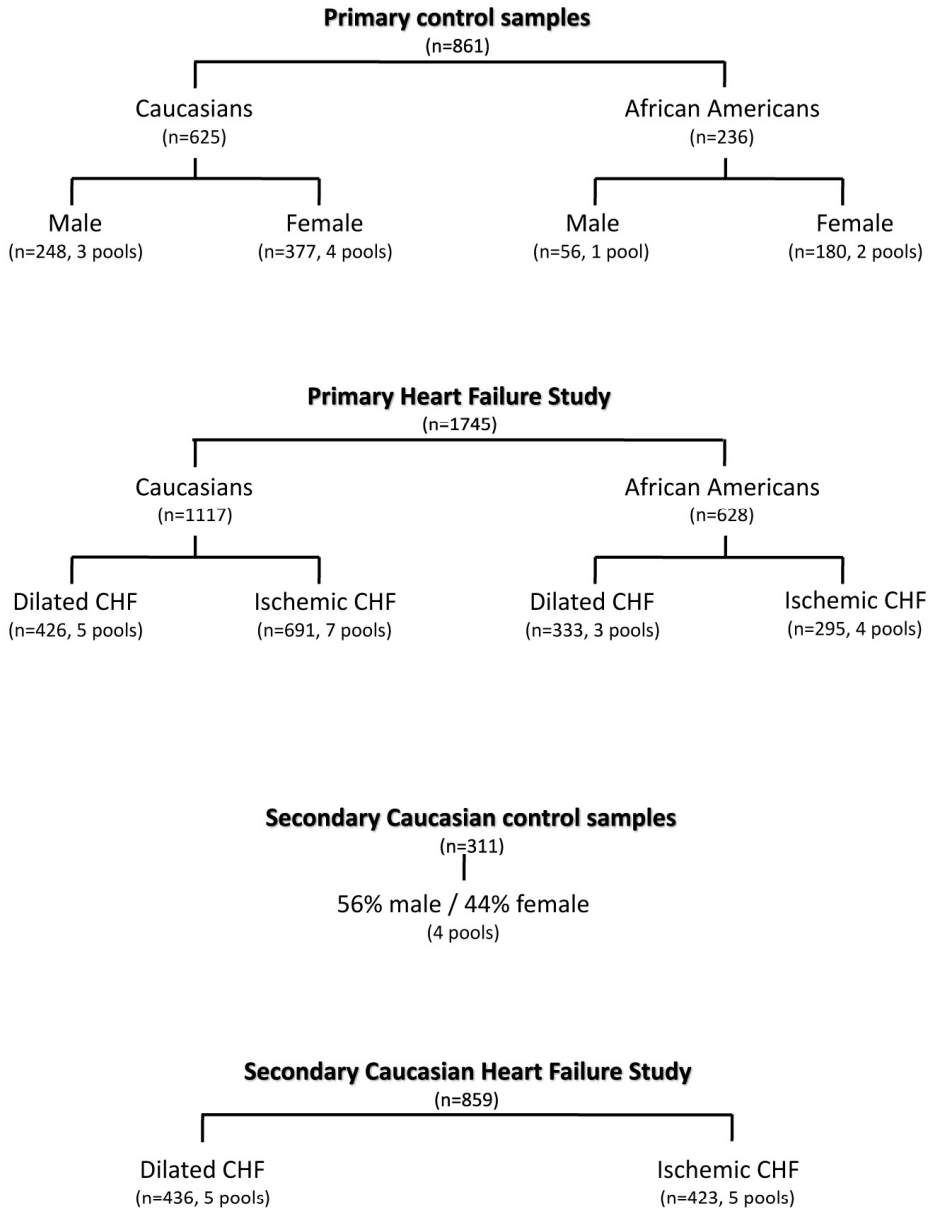
SUPPLEMENTAL DATA



Supplemental Figure 1. Schematic depicting DNA pooling strategy for subgroup analyses of SNPs detected by Illumina sequencing.

Supplemental Table 1 – Comparative allele frequencies of target gene SNPs in Caucasians and African Americans.

