Whole Exome Sequencing
Gene package Congenital Heart Defects (CHD), version 4, 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
ACTC1	Atrial septal defect 5, 612794 Cardiomyopathy, dilated, 1R, 613424 Cardiomyopathy, hypertrophic, 11, 612098 Left ventricular noncompaction 4, 613424	102540	194	100	100	100
ACVR1	Fibrodysplasia ossificans progressiva, 135100	102576	73	100	100	99
ACVR2B	Heterotaxy, visceral, 4, autosomal, 613751	602730	105	100	100	98
ANKRD1	No OMIM phenotype	609599	91	100	100	97
CFAP53	Heterotaxy, visceral, 6, 614779	614759	98	100	100	98
CFC1	Heterotaxy, visceral, 2, autosomal, 605376	605194	70	41	34	28
CHD7	CHARGE syndrome, 214800 Hypogonadotropic hypogonadism 5 with or without anosmia, 612370	608892	87	100	100	97
CITED2	Atrial septal defect 8, 614433 Ventricular septal defect 2, 614431	602937	93	100	100	100
CRELD1	Atrioventricular septal defect, partial, with heterotaxy syndrome, 606217 {Atrioventricular septal defect, susceptibility to, 2}, 606217	607170	100	100	100	100
DCHS1	Mitral valve prolapse 2, 607829 Van Maldergem syndrome 1, 601390	603057	128	100	100	100
DNAAF1	Ciliary dyskinesia, primary, 13, 613193	613190	131	100	100	99

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ELN	Cutis laxa, 123700 Supravalvar aortic stenosis, 185500	130160	85	100	100	98
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
FLT4	Hemangioma, capillary infantile, somatic, 602089 Lymphatic malformation 1, 153100	136352	132	100	100	100
FOXH1	No OMIM phenotype	603621	78	100	100	97
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
GATA5	Congenital heart defects, multiple types, 5, 617912	611496	78	100	99	95
GATA6	Atrial septal defect 9, 614475 Atrioventricular septal defect 5, 614474 Pancreatic agenesis and congenital heart defects, 600001 Persistent truncus arteriosus, 217095 Tetralogy of Fallot, 187500	601656	128	100	95	91
GDF1	Congenital heart defects, multiple types, 6, 613854 Right atrial isomerism (Ivemark), 208530	602880	69	100	93	81
GJA1	Atrioventricular septal defect 3, 600309 Craniometaphyseal dysplasia, 218400 Erythrokeratodermia variabilis et progressiva 3, 617525 Hypoplastic left heart syndrome 1, 241550 Oculodentodigital dysplasia, 164200 Oculodentodigital dysplasia, 257850 Palmoplantar keratoderma with congenital alopecia, 104100 Syndactyly, type III, 186100	121014	101	100	100	100
HAND1	No OMIM phenotype	602406	146	100	100	98
HAND2	No OMIM phenotype	602407	99	100	100	100

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HEY2	No OMIM phenotype	604674	160	100	99	96
IRX4	No OMIM phenotype	606199	149	98	96	96
JAG1	Alagille syndrome 1, 118450 ?Deafness, congenital heart defects, and posterior embryotoxon, 617992 Tetralogy of Fallot, 187500	601920	96	100	100	96
LEFTY2	No OMIM phenotype	601877	144	100	100	99
MATR3	Amyotrophic lateral sclerosis 21, 606070	164015	63	100	100	95
MED13L	Mental retardation and distinctive facial features with or without cardiac defects, 616789 Transposition of the great arteries, dextro-looped 1, 608808	608771	73	100	100	97
MMP21	Heterotaxy, visceral, 7, autosomal, 616749	608416	81	100	96	88
MYH11	Aortic aneurysm, familial thoracic 4, 132900	160745	136	100	100	99
MYH6	Atrial septal defect 3, 614089 Cardiomyopathy, dilated, 1EE, 613252 Cardiomyopathy, hypertrophic, 14, 613251 {Sick sinus syndrome 3}, 614090	160710	145	100	99	98
MYH7	Cardiomyopathy, dilated, 1S, 613426 Cardiomyopathy, hypertrophic, 1, 192600 Laing distal myopathy, 160500 Left ventricular noncompaction 5, 613426 Myopathy, myosin storage, 608358 Myopathy, myosin storage, 255160 Scapuloperoneal syndrome, myopathic type, 181430	160760	176	100	100	100
MYOCD	No OMIM phenotype	606127	121	100	100	100
NKX2-5	Atrial septal defect 7, with or without AV conduction defects, 108900 Conotruncal heart malformations, variable, 217095 Hypoplastic left heart syndrome 2, 614435 Hypothyroidism, congenital nongoitrous, 5, 225250 Tetralogy of Fallot, 187500 Ventricular septal defect 3, 614432	600584	101	100	100	97
NKX2-6	Conotruncal heart malformations, 217095 Persistent truncus arteriosus, 217095	611770	145	100	100	100
NODAL	Heterotaxy, visceral, 5, 270100	601265	119	100	100	100
NOTCH1	Adams-Oliver syndrome 5, 616028 Aortic valve disease 1, 109730	190198	117	100	99	98
NOTCH2	Alagille syndrome 2, 610205 Hajdu-Cheney syndrome, 102500	600275	98	100	99	98
NR2F2	Congenital heart defects, multiple types, 4, 615779	107773	232	100	100	100
PKD1L1	Heterotaxy, visceral, 8, autosomal, 617205	609721	69	100	98	91

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PRDM6	Patent ductus arteriosus 3, 617039	616982	85	100	100	98
PTPN11	LEOPARD syndrome 1, 151100 Leukemia, juvenile myelomonocytic, somatic, 607785 Metachondromatosis, 156250 Noonan syndrome 1, 163950	176876	77	100	99	90
ROBO1	No OMIM phenotype	602430	102	100	100	98
ROBO4	Aortic valve disease 8, 618496	607528	91	100	100	98
SMAD2	No OMIM phenotype	601366	69	100	100	97
SMAD6	Aortic valve disease 2, 614823 {Craniosynostosis 7, susceptibility to}, 617439	602931	165	100	97	87
SMO	Basal cell carcinoma, somatic, 605462 Curry-Jones syndrome, somatic mosaic, 601707	601500	124	100	100	100
SOS1	?Fibromatosis, gingival, 1, 135300 Noonan syndrome 4, 610733	182530	71	100	100	95
TAB2	Congenital heart defects, nonsyndromic, 2, 614980	605101	76	100	100	99
TBX1	Conotruncal anomaly face syndrome, 217095 DiGeorge syndrome, 188400 Tetralogy of Fallot, 187500 Velocardiofacial syndrome, 192430	602054	94	94	85	80
TBX20	Atrial septal defect 4, 611363	606061	80	100	100	97
TBX5	Holt-Oram syndrome, 142900	601620	77	100	100	99
TDGF1	Forebrain defects	187395	127	100	100	100
TFAP2B	Char syndrome, 169100 Patent ductus arteriosus 2, 617035	601601	142	100	100	100
TLL1	Atrial septal defect 6, 613087	606742	67	100	100	96
ZFPM2	Diaphragmatic hernia 3, 610187 Tetralogy of Fallot, 187500 46XY sex reversal 9, 616067	603693	82	100	100	100
ZIC3	Congenital heart defects, nonsyndromic, 1, 306955 Heterotaxy, visceral, 1, 306955 VACTERL association, 314390	300265	101	100	100	97

- 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

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