

Supplementary Table S1. Genes included in the NGS

Gene	Chr	Num. Amplicons	Total Bases	Covered Bases	Missed Bases	Overall Coverage
<i>ABCC8</i>	chr11	47	5139	5139	0	1
<i>ABCC9</i>	chr12	44	5178	5178	0	1
<i>ACTA2</i>	chr10	8	1214	1214	0	1
<i>ACTC1</i>	chr15	8	1194	1194	0	1
<i>ACTN2</i>	chr1	28	3112	3112	0	1
<i>ACVRL1</i>	chr12	14	1602	1602	0	1
<i>ADAMTSL4</i>	chr1	31	4269	4269	0	1
<i>AGL</i>	chr1	52	6024	6024	0	1
<i>AKAP9</i>	chr7	90	12224	12224	0	1
<i>ALMS1</i>	chr2	85	12734	12734	0	1
<i>ANK2</i>	chr4	93	12411	12411	0	1
<i>ANKRD1</i>	chr10	9	1050	1050	0	1
<i>APOB</i>	chr2	85	13982	13982	0	1
<i>ATP7A</i>	chrX	41	4723	4723	0	1
<i>B3GAT3</i>	chr11	13	1474	1471	3	.998
<i>BAG3</i>	chr10	12	1768	1768	0	1
<i>BGN</i>	chrX	12	1457	1457	0	1
<i>BLK</i>	chr8	21	2118	2118	0	1
<i>BMP10</i>	chr2	9	1375	1375	0	1
<i>BMPR1A</i>	chr10	13	1709	1709	0	1
<i>BMPR1B</i>	chr4	13	1709	1709	0	1
<i>BMPR2</i>	chr2	25	3247	3247	0	1
<i>BRAF</i>	chr7	23	2481	2481	0	1
<i>CACNA1C</i>	chr12	64	7626	7626	0	1
<i>CACNA1D</i>	chr3	64	7150	7150	0	1
<i>CACNA2D1</i>	chr7	51	5327	5327	0	1
<i>CACNB2</i>	chr10	26	3269	3269	0	1
<i>CALM1</i>	chr14	7	690	690	0	1
<i>CALM2</i>	chr2	7	664	664	0	1
<i>CALM3</i>	chr19	8	750	750	0	1
<i>CALR3</i>	chr19	14	1605	1574	31	.9807
<i>CASQ2</i>	chr1	13	1750	1750	0	1
<i>CAV3</i>	chr3	4	476	476	0	1
<i>CBL</i>	chr11	23	2881	2881	0	1
<i>CBS</i>	chr21	21	1806	1806	0	1
<i>CHRM2</i>	chr7	8	1451	1451	0	1
<i>COL1A1</i>	chr17	56	4905	4905	0	1
<i>COL1A2</i>	chr7	55	4621	4621	0	1
<i>COL3A1</i>	chr2	57	4911	4911	0	1
<i>COL5A1</i>	chr9	78	6256	6256	0	1
<i>COL5A2</i>	chr2	64	7200	7200	0	1
<i>CRYAB</i>	chr11	5	678	678	0	1
<i>CSRP3</i>	chr11	6	635	635	0	1