Gene	dbSNP	Position	Type	Major Allele	Minor Allele	Codon	Cauc controls	AA controls	P-value
ADRA1A		-347	5'UTR	T	C		--	0.0112	--
		-27	5'UTR	G	A		--	0.0030	--
		+226	Coding NS	A	C	T76P	0.0006	--	--
		+320	Coding NS	T	G	V17G	0.0024	0.0079	0.0945
		+435	Coding NS	G	T	M145I	--	0.0028	--
	rs617579	+460	Coding NS	T	G	S154A	0.0046	--	--
	rs2229124	+462	Coding S	C	G	S154S	0.0092	--	--
		+481	Coding NS	C	T	P161S	0.0007	--	--
	rs56233953	+497	Coding NS	G	A	R166K	0.0048	--	--
		+581	Coding NS	A	C	Y194S	0.0014	--	--
	rs2229125	+599	Coding NS	T	G	I200S	0.0216	0.0017	0.0022
		+695	Coding NS	T	G	V232G	0.0008	--	--
		+746	Coding NS	C	A	A249D	--	0.0027	--
	rs617577	+819	Coding S	G	T	T273T	0.0012	--	--
	rs382423	I1+53	intronic	G	T		0.0162	0.0095	0.3555
		+996	Coding S	G	A	E332E	--	0.0053	--
	rs14811	+1039	Coding NS	T	C	C347R	0.4317	0.7023	**<0.0001**
	rs5631822	+1074	Coding S	C	T	Y358Y	0.0010	--	--
	rs61731555	+1123	Coding NS	G	T	V375L	--	0.0017	--
		+1124	Coding NS	T	G	V375G	0.0016	--	--
		+1173	Coding S	G	A	T391T	--	0.0026	--
		+1311	Coding S	G	T	G437G	0.0008	--	--
	rs2229126	+1395	Coding NS	A	T	E465D	0.0243	0.0226	1.0000
	rs6176513	+1460	3'UTR	C	A		0.0008	0.0110	0.0071
	rs6176511	+1563	3'UTR	G	T		0.0030	0.0021	1.0000
	rs73678233	+1617	3'UTR	C	T		0.0011	0.0591	**<0.0001**
		+1792	3'UTR	G	A		--	0.0028	--
	rs1755967	+1802	3'UTR	T	C		0.0081	--	--
	rs3739216	+1818	3'UTR	C	G		0.0742	0.1800	**<0.0001**
ADRB2	rs33947624	-262	5'FR	G	A		--	0.0583	--
		-217	5'UTR	T	C		0.0023	--	--
	rs35883484	-75	5'UTR	G	A		--	0.0064	--
	rs142711	-47	5'UTR	C	T		0.6161	0.8451	**<0.0001**
	rs18174	-20	5'UTR	C	T		0.6185	0.8415	**<0.0001**
	rs3397363	+44	Coding NS	A	G	N15S	--	0.0041	--
	rs142713	+46	Coding NS	G	A	G16R	0.3985	0.4781	0.0031
	rs142714	+79	Coding NS	G	C	E27Q	0.5716	0.8165	**<0.0001**

