



**Supp. Figure S1.** Gene structure of three isoforms of human *TBX1* gene. There are three isoforms of human *TBX1* protein, isoform A (NM\_080646, 18,124,226-18,147,068), B (NM\_005992, 18,124,226-18,151,112) and C (NM\_080647, 124,226-18,134,855). The enhancer track shows the human orthologous region to a previously defined enhancer for mouse *Tbx1* (18,115,184-18,115,529; Garg et al., 1999). Potential regulatory regions such as promoters have been associated with high CpG content referred to as CpG islands. First EF (First exon prediction) track shows the prediction of alternative start sites in the *TBX1* gene. CpG islands, which associated with potential regulatory regions such as promoters are shown in “CpG islands” track.

**Supp. Table S1. Primers used for *TBX1* resequencing**

Amplicon ID	Amplicon Begin	Amplicon End	Amplicon Length	Forward Primer Sequence	Reverse Primer Sequence
R010_00000_1000_1109494573895	18109737	18110083	346	TGTA AACGACG GCCAGT GAGGAGTCTGTG TCCGTGCC	CAGGAAACAGCTATGACCACTCACCTGATGCCAGAGG
R010_00100_1001_1109494573961	18116649	18116997	348	TGTA AACGACG GCCAGT CAGACTCAGGGACACCTCC	CAGGAAACAGCTATGACCCGATGAAGAAGGAGGCCGTT
R010_00101_1002_1109494573964	18116895	18117211	316	TGTA AACGACG GCCAGT AGGCAAGTCAAGGAGCAG	CAGGAAACAGCTATGACCTAGGCAGTGGTTTGACGCC
R010_00102_1003_1109494573967	18117053	18117391	338	TGTA AACGACG GCCAGT CCTGGCAGGCAGGGAAGTA	CAGGAAACAGCTATGACCCCTGCCCCCTCGTCGGA
R010_00200_1004_1109494573970	18117191	18117541	350	TGTA AACGACG GCCAGT GGCTGCAAAACCACTGCCT	CAGGAAACAGCTATGACCCCATCCCACGAAAGTGCTTG
R010_00201_1005_1109494573973	18117443	18117788	345	TGTA AACGACG GCCAGT GCCTCCCAGGCTCGGGGT	CAGGAAACAGCTATGACCCCTCGGGGTCTCGGGGAAG
R010_00202_1006_1109494573976	18117687	18118022	335	TGTA AACGACG GCCAGT AGCCGCCGCCCTTCTCT	CAGGAAACAGCTATGACCCAGCATTGGTCCCAGGCTAC
R010_00300_1007_1109494573979	18117732	18118082	350	TGTA AACGACG GCCAGT GGGAGGGAGGACGGTGAG	CAGGAAACAGCTATGACCCGGCAGACAGTATACCAGGATCTT
R010_00301_1008_1109494573982	18117951	18118301	350	TGTA AACGACG GCCAGT CGTGCACTCGAACCTCC	CAGGAAACAGCTATGACCCCGCTGGAGAATTGTGGC
R010_00302_1009_1109494573985	18118205	18118544	339	TGTA AACGACG GCCAGT TGAGGGTGCTGTCTGAA	CAGGAAACAGCTATGACCAACCGAAGCTTGGCTCCAC
R010_00400_1010_1109494573988	18118258	18118589	331	TGTA AACGACG GCCAGT CGGAACTGGGCAGACAGAT	CAGGAAACAGCTATGACCCGAGGGGGCAGATGGGA
R010_00401_1011_1109494573991	18118477	18118817	340	TGTA AACGACG GCCAGT CTCCTGCACTCAGCCAAGCC	CAGGAAACAGCTATGACCCCGCCGCGGTTCCCTTC
R010_00402_1012_1109494573994	18118711	18119061	350	TGTA AACGACG GCCAGT CTCACCTCTGATCCACGC	CAGGAAACAGCTATGACCCAGGATAGGGCTCCTCCGACC
R010_00500_1013_1109494573997	18120572	18120885	313	TGTA AACGACG GCCAGT CCAGGCAGAGCGCGGGCCT	CAGGAAACAGCTATGACCTGCGCAGCCCGGAGCCCGA
R010_00501_1014_1109494574000	18120700	18121049	349	TGTA AACGACG GCCAGT ACATGTCTCGTCTCGG	CAGGAAACAGCTATGACCCAGCTTGGGCTCTCGCAC
R010_00600_1015_1109494574003	18121278	18121628	350	TGTA AACGACG GCCAGT ATGTTCAAGGGCGTTGGTC	CAGGAAACAGCTATGACCCAGAGAGGCGATGTGAAC
R010_00601_1016_1109494574006	18121520	18121865	345	TGTA AACGACG GCCAGT GGCTGGGCACACGCAATC	CAGGAAACAGCTATGACCCGAGGCCACGCTACCAAGAG
R010_00602_1017_1109494574009	18121757	18122103	346	TGTA AACGACG GCCAGT AGCCTCCAGGCGGTCTA	CAGGAAACAGCTATGACCTCGAGGCTTCTCTCTCTGTG
R010_00700_1018_1109494574012	18122793	18123112	319	TGTA AACGACG GCCAGT TCGGGCCGCCCTGCGGTGT	CAGGAAACAGCTATGACCCGCGCGCACGGTCTGTAG
R010_00701_1019_1109494574015	18122972	18123320	348	TGTA AACGACG GCCAGT ACCTTGACGCTTCCACGG	CAGGAAACAGCTATGACCCGTTGAACTCGTCCACAGC
R010_00702_1020_1109494574018	18123147	18123490	343	TGTA AACGACG GCCAGT GCACGCCCTACCCGTTTGC	CAGGAAACAGCTATGACCCAGAGGGCCCGCAGGTG
R010_00703_1021_1109494574021	18123385	18123735	350	TGTA AACGACG GCCAGT CCTCCCACGTGCTGCCG	CAGGAAACAGCTATGACCCGGTGAGGCCCTGGAC
R010_00800_1022_1109494574024	18123853	18124181	328	TGTA AACGACG GCCAGT GGATTACCCCTAAAACAGCGTG	CAGGAAACAGCTATGACCCGTTCTCAGAAAGGACGCC
R010_00801_1023_1109494574027	18124034	18124380	346	TGTA AACGACG GCCAGT TTGACCGTAGACAAGGGCG	CAGGAAACAGCTATGACCCCCCAACCGAAGCTCT
R010_00900_1024_1109494574030	18125138	18125480	342	TGTA AACGACG GCCAGT TAGGGCCCTGCCAGATTAG	CAGGAAACAGCTATGACCCGAGACCCGCCACTTCC
R010_00901_1025_1109494574033	18125378	18125712	334	TGTA AACGACG GCCAGT CTGCTCATGGACTTCGTGCC	CAGGAAACAGCTATGACCGAAGAAGTCCGGGGCTGAGT
R010_00000_1026_1109494573898	18126103	18126446	343	TGTA AACGACG GCCAGT GGCAGCAGAGGGTTCAATCTC	CAGGAAACAGCTATGACCCAGGCCCTGGGGGACACC
R010_00001_1027_1109494573922	18126348	18126695	347	TGTA AACGACG GCCAGT CGTGTCTTCGACAAGCTCA	CAGGAAACAGCTATGACCAATCAGGAGTGGGGTGAGAGAA
R010_00000_1028_1109494573901	18126910	18127240	330	TGTA AACGACG GCCAGT GGGTTTTGCCAACTCATCC	CAGGAAACAGCTATGACCCGTTTTCCAGAGCGTTGAA
R010_00001_1029_1109494573925	18127104	18127454	350	TGTA AACGACG GCCAGT GCGAGAAATATGCCAGGAGA	CAGGAAACAGCTATGACCCGGAATGTTCCGAAAACAA
R010_00000_1030_1109494573904	18127599	18127899	300	TGTA AACGACG GCCAGT ACCTGGGGACACCAGAGAG	CAGGAAACAGCTATGACCTCCTCAGGGTCACAGTCCC