<i>CTNNA3</i>	chr10	29	3758	3758	0	1
<i>CTNNB1</i>	chr3	19	2486	2486	0	1
<i>DES</i>	chr2	15	1503	1503	0	1
<i>DMD</i>	chrX	106	12161	12161	0	1
<i>DNAJC19</i>	chr3	6	411	411	0	1
<i>DOLK</i>	chr9	9	1667	1667	0	1
<i>DSC2</i>	chr18	25	2912	2912	0	1
<i>DSG2</i>	chr18	28	3507	3507	0	1
<i>DSP</i>	chr6	57	8856	8856	0	1
<i>DTNA</i>	chr18	29	3795	3795	0	1
<i>EIF2AK3</i>	chr2	32	4201	4201	0	1
<i>EIF2AK4</i>	chr15	51	6900	6900	0	1
<i>ELN</i>	chr7	37	4094	4094	0	1
<i>EMD</i>	chrX	9	1005	1005	0	1
<i>ENG</i>	chr9	22	2753	2753	0	1
<i>EYA4</i>	chr6	26	3039	3039	0	1
<i>FBN1</i>	chr15	73	9266	9266	0	1
<i>FBN2</i>	chr5	88	9389	9389	0	1
<i>FHL1</i>	chrX	11	1472	1466	6	.9959
<i>FHL2</i>	chr2	9	1090	1090	0	1
<i>FKRP</i>	chr19	11	1498	1498	0	1
<i>FKTN</i>	chr9	13	1509	1509	0	1
<i>FLNA</i>	chrX	76	10294	10294	0	1
<i>FLNC</i>	chr7	75	8658	8658	0	1
<i>GAA</i>	chr17	27	3049	3049	0	1
<i>GATA4</i>	chr8	12	1392	1392	0	1
<i>GATA5</i>	chr20	12	1494	1494	0	1
<i>GATAD1</i>	chr7	9	1060	1060	0	1
<i>GCK</i>	chr7	17	1608	1608	0	1
<i>GDF2</i>	chr10	7	1390	1390	0	1
<i>GJA1</i>	chr6	6	1159	1159	0	1
<i>GJA5</i>	chr1	8	1117	1117	0	1
<i>GLA</i>	chrX	10	1360	1360	0	1
<i>GLIS3</i>	chr9	22	3293	3293	0	1
<i>GPD1L</i>	chr3	11	1376	1376	0	1
<i>HFE</i>	chr6	9	1125	1107	18	.984
<i>HNFB1A</i>	chr12	16	2017	2017	0	1
<i>HNFB1B</i>	chr17	16	1856	1856	0	1
<i>HNFB4A</i>	chr20	20	1860	1860	0	1
<i>HRAS</i>	chr11	5	683	683	0	1
<i>ILK</i>	chr11	14	1959	1959	0	1
<i>JPH2</i>	chr20	17	2402	2402	0	1
<i>JUP</i>	chr17	21	2368	2368	0	1
<i>KCNA5</i>	chr12	11	1892	1892	0	1
<i>KCND2</i>	chr7	15	2193	2193	0	1

<i>KCND3</i>	chr1	17	2318	2318	0	1
<i>KCNE1</i>	chr21	2	400	400	0	1
<i>KCNE2</i>	chr21	2	382	382	0	1
<i>KCNE3</i>	chr11	2	362	362	0	1
<i>KCNE5</i>	chrX	3	479	479	0	1
<i>KCNH2</i>	chr7	28	4017	4017	0	1
<i>KCNJ11</i>	chr11	6	1183	1183	0	1
<i>KCNJ2</i>	chr17	8	1294	1294	0	1
<i>KCNJ5</i>	chr11	9	1340	1340	0	1
<i>KCNJ8</i>	chr12	8	1375	1375	0	1
<i>KCNK3</i>	chr2	9	1285	1285	0	1
<i>KCNQ1</i>	chr11	20	2206	2206	0	1
<i>KLF11</i>	chr2	11	1739	1739	0	1
<i>KRAS</i>	chr12	6	737	737	0	1
<i>LAMA4</i>	chr6	55	7540	7540	0	1
<i>LAMP2</i>	chrX	15	1626	1626	0	1
<i>LDB3</i>	chr10	24	2668	2664	4	.9985
<i>LDLR</i>	chr19	21	2763	2763	0	1
<i>LDLRAP1</i>	chr1	14	1377	1377	0	1
<i>LIPA</i>	chr10	14	1650	1650	0	1
<i>LMNA</i>	chr1	18	2369	2369	0	1
<i>LOX</i>	chr5	13	1604	1604	0	1
<i>LZTR1</i>	chr22	29	2733	2733	0	1
<i>MAP2K1</i>	chr15	12	1292	1292	0	1
<i>MAP2K2</i>	chr19	13	1313	1313	0	1
<i>MAT2A</i>	chr2	11	1638	1638	0	1
<i>MED12</i>	chrX	59	6984	6984	0	1
<i>MFAP5</i>	chr12	9	972	972	0	1
<i>MIB1</i>	chr18	36	4071	4071	0	1
<i>MURC</i>	chr9	7	1195	1195	0	1
<i>MYBPC3</i>	chr11	35	4155	4155	0	1
<i>MYH11</i>	chr16	51	6391	6391	0	1
<i>MYH6</i>	chr14	51	6190	6190	0	1
<i>MYH7</i>	chr14	45	6188	6188	0	1
<i>MYL2</i>	chr12	7	571	571	0	1
<i>MYL3</i>	chr3	6	648	648	0	1
<i>MYLK</i>	chr3	41	6055	6055	0	1
<i>MYLK2</i>	chr20	21	2391	2391	0	1
<i>MYOM1</i>	chr18	56	6908	6908	0	1
<i>MYOZ2</i>	chr4	8	1045	1045	0	1
<i>MYPN</i>	chr10	36	4983	4983	0	1
<i>NEBL</i>	chr10	38	5002	5002	0	1
<i>NEUROD1</i>	chr2	6	1121	1121	0	1
<i>NEUROG3</i>	chr10	5	695	695	0	1
<i>NEXN</i>	chr1	21	2628	2628	0	1