Gene	dbSNP	Position	Type	Major Allele	Minor Allele	Codon	Cauc controls	AA controls	P-value
	rs142717	+252	Coding S	G	A	L84L	0.2165	0.3965	**<0.0001**
ADRB2		+328	Coding NS	A	C	T11P	0.0008	--	--
	rs18888	+491	Coding NS	C	T	T164I	0.0208	--	--
	rs142718	+523	Coding S	C	A	R175R	0.2004	0.3892	**<0.0001**
		+587	Coding NS	A	C	N196T	0.0010	--	--
	rs3729943	+659	Coding NS	C	G	S22C	--	0.0330	--
		+847	Coding NS	A	C	T283P	0.0010	--	--
	rs142719	+1053	Coding S	G	C	G351G	0.2995	0.3851	**0.0008**
		+1062	Coding NS	C	A	Y354*	0.0018	--	--
	rs41354346	+1098	Coding S	T	C	Y366Y	0.0010	--	--
		+1108	Coding NS	C	A	Q37K	0.0008	--	--
	rs14272	+1239	Coding S	G	A	L413L	0.3256	0.5402	**<0.0001**
	rs41478145	+1245	3'UTR	C	T		0.0011	--	--
	rs71739194	+1267	3'UTR	C	A		--	0.0027	--
	rs28763957	+1268	3'UTR	C	A		0.0015	--	--
	rs687922	+1273	3'UTR	C	A		--	0.0114	--
	rs142721	+1275	3'UTR	C	A		--	0.0414	--
	rs3579595	+1276	3'UTR	C	A		--	0.1332	--
		+1409	3'UTR	A	C		--	0.0027	--
	rs8192451	+1620	3'UTR	C	T		0.0150	0.0064	0.2267
		+1698	3'UTR	C	T		--	0.0012	--
HSPB7		-12	5'UTR	C	T		--	0.0125	--
	rs373864	-8	5'UTR	G	A		0.1061	0.0410	**<0.0001**
	rs945416	+57	Coding S	C	T	S19S	0.5383	0.6737	**<0.0001**
	rs732286	+99	Coding S	T	C	A33A	0.5171	0.6639	**<0.0001**
		+151	Coding NS	G	A	D51N	--	0.0085	--
		+152	Coding NS	A	G	D51G	--	0.0115	--
		I1+34	intronic	G	T		0.0006	--	--
	rs3883891	I1+177	intronic	A	G		0.3730	0.3590	0.5762
	rs1763596	I1-133	intronic	G	A		0.5383	0.6975	
	rs1739845	I1-113	intronic	G	T		0.0501	0.0788	0.0369
		I1-75	intronic	A	G		--	0.0381	--
		I1-53	intronic	G	A		--	0.0037	--
		I2+121	intronic	T	A		--	0.0051	--
		I2+134	intronic	A	G		--	0.0462	--
	rs3738643	I2+245	intronic	C	G		0.1116	0.0404	**<0.0001**
	rs1739844	I2+247	intronic	A	G		0.5109	0.6735	**<0.0001**
	rs1763597	I2+272	intronic	G	A		0.5276	0.6988	**<0.0001**
	rs1739843	I2+315	intronic	A	G		0.5432	0.7014	**<0.0001**
		I2+422	intronic	T	G		0.0010	--	--
	rs12758813	I2+490	intronic	C	T		0.4173	0.4350	0.5476

Gene	dbSNP	Position	Type	Major Allele	Minor Allele	Codon	Cauc controls	AA controls	P-value
		I2+511	intronic	T	C		--	0.0019	--
HSPB7		I2+651	intronic	G	C		--	0.0424	--
		I2-644	intronic	G	C		--	0.0046	--
	rs1739842	I2-594	intronic	A	C		0.5235	0.6975	**<0.0001**
	rs1187649	I2-524	intronic	G	A		--	0.0421	--
	rs1763598	I2-483	intronic	A	G		0.8775	0.8424	0.0662
	rs1739841	I2-473	intronic	T	C		0.4802	0.6451	**<0.0001**
		I2-455	intronic	C	T		--	0.0034	--
	rs1763599	I2-348	intronic	G	A		0.6009	0.7442	**<0.0001**
	rs61783988	I2-343	intronic	T	C		0.0779	0.0305	**0.0002**
	rs1182877	I2-325	intronic	T	G		--	0.0366	--
		I2-184	intronic	G	A		--	0.0131	--
	rs76176	I2-165	intronic	T	C		0.5307	0.6803	**<0.0001**
		I2-98	intronic	G	A		--	0.0042	--
	rs761759	I2-96	intronic	T	A		0.5519	0.7080	**<0.0001**
	rs173984	+351	Coding S	C	T	T117T	0.4735	0.3096	**<0.0001**
		+387	Coding S	G	A	P129P	--	0.0526	--
		+485	Coding NS	A	C	Q162P	--	0.0089	--
		+556	3'UTR	G	A		--	0.0478	--
PLN	rs73526175	I1-206	intronic	G	T		0.0030	0.0710	**<0.0001**
		I1-105	intronic	A	G		0.0013	0.0043	0.3029
		I1-53	intronic	T	A		--	0.0316	--
		-56	5'UTR	C	T		0.0025	--	--
	rs28763979	+248	3'UTR	A	G		--	0.0378	--
	rs12198461	+556	3'UTR	T	G		0.5238	0.4181	**<0.0001**
		+954	3'UTR	T	A		--	0.0088	--
		+999	3'UTR	C	A		--	0.0184	--
		+1402	3'UTR	C	T		0.0028	--	--
		+1575	3'FR	G	A		0.0209	0.0624	**<0.0001**
		+1591	3'FR	T	C		--	0.0075	--
	rs9489441	+1736	3'FR	G	C		0.0029	0.0781	**<0.0001**
	rs151429	+1737	3'FR	C	T		0.7017	0.7003	0.9529