Amplicon ID	Amplicon Begin	Amplicon End	Amplicon Length	Forward Primer Sequence	Reverse Primer Sequence
R010_00001_1031_1109494573928	18127800	18128129	329	TGTA AACGACGGCCAGTCTCCAGCGGCTTGCTCAC	CAGGAAACAGCTATGACCCGGTAGAGCGCGCACAGGG
R010_00002_1032_1109494573946	18128029	18128354	325	TGTA AACGACGGCCAGTCTCGCGGAACCCCGTGGC	CAGGAAACAGCTATGACCCGACCACTCGGTGCCAGC
R010_00000_1033_1109494573907	18128318	18128653	335	TGTA AACGACGGCCAGTACTTGGGGTCTCGGGCAC	CAGGAAACAGCTATGACCCCTCGGGGTTCTGGGGGACT
R010_00001_1034_1109494573931	18128545	18128848	303	TGTA AACGACGGCCAGTCTGTGGCCCGGGTGCTA	CAGGAAACAGCTATGACCCGCGGGGCTGGACTCAC
R010_00000_1036_1109494573910	18128725	18129053	328	TGTA AACGACGGCCAGTGACCACTATCTCGGGGCCAA	CAGGAAACAGCTATGACCCCTGGGGCTGGGGGAAC
R010_00002_1035_1109494573949	18128727	18129077	350	TGTA AACGACGGCCAGTCCACTATCTCGGGGCCAA	CAGGAAACAGCTATGACCCGGGAAGGGGAGAGCCGC
R010_00001_1037_1109494573934	18128918	18129268	350	TGTA AACGACGGCCAGTGTCTCTACGACTATTGCCCC	CAGGAAACAGCTATGACCCGGTCTCGGGGAGAACAATA
R010_00002_1038_1109494573952	18129154	18129497	343	TGTA AACGACGGCCAGTAGCCACCGGGTCTCTTC	CAGGAAACAGCTATGACCCGAGGCCCTGAGCTACCCC
R010_00003_1039_1109494573958	18129375	18129717	342	TGTA AACGACGGCCAGTGCGCCGACTTGATAAACGGT	CAGGAAACAGCTATGACCATGCACACCTGGGCGGTA
R010_00000_1040_1109494573913	18141158	18141498	340	TGTA AACGACGGCCAGTTCGTGGGAGATGCAGTCTCT	CAGGAAACAGCTATGACCCCGGCCCTCAGATTCAA
R010_00000_0000_1109494573874	18141273	18141952	679	TGTA AACGACGGCCAGTCAATTGGATGGGTTGTCACC	CAGGAAACAGCTATGACCCGGCTTTTCCCGAGTGATGT
R010_00001_1041_1109494573937	18141361	18141670	309	TGTA AACGACGGCCAGTGTGGAGCTTCTGAGGGATGC	CAGGAAACAGCTATGACCAACAAGTTTTGATTTATCAACTGGG
R010_00002_1042_1109494573955	18141509	18141843	334	TGTA AACGACGGCCAGTTGGAGTTGTCTGTTCCCTT	CAGGAAACAGCTATGACCGAACCAGTTTGAGGGAATCATCCT
R010_00000_1043_1109494573916	18144851	18145200	349	TGTA AACGACGGCCAGTGGGGCCTCAGCTGTCTGTGT	CAGGAAACAGCTATGACCCGCTGGAGGATTGCTTCCAT
R010_00001_1044_1109494573940	18145097	18145433	336	TGTA AACGACGGCCAGTGAAGGTA CTGAGTTGGTGGTCC	CAGGAAACAGCTATGACCCCTCTTGCATGCACACTTGA
R010_00000_1045_1109494573919	18146065	18146415	350	TGTA AACGACGGCCAGTTGGGGACCGTGCAGCAG	CAGGAAACAGCTATGACCAGCAGCCAGGACCCG
R010_00001_1046_1109494573943	18146313	18146653	340	TGTA AACGACGGCCAGTGGTGGGAAACACTGATTGAA	CAGGAAACAGCTATGACCCGAGCACTACCCAGCGT

