

Haploinsufficiency of TAB2 Causes

Congenital Heart Defects in Humans

Bernard Thienpont, Litu Zhang, Alex V. Postma, Jeroen Breckpot, Léon-Charles Tranchevent, Peter Van Loo, Kjeld Møllgård, Niels Tommerup, Iben Bache, Zeynep Tümer, Klaartje van Engelen, Björn Menten, Geert Mortier, Darrel Waggoner, Marc Gewillig, Yves Moreau, Koen Devriendt, and Lars Allan Larsen

SUPPLEMENTAL FIGURES

Figure S1. Representation of Spearman Rank Correlations between Data Sources upon Prioritization, Here Using the Vascularisation Training Set

The Cis-regulatory modules (Cr) data source is not strongly correlated with any other source, while the Textmining (Te) and the Gene Ontology (Go) data source, or both micro-array expression analysis data sources for adult human tissues (Sy and So) are strongly correlated. All data sources are perfectly correlated with themselves.

Legend: Go: GeneOntology, Sw: Swissprot, Ip: Interpro, Ke: Kegg, Es: EnsemblEst, Bi: Bind, St: String, Su: SuEtAl, So: Son et al microarray expression, Ch: microarray expression developing heart (GEO GSE1479), Ho: Homologene, Ma: Biomart, In: Inparanoid, Sy: Shyamsundar et al microarray expression, Cl: Clark et al microarray expression, Mo: Motif, Cr: CisRegModule, Bl: Blast, Tx: Text, Ou: Ouzounis, Pr: Prospectr,

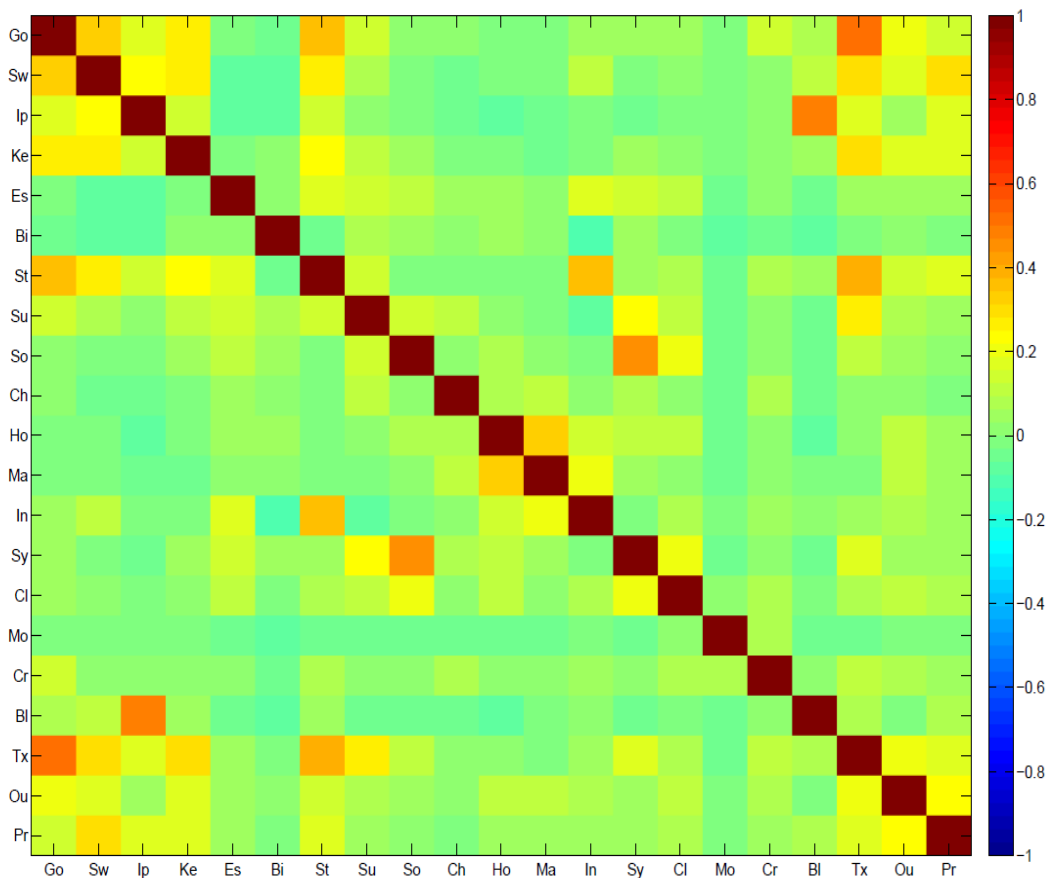


Figure S2. Performance of the Different Data Sources for Prioritization as Assessed by Leave-One-Out Cross-Validations (LOOCV)

Performance measures displayed are the area under the ROC curve of the LOOCV (specificity/sensitivity plot). Performance of the data source in prioritizations depends on the training set. For example: the chdma (microarray expression data for heart development) is highly informative for first heart field and the neural crest cells, but performs poorly for the other training sets. Similarly, Gene Ontology does not contain information to significantly prioritize genes involved in valve formation, while it does contribute to prioritizations according to the other training sets. Information on the standard data sources can be found on the [Endeavour website](#), other data sources are as described in the main text. Similar LOOCV results have been used to decide which data sources were excluded from prioritization (LOOCV <0.6; striped boxes).