Allele frequencies from Illumina resequencing of 7 DNA pools comprising 625 non-affected Caucasians and 3 DNA pools comprising 237 non-affected African Americans. Position of exonic SNPs is relative to +1 position of the translation initiation codon, and of SNPs within introns is relative to the nearest exon; I1 = first intron; I2 = second intron. UTR = untranslated region; FR = flanking region. Significance threshold is $P<0.0005$ (alpha = 0.05, n=110).

Supplemental Table 2. Comparative allele frequencies of common target gene SNPs in Caucasian Heart Failure

Gene	dbSNP	Pos	Type	Maj Allele	Min Allele	Codon	1° control	1° cases	Fisher	Adj χ^2	2° control	2° cases	Fisher	Adj χ^2
ADRA1A	rs2229125	+599	Code NS	T	G	I200S	0.022	0.027	0.4264	0.4613				
	rs3824230	I1+53	intronic	G	T		0.016	0.024	0.1130	0.2253				
	rs1048101	+1039	Code NS	T	C	C347R	0.432	0.440	0.6183	0.6550				
	rs2229126	+1395	Code NS	A	T	E465D	0.024	0.034	0.1010	0.1727				
	rs3739216	+1818	3UTR	C	G		0.074	0.069	0.5820	0.6080				
ADRB2	rs1042711	-47	5UTR	C	T		0.616	0.617	0.9421	0.9546				
	rs1801704	-20	5UTR	C	T		0.619	0.603	0.3852	0.3641				
	rs1042713	+46	Code NS	G	A	G16R	0.399	0.389	0.5874	0.5706				
	rs1042714	+79	Code NS	G	C	E27Q	0.572	0.548	0.3381	0.1807				
	rs1042717	+252	Code S	G	A	L84L	0.217	0.213	0.8298	0.7891				
	rs1800888	+491	Code NS	C	T	T164I	0.021	0.014	0.1214	0.2081				
	rs1042718	+523	Code S	C	A	R175R	0.200	0.202	0.9649	0.8913				
	rs1042719	+1053	Code S	G	C	G351G	0.300	0.278	0.1836	0.1789				
	rs1042720	+1239	Code S	G	A	L413L	0.326	0.313	0.4711	0.4403				
	rs8192451	+1620	3UTR	C	T		0.015	0.008	0.0371	0.1398				
HSPB7	rs3738640	-8	5UTR	G	A		0.106	0.102	0.6847	0.7246				
	rs945416	+57	Code S	C	T	S19S	0.538	0.606	**0.0001**	**0.0001**	0.510	0.582	**0.0025**	**0.0001**
	rs732286	+99	Code S	T	C	A33A	0.517	0.594	**<0.0001**	**<0.0001**	0.489	0.575	**0.0003**	**<0.0001**
	rs3883891	I1+177	intronic	A	G		0.373	0.424	0.0032	0.0040				
	rs1763596	I1-133	intronic	G	A		0.538	0.619	**<0.0001**	**<0.0001**	0.506	0.576	**0.003**	**0.0001**
	rs1739845	I1-113	intronic	G	T		0.050	0.052	0.8732	0.8168				
	rs3738643	I2+245	intronic	C	G		0.112	0.098	0.2454	0.2156				
	rs1739844	I2+247	intronic	A	G		0.511	0.589	**<0.0001**	**<0.0001**	0.480	0.571	**0.0001**	**<0.0001**
	rs1763597	I2+272	intronic	G	A		0.528	0.618	**<0.0001**	**<0.0001**	0.515	0.575	**0.0109**	**0.0008**
	rs1739843	I2+315	intronic	A	G		0.543	0.624	**<0.0001**	**<0.0001**	0.495	0.585	**0.0001**	**<0.0001**
	rs12758813	I2+490	intronic	C	T		0.417	0.450	0.0696	0.0654				
HSPB7	rs1739842	I2-594	intronic	A	C		0.524	0.615	**<0.0001**	**<0.0001**	0.480	0.568	**0.0002**	**<0.0001**
	rs1763598	I2-483	intronic	A	G		0.878	0.898	0.0796	0.0836				
	rs1739841	I2-473	intronic	T	C		0.480	0.578	**<0.0001**	**<0.0001**	0.405	0.506	**<0.0001**	**<0.0001**
	rs1763599	I2-348	intronic	G	A		0.601	0.666	**0.0001**	**0.0002**	0.554	0.633	**0.0006**	**<0.0001**

