Supplementary Table 1. AVSD-associated gene list from Phenolyzer

Gene	OMIM ID	CHD-associated syndromes or diseases	CHD phenotypes
ABCD3	170995	Zellweger syndrome	Heart septal defect
ABCD4	603214	Methylmalonic aciduria and homocystinuria cblj type	Heart septal defect
ACF	603375	Cayler cardiofacial syndrome	Heart septal defect
ACTC1	102540	Atrial septal defect 5; dilated cardiomyopathy 1r; hypertrophic cardiomyopathy 11; left ventricular noncompaction 4	Heart septal defect; heart atrial septal defect
ACVR2B	602730	Situs ambiguus; heterotaxy visceral 4 autosomal	Heart septal defect; atrioventricular septal defect
ADAMTS10	608990	Weill marchesani syndrome	Heart septal defect
ADAMTSL2	612277	Geleophysic dysplasia	Heart septal defect
ADK	102750	Hypermethioninemia due to adenosine kinase deficiency	Heart septal defect
AGGF1	608464	Klippel trenaunay weber syndrome	Heart septal defect
AHI1	608894	Acrocallosal syndrome; joubert syndrome	Heart septal defect
ALG1	605907	Congenital disorder of glycosylation	Heart septal defect
ALG11	613666	Congenital disorder of glycosylation	Heart septal defect
ALG12	607144	Congenital disorder of glycosylation	Heart septal defect
ALG13	300776	Congenital disorder of glycosylation	Heart septal defect
ALG2	607905	Congenital disorder of glycosylation	Heart septal defect
ALG3	608750	Congenital disorder of glycosylation	Heart septal defect
ALG6	604566	Congenital disorder of glycosylation	Heart septal defect
ALG8	608103	Congenital disorder of glycosylation	Heart septal defect
ALG9	606941	Congenital disorder of glycosylation	Heart septal defect
ANK1	612641	8p11.2 deletion syndrome	Heart septal defect
ANKRD11	611192	16q24.3 microdeletion syndrome	Heart septal defect
ARHGAP31	610911	Adams oliver syndrome	Heart septal defect
ARID1A	603024	Coffin siris syndrome	Heart septal defect
ARID1B	614556	Coffin siris syndrome	Heart septal defect
ARL13B	608922	Acrocallosal syndrome; joubert syndrome	Heart septal defect
ARVCF	602269	22q11.2 deletion syndrome	Heart septal defect
ARX	300382	Lissencephaly x linked 2	Heart septal defect
ASXL1	612990	Bohring opitz syndrome; c like syndrome	Heart septal defect
ATIC	601731	Aicar transformylase imp cyclohydrolase deficiency	Heart septal defect
ATP6V0A2	611716	Cutis laxa; wrinkly skin syndrome	Heart septal defect
ATRX	300032	Atr x syndrome	Heart septal defect
B3GALTL	610308	Peters plus syndrome	Heart septal defect
B3GAT3	606374	Multiple joint dislocations short stature craniofacial dysmorphism and congenital heart defects	Heart septal defect
B4GALT1	137060	Congenital disorder of glycosylation	Heart septal defect
BAZ1B	605681	Williams syndrome	Heart septal defect
BCL7B	605846	Williams syndrome	Heart septal defect
BCOR	300485	Microphthalmia syndromic 2	Heart septal defect
BMP2	112261	20p12.3 microdeletion syndrome	Heart septal defect
BMP4	112262	Microphthalmia syndromic 3	Heart septal defect
BPIFA1	607412	Fetal alcohol syndrome	Heart septal defect
BRAF	164757	Cardiofaciocutaneous syndrome; leopard syndrome; noonan syndrome	Heart septal defect; atrioventricular septal defect
BRCA2	600185	Fanconi anemia	Heart septal defect
BRIP1	605882	Fanconi anemia	Heart septal defect
BUB1	602452	Mosaic variegated aneuploidy syndrome	Heart septal defect
BUB1B	602860	Mosaic variegated aneuploidy syndrome	Heart septal defect
BUB3	603719	Mosaic variegated aneuploidy syndrome	Heart septal defect
C5ORF42	614571	Acrocallosal syndrome; joubert syndrome	Heart septal defect
CACNA1D	114206	Primary aldosteronism seizures and neurologic abnormalities	Heart septal defect
CANT1	613165	Desbuquois syndrome	Heart septal defect
CC2D2A	612013	Acrocallosal syndrome; joubert syndrome	Heart septal defect
CCBE1	612753	Hennekam lymphangiectasia lymphedema syndrome	Heart septal defect
CD96	606037	Bohring syndrome; opitz trigonocephaly syndrome	Heart septal defect
CDKN1C	600856	Williams beuren syndrome	Heart septal defect