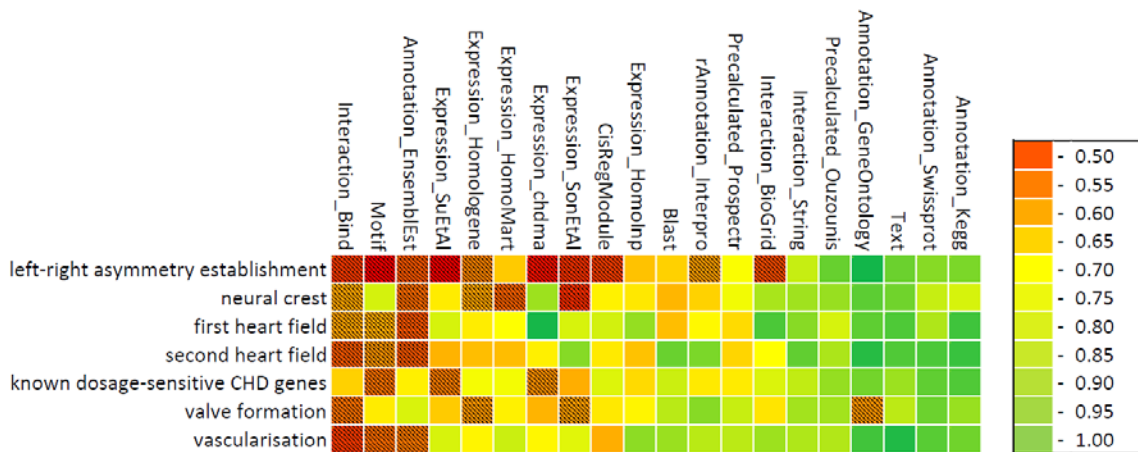


Figure S3. Mapping of Translocation Breakpoints of Family N

The top 5 ranking genes after prioritizations of all 106 genes on 6q24q25 using the adapted Endeavour and training genes involved in different processes of cardiac development, as indicated on top. LR = left-right; HF = heart field. Final = result upon combining individual prioritizations.

rank	final	vasculogenesis	neural crest	valve formation	LR asymmetry establishment	first HF	second HF	human CHDs
1	TAB2	GPR126	CITED2	TAB2	CITED2	HIVE P2	HIVE P2	TAB2
2	HIVE P2	UTRN	TAB2	UTRN	IGF2R	PPP1 R14C	FBX O30	GTF 2H5
3	CITED 2	IGF2 R	FBX O30	HIVE P2	GRM1	TXLNB	PPP1 R14C	GRM1
4	GRM1	CITED2	GRM1	ZBTB2	MTRF 1L	OPRM 1	TXLNB	HIVE P2
5	FBX O30	TAB2	HIVE P2	PEX3	FBX O30	GPR12 6	OPRM 1	HECA

Figure S4. Mapping of Translocation Breakpoints of Family N

(A) Breakpoint on chromosome 2 as determined by two breakpoint spanning fosmid probes, G248P8673B4 and G248P8684C9. This breakpoint is within the POTE ankyrin domain family, member E (POTEE) gene. This gene is variable in copy number as described by the several independent reports in the Database of Genomic Variants. **(B)** Breakpoint on chromosome 6 as determined by the breakpoint spanning fosmid probe G248P8912A2. FISH moreover showed a proximal position of the probes AL031056 and G248P8121B5 and a distal position of the probes RP11-455K21 and G248P82418C3 compared to the breakpoint, thus indicating that the breakpoint lies within a 17 kb region at chromosome position 149,678,240-149,695,219, within the first intron or the promoter region of TAB2.

Depicted Database of Genomic Variants entries:

3393: Pub Med ID: 17122850; Sample Size: 270 control samples (HapMap); Total Gain/Loss: 121

2409: Pub Med ID: 17122850; Sample Size: 270 control samples (HapMap); Observed Gain: 4; Observed Loss: 4

32374: Pub Med ID: 18304495; Sample Size: 30 control samples (HapMap); Observed Gain: 0; Observed Loss: 20

8388: Pub Med ID: 17911159; Sample Size: 776 control samples (506 Germans, 270 HapMap); Observed Gain: 1