Gene	dbSNP	Pos	Type	Maj Allele	Min Allele	Codon	1° control	1° cases	Fisher	Adj χ^2	2° control	2° cases	Fisher	Adj χ^2
	rs61783988	I2-343	intronic	T	C		0.078	0.075	0.7903	0.7652				
	rs761760	I2-165	intronic	T	C		0.531	0.598	**0.0001**	**0.0002**	0.484	0.570	**0.0003**	**<0.0001**
	rs761759	I2-96	intronic	T	A		0.552	0.632	**<0.0001**	**<0.0001**	0.456	0.581	**<0.0001**	**<0.0001**
	rs1739840	+351	Code S	C	T	T117T	0.473	0.399	**<0.0001**	**<0.0001**	0.561	0.443	**<0.0001**	**<0.0001**
PLN	rs12198461	+556	3'UTR	T	G		0.524	0.540	0.3575	0.3740				
		+1575	3'FR	G	A		0.021	0.015	0.2248	0.2896				
	rs1051429	+1737	3'FR	C	T		0.702	0.718	0.2924	0.3292				

Allele frequencies of 37 common SNPs from Illumina resequencing of 7 DNA pools comprising 625 non-affected Caucasians (**1° control**), 12 DNA pools comprising 1117 Caucasians with systolic heart failure (**1° cases**), 4 pools comprising 311 non-affected Caucasians (**2° control**) and 10 pools comprising 825 Caucasians with systolic heart failure (**2° cases**). SNPs are numbered as in Tables 1 and 2. Statistical comparisons used Fisher's exact test (**Fisher**), and adjusted chi-squared test (**Adj χ^2**), as described in methods. P value threshold for primary study was <0.0014 (alpha = 0.05, two-tailed test, with n=37), and for replication study was <0.0212 (alpha = 0.05, two-tailed test, with Meff = 2.36).

Supplemental Table 3. *HSPB7* SNPs in ischemic and non-ischemic heart failure.

Gene	dbSNP	Posit.	Type	Major Allele	Minor Allele	Codon	Controls	Primary cases, ischemic	P-value	Replication cases, ischemic	P-value
HSPB7	rs945416	+57	Coding S	C	T	S19S	0.5383	0.5989	0.0018	0.5714	0.1012
	rs732286	+99	Coding S	T	C	A33A	0.5171	0.5882	0.0003	0.5726	**0.0139**
	rs1763596	I1-133	intronic	G	A		0.5383	0.6141	**<0.0001**	0.5732	0.0894
	rs1739844	I2+247	intronic	A	G		0.5109	0.5835	0.0002	0.5719	**0.0093**
	rs1763597	I2+272	intronic	G	A		0.5276	0.6121	**<0.0001**	0.5795	0.0228
	rs1739843	I2+315	intronic	A	G		0.5432	0.6148	0.0002	0.5753	0.1105
	rs1739842	I2-594	intronic	A	C		0.5235	0.6068	**<0.0001**	0.5969	**0.0021**
	rs1739841	I2-473	intronic	T	C		0.4802	0.5726	0.0057	0.5403	**0.0098**
	rs1763599	I2-348	intronic	G	A		0.6009	0.6601	0.0018	0.6501	**0.0243**
	rs761760	I2-165	intronic	T	C		0.5307	0.5920	0.0016	0.5745	0.0417
	rs761759	I2-96	intronic	T	A		0.5519	0.6219	0.0003	0.6140	**0.0077**
	rs1739840	+351	Coding S	C	T	T117T	0.4735	0.4126	0.0017	0.4199	**0.0179**