CEP290	610142	Acrocallosal syndrome; joubert syndrome 18; meckel syndrome type 4	Heart septal defect
CEP41	610523	Acrocallosal syndrome; joubert syndrome	Heart septal defect
CEP57	607951	Mosaic variegated aneuploidy syndrome	Heart septal defect
CFC1	605194	Conotruncal heart malformations; double outlet right ventricle; situs ambiguus; heterotaxy visceral 2 autosomal	Heart septal defect; atrioventricular septal defect
CHD7	608892	Charge syndrome	Heart septal defect
CHST14	608429	Ehlers danlos syndrome musculocontractural type	Heart septal defect
CHST3	603799	Multiple joint dislocations short stature craniofacial dysmorphism and congenital heart defects	Heart septal defect
CITED2	602937	Tetralogy of fallot; ventricular septal defect 2; atrial septal defect 8	Heart septal defect; atrioventricular septal defect
CKAP2L	616174	Filippi syndrome	Heart septal defect
CLIP2	603432	Williams syndrome	Heart septal defect
COG1	606973	Congenital disorder of glycosylation	Heart septal defect
COG4	606976	Congenital disorder of glycosylation	Heart septal defect
COG5	606821	Congenital disorder of glycosylation	Heart septal defect
COG6	606977	Congenital disorder of glycosylation	Heart septal defect
COG7	606978	Congenital disorder of glycosylation	Heart septal defect
COG8	606979	Congenital disorder of glycosylation	Heart septal defect
COL11A1	120280	Stickler syndrome, type II	Heart septal defect
COL11A2	120290	Otospondylomegaepiphyseal dysplasia	Heart septal defect
COL1A1	120150	Ehlers danlos syndrome classic type	Heart septal defect
COL2A1	120140	Otospondylomegaepiphyseal dysplasia	Heart septal defect
COL5A1	120215	Ehlers danlos syndrome classic type	Heart septal defect
COL5A2	120190	Ehlers danlos syndrome classic type	Heart septal defect
COMT	116790	22q11.2 deletion syndrome	Heart septal defect
CREBBP	600140	Rubinstein taybi syndrome 1	Heart septal defect
CRELD1	607170	Atrioventricular septal defect partial	Heart septal defect; heart ventricular septal defect; atrioventricular septal defect
CRKL	602007	Digeorge syndrome	Heart septal defect
CSGALNACT2	616616	Hirschsprung disease	Heart septal defect; heart ventricular septal defect
CTCF	604167	Mental retardation autosomal dominant 21	Heart septal defect
DDOST	602202	Congenital disorder of glycosylation	Heart septal defect
DDX11	601150	Warsaw breakage syndrome	Heart septal defect
DHCR7	602858	Smith lemli opitz syndrome	Heart septal defect; atrioventricular septal defect
DHFR	126060	Smith lemli opitz syndrome	Heart septal defect; atrioventricular canal defect
DLG4	602887	Williams syndrome	Heart septal defect
DOCK6	614194	Adams oliver syndrome	Heart septal defect
DOLK	610746	Congenital disorder of glycosylation	Heart septal defect
DPAGT1	191350	Congenital disorder of glycosylation	Heart septal defect
DPM1	603503	Congenital disorder of glycosylation	Heart septal defect
DPM2	603564	Congenital disorder of glycosylation	Heart septal defect
DPM3	605951	Congenital disorder of glycosylation	Heart septal defect
DSE	605942	Ehlers danlos syndrome musculocontractural type	Heart septal defect
DTNA	601239	Left ventricular noncompaction	Heart septal defect
ECE1	600423	Hirschsprung disease	Heart septal defect; heart ventricular septal defect
EDN3	131242	Hirschsprung disease	Heart septal defect; heart ventricular septal defect
EDNRB	131244	Hirschsprung disease	Heart septal defect; heart ventricular septal defect
EFTUD2	603892	Growth and mental retardation mandibulofacial dysostosis microcephaly and cleft palate; mandibulofacial dysostosis guion almeida type	Heart septal defect
EHMT1	607001	Kleefstra syndrome; kleefstra syndrome due to 9q34 microdeletion	Heart septal defect
EIF4H	603431	Williams syndrome	Heart septal defect
ELN	130160	Williams syndrome	Heart septal defect