<i>NF1</i>	chr17	74	9161	9161	0	1
<i>NKX2-5</i>	chr5	9	1142	1142	0	1
<i>NKX2-6</i>	chr8	6	926	926	0	1
<i>NNT</i>	chr5	37	4311	4306	5	.9988
<i>NOTCH1</i>	chr9	63	8008	7987	21	.9974
<i>NOTCH3</i>	chr19	51	7296	7296	0	1
<i>NPPA</i>	chr1	4	486	486	0	1
<i>NRAS</i>	chr1	5	610	610	0	1
<i>PAX6</i>	chr11	13	2035	2035	0	1
<i>PCSK9</i>	chr1	16	2199	2199	0	1
<i>PDLIM3</i>	chr4	13	1733	1733	0	1
<i>PDX1</i>	chr13	7	952	952	0	1
<i>PITX2</i>	chr4	11	1209	1209	0	1
<i>PKP2</i>	chr12	21	2786	2786	0	1
<i>PLN</i>	chr6	1	169	169	0	1
<i>PLOD1</i>	chr1	28	3325	3325	0	1
<i>PPARG</i>	chr3	12	1588	1588	0	1
<i>PRDM16</i>	chr1	37	4681	4654	27	.9942
<i>PRKAG2</i>	chr7	19	1974	1974	0	1
<i>PRKG1</i>	chr10	26	3087	3087	0	1
<i>PSEN1</i>	chr14	12	1504	1504	0	1
<i>PSEN2</i>	chr1	15	1447	1447	0	1
<i>PTPN11</i>	chr12	16	1936	1936	0	1
<i>RAF1</i>	chr3	18	2107	2107	0	1
<i>RANGRF</i>	chr17	8	853	853	0	1
<i>RASA1</i>	chr5	39	3412	3411	1	.9997
<i>RASA2</i>	chr3	38	3815	3793	22	.9942
<i>RBM20</i>	chr10	27	3824	3817	7	.9982
<i>RFX6</i>	chr6	30	3737	3737	0	1
<i>RIT1</i>	chr1	8	771	771	0	1
<i>RYR2</i>	chr1	134	15954	15954	0	1
<i>SCN10A</i>	chr3	49	7221	7221	0	1
<i>SCN1B</i>	chr19	9	1066	1066	0	1
<i>SCN2B</i>	chr11	7	848	848	0	1
<i>SCN3B</i>	chr11	8	898	898	0	1
<i>SCN4B</i>	chr11	7	887	887	0	1
<i>SCN5A</i>	chr3	44	6423	6423	0	1
<i>SDHA</i>	chr5	19	2145	2145	0	1
<i>SGCD</i>	chr5	8	1025	1025	0	1
<i>SHOC2</i>	chr10	14	1829	1829	0	1
<i>SLC19A2</i>	chr1	13	1794	1794	0	1
<i>SLC22A5</i>	chr5	14	1856	1856	0	1
<i>SLC2A10</i>	chr20	14	1876	1876	0	1
<i>SLMAP</i>	chr3	33	3799	3799	0	1
<i>SMAD1</i>	chr4	12	1698	1698	0	1

