	99
CCDC50	?Deafness 44, 607453	611051	69	100	100
CD164	?Deafness 66, 616969	603356	47	93	91
CDC14A	Deafness 105, 616958	603504	60	94	76
CDH23	Deafness 12, 601386 Usher syndrome, type 1D, 601067 Usher syndrome, type 1D/F digenic, 601067	605516	119	100	100
CEACAM16	Deafness 4B, 614614	614591	88	100	100
CEP78	Cone-rod dystrophy and hearing loss, 617236	617110	45	95	84
CIB2	Deafness 48, 609439 Usher syndrome, type IJ, 614869	605564	109	100	100
CLDN14	Deafness 29, 614035	605608	55	100	100
CLIC5	?Deafness 103, 616042	607293	44	100	94
CLPP	Perrault syndrome 3, 614129	601119	60	97	90
CLRN1	Retinitis pigmentosa 61, 614180 Usher syndrome, type 3A, 276902	606397	105	100	100
COCH	Deafness 9, 601369	603196	111	100	100
COL11A1	Fibrochondrogenesis 1, 228520 {Lumbar disc herniation, susceptibility to}, 603932 Marshall syndrome, 154780 Stickler syndrome, type II, 604841	120280	56	98	88
COL11A2	Deafness 13, 601868 Deafness 53, 609706 Fibrochondrogenesis 2, 614524 Otospondylomegaepiphyseal dysplasia, 215150 Stickler syndrome, type III, 184840 Weissenbacher-Zweymuller syndrome, 277610	120290	64	100	97

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
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	74	100	99
COL4A3	Alport syndrome, 104200 Alport syndrome, 203780 Hematuria, benign familial, 141200	120070	62	98	97
COL4A4	Alport syndrome, 203780 Hematuria, familial benign	120131	62	100	96
COL4A5	Alport syndrome, 301050	303630	34	97	79
COL4A6	?Deafness 6, 300914	303631	40	98	87
COL9A1	?Epiphyseal dysplasia, multiple, 6, 614135 Stickler syndrome, type IV, 614134	120210	71	99	95
COL9A2	Epiphyseal dysplasia, multiple, 2, 600204 ?Stickler syndrome, type V, 614284	120260	50	100	94
CRYM	Deafness 40, 616357	123740	70	100	100
DCDC2	?Deafness 66, 610212 Nephronophthisis 19, 616217 Sclerosing cholangitis, neonatal, 617394	605755	58	100	93
DFNA5	Deafness 5, 600994	608798	88	100	100
DFNB59	Deafness 59, 610220	610219	79	100	97
DIABLO	Deafness 64, 614152	605219	107	100	100
DIAPH1	Deafness 1, 124900 Seizures, cortical blindness, microcephaly syndrome, 616632	602121	80	100	96
DIAPH3	Auditory neuropathy, 1, 609129	614567	54	100	92

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
DSPP	Deafness 39, with dentinogenesis, 605594 Dentin dysplasia, type II, 125420 Dentinogenesis imperfecta, Shields type II, 125490 Dentinogenesis imperfecta, Shields type III, 125500	125485	49	84	61
EDN3	Central hypoventilation syndrome, congenital, 209880 {Hirschsprung disease, susceptibility to, 4}, 613712 Waardenburg syndrome, type 4B, 613265	131242	103	100	100
EDNRB	ABCD syndrome, 600501 {Hirschsprung disease, susceptibility to, 2}, 600155 Waardenburg syndrome, type 4A, 277580	131244	93	100	100
ELMOD3	?Deafness 88, 615429	615427	65	100	94
EPS8	?Deafness 102, 615974	600206	41	90	75
ESPN	Deafness 36, 609006 Deafness, neurosensory, without vestibular involvement	606351	37	84	66
ESRRB	Deafness 35, 608565	602167	80	100	100
EXOSC2	No OMIM phenotype	602238	41	100	86
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	78	100	96
EYA4	Cardiomyopathy, dilated, 1J, 605362 Deafness 10, 601316	603550	82	100	100
FGF3	Deafness, congenital with inner ear agenesis, microtia, and microdontia, 610706	164950	60	100	97
FOXI1	Enlarged vestibular aqueduct, 600791	601093	84	100	100
GATA3	Hypoparathyroidism, sensorineural deafness, and renal dysplasia, 146255	131320	86	100	100
GIPC3	Deafness 15, 601869	608792	70	94	88
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	122	100	100
GJB3	Deafness 2B, 612644 Deafness, with peripheral neuropathy Deafness Deafness, digenic, GJB2/GJB3, 220290 Erythrokeratodermia variabilis et progressiva, 133200	603324	114	100	100