EOGT	614789	Adams oliver syndrome	Heart septal defect
EPO	133170	Heart septal defects ventricular	Heart septal defect; heart ventricular septal defects
ERBB3	190151	Lethal congenital contracture syndrome 2	Heart septal defect
ERCC4	133520	Fanconi anemia	Heart septal defect
ESCO2	609353	Roberts syndrome	Heart septal defect
EVC	604831	Ellis van creveld syndrome	Heart septal defect; atrioventricular septal defect
EVC2	607261	Ellis van creveld syndrome	Heart septal defect; atrioventricular septal defect
EYA1	601653	Cayler cardiofacial syndrome	Heart septal defect
FAM58A	300708	Syndactyly telecanthus anogenital and renal malformations	Heart septal defect
FANCA	607139	Fanconi anemia	Heart septal defect
FANCB	300515	Vacterl association; fanconi anemia	Heart septal defect
FANCC	613899	Fanconi anemia	Heart septal defect
FANCD2	613984	Fanconi anemia	Heart septal defect
FANCE	613976	Fanconi anemia	Heart septal defect
FANCF	613897	Fanconi anemia	Heart septal defect
FANCG	602956	Fanconi anemia	Heart septal defect
FANCI	611360	Fanconi anemia	Heart septal defect
FANCL	608111	Fanconi anemia	Heart septal defect
FANCM	609644	Fanconi anemia	Heart septal defect
FBN1	134797	Aortic aneurysm familial thoracic 4; marfan syndrome; shprintzen goldberg syndrome; geleophysic dysplasia; weill marchesani syndrome	Heart septal defect
FGF8	600483	Digeorge syndrome	Heart septal defect
FGFR1	136350	Apert syndrome; encephalocraniocutaneous lipomatosis	Heart septal defect
FGFR2	176943	Acrocephalosyndactyly type I; apert syndrome	Heart septal defect
FGFR3	134934	Apert syndrome; thanatophoric dysplasia	Heart septal defect
FIG4	609390	Yunis varon syndrome	Heart septal defect
FKBP6	604839	Williams syndrome	Heart septal defect
FKTN	607440	Fukuyama congenital muscular dystrophy	Heart septal defect
FLNA	300017	Cardiac valvular dysplasia x linked; frontometaphyseal dysplasia; melnick needles syndrome; otopalatodigital syndrome type II	Heart septal defect; atrioventricular septal defect
FLNB	603381	Larsen syndrome	Heart septal defect
FOXC1	601090	Axenfeld rieger syndrome type 3	Heart septal defect
FOXC2	602402	Lymphedema distichiasis syndrome	Heart septal defect
FOXE3	601094	Anterior segment mesenchymal dysgenesis	Heart septal defect
FOXG1	164874	Acrocallosal syndrome	Heart septal defect
G6PC3	611045	Dursun syndrome	Heart septal defect; heart atrial septal defect
GAS1	139185	Holoprosencephaly	Heart septal defect
GATA1	305371	Diamond blackfan anemia	Heart septal defect
GATA4	600576	Atrial septal defect 2; atrioventricular septal defect 4; tetralogy of fallot; ventricular septal defect 1; 8p23.1 microdeletion syndrome	Heart septal defect; heart atrial septal defect; heart ventricular septal defect; atrioventricular septal defect
GATA6	601656	Conotruncal heart malformations; persistent truncus arteriosus; tetralogy of fallot; atrioventricular septal defect 5; pancreatic agenesis and congenital heart defects; atrial septal defect 9	Heart septal defect; atrioventricular septal defect
GDF1	602880	Conotruncal heart malformations; double outlet right ventricle; right atrial isomerism; tetralogy of fallot	Heart septal defect; atrioventricular septal defect
GDF3	606522	Isolated klippel feil syndrome	Heart septal defect
GDF6	601147	Isolated klippel feil syndrome	Heart septal defect
GDNF	600837	Hirschsprung disease	Heart septal defect; heart ventricular septal defects
GH1	139250	Turner syndrome	Heart septal defect
GJA1	121014	Atrioventricular septal defect 3; hypoplastic left heart syndrome; palmoplantar keratoderma; oculodentodigital dysplasia	Heart septal defect; atrioventricular septal defect
GLA	300644	Fabry disease	Heart septal defect
GLI3	165240	Acrocallosal syndrome; pallister hall syndrome	Heart septal defect
GP1BB	138720	22q11.2 deletion syndrome	Heart septal defect
GPC3	300037	Simpson golabi behmel syndrome	Heart septal defect

GPC4	300168	Simpson golabi behmel syndrome	Heart septal defect
GPC6	604404	Omodysplasia 1	Heart septal defect
GPX4	138322	Spondylometaphyseal dysplasia sedaghatian type	Heart septal defect
GTF2I	601679	Williams syndrome	Heart septal defect
GTF2IRD1	604318	Williams syndrome	Heart septal defect
HCCS	300056	Microphthalmia syndromic 7	Heart septal defect
HDAC8	300269	Cornelia de lange syndrome; de lange syndrome	Heart septal defect
HIRA	600237	22q11.2 deletion syndrome	Heart septal defect
HOXA13	142959	Hand foot genital syndrome	Heart septal defect
HRAS	190020	Costello syndrome	Heart septal defect
HSD17B4	601860	Zellweger syndrome	Heart septal defect
HSPG2	142461	Dyssegmental dysplasia silverman handmaker type	Heart septal defect
HYLS1	610693	Hydrolethalus syndrome	Heart septal defect; atrioventricular septal defect
IMPAD1	614010	Catel manzke syndrome	Heart septal defect
INPP5E	613037	Acrocallosal syndrome; joubert syndrome	Heart septal defect
IRX5	606195	Hamamy syndrome	Heart septal defect
JAG1	601920	Alagille syndrome; deafness congenital heart defects and posterior embryotoxon; tetralogy of fallot	Heart septal defect
KANSL1	612452	Koolen de vries syndrome	Heart septal defect
KAT6B	605880	Noonan syndrome; young simpson syndrome; blepharophimosis intellectual deficit syndrome sbbys type; genitopatellar syndrome; noonan syndrome	Heart septal defect; atrioventricular septal defect
KDM6A	300128	Kabuki make up syndrome	Heart septal defect
KIAA0196	610657	3c syndrome; dandy walker like malformation	Heart septal defect; heart atrial septal defect
KIF7	611254	Acrocallosal syndrome; joubert syndrome 18	Heart septal defect
KMT2D	602113	Kabuki make up syndrome	Heart septal defect
KRAS	190070	Cardiofaciocutaneous syndrome; noonan syndrome; costello syndrome	Heart septal defect
L1CAM	308840	Hirschsprung disease	Heart ventricular septal defect
LAT2	605719	Williams syndrome	Heart septal defect
LBR	600024	Pelger huet anomaly	Heart septal defect
LETM1	604407	Wolf hirschhorn syndrome	Heart septal defect
LIMK1	601329	Williams syndrome	Heart septal defect
LMNA	150330	Heart hand syndrome slovenian type; left ventricular noncompaction; restrictive dermopathy lethal	Heart septal defect
LONP1	605490	Codas syndrome	Heart septal defect
LRP2	600073	Donnai barrow syndrome	Heart septal defect
LRP5	603506	Osteoporosis pseudoglioma syndrome	Heart septal defect
LTBP2	602091	Weill marchesani syndrome	Heart septal defect
LTBP4	604710	Cutis laxa	Heart septal defect
MAGT1	300715	Congenital disorder of glycosylation	Heart septal defect
MAP2K1	176872	Cardiofaciocutaneous syndrome; noonan syndrome	Heart septal defect
MAP2K2	601263	Cardiofaciocutaneous syndrome	Heart septal defect
MED12	300188	Lujan fryns syndrome; x linked intellectual deficit; x linked mental retardation	Heart septal defect
MEGF8	604267	Carpenter syndrome	Heart septal defect
MEOX1	600147	Isolated klippel feil syndrome	Heart septal defect
MGAT2	602616	Congenital disorder of glycosylation type iia	Heart septal defect
MGP	154870	Keutel syndrome	Heart septal defect
MID1	300552	Opitz frias syndrome	Heart septal defect; atrioventricular septal defect
MKKS	604896	Mckusick kaufman syndrome	Heart septal defect
MKS1	609883	Meckel syndrome type 1	Heart septal defect; atrioventricular septal defect
MLXIPL	605678	Williams syndrome	Heart septal defect
MMP14	600754	Torg winchester syndrome	Heart septal defect
MMP2	120360	Torg winchester syndrome	Heart septal defect
MOGS	601336	Congenital disorder of glycosylation	Heart septal defect
MPDU1	604041	Congenital disorder of glycosylation	Heart septal defect
MPI	154550	Congenital disorder of glycosylation	Heart septal defect
MSX1	142983	Wolf hirschhorn syndrome	Heart septal defect

