Whole Exome Sequencing
Gene package Hereditary Congenital Defects, version 5, 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).

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HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x	% covered >30x
Oesophagus atresia						
CHD7	CHARGE syndrome, 214800 Hypogonadotropic hypogonadism 5 with or without anosmia, 612370	608892	87	100	100	97
EFTUD2	Mandibulofacial dysostosis, Guion-Almeida type, 610536	603892	85	100	100	99
GLI3	Greig cephalopolysyndactyly syndrome, 175700 {Hypothalamic hamartomas, somatic}, 241800 Pallister-Hall syndrome, 146510 Polydactyly, postaxial, types A1 and B, 174200 Polydactyly, preaxial, type IV, 174700	165240	110	100	100	99
MID1	Opitz GBBB syndrome, type I, 300000	300552	89	100	100	93
MYCN	Feingold syndrome 1, 164280	164840	169	100	100	100
SOX2	Microphthalmia, syndromic 3, 206900 Optic nerve hypoplasia and abnormalities of the central nervous system, 206900	184429	183	100	100	100
Congenital Hernia Diaphragmatica						
GATA4	Atrial septal defect 2, 607941 Atrioventricular septal defect 4, 614430 ?Testicular anomalies with or without congenital heart disease, 615542 Tetralogy of Fallot, 187500 Ventricular septal defect 1, 614429	600576	81	100	87	80

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GPC3	Simpson-Golabi-Behmel syndrome, type 1, 312870 Wilms tumor, somatic, 194070	300037	53	100	99	91
LRP2	Donnai-Barrow syndrome, 222448	600073	69	100	100	96
MYRF	Cardiac-urogenital syndrome, 618280 Encephalitis/encephalopathy, mild, with reversible myelin vacuolization, 618113	608329	118	98	97	96
NIPBL	Cornelia de Lange syndrome 1, 122470	608667	65	100	98	92
SMC3	Cornelia de Lange syndrome 3, 610759	606062	69	100	97	88
STRA6	Microphthalmia, isolated, with coloboma 8, 601186 Microphthalmia, syndromic 9, 601186	610745	98	100	100	100
WT1	Denys-Drash syndrome, 194080 Frasier syndrome, 136680 Meacham syndrome, 608978 Mesothelioma, somatic, 156240 Nephrotic syndrome, type 4, 256370 Wilms tumor, type 1, 194070	607102	117	100	100	98
ZFPM2	Diaphragmatic hernia 3, 610187 Tetralogy of Fallot, 187500 46XY sex reversal 9, 616067	603693	82	100	100	100
Ano-rectal Marformation						
CASK	FG syndrome 4, 300422 Mental retardation and microcephaly with pontine and cerebellar hypoplasia, 300749 Mental retardation, with or without nystagmus, 300422	300172	51	100	96	80
CCNB1	No OMIM phenotype	123836	57	100	97	89
CCNQ	STAR syndrome, 300707	300708	62	81	81	81
FLNA	Cardiac valvular dysplasia, 314400 Congenital short bowel syndrome, 300048 ?FG syndrome 2, 300321 Frontometaphyseal dysplasia 1, 305620 Heterotopia, periventricular, 1, 300049 Intestinal pseudoobstruction, neuronal, 300048 Melnick-Needles syndrome, 309350 Otopalatodigital syndrome, type I, 311300 Otopalatodigital syndrome, type II, 304120 Terminal osseous dysplasia, 300244	300017	110	100	100	100

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GLI3	Greig cephalopolysyndactyly syndrome, 175700 {Hypothalamic hamartomas, somatic}, 241800 Pallister-Hall syndrome, 146510 Polydactyly, postaxial, types A1 and B, 174200 Polydactyly, preaxial, type IV, 174700	165240	110	100	100	99
JAG1	Alagille syndrome 1, 118450 ?Deafness, congenital heart defects, and posterior embryotoxon, 617992 Tetralogy of Fallot, 187500	601920	96	100	100	96
KDM6A	Kabuki syndrome 2, 300867	300128	52	100	95	80
KMT2D	Kabuki syndrome 1, 147920	602113	114	100	100	99
MED12	Lujan-Fryns syndrome, 309520 Ohdo syndrome, 300895 Opitz-Kaveggia syndrome, 305450	300188	68	100	100	97
MID1	Opitz GBBB syndrome, type I, 300000	300552	89	100	100	93
MNX1	Currarino syndrome, 176450	142994	44	77	69	57
MYCN	Feingold syndrome 1, 164280	164840	169	100	100	100
NOTCH2	Alagille syndrome 2, 610205 Hajdu-Cheney syndrome, 102500	600275	114	100	100	99
SALL1	Townes-Brocks branchiootorenal-like syndrome, 107480 Townes-Brocks syndrome 1, 107480	602218	120	100	100	99
SALL4	Duane-radial ray syndrome, 607323 IVIC syndrome, 147750	607343	155	100	100	97
USP9X	Mental retardation 99, 300919 Mental retardation 99, syndromic, female-restricted, 300968	300072	67	100	98	94
HSCR/CIPO/MMIHS						
AAAS	Achalasia-addisonianism-alacrimia syndrome, 231550	605378	102	100	100	100
ACTG2	Visceral myopathy, 155310	102545	95	100	100	100
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

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KIFBP	Goldberg-Shprintzen megacolon syndrome, 609460	609367	76	100	100	98
LMOD1	No OMIM phenotype	602715	128	100	100	100
MYH11	Aortic aneurysm, familial thoracic 4, 132900	160745	136	100	100	99
MYL9	No OMIM phenotype	609905	102	100	100	98
MYLK	Aortic aneurysm, familial thoracic 7, 613780	600922	121	100	100	99
NOS1	No OMIM phenotype	163731	89	100	100	98
PHOX2B	Central hypoventilation syndrome, congenital, with or without Hirschsprung disease, 209880 Neuroblastoma with Hirschsprung disease, 613013 {Neuroblastoma, susceptibility to, 2}, 613013	603851	149	100	100	100
RAD21	Cornelia de Lange syndrome 4, 614701 ?Mungan syndrome, 611376	606462	69	100	99	92
RET	Central hypoventilation syndrome, congenital, 209880 {Hirschsprung disease, protection against}, 142623 {Hirschsprung disease, susceptibility to, 1}, 142623 Medullary thyroid carcinoma, 155240 Multiple endocrine neoplasia IIA, 171400 Multiple endocrine neoplasia IIB, 162300 Pheochromocytoma, 171300	164761	173	100	100	100
SGO1	Chronic atrial and intestinal dysrhythmia, 616201	609168	54	100	99	91
SOX10	PCWH syndrome, 609136 Waardenburg syndrome, type 2E, with or without neurologic involvement, 611584 Waardenburg syndrome, type 4C, 613266	602229	72	100	97	89
VCL	Cardiomyopathy, dilated, 1W, 611407 Cardiomyopathy, hypertrophic, 15, 613255	193065	89	100	99	93
ZEB2	Mowat-Wilson syndrome, 235730	605802	85	100	100	100

- 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

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- 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