**Supp. Table S2. DNA variants identified from *TBX1* resequencing**

Order	SNPs	A1/A2 <sup>a</sup>	Position	MAF	Function	Table 2 <sup>b</sup>	Figure 4 <sup>c</sup>	Figure 6 <sup>d</sup>
1	rs41298611	A/g	18122193	0.008	promotor		1	1
2	rs41298613	C/a	18122208	0.003	promotor		2	2
3	rs72646935	G/a	18122493	0.016	promotor			3
4	rs41298615	C/t	18122522	0.009	promotor		3	4
5	rs72646936	G/c	18122714	0.003	promotor		4	5
6	rs41298621	C/g	18122743	0.003	promotor		5	6
7	rs41298623	A/c	18122848	0.003	promotor		6	7
8	rs41298627	G/a	18123121	0.003	promotor		7	8
9	rs72646937	GAG/-	18123390	0.003	promotor		8	9
10	rs41260844	C/t	18123424	0.235	promotor	1		
11	rs41298629	C/t	18123473	0.011	promotor			10
12	rs41298631	C/g	18123497	0.003	promotor		9	11
13	rs41298635	A/g	18123549	0.003	promotor		10	12
14	rs5993823	G/a	18123640	0.003	promotor		11	13
15	rs72646938	G/t	18124228	0.003	promotor		12	14
16	rs72646939	G/a	18126195	0.003	intron		13	15
17	rs41299453	G/a	18126338	0.003	intron		14	16
18	rs41299455	G/a	18126354	0.032	intron			17
19	rs737867	T/a	18126903	0.389	intron			
20	rs72646948	C/g	18127033	0.006	intron		15	18
21	rs41299457	C/t	18127042	0.003	intron		16	19
22	rs72646949	G/a	18127051	0.003	intron		17	20
23	rs737868	C/g	18127082	0.383	intron	2		
24	rs72646950	C/t	18127128	0.003	intron		18	21
25	rs12158927	G/c	18127485	0.006	intron		19	22
26	rs41298790	G/t	18127486	0.008	intron		20	23
27	rs41298792	G/a	18127487	0.008	intron		21	24
28	rs72646951	G/c	18128312	0.077	intron			
29	rs72646952	G/t	18128468	0.011	intron			25
30	rs72646953	G/a	18128690	0.044	Ala99Ala			26
31	rs72646954	T/c	18128960	0.006	intron		22	27
32	rs72646955	C/g	18128967	0.003	intron		23	28
33	Novel23	-/tcgc	18129079	0.003	intron		24	29
34	rs72646957	T/c	18129375	0.003	intron		25	30
35	rs41298798	C/g	18129508	0.006	intron		26	31
36	rs1978060	G/a	18129525	0.309	intron			
37	rs41298802	G/a	18129713	0.045	intron			32
38	rs41298804	G/t	18129725	0.006	intron		27	33
39	rs72646958	G/a	18130645	0.011	intron			34
40	rs41298814	T/c	18130773	0.176	Phe140Phe	3		
41	rs72646959	G/a	18130919	0.003	intron		28	35
42	rs41298818	C/t	18131065	0.014	intron	4		36
43	rs72646960	C/t	18131670	0.003	intron		29	37