MX1	147150	Fanconi anemia	Heart septal defect
MYH6	160710	Atrial septal defect 3; dilated cardiomyopathy 1ee; hypertrophic cardiomyopathy 14	Heart septal defect; heart atrial septal defect
MYL2	160781	Cardiomyopathy familial hypertrophic 10	Heart septal defect
NAA10	300013	N-terminal acetyltransferase deficiency; ogden syndrome	Heart septal defect
NEK8	609799	Renal hepatic pancreatic dysplasia	Heart septal defect
NEK9	609798	Arthrogryposis perthes disease and upward gaze palsy	Heart septal defect
NELFA	606026	Wolf hirschhorn syndrome	Heart septal defect
NFIX	164005	Marshall smith syndrome; sotos syndrome	Heart septal defect
NIPBL	608667	Cornelia de lange syndrome	Heart septal defect
NKX2-5	600584	Atrial septal defect 7; conotruncal heart malformations; tetralogy of fallot; ventricular septal defect 3	Heart atrial septal defect; heart septal defect
NKX2-6	611770	Conotruncal heart malformations; persistent truncus arteriosus	Heart septal defect
NODAL	601265	Heterotaxy visceral 5 autosomal	Heart septal defect
NOS3	163729	Fabry disease	Heart septal defect
NOTCH2	600275	Alagille syndrome; hajdu cheney syndrome	Heart septal defect
NOTCH3	600276	Lateral meningocele syndrome	Heart septal defect
NPHP1	607100	Acrocallosal syndrome; joubert syndrome	Heart septal defect
NPHP3	608002	Renal hepatic pancreatic dysplasia	Heart septal defect
NRAS	164790	Noonan syndrome	Heart septal defect
NRG1	142445	Hirschsprung disease	Heart septal defect; heart ventricular septal defect
NRTN	602018	Hirschsprung disease	Heart septal defect; heart ventricular septal defect
NSD1	606681	Sotos syndrome	Heart septal defect
NSDHL	300275	Child syndrome	Heart septal defect
OFD1	300170	Primary ciliary dyskinesia; acrocallosal syndrome; joubert syndrome 18	Heart septal defect
OTX2	600037	Microphthalmia syndromic 3	Heart septal defect
PALB2	610355	Fanconi anemia	Heart septal defect
PAX2	167409	Microphthalmia syndromic 3	Heart septal defect
PAX3	606597	Waardenburg syndrome type 3	Heart septal defect
PCNT	605925	Microcephalic osteodysplastic primordial dwarfism type II	Heart septal defect
PCSK5	600488	Heart septal defects; heart ventricular septal defects	Heart septal defects; heart ventricular septal defects
PEX1	602136	Zellweger syndrome	Heart septal defect
PEX10	602859	Zellweger syndrome	Heart septal defect
PEX11B	603867	Zellweger syndrome	Heart septal defect
PEX12	601758	Zellweger syndrome	Heart septal defect
PEX13	601789	Zellweger syndrome	Heart septal defect
PEX14	601791	Zellweger syndrome	Heart septal defect
PEX16	603360	Zellweger syndrome	Heart septal defect
PEX19	600279	Zellweger syndrome	Heart septal defect
PEX2	170993	Zellweger syndrome	Heart septal defect
PEX26	608666	Zellweger syndrome	Heart septal defect
PEX3	603164	Zellweger syndrome	Heart septal defect
PEX5	600414	Zellweger syndrome	Heart septal defect
PEX6	601498	Zellweger syndrome	Heart septal defect
PGM1	171900	Congenital disorder of glycosylation	Heart septal defect
PHOX2B	603851	Hirschsprung disease	Heart septal defects; heart ventricular septal defects
PIEZO2	613629	Marden walker syndrome	Heart septal defect
PIGA	311770	Multiple congenital anomalies hypotonia seizures syndrome 2	Heart septal defect
PIGL	605947	Chime syndrome; zunich neuroectodermal syndrome	Heart septal defect
PIGN	606097	Multiple congenital anomalies hypotonia seizures syndrome 1	Heart septal defect
PIK3CA	171834	Megalencephaly capillary malformation polymicrogyria syndrome; megalencephaly cutis marmorata telangiectatica congenita	Heart septal defect
PIK3R2	603157	Megalencephaly polymicrogyria polydactyly hydrocephalus syndrome	Heart septal defect