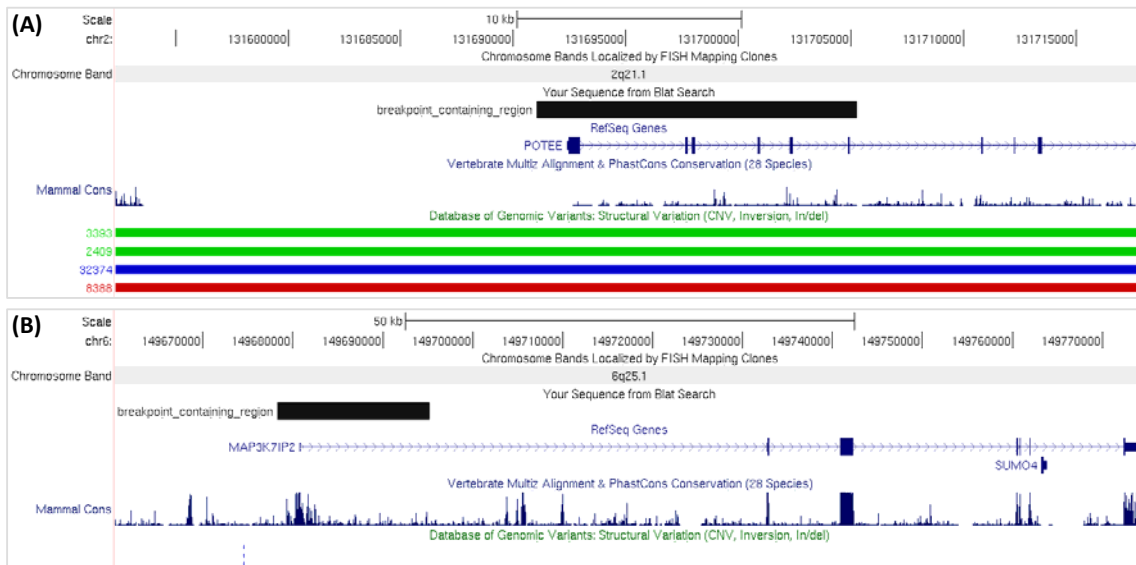


TABLE S1. PHENOTYPES ASSOCIATED WITH DELETIONS IN 6Q24 OR 6Q25

ref ^a	breakpoint regions on chromosome 6 (Mb)		heart defect	develop-mental delay	micro-ceph	IUGR	PNGR	CNS	oral	phenotypic features			CHD Wiki case report
	proximal	Distal								eye	hearing	Dysmorphism	
A *	143.72-143.74	150.21-150.22	hypopl AoA, CoAo, VSD	mild-mod	?	Y	Y	nl	nl	strabism	/	hypospadias, epicanthic folds, micrognathia, small ears	439
B *,I1	142.34-142.35	152.48-152.49	tricuspid & pulmonic valve dyspl, mvp, premature ventr. contractions	mild	N	Y	Y	nl	nl	astigmatism	/	frontal bossing, bitemporal narrowing, PF short & slant up, hooded eyelids, sparse eyelashes, infraorbital folds, anteverted nares, thin upper lip, fetal pads (hands), low set dyspl ears	464
C *,I2	146.17-146.18	156.55-156.59	ASD-II	mild	N	Y	Y	/	nl	retinal pigment changes, minimal optic nerve hypopl	/	sacral dimple, narrow thorax, frontal bossing, bitemporal narrowing, PF short & slant up, sparse eyelashes, infraorbital folds, anteverted nares, thin upper lip, flat long philtrum, low posterior hair line, low set dyspl ears	465
D II	148.70-148.78	151.38-151.35	tricuspid insufficiency, ASD, PDA	mild	N	N	Y	nl	HP	nl	nl	facial asymmetry, short PF, medial flare eyebrows, anteverted nares, thin upper lip, long & smooth philtrum, sandal gap, cupshaped left ear	400
E III1	149.09-149.23	156.06-156.30	VSD	mild	/	N	Y	/	nl	/	/	short nose, full cheeks, smooth philtrum, thin upper lip, almond eyes, low set protruding ears, dyspl left ear	399
F _p *	148.79-148.84	150.78-151.16	centrovalvular insufficiency of aortic & pulmonic valve	N	Y	N	Y	/	/	/	/	phimosis; high forehead; almond-shaped, upslanting palpebral fissures; midface hypopl; micrognathia; large, normally placed ears	462
F _m			mild aortic & mitral valve stenosis, sinus tachycardia	N	/	/	Y	/	/	/	/	facial features similar to her son (Fp)	463
G IV			N	/	/	/	/	nl	CLP	/	/	/	
H V3	149.95-149.96	160.27-160.28	N	Y	Y	N	Y	Acc	HP, BU	/	mild cHL	midface hypopl, clinodact 5, plagiocephaly, low set, posteriorly roated ears	
I *,I3	140.33-140.35	146.47-146.48	N	N	N	Y	Y	NI	nl	/	nl	N	
J VI	151.16-152.37	157.79-158.68	N	mild-mod	Y	N	Y	Acc	CHP	nystagmus	/	dolichocephaly, anteriorly placed anus, low set ears	
K V1	155.09	158.87-158.88	N	Y	Y	N	N	/	N	N	snHL	long philtrum, micrognathia, PF slant down, epicanthus, low set ears	

^a *: this report; I:Nowaczyk¹; II: Caselli²; III: Bisgaard³; IV: Osoegawa⁴; V: Nagamani^{4,5}; VI: Pirola⁶. CHDWiki case reports are accessible through homes.esat.kuleuven.be/~bioiuser/chdwiki

Acc = Agenesis of the corpus callosum, AoA = aortic arch, AoS = aortic stenosis, ASD = atrial septal defect, BU = bifid uvula, cHL = conductive hearing loss, CHP = cleft and high palate, CLP = cleft lip and palate, CNS = Central nervous system, CoAo = coarctation of the aorta, dyspl = dysplastic, G_p = proband of family G, G_m = mother of G_p, HP = high palate, hypopl = hypoplasia, IUGR = intra-uterine growth retardation, LS = low-set, mod = moderate, mvp = mitral valve prolapse, N = no, nl = normal, PNGR = post-natal growth retardation, SNHL = sensorineural hearing loss, PDA = patent ductus arteriosus, PF = palpebral fissures, VSD = ventricular septal defect, Y = yes, / = not available.