<i>SMAD2</i>	chr18	13	1504	1504	0	1
<i>SMAD3</i>	chr15	14	1452	1452	0	1
<i>SMAD4</i>	chr18	18	1769	1769	0	1
<i>SMAD9</i>	chr13	13	1704	1704	0	1
<i>SNTA1</i>	chr20	17	1918	1918	0	1
<i>SOS1</i>	chr2	40	4232	4232	0	1
<i>SOS2</i>	chr14	46	4919	4919	0	1
<i>SPRED1</i>	chr15	13	1405	1405	0	1
<i>STAP1</i>	chr4	10	1248	1248	0	1
<i>TAZ</i>	chrX	14	1043	1043	0	1
<i>TBX5</i>	chr12	12	1637	1637	0	1
<i>TCAP</i>	chr17	5	524	524	0	1
<i>TGFB2</i>	chr1	12	1409	1409	0	1
<i>TGFB3</i>	chr14	10	1589	1589	0	1
<i>TGFBR1</i>	chr9	13	1614	1614	0	1
<i>TGFBR2</i>	chr3	12	1859	1859	0	1
<i>TMEM43</i>	chr3	13	1323	1323	0	1
<i>TMPO</i>	chr12	25	3385	3385	0	1
<i>TNNC1</i>	chr3	7	546	546	0	1
<i>TNNI3</i>	chr19	7	702	702	0	1
<i>TNNI3K</i>	chr1	30	3758	3710	48	.9872
<i>TNNT2</i>	chr1	17	1081	1081	0	1
<i>TOPBP1</i>	chr3	51	5919	5919	0	1
<i>TPM1</i>	chr15	15	1500	1500	0	1
<i>TRDN</i>	chr6	48	4418	4418	0	1
<i>TRPM4</i>	chr19	32	3895	3895	0	1
<i>TTN</i>	chr2	800	132581	129775	2806	.9788
<i>TTR</i>	chr18	5	484	484	0	1
<i>TXNRD2</i>	chr22	23	2543	2543	0	1
<i>VCL</i>	chr10	36	4505	4505	0	1
<i>WFS1</i>	chr4	19	2743	2743	0	1
<i>ZDHHC9</i>	chrX	10	1545	1545	0	1

Supplementary. Table S2. Transcripts for the genes with candidate variants.

GENE	Transcript ID	RefSeq Match
<i>AKAP9</i>	ENST00000356239	NM_005751
<i>ANK2</i>	ENST00000357077	NM_001148
<i>APOB</i>	ENST00000233242	NM_000384
<i>BAG3</i>	ENST00000369085	NM_004281
<i>BMPR2</i>	ENST00000374580	NM_001204
<i>DMD</i>	ENST00000357033	NM_004006
<i>DSP</i>	ENST00000379802	NM_004415
<i>ELN</i>	ENST00000252034	NM_000501
<i>EMD</i>	ENST00000369842	NM_000117
<i>FBN1</i>	ENST00000316623	NM_000138
<i>FKRP</i>	ENST00000391909	NM_001039885
<i>FLNC</i>	ENST00000325888	NM_001458
<i>GAA</i>	ENST00000390015	NM_001079804
<i>GDF2</i>	ENST00000581492	NM_016204
<i>GLA</i>	ENST00000218516	NM_000169
<i>JPH2</i>	ENST00000372980	NM_020433
<i>JUP</i>	ENST00000393931	NM_002230
<i>KCNH2</i>	ENST00000262186	NM_000238
<i>LAMA4</i>	ENST00000230538	NM_001105206
<i>LDB3</i>	ENST00000361373	NM_007078
<i>LDLR</i>	ENST00000558518	NM_000527
<i>LMNA</i>	ENST00000368300	NM_170707
<i>MIB1</i>	ENST00000261537	NM_020774
<i>MYBPC3</i>	ENST00000545968	NM_000256
<i>MYH6</i>	ENST00000405093	NM_002471
<i>MYH7</i>	ENST00000355349	NM_000257
<i>MYH11</i>	ENST00000396324	NM_001040114
<i>MYLK</i>	ENST00000360304	NM_053025
<i>MYPN</i>	ENST00000540630	NM_001256267
<i>NEBL</i>	ENST00000377122	NM_006393
<i>NOTCH1</i>	ENST00000651671	NM_017617
<i>PDX1</i>	ENST00000381033	NM_000209
<i>PKP2</i>	ENST00000070846	NM_004572
<i>RBM20</i>	ENST00000369519	NM_001134363
<i>RIT1</i>	ENST00000368322	NM_001256821
<i>RYR2</i>	ENST00000366574	NM_001035
<i>SCN5A</i>	ENST00000413689	NM_001160161
<i>SMAD9</i>	ENST00000379826	NM_001127217
<i>TCAP</i>	ENST00000309889	NM_003673
<i>TMEM43</i>	ENST00000306077	NM_024334
<i>TNNI3</i>	ENST00000344887	NM_000363
<i>TNNT2</i>	ENST00000236918	NM_001276345
<i>TRPM4</i>	ENST00000252826	NM_017636
<i>TTN</i>	ENST00000460472	NM_003319