PITX2	601542	Microphthalmia syndromic 3	Heart septal defect
PITX3	602669	Anterior segment mesenchymal dysgenesis; microphthalmia syndromic 3	Heart septal defect
PMM2	601785	Congenital disorder of glycosylation	Heart septal defect
PORCN	300651	Focal dermal hypoplasia	Heart septal defect
PQBP1	300463	Hamel cerebro palato cardiac syndrome; renpenning syndrome 1	Heart septal defect
PTEN	601728	Leopard syndrome	Heart septal defects; atrioventricular canal defect
PTPN11	176876	Leopard syndrome; noonan syndrome; tetralogy of fallot	Heart septal defect; atrioventricular septal defect
PUF60	604819	Verheij syndrome	Heart septal defect
PYCR1	179035	Cutis laxa	Heart septal defect
RAB23	606144	Carpenter syndrome	Heart septal defect
RAD21	606462	Cornelia de lange syndrome	Heart septal defect
RAD51C	602774	Fanconi anemia	Heart septal defect
RAF1	164760	Leopard syndrome; noonan syndrome; dilated cardiomyopathy 1nn	Heart septal defect; atrioventricular septal defect
RAI1	607642	Potocki lupski syndrome	Heart septal defect
RARB	180220	Microphthalmia syndromic 12	Heart septal defect
RASGEF1A	614531	Hirschsprung disease	Heart septal defect; heart ventricular septal defect
RAX	601881	Microphthalmia syndromic 3	Heart septal defect
RBM10	300080	Tarp syndrome	Heart septal defect
RBM8A	605313	Thrombocytopenia absent radius syndrome	Heart septal defect
RBPJ	147183	Adams oliver syndrome	Heart septal defect
RECQL4	603780	Rapadilino syndrome; baller gerold syndrome	Heart septal defect; heart atrial septal defect
RET	164761	Hirschsprung disease	Heart septal defect; heart ventricular septal defect
RFC2	600404	Williams syndrome	Heart septal defect
RFT1	611908	Congenital disorder of glycosylation	Heart septal defect
RIT1	609591	Noonan syndrome	Heart septal defect
RMRP	157660	Cartilage hair hypoplasia	Heart septal defect
RNU4ATAC	601428	Microcephalic osteodysplastic primordial dwarfism type I	Heart septal defect
ROR2	602337	Brachydactyly type b; robinow syndrome autosomal recessive	Heart septal defect
RPGRIP1L	610937	Acrocallosal syndrome; joubert syndrome	Heart septal defect
RPL11	604175	Diamond blackfan anemia	Heart septal defect
RPL15	604174	Diamond blackfan anemia	Heart septal defect
RPL26	603704	Diamond blackfan anemia	Heart septal defect
RPL35A	180468	Diamond blackfan anemia	Heart septal defect
RPL5	603634	Aase syndrome; diamond blackfan anemia	Heart septal defect
RPS10	603632	Diamond blackfan anemia	Heart septal defect
RPS17	180472	Diamond blackfan anemia	Heart septal defect
RPS19	603474	Diamond blackfan anemia	Heart septal defect
RPS24	602412	Diamond blackfan anemia	Heart septal defect
RPS26	603701	Diamond blackfan anemia	Heart septal defect
RPS28	603685	Diamond blackfan anemia	Heart septal defect
RPS7	603658	Diamond blackfan anemia	Heart septal defect
SALL1	602218	Townes brocks syndrome	Heart septal defect
SALL4	607343	Duane radial ray syndrome	Heart septal defect
SEMA3C	602645	Truncus arteriosus persistent	Heart septal defect
SEMA3E	608166	Charge syndrome	Heart septal defect
SETBP1	611060	Schinzel giedion midface retraction syndrome	Heart septal defect
SH2B1	608937	Proximal 16p11 2 microdeletion syndrome	Heart septal defect
SHANK3	606230	Phelan mcdermid syndrome	Heart septal defect
SHH	600725	Single upper central incisor	Heart septal defect; atrioventricular septal defect
SHOC2	602775	Noonan syndrome	Heart septal defect
SIX3	603714	Microphthalmia syndromic 3	Heart septal defect
SIX6	606326	Microphthalmia syndromic 3	Heart septal defect
SLC19A2	603941	Thiamine responsive megaloblastic anemia syndrome	Heart septal defect