TABLE S2. PATIENT POPULATION SCREENED FOR *TAB2* MUTATIONS

n	CHD
<u>Patients from the CONCOR national registry database and DNA-bank</u>	
18	Aortic stenosis
4	Subaortic stenosis
74	Subaortic stenosis due to fibromuscular shelf
13	Aortic valvar abnormality
62	Congenital aortic valvar stenosis
42	Congenital aortic regurgitation
62	Bicuspid aortic valve
11	Ascending aorta abnormality
1	Ascending aorta hypoplasia
18	Supravalvar aortic stenosis
26	Ascending aorta dilation
331 heart defects in total, found in 282 unique patients	
<u>Patients from the paediatric cardiology unit of the University Hospitals Leuven</u>	
25	Aortic stenosis
42	Pulmonic stenosis
24	Aortic coarctation
11	Atrial septal defect
30	Ventricular septal defect
58	Tetralogy of Fallot
4	Univentricular heart
194 heart defects in total, found in 126 unique patients	

The patients from these patient populations were not analyzed systematically by aCGH.

TABLE S3. OLIGONUCLEOTIDE PRIMERS USED FOR TAB2 SEQUENCING

name	Forward (5'→3')	Reverse (5'→3')
Exon1	GTTTTTGATCTGCTGCAGCC	GCTCGATTCCAATGAAGCTC
Exon1_alt	GAGGCACATGTGAAGATTGG	GGCTGTTTTGAGAGATGGAATAC
Exon2	GCTAAAGCACATATTCTTTTGTACTGA	AACAAGAAGATAACCTAAAAGAGTTTTTC
Exon2_alt	GAGACCCATTTTCCCTTCAG	AAACTCAATACTAGCTGCATGTTACC
Exon3a	GCCAGTCACTTGGTAATCATGTATT	TGTAGACATGAGAGGTCTGGTG
Exon3b	GCCCCAAATATCCAGACTGG	GGCAGAAGACTGTGAGCTACC
Exon3c	GCCCCAAATATCCAGACTGG	GTGAAATCAAATGCACACCAAC
Exon4	GTTTTAATAAGCAACTAGTTGACTCTCTT	GGCAGAGTGGTATGGTCAC
Exon5	GTTTGCTTTTCCAAGTCTGCTTA	CCACAGAAAACTGCTGGTG
Exon6	GTTTTTGAGCTATAAGCATTGATATATT	TCTAGAGAGGAAGGTTGCTGAAC
Exon7	GGTGTTTAAAGTTGCCTGTAATTTT	CCTCCTGTCAAATTCAGTAGTGAC