Supplementary Table S3. Main clinical characteristics of the ischemic cases.

		Ischemic Patients (N=63)
Deceased n(%)		37 (58.7)
Smokers pre-HT n(%)		51 (80.9)
Arterial hypertension pre-HT n(%)		39 (61.9)
Mellitus Diabetes (%)	No	61.9
	Type 1	27.0
	Type 2	11.1
Dyslipidemia n(%)		30 (47.6)
Renal Disease n(%)		3 (4.8)
Family history of severe HF n(%)		10 (15.8)
Myocardial infarction n(%)		50 (79.4)
LVEF (%)	>53	6.4
	45-53	1.6
	35-45	9.5
	<35	82.5
Coronary heart disease (%)	No	—
	LMCA	10.3
	A blood vessel	22.4
	Two blood vessel	25.9
	Three blood vessel	41.4
Revascularization (%)	No	49.2
	Complete	23.8
	Incomplete	27.0
Fibrinolysis n(%)		20 (31.7)
PCI n(%)		22 (34.9)
CABG n(%)		11 (17.5)

HT: heart transplantation; HF: heart failure; LMCA: left main coronary artery; LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft.

Supplementary Table S4. Family studies in available patients.

Patient ID	Variant	Age	Sex	Genetic status	Clinical status
2	LMNA p.R190W	38	Male	Carrier	DCM non-ischemic (Transplanted)
2.2		13	Female	Non carrier	Normal
2.3		8	Male	Non carrier	Normal
2.4		57	Female	Non carrier	Normal
2.5		75	Female	Non carrier	Normal
3	LMNA p.R190W	67	Female	Carrier	DCM non-ischemic (Transplanted)
3.2		71	Female	Non carrier	Normal
3.3		61	Female	Non carrier	Normal
3.4		45	Male	Carrier	DCM non-ischemic
3.5		4	Female	Carrier	Normal
3.7		36	Male	Carrier	DCM non-ischemic
3.8		14	Male	Carrier	Normal
5	MYBC3 c.2308+1G>A	76	Male	Carrier	HCM (Transplanted)
5.2		40	Male	Carrier	HCM
5.3		46	Male	Carrier	HCM
5.4		8	Female	Non carrier	Normal
5.5		8	Male	Non carrier	Normal
5.6		65	Female	Non carrier	Normal
5.7		69	Female	Non carrier	Normal
5.8		51	Male	Non carrier	Normal
5.9		48	Female	Carrier	Normal
5.10		27	Female	Non carrier	Normal
5.11		18	Male	Carrier	HCM
7	MYH7 p.R663C	63	Male	Carrier	HCM (Transplanted)
7.2		39	Male	Carrier	HCM
8	MYH7 p.R403Q	53	Female	Carrier	HCM (Transplanted)
8.2		25	Female	Non carrier	Normal
8.3		22	Male	Carrier	HCM
10	TNNT2 p.E173del	70	Female	Carrier	HCM (Transplanted)
10.2		51	Female	Carrier	HCM
10.3		66	Female	Carrier	HCM
10.4		45	Female	Non carrier	Normal
10.5		68	Female	Non carrier	Normal
10.6		50	Male	Non carrier	Normal
13	TTN c.29453-1G>A	76	Male	Carrier	DCM non-ischemic (Transplanted)
13.2		72	Female	Carrier	Normal
13.3		74	Female	Non carrier	Normal
13.5		50	Female	Carrier	Normal
13.6		51	Female	Carrier	Normal
13.7		30	Male	Carrier	Normal
13.8		21	Male	Carrier	Normal

13.9		37	Male	Non carrier	Normal
13.10		13	Female	Carrier	Normal