SLC29A3	612373	Dysosteosclerosis; faisalabad histiocytosis; h syndrome; histiocytosis lymphadenopathy plus syndrome	Heart septal defect
SLC35A1	605634	Congenital disorder of glycosylation	Heart septal defect
SLC35C1	605881	Congenital disorder of glycosylation	Heart septal defect
SLX4	613278	Fanconi anemia	Heart septal defect
SMAD4	600993	Myhre syndrome	Heart septal defect
SMARCA2	600014	Coffin siris syndrome	Heart septal defect
SMARCA4	603254	Coffin siris syndrome	Heart septal defect
SMARCB1	601607	Coffin siris syndrome	Heart septal defect
SMARCE1	603111	Coffin siris syndrome	Heart septal defect
SMC1A	300040	Cornelia de lange syndrome	Heart septal defect
SMC3	606062	Cornelia de lange syndrome	Heart septal defect
SNRPB	182282	Cerebrocostomandibular syndrome	Heart septal defect
SNX3	605930	Microphthalmia syndromic 8	Heart septal defect
SOS1	182530	Noonan syndrome	Heart septal defect
SOX2	184429	Microphthalmia syndromic 3	Heart septal defect
SPECC1L	614140	Opitz gbbb syndrome type ii	Heart septal defect
SRCAP	611421	Floating harbor syndrome	Heart septal defect; heart ventricular septal defect
SRD5A3	611715	Congenital disorder of glycosylation	Heart septal defect
STAMBP	606247	Microcephaly capillary malformation syndrome	Heart septal defect
STRA6	610745	Microphthalmia syndromic 9	Heart septal defect
STRADA	608626	Polyhydramnios megalencephaly and symptomatic epilepsy	Heart septal defect
SYNE1	608441	Emery dreifuss muscular dystrophy 4 autosomal dominant	Heart septal defect
TBL2	605842	Williams syndrome	Heart septal defect
TBX1	602054	22q11.2 deletion syndrome; conotruncal anomaly face syndrome; conotruncal heart malformations; digeorge syndrome; shprintzen syndrome; tetralogy of fallot; velocardiofacial syndrome	Heart septal defect
TBX20	606061	Atrial septal defect 4	Heart septal defect; heart atrial septal defect
TBX3	601621	Ulnar mammary syndrome	Heart septal defect
TBX5	601620	Holt oram syndrome	Heart septal defect; heart atrial septal defect; atrioventricular septal defect
TCF4	602272	Pallister hall syndrome	Heart septal defect
TCTN1	609863	Acrocallosal syndrome; joubert syndrome	Heart septal defect
TCTN2	613846	Acrocallosal syndrome; joubert syndrome	Heart septal defect
TCTN3	613847	Acrocallosal syndrome; joubert syndrome 18	Heart septal defect
TDGF1	187395	Holoprosencephaly	Heart septal defect
TFAP2B	601601	Char syndrome; patent ductus arteriosus 2	Heart septal defect
TGDS	616146	Catel manzke syndrome	Heart septal defect
TGFBR1	190181	loeys dietz syndrome type 1a	Heart septal defect
TGFBR2	190182	loeys dietz syndrome type 1b	Heart septal defect
TGIF1	602630	Holoprosencephaly	Heart septal defect
TLL1	606742	Atrial septal defect 6	Heart septal defect; heart atrial septal defect
TMEM138	614459	Acrocallosal syndrome; joubert syndrome	Heart septal defect
TMEM165	614726	Congenital disorder of glycosylation	Heart septal defect
TMEM216	613277	Acrocallosal syndrome; joubert syndrome	Heart septal defect
TMEM231	614949	Acrocallosal syndrome; joubert syndrome	Heart septal defect
TMEM237	614423	Acrocallosal syndrome; joubert syndrome	Heart septal defect
TMEM67	609884	Acrocallosal syndrome; joubert syndrome	Heart septal defect
TNF	191160	Fanconi anemia	Heart septal defect
TP63	603273	Ankyloblepharon ectodermal defects cleft lip palate; hay wells syndrome	Heart septal defect
TSFM	604723	Combined oxidative phosphorylation deficiency 3	Heart septal defect
TTC21B	612014	Acrocallosal syndrome; joubert syndrome	Heart septal defect
TTC37	614589	Trichohepatoenteric syndrome 1	Heart septal defect
TUSC3	601385	Congenital disorder of glycosylation	Heart septal defect
TWSG1	605049	Holoprosencephaly	Heart septal defect
TXNL4A	611595	Burn mckeown syndrome	Heart septal defect

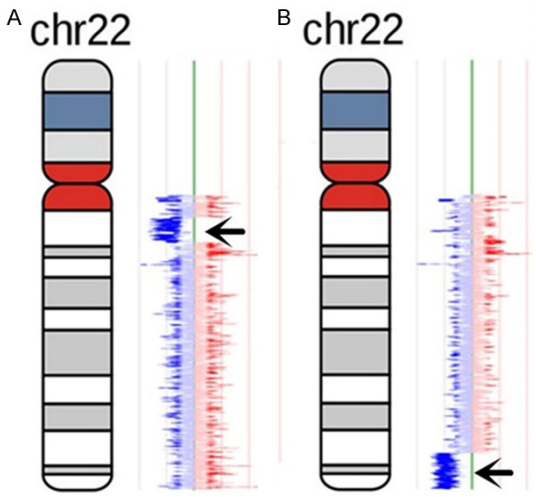
UBR1	605981	Johanson blizzard syndrome	Heart septal defect
UFD1L	601754	22q11.2 deletion syndrome	Heart septal defect
UMPS	613891	Orotic aciduria	Heart septal defect
VAX1	604294	Microphthalmia syndromic 3	Heart septal defect
VEGFA	192240	Heart septal defects ventricular	Heart septal defect; heart ventricular septal defects
VIPAS39	613401	Arthrogryposis renal dysfunction and cholestasis 2	Heart septal defect
VPS13B	607817	Cohen syndrome	Heart septal defect
VPS33B	608552	Arthrogryposis renal dysfunction and cholestasis 1	Heart septal defect
VSX2	142993	Microphthalmia syndromic 3	Heart septal defect
WBSCR22	615733	Williams syndrome	Heart septal defect
WBSCR27	612546	Williams syndrome	Heart septal defect
WDPCP	613580	Congenital heart defects hamartomas of tongue and polysyndactyly; orstavik lindemann solberg syndrome	Heart septal defect; atrioventricular septal defect
WHSC1	602952	Wolf hirschhorn syndrome	Heart septal defect
WT1	607102	Meacham syndrome	Heart septal defect
YY1AP1	607860	Grange syndrome	Heart septal defect
ZEB2	605802	Mowat wilson syndrome	Heart septal defect
ZIC3	300265	Double outlet right ventricle; heterotaxy visceral x linked; situs ambiguus; vacterl association; vacterl association x linked	Heart septal defect
ZMPSTE24	606480	Restrictive dermopathy lethal	Heart septal defect