TABLE S4. RESULTS OF ENDEAVOUR PRIORITISATION

rank	Ensembl ID	name	description	p-value	genome-wide rank
1	ENSG00000055208	MAP3K7IP2	Mitogen-activated protein kinase kinase kinase 7-interacting protein 2 (TAK1-binding protein 2)	4.17E-07	44
2	ENSG00000010818	HIVEP2	Human immunodeficiency virus type 1 enhancer-binding protein 2	1.19E-05	190
3	ENSG00000164442	CITED2	Cbp/p300-interacting transactivator 2	1.62E-05	216
4	ENSG00000152822	GRM1	Metabotropic glutamate receptor 1 precursor	4.69E-05	337
5	ENSG00000118496	FBXO30	F-box only protein 30	7.26E-05	383
6	ENSG00000152818	UTRN	Utrophin	0.000155	494
7	ENSG00000112414	GPR126	Probable G-protein coupled receptor 126 precursor	0.000342	680
8	ENSG00000197081	IGF2R	Cation-independent mannose-6-phosphate receptor precursor	0.000455	745
9	ENSG00000112038	OPRM1	Mu-type opioid receptor	0.002236	1386
10	ENSG00000118495	PLAGL1	Zinc finger protein PLAGL1	0.003608	1669
11	ENSG00000164440	TXLNB	Beta-taxilin	0.00393	1722
12	ENSG00000034693	PEX3	Peroxisomal biogenesis factor 3	0.004048	1746
13	ENSG00000130338	TULP4	Tubby-related protein 4	0.008736	2368
14	ENSG00000198729	PPP1R14C	Protein phosphatase 1 regulatory subunit 14C	0.010421	2529
15	ENSG00000112406	HECA	Headcase protein homolog	0.012274	2677
16	ENSG00000112096	SOD2	Superoxide dismutase [Mn], mitochondrial precursor	0.013638	2805
17	ENSG00000181472	ZBTB2	Zinc finger and BTB domain-containing protein 2	0.013665	2811
18	ENSG00000091831	ESR1	Estrogen receptor	0.016179	3030
19	ENSG00000112031	MTRF1L	mitochondrial translational release factor 1-like	0.016263	3037
20	ENSG00000146457	WTAP	Wilms' tumor 1-associating protein	0.023454	3499
21	ENSG00000175048	ZDHHC14	Probable palmitoyltransferase ZDHHC14	0.023796	3521
22	ENSG00000074706	NP_056368.1	phosphoinositide-binding protein PIP3-E	0.025931	3629
23	ENSG00000092820	VIL2	Ezrin	0.027138	3703
24	ENSG00000112029	FBXO5	F-box only protein 5	0.029822	3833
25	ENSG00000120265	PCMT1	Protein-L-isoaspartate	0.032716	3983
26	ENSG00000131018	C6orf98	Nesprin-1	0.034277	4058
27	ENSG00000112419	PHACTR2	Phosphatase and actin regulator 2	0.043925	4418
28	ENSG00000186625	KATNA1	Katanin p60 ATPase-containing subunit A1	0.062688	5055
29	ENSG00000185068	GTF2H5	TFIIH basal transcription factor complex TTD-A subunit	0.06391	5093
30	ENSG00000146477	SLC22A3	Organic cation transporter 3	0.065952	5161
31	ENSG00000111961	SASH1	SAM and SH3 domain-containing protein 1	0.067992	5218
32	ENSG00000164674	SYTL3	synaptotagmin-like 3	0.074042	5374
33	ENSG00000009844	VTA1	Vacuolar protein sorting-associated protein VTA1 homolog	0.075066	5394
34	ENSG00000120254	MTHFD1L	methylenetetrahydrofolate dehydrogenase	0.076261	5422
35	ENSG00000135604	STX11	Syntaxin-11	0.094487	5888
36	ENSG00000122335	SERAC1	Protein SERAC1	0.095663	5914

37	ENSG00000120438	TCP1	T-complex protein 1 subunit alpha	0.095825	5920
38	ENSG00000029639	TFB1M	Mitochondrial dimethyladenosine transferase 1, mitochondrial precursor	0.096437	5941
39	ENSG00000120278	PLEKHG1	Pleckstrin homology domain-containing family G member 1	0.106406	6156
40	ENSG00000112425	EPM2A	Laforin	0.108274	6206
41	ENSG00000055211	C6orf72	Uncharacterized protein C6orf72 precursor	0.111094	6263
42	ENSG00000146469	VIP	VIP peptides precursor	0.113626	6332
43	ENSG00000120279	MYCT1	myc target 1	0.11487	6359
44	ENSG00000091844	RGS17	Regulator of G-protein signaling 17	0.125839	6571
45	ENSG00000078269	SYNJ2	Synaptojanin-2	0.142887	6912
46	ENSG00000146425	DYNLT1	Dynein light chain Tctex-type 1	0.170058	7438
47	ENSG00000049618	ARID1B	AT-rich interactive domain-containing protein 1B	0.171981	7475
48	ENSG00000130340	SNX9	Sorting nexin-9	0.174483	7516
49	ENSG00000203711	C6orf99		0.175808	7543
50	ENSG00000203727	SAMD5	sterile alpha motif domain containing 5	0.192814	7816
51	ENSG00000135577	NMBR	Neuromedin-B receptor	0.193228	7829
52	ENSG00000131013	PPIL4	Peptidyl-prolyl cis-trans isomerase-like 4	0.19765	7888
53	ENSG00000112110	MRPL18	39S ribosomal protein L18, mitochondrial precursor	0.197794	7890
54	ENSG00000001036	FUCA2	Plasma alpha-L-fucosidase precursor	0.223905	8276
55	ENSG00000130363	RSPH3	radial spoke head 3 homolog	0.262823	8836
56	ENSG00000153721	CNKSR3	CNKSR family member 3	0.275909	9014
57	ENSG00000164691	TAGAP	T-cell activation Rho GTPase-activating protein	0.303527	9407
58	ENSG00000131016	AKAP12	A-kinase anchor protein 12	0.316981	9559
59	ENSG00000120256	LRP11	Low-density lipoprotein receptor-related protein 11 precursor.	0.331013	9721
60	ENSG00000135597	REPS1	RalBP1-associated Eps domain-containing protein 1	0.346337	9916
61	ENSG00000146426	TIAM2	T-cell lymphoma invasion and metastasis 2 isoform b	0.382258	10332
62	ENSG00000009765	IYD	Iodotyrosine dehalogenase 1 precursor	0.382923	10341
63	ENSG00000120437	ACAT2	Acetyl-CoA acetyltransferase, cytosolic	0.39124	10449
64	ENSG00000024862	CCDC28A	Coiled-coil domain-containing protein 28A	0.395685	10507
65	ENSG00000146386	C6orf115	Uncharacterized protein C6orf115.	0.440162	11033
66	ENSG00000171217	CLDN20	Claudin-20.	0.441675	11045
67	ENSG00000146416	AIG1	Androgen-induced protein 1	0.446371	11101
68	ENSG00000146453	PNLDC1	poly(A)-specific ribonuclease (PARN)-like domain containing 1	0.459979	11261
69	ENSG00000135521	LTV1	LTV1 homolog	0.47354	11422
70	ENSG00000130368	MAS1	MAS proto-oncogene.	0.572183	12591
71	ENSG00000120253	NUP43	Nucleoporin Nup43	0.578863	12683
72	ENSG00000203725			0.598758	12917
73	ENSG00000203734	C6orf91	Lung specific F-box and DH domain containing protein.	0.604803	12989
74	ENSG00000120262	C6orf97	Coiled coil-containing protein C6orf97.	0.605512	12993
75	ENSG00000203715	Q6ZUJ7	CDNA FLJ43649 fis, clone SYNOV4001326.	0.616374	13115
76	ENSG00000203733			0.622915	13186
77	ENSG00000111981	ULBP1	NKG2D ligand 1 precursor	0.673845	13760
78	ENSG00000146433	TMEM181	Transmembrane protein 181.	0.723806	14369
79	ENSG00000131023	LATS1	Serine/threonine-protein kinase LATS1	0.739113	14538
80	ENSG00000164694	FNDC1	Fibronectin type III domain-containing	0.746304	14644