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
GJB6	Deafness 3B, 612643 Deafness 1B, 612645 Deafness, digenic GJB2/GJB6, 220290 Ectodermal dysplasia 2, Clouston type, 129500	604418	90	100	100
GPSM2	Chudley-McCullough syndrome, 604213	609245	76	100	97
GRHL2	Deafness 28, 608641 Ectodermal dysplasia/short stature syndrome, 616029	608576	75	100	99
GRXCR1	Deafness 25, 613285	613283	93	100	100
GRXCR2	?Deafness 101, 615837	615762	47	100	96
HARS	Charcot-Marie-Tooth disease, axonal, type 2W, 616625 Usher syndrome type 3B, 614504	142810	86	100	99
HARS2	?Perrault syndrome 2, 614926	600783	107	100	100
HGF	Deafness 39, 608265	142409	83	100	99
HOMER2	?Deafness 68, 616707	604799	50	99	91
HSD17B4	D-bifunctional protein deficiency, 261515 Perrault syndrome 1, 233400	601860	63	99	96
ILDR1	Deafness 42, 609646	609739	63	100	97
KARS	?Charcot-Marie-Tooth disease, recessive intermediate, B, 613641 Deafness 89, 613916	601421	100	100	100
KCNE1	Jervell and Lange-Nielsen syndrome 2, 612347 Long QT syndrome 5, 613695	176261	163	100	100
KCNJ10	Enlarged vestibular aqueduct, digenic, 600791 SESAME syndrome, 612780	602208	122	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	75	93	90
KCNQ4	Deafness 2A, 600101	603537	98	95	94
KITLG	Deafness 69, unilateral or asymmetric, 616697 Hyperpigmentation with or without hypopigmentation, 145250 [Skin/hair/eye pigmentation 7, blond/brown hair], 611664	184745	55	100	95
LARS2	?Hydrops, lactic acidosis, and sideroblastic anemia, 617021 Perrault syndrome 4, 615300	604544	50	100	97
LHFPL5	Deafness 67, 610265	609427	123	100	100
LMX1A	No OMIM phenotype	600298	43	99	85
LOXHD1	Deafness 77, 613079	613072	100	100	100
LRTOMT	Deafness 63, 611451	612414	98	100	100
MARVELD2	Deafness 49, 610153	610572	91	100	98

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
MCM2	?Deafness 70, 616968	116945	62	100	98
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	95	100	100
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	54	100	98
MPZL2	No OMIM phenotype	604873	40	100	86
MSRB3	Deafness 74, 613718	613719	72	100	99
MYH14	Deafness 4A, 600652 ?Peripheral neuropathy, myopathy, hoarseness, and hearing loss, 614369	608568	70	99	95
MYH9	Deafness 17, 603622 Epstein syndrome, 153650 Fechtner syndrome, 153640 Macrothrombocytopenia and progressive sensorineural deafness, 600208 May-Hegglin anomaly, 155100 Sebastian syndrome, 605249	160775	91	100	100
MYO15A	Deafness 3, 600316	602666	83	98	94
MYO3A	Deafness 30, 607101	606808	70	100	98
MYO6	Deafness 22, 606346 Deafness 22, with hypertrophic cardiomyopathy, 606346 Deafness 37, 607821	600970	59	100	94
MYO7A	Deafness 11, 601317 Deafness 2, 600060 Usher syndrome, type 1B, 276900	276903	100	100	98
NARS2	Combined oxidative phosphorylation deficiency 24, 616239	612803	67	97	97
NLRP3	CINCA syndrome, 607115 Familial cold-induced inflammatory syndrome 1, 120100 Muckle-Wells syndrome, 191900	606416	102	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	69	100	93
OSBPL2	Deafness 67, 616340	606731	54	100	94

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
OTOA	Deafness 22, 607039	607038	88	100	98
OTOF	Auditory neuropathy, 1, 601071 Deafness 9, 601071	603681	90	100	99
OTOG	Deafness 18B, 614945	604487	82	100	99
OTOGL	Deafness 84B, 614944	614925	68	100	96
P2RX2	Deafness 41, 608224	600844	61	100	95
PAX3	Craniofacial-deafness-hand syndrome, 122880 Rhabdomyosarcoma 2, alveolar, 268220 Waardenburg syndrome, type 1, 193500 Waardenburg syndrome, type 3, 148820	606597	71	100	100
PCDH15	Deafness 23, 609533 Usher syndrome, type 1D/F digenic, 601067 Usher syndrome, type 1F, 602083	605514	89	100	98
PDZD7	{Retinal disease in Usher syndrome type IIA, modifier of}, 276901 Usher syndrome, type IIC, GPR98/PDZD7 digenic, 605472	612971	60	99	96
PET100	Mitochondrial complex IV deficiency, 220110	614770	35	97	64
PEX1	Heimler syndrome 1, 234580 Peroxisome biogenesis disorder 1A (Zellweger), 214100 Peroxisome biogenesis disorder 1B (NALD/IRD), 601539	602136	67	100	98
PEX6	Heimler syndrome 2, 616617 Peroxisome biogenesis disorder 4A (Zellweger), 614862 Peroxisome biogenesis disorder 4B, 614863	601498	71	95	91
PNPT1	Combined oxidative phosphorylation deficiency 13, 614932 Deafness 70, 614934	610316	33	87	63
POU3F4	Deafness 2, 304400	300039	49	100	100
POU4F3	Deafness 15, 602459	602460	131	100	100
PRKCB	No OMIM phenotype	176970	50	100	95
PRPS1	Arts syndrome, 301835 Charcot-Marie-Tooth disease recessive, 5, 311070 Deafness 1, 304500 Gout, PRPS-related, 300661 Phosphoribosylpyrophosphate synthetase superactivity, 300661	311850	59	100	100
PTPRQ	Deafness 84A, 613391	603317	69	99	95
RAI1	Smith-Magenis syndrome, 182290	607642	91	100	100
RDX	Deafness 24, 611022	179410	51	100	93
RIPOR2	?Deafness 104, 616515	611410	46	99	91
S1PR2	Deafness 68, 610419	605111	83	97	89
SERPINB6	?Deafness 91, 613453	173321	99	100	100