Abbreviations: AVSD, atrioventricular septal defect; CHD, congenital heart disease.

Supplementary Table 2. AVSD-associated gene list from related published literatures

Gene	OMIM ID	CHD-associated syndromes or diseases	CHD Phenotypes	Genetic variation in human AVSD	Play a role in AVSD formation in animal models
COL1A2	120160	Ehlers danlos syndrome autosomal recessive cardiac valvular form; osteogenesis imperfecta	Heart septal defect; atrioventricular septal defect	No	Yes
COL6A1	120220	-	Heart septal defect; atrioventricular septal defect	Yes	Yes
COL6A2	120240	-	Heart septal defect; atrioventricular septal defect	Yes	Yes
NR2F2	107773	Congenital heart defects multiple types, 4	Heart septal defect; atrioventricular septal defect	Yes	Yes
DSCAM	602523	Down's syndrome	Heart septal defect; atrioventricular septal defect	Yes	No
DNAHC11	603339	Ciliary dyskinesia, primary, 7, with or without situs inversus	Heart septal defect; atrioventricular septal defect	No	Yes
FOXP1	605515	Mental retardation with language impairment and with or without autistic features	Heart septal defect; atrioventricular septal defect	Yes	Yes
ACVR1 (*ALK2*)	102576	Cardiac death sudden	Heart septal defect; atrioventricular septal defect	Yes	Yes
BMP5	112265	-	Heart septal defect; atrioventricular septal defect	No	Yes
COL18A1	120328	Heart valve diseases	Heart septal defect; atrioventricular septal defect	No	Yes
CYR61 (*CCN1*)	602369	-	Heart septal defect; atrioventricular septal defect	No	Yes
FBLN2	135821	-	Heart septal defect; atrioventricular septal defect	Yes	Yes
FGF2	134920	Cardiomegaly; myocardial ischemia	Heart septal defect; atrioventricular septal defect	No	Yes
FRZB	605083	-	Heart septal defect; atrioventricular septal defect	Yes	Yes
GATA5	611496	Familial atrial fibrillation	Heart septal defect; atrioventricular septal defect	Yes	Yes
HEY2	604674	Brugada syndrome; cardiomyopathy hypertrophic	Heart septal defect; atrioventricular septal defect	Yes	Yes
ROCK1	601702	-	Heart septal defect; atrioventricular septal defect	No	Yes
WNT9A	602863	-	Heart septal defect; atrioventricular septal defect	No	Yes
ALDH1A2	603687	-	Tetralogy of Fallot	No	Yes
HAND1	602406	-	Atrial Septal Defect, Hypoplastic Left Heart	No	Yes
SMAD6	602931	-	Aortic Valve Disease	No	Yes

Abbreviations: AVSD, atrioventricular septal defect; CHD, congenital heart disease.



Supplementary Figure 1. Two CNVs larger than 1 Mb were detected by low-pass WGS. They were heterozygous deletions at chromosome 22q11.21 (A) and chromosome 22q13.31q13.33 (B), the length of them were 2.78 Mb and 4.29 Mb, respectively.

Supplementary Table 3. Primers Design for AVSD-associated genes contained in CNVs

Gene	Forward Primer	Reverse Primer	Product Length
NOTCH2	AGGCACCTGTATTGACCTTG	TCCAATCCTATCCATGCACTG	142 Bp
COL11A1	CAGGTGGAACTTTCCCAGAA	GCAGGTTTTCCAGTGTGGTC	169 Bp
NIPBL	GCTGGCACCTGAACTAAGTAC	GTAAAGGAGATGGAAGAGGCAG	150 Bp
EHMT1	GCCAGTAAAGATCCCAGAGAAG	GTAGCACTGGTTCTGAGGTAG	150 Bp
NR2F2	TCAAAGTGGGCATGAGACG	CGCAACAGCAGGGAAATATATC	142 Bp
COL6A1	CGAATGCGAGATTTTGGACATC	ACGAAGTCCTTGGCAATCTC	138 Bp
COL6A2	CAGCCCTCAAGTTTGCCTAC	TCACTCTCGTGCTTCTCGTG	196 Bp
SMC1A	GGTAGAGGATGAGGTGTTTGAAG	ACTGAATGCCCAAGCGAG	149 Bp