protein 1					
81	ENSG00000164506	STXBP5	Syntaxin-binding protein 5	0.774888	15036
82	ENSG00000146414	SHPRH	E3 ubiquitin-protein ligase SHPRH	0.800801	15387
83	ENSG00000155906	RMND1	Required for meiotic nuclear division protein 1 homolog.	0.808266	15510
84	ENSG00000112499	SLC22A2	solute carrier family 22 member 2	0.820311	15698
85	ENSG00000189007	ADAT2	tRNA-specific adenosine deaminase 2	0.828169	15815
86	ENSG00000118492	C6orf103	Uncharacterized protein C6orf103.	0.828857	15826
87	ENSG00000169976	SF3B5	Splicing factor 3B subunit 5	0.834561	15912
88	ENSG00000146476	C6orf211	UPF0364 protein C6orf211.	0.853991	16254
89	ENSG00000177688	SUMO4	Small ubiquitin-related modifier 4 precursor	0.857203	16315
90	ENSG00000122339	C6orf35	CDNA FLJ10029 fis, clone HEMBA1000817	0.887182	16911
91	ENSG00000118508	RAB32	Ras-related protein Rab-32.	0.89588	17112
92	ENSG00000074771	NOX3	NADPH oxidase 3	0.90021	17220
93	ENSG00000131015	ULBP2	NKG2D ligand 2 precursor	0.912752	17524
94	ENSG00000131019	ULBP3	NKG2D ligand 3 precursor	0.940166	18306
95	ENSG00000111962	UST	Uronyl 2-sulfotransferase	0.949789	18691
96	ENSG00000198670	LPA	Apolipoprotein	0.955294	18926
97	ENSG00000118491	C6orf94	UPF0418 protein C6orf94.	0.964293	19332
98	ENSG00000164520	RAET1E	NKG2D ligand 4 precursor	0.970816	19698
99	ENSG00000175003	SLC22A1	solute carrier family 22 member 1 isoform b	0.971006	19713
100	ENSG00000164711	LPAL2	Lipoprotein Lp	0.974121	19894
101	ENSG00000155918	RAET1L	retinoic acid early transcript 1L	0.984489	20777
102	ENSG00000203722	RAET1G	Retinoic acid early transcript 1G protein precursor.	0.988129	21198
103	ENSG00000178199	ZC3H12D	zinc finger CCCH-type containing 12D	0.991595	21785
104	ENSG00000196492	NM_207500	CDNA FLJ44955 fis, clone BRAWH2010619	0.993465	22221
105	ENSG00000198213	NM_207501	CDNA FLJ27255 fis, clone SYN09519.	0.994379	22468

