Whole Exome Sequencing
Gene package Congenital Heart Defects (CHD), version 1.1, 22-11-2017

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	124	100	100	100
ACVR1	Fibrodysplasia ossificans progressiva, 135100	102576	51	100	99	89
ACVR2B	Heterotaxy, visceral, 4, autosomal, 613751	602730	74	100	100	96
ANKRD1	No OMIM phenotype	609599	64	100	98	85
CFC1	Heterotaxy, visceral, 2, autosomal, 605376	605194	130	100	96	83
CITED2	Atrial septal defect 8, 614433 Ventricular septal defect 2, 614431	602937	117	100	100	100
CRELD1	Atrioventricular septal defect, partial, with heterotaxy syndrome, 606217 {Atrioventricular septal defect, susceptibility to, 2}, 606217	607170	66	100	100	99
DCHS1	Mitral valve prolapse 2, 607829 Van Maldergem syndrome 1, 601390	603057	94	100	100	100
ELN	Cutis laxa, 123700 Supravalvar aortic stenosis, 185500	130160	70	100	100	98

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x	% covered >30x
FLNA	Cardiac valvular dysplasia, 314400 Congenital short bowel syndrome, 300048 FG syndrome 2, 300321 Frontometaphyseal dysplasia 1, 305620 Heterotopia, periventricular, 300049 Intestinal pseudoobstruction, neuronal, 300048 Melnick-Needles syndrome, 309350 Otopalatodigital syndrome, type I, 311300 Otopalatodigital syndrome, type II, 304120 Terminal osseous dysplasia, 300244	300017	79	100	100	100
FOXH1	No OMIM phenotype	603621	75	100	100	100
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	42	100	86	65
GATA5	No OMIM phenotype	611496	66	100	100	99
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	61	100	91	74
GDF1	Double-outlet right ventricle, 217095 Right atrial isomerism, 208530 Tetralogy of Fallot, 187500 Transposition of great arteries, dextro-looped 3, 613854	602880	40	100	90	65
GJA1	Atrioventricular septal defect 3, 600309 Craniometaphyseal dysplasia, 218400 Erythrokeratodermia variabilis et progressiva, 133200 Hypoplastic left heart syndrome 1, 241550 Oculodentodigital dysplasia, 164200 Oculodentodigital dysplasia, 257850 Palmoplantar keratoderma with congenital alopecia, 104100 Syndactyly, type III, 186100	121014	79	100	100	100
HAND1	No OMIM phenotype	602406	103	100	100	100
HEY2	No OMIM phenotype	604674	72	100	97	85
IRX4	No OMIM phenotype	606199	95	100	98	96

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x	% covered >30x
JAG1	Alagille syndrome 1, 118450 ?Deafness, congenital heart defects, and posterior embryotoxon Tetralogy of Fallot, 187500	601920	62	100	100	92
LEFTY2	Left-right axis malformations	601877	87	100	100	100
MATR3	Amyotrophic lateral sclerosis 21, 606070	164015	58	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	56	100	97	87
MMP21	Heterotaxy, visceral, 7, autosomal, 616749	608416	52	100	94	83
MYH11	Aortic aneurysm, familial thoracic 4, 132900	160745	76	100	99	91
MYH6	Atrial septal defect 3, 614089 Cardiomyopathy, dilated, 1EE, 613252 Cardiomyopathy, hypertrophic, 14, 613251 {Sick sinus syndrome 3}, 614090	160710	97	99	98	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	114	100	100	100
MYOCD	No OMIM phenotype	606127	68	100	100	95
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	84	100	100	100
NKX2-6	Conotruncal heart malformations, 217095 Persistent truncus arteriosus, 217095	611770	87	100	100	100
NODAL	Heterotaxy, visceral, 5, 270100	601265	79	100	100	100
NOTCH1	Adams-Oliver syndrome 5, 616028 Aortic valve disease 1, 109730	190198	87	100	99	98
NOTCH2	Alagille syndrome 2, 610205 Hajdu-Cheney syndrome, 102500	600275	75	100	100	96
NR2F2	Congenital heart defects, multiple types, 4, 615779	107773	111	100	100	100
SMAD2	No OMIM phenotype	601366	47	100	97	88
SMAD6	Aortic valve disease 2, 614823 {Craniosynostosis 7, susceptibility to}, 617439	602931	90	100	100	99

HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x	% covered >30x
SMO	Basal cell carcinoma, somatic, 605462 Curry-Jones syndrome, somatic mosaic, 601707	601500	76	100	100	99
TAB2	Congenital heart defects, nonsyndromic, 2, 614980	605101	58	100	100	95
TBX1	Conotruncal anomaly face syndrome, 217095 DiGeorge syndrome, 188400 Tetralogy of Fallot, 187500 Velocardiofacial syndrome, 192430	602054	44	91	78	67
TBX20	Atrial septal defect 4, 611363	606061	62	100	97	90
TBX5	Holt-Oram syndrome, 142900	601620	72	100	100	94
TDGF1	Forebrain defects	187395	86	100	100	96
TFAP2B	Char syndrome, 169100 Patent ductus arteriosus 2, 617035	601601	68	100	100	94
TLL1	Atrial septal defect 6, 613087	606742	46	100	97	82
ZFPM2	Diaphragmatic hernia 3, 610187 Tetralogy of Fallot, 187500 46XY sex reversal 9, 616067	603693	60	100	100	100
ZIC3	Congenital heart defects, nonsyndromic, 1, 306955 Heterotaxy, visceral, 1, 306955 VACTERL association, 314390	300265	60	100	97	86

- 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 96 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 describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 10x
- % Covered 20x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 20x