Supplementary Table 4. CNVs containing the AVSD-associated genes in DECIPHER

Candidate gene	Patients, CNVs and phenotypes
NOTCH2	Patient 250,335 with 14.55 Mb deletion at 1p12p21.1 has ASD, VSD
	Patient 317,280 with 4.20 Mb deletion at 1p12p13.2 has VSD
COL11A1	None
NIPBL	Patient 4,651 with 177.78 Kb deletion at 5p13.2 with VSD
	Patient 285,915 with 22.17 Mb duplication at 5p13.2q11.2 has ASD
	Patient 341,218 with 422.15 Kb duplication at 5p13.2 has ASD
	Patient 350,097 with a heterozygous and definitely pathogenic frameshift variant (Val2227PhefsTer25) has complete AVSD (SNV)
EHMT1	Patient 771 with 3.03 Mb deletion at 9q34.3 has VSD
	Patient 1,003 with 2.22 Mb deletion at 9q34.3 has ASD, VSD
	Patient 250,053 with 192.76 Kb deletion at 9q34.3 has ASD
	Patient 251,553 with 561.12 Kb deletion at 9q34.3 has ASD
	Patient 269,405 with 293.64 Kb deletion at 9q34.3 has ASD
	Patient 285,975 with 589.35 Kb definitely pathogenic deletion at 9q34.3 has ASD, VSD
NR2F2	Patient 2,219 with 8.54 Mb duplication at 15q26.1q26.3 has AVSD
	Patient 251,099 with 6.60 Mb deletion at 15q26.2q26.3 has VSD
	Patient 256,144 with 10.65 Mb duplication at 15q26.1q26.3 has ASD

	Patient 259,934 with 7.10 Mb deletion at 15q26.2q26.3 has VSD
	Patient 277,356 with 3.56 Mb deletion at 15q26.2q26.3 has VSD
	Patient 286,739 with 3.71 Mb likely pathogenic deletion at 15q26.2q26.3 has VSD
	Patient 259,383 with a likely pathogenic SNV has complete AVSD
COL6A1	None
COL6A2	None
TBX1	Patient 256,300 with 2.40 Mb deletion at 22q11.21 has AVSD
	Patient 286,085 with 2.49 Mb definitely pathogenic deletion at 22q11.1q11.21 has ASD, VSD
	Patient 300,420 with 2.42 Mb definitely pathogenic duplication at 22q11.21 has ASD, VSD
SHANK3	Patient 253,900 with 86.55 Kb duplication at 22q13.33 has AVSD
	Patient 353,765 with 55.33 Kb duplication at 22q13.33 has VSD
SMC1A	Patient 256,035 with 1.32 Mb duplication at Xp11.22 has VSD

Abbreviations: CNV, copy number variation; AVSD, atrioventricular septal defect; ASD, atrial septal defect; VSD, ventricular septal defect; SNV, single nucleotide variants.

Supplementary Table 5. Primers Design for Sanger sequencing

Gene	Position	Nucleotide changes	Forward Primer	Reverse Primer	Product Length
COL11A1	1:103496805	652-5->TT	TTTCCTGAGCCAGAAGATAACA	CAAAAACTGCACTGCGATGT	427 Bp
	1:103412451	3266C>T	ACATGCCAGACACATATGCAG	TGGATTCAACTGTTTCTCTTTGG	388 Bp
COL6A2	21:47532276	499G>A	ATCCACGTGTACTTCGTGCTG	TCACCATGACCTTGATGATGC	586 Bp
	21:47532456	679G>A	CTGGCCAACATGACGGAG	GGTAAAGTGAGGCCCGGAG	384 Bp
	21:47552204	2798G>A	ACGACGACCCTCTCAACG	AGGAGCTGGAGAGGTGCAG	588 Bp
C5ORF42	5:37170162	6443A>G	CACCCGGCTGACTTTTGTAT	CTGTGCATTTAGGGGAAAGC	355 Bp
	5:37125396	8746G>A	TGCCAAATTACAAATGTATCCAA	AGGTAACAAATTGGAGTGAGTTGAC	434 Bp
	5:37243184	608A>G	AAGGCAGGAGGACTGCTTG	CTGCCTCTGGCTCAGAAAAA	504 Bp
GLI3	7:42188023	169G>A	ATAAAGCGCGCACACACAC	GCTCTCAAAGTTGCTGTGAATG	481 Bp
	7:42188028	164G>A	ATAAAGCGCGCACACACAC	GCTCTCAAAGTTGCTGTGAATG	481 Bp
LRP2	2:170038738	9937G>A	TTACATGAACAGCCTTCTCGG	TAGCTTGGGTAGGAAACTGGG	315 Bp
	2:170038761	9914G>A	TTACATGAACAGCCTTCTCGG	TAGCTTGGGTAGGAAACTGGG	315 Bp
GATA6	18:19751148	43G>C	CTTGTTAACCCGTCGATCTCC	TCAGTGAACAGCAGCAAGTCC	439 Bp
	18:19751656	551G>A	CTGCTGTTCACTGACCTCGAC	GTATGGAGGGCTGTCGGC	369 Bp
HSPG2	1:22161303	10589G>A	TGTCCCAAGTGAACAGAAAGG	TTGGGCAGTCTATGGCCTC	454 Bp
	1:22206994	2057T>C	GACAAGCCAGAATAGCCAATG	TAGGGCTGGGAGCAAAGG	408 Bp
	1:22217079	353C>T	TCAAGTACTCCGACTCCAGCTG	TATTTCCGAGCCCTGGTGA	226 Bp