TABLE S5. TRAINING SETS FOR GENE PRIORITISATION

Ensembl Gene ID	HGNC symbol	Description
vascularisation		
ENSG00000004399	PLXND1	Plexin-D1 Precursor
ENSG00000074181	NOTCH3	Neurogenic locus notch homolog protein 3 Precursor
ENSG00000075213	SEMA3A	Semaphorin-3A Precursor
ENSG00000075223	SEMA3C	Semaphorin-3C Precursor
ENSG00000078401	EDN1	Endothelin-1 Precursor
ENSG00000099250	NRP1	Neuropilin-1 Precursor
ENSG00000105329	TGFB1	Transforming growth factor beta-1 Precursor
ENSG00000106799	TGFBR1	TGF-beta receptor type-1 Precursor
ENSG00000106991	ENG	Endoglin Precursor
ENSG00000112715	VEGFA	Vascular endothelial growth factor A Precursor
ENSG00000120156	TEK	Angiopoietin-1 receptor Precursor
ENSG00000125845	BMP2	Bone morphogenetic protein 2 Precursor
ENSG00000134250	NOTCH2	Neurogenic locus notch homolog protein 2 Precursor
ENSG00000137834	SMAD6	Mothers against decapentaplegic homolog 6
ENSG00000148400	NOTCH1	Neurogenic locus notch homolog protein 1 Precursor
ENSG00000154188	ANGPT1	Angiopoietin-1 Precursor
ENSG00000162692	VCAM1	Vascular cell adhesion protein 1 Precursor
ENSG00000163513	TGFBR2	TGF-beta receptor type-2 Precursor
ENSG00000170381	SEMA3E	Semaphorin-3E Precursor
ENSG00000185551	NR2F2	COUP transcription factor 2
left-right asymmetry establishment		
ENSG00000105877	DNAH11	Dynein heavy chain 11, axonemal
ENSG00000114739	ACVR2B	Activin receptor type-2B Precursor
ENSG00000124181	PLCG1	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma-1
ENSG00000125378	BMP4	Bone morphogenetic protein 4 Precursor
ENSG00000136698	CFC1	Cryptic protein Precursor
ENSG00000143768	LEFTY2	Left-right determination factor 2 Precursor
ENSG00000156574	NODAL	Nodal homolog Precursor
ENSG00000156925	ZIC3	Zinc finger protein ZIC 3
ENSG00000164093	PITX2	Pituitary homeobox 2
ENSG00000164442	CITED2	Cbp/p300-interacting transactivator 2
ENSG00000164690	SHH	Sonic hedgehog protein Precursor
human CHDs		
ENSG00000008196	TFAP2B	Transcription factor AP-2 beta
ENSG00000072840	EVC	Ellis-van Creveld syndrome protein
ENSG00000085224	ATRX	Transcriptional regulator ATRX
ENSG00000089225	TBX5	T-box transcription factor TBX5
ENSG00000101384	JAG1	Protein jagged-1 Precursor
ENSG00000101871	MID1	Midline-1
ENSG00000106799	TGFBR1	TGF-beta receptor type-1 Precursor
ENSG00000114739	ACVR2B	Activin receptor type-2B Precursor
ENSG00000115904	SOS1	Son of sevenless homolog 1
ENSG00000123066	MED13L	Mediator of RNA polymerase II transcription subunit 13-like
ENSG00000126934	MAP2K2	Dual specificity mitogen-activated protein kinase kinase 2
ENSG00000133703	KRAS	GTPase KRas Precursor
ENSG00000136574	GATA4	Transcription factor GATA-4
ENSG00000136698	CFC1	Cryptic protein Precursor
ENSG00000138829	FBN2	Fibrillin-2 Precursor

ENSG00000143768	LEFTY2	Left-right determination factor 2 Precursor
ENSG00000148400	NOTCH1	Neurogenic locus notch homolog protein 1 Precursor
ENSG00000156925	ZIC3	Zinc finger protein ZIC 3
ENSG00000157764	BRAF	B-Raf proto-oncogene serine/threonine-protein kinase
ENSG00000163513	TGFBR2	TGF-beta receptor type-2 Precursor
ENSG00000163703	CRELD1	Cysteine-rich with EGF-like domain protein 1 Precursor
ENSG00000164442	CITED2	Cbp/p300-interacting transactivator 2
ENSG00000169032	MAP2K1	Dual specificity mitogen-activated protein kinase kinase 1
ENSG00000169554	ZEB2	Zinc finger E-box-binding homeobox 2
ENSG00000169946	ZFPM2	Zinc finger protein ZFPM2
ENSG00000170381	SEMA3E	Semaphorin-3E Precursor
ENSG00000171316	CHD7	Chromodomain-helicase-DNA-binding protein 7
ENSG00000174775	HRAS	GTPase HRas Precursor
ENSG00000175206	NPPA	Atrial natriuretic factor Precursor
ENSG00000179295	PTPN11	Tyrosine-protein phosphatase non-receptor type 11
ENSG00000181090	EHMT1	Histone-lysine N-methyltransferase, H3 lysine-9 specific 5
ENSG00000183072	NKX2-5	Homeobox protein Nkx-2.5
ENSG00000184058	TBX1	T-box transcription factor TBX1
neural crest cells		
ENSG00000004975	DVL2	Segment polarity protein dishevelled homolog DVL-2
ENSG00000006377	DLX6	Homeobox protein DLX-6
ENSG000000054598	FOXC1	Forkhead box protein C1
ENSG000000070010	UFD1L	Ubiquitin fusion degradation protein 1 homolog
ENSG000000076356	PLXNA2	Plexin-A2 Precursor
ENSG000000077092	RARB	Retinoic acid receptor beta
ENSG000000087245	MMP2	72 kDa type IV collagenase Precursor
ENSG000000099942	CRKL	Crk-like protein
ENSG00000100027	YPEL1	Protein yippee-like 1
ENSG00000100084	HIRA	Protein HIRA
ENSG00000101384	JAG1	Protein jagged-1 Precursor
ENSG00000105329	TGFB1	Transforming growth factor beta-1 Precursor
ENSG00000107779	BMPRI1A	Bone morphogenetic protein receptor type-1A Precursor
ENSG00000107831	FGF8	Fibroblast growth factor 8 Precursor
ENSG00000108557	RAI1	Retinoic acid-induced protein 1
ENSG00000112715	VEGFA	Vascular endothelial growth factor A Precursor
ENSG00000115170	ACVR1	Activin receptor type-1 Precursor
ENSG00000118257	NRP2	Neuropilin-2 Precursor
ENSG00000120149	MSX2	Homeobox protein MSX-2
ENSG00000125084	WNT1	Proto-oncogene protein Wnt-1 Precursor
ENSG00000131759	RARA	Retinoic acid receptor alpha
ENSG00000135503	ACVR1B	Activin receptor type-1B Precursor
ENSG00000135547	HEY2	Hairy/enhancer-of-split related with YRPW motif protein 2
ENSG00000135903	PAX3	Paired box protein Pax-3
ENSG00000138136	LBX1	Transcription factor LBX1
ENSG00000141448	GATA6	Transcription factor GATA-6
ENSG00000143171	RXRG	Retinoic acid receptor RXR-gamma
ENSG00000146457	WTAP	Pre-mRNA-splicing regulator WTAP
ENSG00000148400	NOTCH1	Neurogenic locus notch homolog protein 1 Precursor
ENSG00000151617	EDNRA	Endothelin-1 receptor Precursor
ENSG00000152661	GJA1	Gap junction alpha-1 protein
ENSG00000164442	CITED2	Cbp/p300-interacting transactivator 2
ENSG00000169756	LIMS1	LIM and senescent cell antigen-like-containing domain protein 1