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
SIX1	Branchiootic syndrome 3, 608389 Deafness 23, 605192	601205	90	100	100
SIX5	Branchiootorenal syndrome 2, 610896	600963	45	94	82
SLC17A8	Deafness 25, 605583	607557	81	100	99
SLC22A4	{Rheumatoid arthritis, susceptibility to}, 180300	604190	97	100	100
SLC26A4	Deafness 4, with enlarged vestibular aqueduct, 600791 Pendred syndrome, 274600	605646	82	100	98
SLC26A5	?Deafness 61, 613865	604943	90	100	100
SLC33A1	Congenital cataracts, hearing loss, and neurodegeneration, 614482 Spastic paraplegia 42, 612539	603690	62	100	96
SLITRK6	Deafness and myopia, 221200	609681	93	100	100
SMPX	Deafness 4, 300066	300226	50	100	94
SNAI2	Piebaldism, 172800 Waardenburg syndrome, type 2D, 608890	602150	71	100	92
SOX10	PCWH syndrome, 609136 Waardenburg syndrome, type 2E, with or without neurologic involvement, 611584 Waardenburg syndrome, type 4C, 613266	602229	45	99	87
STRC	Deafness 16, 603720	606440	73	100	97
SYNE4	Deafness 76, 615540	615535	36	99	85
TBC1D24	DOOR syndrome, 220500 Deafness 86, 614617 Deafness 65, 616044 Epileptic encephalopathy, early infantile, 16, 615338 Myoclonic epilepsy, infantile, familial, 605021	613577	92	100	100
TECTA	Deafness 8/12, 601543 Deafness 21, 603629	602574	101	100	100
TIMM8A	Mohr-Tranebjaerg syndrome, 304700	300356	42	100	100
TJP2	Cholestasis, progressive familial intrahepatic 4, 615878 Hypercholanemia, familial, 607748	607709	83	100	99
TMC1	Deafness 36, 606705 Deafness 7, 600974	606706	68	100	100
TMEM132E	No OMIM phenotype	616178	54	93	86
TMIE	Deafness 6, 600971	607237	68	99	88
TMPRSS3	Deafness 8/10, 601072	605511	94	100	100
TMTC2	No OMIM phenotype	615856	58	100	95
TNC	Deafness 56, 615629	187380	64	99	92
TPRN	Deafness 79, 613307	613354	49	80	71
TRIOBP	Deafness 28, 609823	609761	120	100	99
TSPEAR	Deafness 98, 614861	612920	97	100	100

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
TWNK	Mitochondrial DNA depletion syndrome 7 (hepatocerebral type), 271245 Perrault syndrome 5, 616138 Progressive external ophthalmoplegia with mitochondrial DNA deletions 3, 609286	606075	103	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	71	100	100
USH1C	Deafness 18A, 602092 Usher syndrome, type 1C, 276904	605242	70	100	91
USH1G	Usher syndrome, type 1G, 606943	607696	86	100	99
USH2A	Retinitis pigmentosa 39, 613809 Usher syndrome, type 2A, 276901	608400	90	100	100
WBP2	No OMIM phenotype	606962	40	100	92
WFS1	?Cataract 41, 116400 Deafness 6/14/38, 600965 {Diabetes mellitus, noninsulin-dependent, association with}, 125853 Wolfram syndrome, 222300 Wolfram-like syndrome, 614296	606201	102	100	100
WHRN	Deafness 31, 607084 Usher syndrome, type 2D, 611383	607928	68	100	98
YAP1	Coloboma, ocular, 120433 Coloboma, ocular, with or without hearing impairment, cleft lip/palate, and/or mental retardation, 120433	606608	40	86	73

- Gene symbols according HGCN
- OMIM release used: 2-6-2017
- "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 50 samples
- Median depth is the median of the mean sequence depth over the protein coding exons of the transcript
- % Covered 10x describes the percentage of a gene's coding sequence that is covered at least 10x
- % Covered 20x describes the percentage of a gene's coding sequence that is covered at least 20x