44	rs2301558	C/t	18131829	0.219	Leu222Leu	5		
45	rs41298826	T/c	18132007	0.175	intron	6		
46	rs72646961	G/t	18133186	0.003	intron		30	38
47	rs41298836	C/t	18133379	0.072	intron			
48	rs41298838	G/a	18133444	0.003	Gly310Ser		31	39
49	rs41298840	A/g	18133449	0.177	Ala311Ala			
50	rs72646963	G/c	18133608	0.003	intron		32	40
51	rs72646964	C/g	18133647	0.008	intron		33	41
52	rs72646965	C/t	18133829	0.006	intron		34	42
53	rs72646966	A/g	18133848	0.142	intron			
54	rs13054377	A/g	18133961	0.072	Ala353Ala			
55	rs72646967	A/c	18134091	0.181	Asn397His	7		
56	rs72646968	C/t	18134303	0.003	Ala467Ala		35	43
57	rs72646969	G/a	18134508	0.014	UTR			44
58	rs72646970	G/t	18134725	0.006	UTR		36	45
59	rs72646971	A/g	18134791	0.003	UTR		37	46
60	rs72646972	C/a	18134817	0.003	UTR		38	47
61	rs4819522	C/t	18146782	0.156	Thr350Met			
62	rs72646973	C/t	18146941	0.003	UTR		39	48
63	rs41298008	C/g	18146954	0.006	UTR		40	49
64	rs5746826	G/t	18147051	0.425	intron	8		
65	rs72646974	G/t	18150562	0.003	intron		41	50
66	rs72646975	C/t	18150566	0.003	intron		42	51
67	rs41298850	A/g	18150706	0.003	intron		43	52
68	rs13055776	C/t	18150707	0.086	intron	9		
69	rs2073762	A/g	18151568	0.436	3' flanking			
70	rs72646976	T/g	18151743	0.006	3' flanking		44	53
71	rs72646977	G/a	18151854	0.006	3' flanking		45	54

<sup>a</sup> A1 is the minor allele and A2 is the major allele. <sup>b</sup> "Table 2" are the common SNPs which were selected to be genotyped in the whole cohort of 1,022 subjects in Table 2. <sup>c</sup> "Figure 4" are the 45 very rare variations which were used for the rare variation enrichment analysis shown in Figure 4. <sup>d</sup> "Figure 6" are 54 rare variations which were used in Figure 6.

**Supp. Table S3. Association between representative common SNPs in *TBX1* and individual CHDs**

Marker	Location (hg18)	A1/A2	P value for individual CHDs						
			ASD	Isolated VSD	TOF	PTA	PS	RAA	IAAB
rs41260844	18123423	T/C	0.39	0.29	0.65	0.71	0.21	0.49	0.62
rs737868	18127081	G/C	0.09	0.08	0.83	0.34	0.75	0.37	0.24
rs41298814	18130772	C/T	0.28	0.20	0.99	0.65	0.81	0.86	0.67
rs2301558	18131828	T/C	0.17	0.15	0.38	0.93	0.15	0.12	0.19
rs41298826	18132006	C/T	0.28	0.37	0.67	0.41	0.72	0.77	0.75
rs72646967	18134090	C/A	0.34	0.37	0.88	0.64	0.78	0.48	0.69
rs4819522	18146781	T/C	0.73	0.47	0.70	0.58	0.20	0.58	0.41
rs5746826	18147050	T/G	0.12	0.26	0.26	0.95	0.11	0.93	0.87
rs13055776	18150706	T/C	0.13	0.28	0.11	0.39	0.31	0.62	0.65

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