ENSG00000170381	SEMA3E	Semaphorin-3E Precursor
ENSG00000171316	CHD7	Chromodomain-helicase-DNA-binding protein 7
ENSG00000176692	FOXC2	Forkhead box protein C2
ENSG00000178568	ERBB4	Receptor tyrosine-protein kinase erbB-4 Precursor
ENSG00000185652	NTF3	Neurotrophin-3 Precursor
ENSG00000186260	MKL2	MKL/myocardin-like protein 2
ENSG00000186350	RXRA	Retinoic acid receptor RXR-alpha
ENSG00000197461	PDGFA	Platelet-derived growth factor subunit A Precursor
ENSG00000204231	RXRB	Retinoic acid receptor RXR-beta
first heart field		
ENSG00000081189	MEF2C	Myocyte-specific enhancer factor 2C
ENSG00000089225	TBX5	T-box transcription factor TBX5
ENSG00000113196	HAND1	Heart- and neural crest derivatives-expressed protein 1
ENSG00000134817	APLNR	Apelin receptor
ENSG00000136574	GATA4	Transcription factor GATA-4
ENSG00000141052	MYOCD	Myocardin
ENSG00000163217	BMP10	Bone morphogenetic protein 10 Precursor
ENSG00000164107	HAND2	Heart- and neural crest derivatives-expressed protein 2
ENSG00000164532	TBX20	T-box transcription factor TBX20
ENSG00000169946	ZFPM2	Zinc finger protein ZFPM2
ENSG00000171388	APLN	Apelin Precursor
ENSG00000183072	NKX2-5	Homeobox protein Nkx-2.5
second heart field		
ENSG00000016082	ISL1	Insulin gene enhancer protein ISL-1
ENSG00000070193	FGF10	Fibroblast growth factor 10 Precursor
ENSG00000081189	MEF2C	Myocyte-specific enhancer factor 2C
ENSG00000100027	YPEL1	Protein yippee-like 1
ENSG00000107831	FGF8	Fibroblast growth factor 8 Precursor
ENSG00000113196	HAND1	Heart- and neural crest derivatives-expressed protein 1
ENSG00000160973	FOXH1	Forkhead box protein H1
ENSG00000164093	PITX2	Pituitary homeobox 2
ENSG00000164107	HAND2	Heart- and neural crest derivatives-expressed protein 2
ENSG00000164532	TBX20	T-box transcription factor TBX20
valve development		
ENSG00000038427	VCAN	Versican core protein Precursor
ENSG00000101384	JAG1	Protein jagged-1 Precursor
ENSG00000106991	ENG	Endoglin Precursor
ENSG00000115170	ACVR1	Activin receptor type-1 Precursor
ENSG00000125398	SOX9	Transcription factor SOX-9
ENSG00000131196	NFATC1	Nuclear factor of activated T-cells, cytoplasmic 1
ENSG00000135074	ADAM19	Disintegrin and metalloproteinase domain-containing protein 19 Precursor
ENSG00000143387	CTSK	Cathepsin K Precursor
ENSG00000148400	NOTCH1	Neurogenic locus notch homolog protein 1 Precursor
ENSG00000163513	TGFBR2	TGF-beta receptor type-2 Precursor
ENSG00000166147	FBN1	Fibrillin-1 Precursor
ENSG00000171316	CHD7	Chromodomain-helicase-DNA-binding protein 7
ENSG00000183337	BCOR	BCL-6 corepressor