Gene	dbSNP	Posit.	Type	Major Allele	Minor Allele	Codon	Controls	Primary cases, nonischemic	P-value	Replication cases, nonischemic	P-value
HSPB7	rs945416	+57	Coding S	C	T	S19S	0.5383	0.6168	0.0003	0.5752	0.0894
	rs732286	+99	Coding S	T	C	A33A	0.5171	0.6035	**0.0001**	0.5726	**0.0163**
	rs1763596	I1-133	intronic	G	A		0.5383	0.6270	**<0.0001**	0.5601	0.2138
	rs1739844	I2+247	intronic	A	G		0.5109	0.5991	**<0.0001**	0.5601	0.0307
	rs1763597	I2+272	intronic	G	A		0.5276	0.6285	**<0.0001**	0.5608	0.0956
	rs1739843	I2+315	intronic	A	G		0.5432	0.6390	**<0.0001**	0.5864	0.0491
HSPB7	rs1739842	I2-594	intronic	A	C		0.5235	0.6292	**<0.0001**	0.5614	0.0714
	rs1739841	I2-473	intronic	T	C		0.4802	0.5876	**<0.0001**	0.4947	0.2970
	rs1763599	I2-348	intronic	G	A		0.6009	0.6758	0.0005	0.6295	0.1301
	rs761760	I2-165	intronic	T	C		0.5307	0.6074	0.0006	0.5531	0.2029
	rs761759	I2-96	intronic	T	A		0.5519	0.6493	**<0.0001**	0.5937	0.0564
	rs1739840	+351	Coding S	C	T	T117T	0.4735	0.3775	**<0.0001**	0.4531	**0.0093**

Case-control analysis of systolic heart failure (HF) in Caucasians, categorized as ischemic or non-ischemic etiology.

Supplemental Table 4 – Case-control analysis of systolic heart failure in African-Americans for significant *HSPB7* SNPs from Caucasian case-control study.

Gene	dbSNP	Position	Type	Major Allele	Minor Allele	Codon	AA controls	AA cases	P-value
HSPB7	rs945416	+57	Coding S	C	T	S19S	0.6737	0.6556	0.4941
	rs732286	+99	Coding S	T	C	A33A	0.6639	0.6574	0.8644
	rs1763596	I1-133	intronic	G	A		0.6975	0.6907	0.8152
	rs1739844	I2+247	intronic	A	G		0.6735	0.6766	0.8627
	rs1763597	I2+272	intronic	G	A		0.6988	0.6953	0.9066
	rs1739843	I2+315	intronic	A	G		0.7014	0.6983	0.9531
	rs1739842	I2-594	intronic	A	C		0.6975	0.7006	0.9063
	rs1739841	I2-473	intronic	T	C		0.6451	0.6513	0.7776
	rs1763599	I2-348	intronic	G	A		0.7442	0.7313	0.6253
	rs761760	I2-165	intronic	T	C		0.6803	0.6829	0.8619
	rs761759	I2-96	intronic	T	A		0.7080	0.7044	0.9528
	rs1739840	+351	Coding S	C	T	T117T	0.3096	0.3260	0.5255

n=236 AA controls; 628 AA HF patients.

Supplemental Table 5 - Analysis of common non-synonymous SNPs in Caucasian and African Americans with systolic heart failure.

Common Synonymous SNPs								Caucasian			African American		
Gene	**dbSNP**	**Position**	**Major Allele**	**Minor Allele**	**Codon**	**SIFT**	**PolyPhen**	**Controls**	**Cases**	**p-value**	**Controls**	**Cases**	**p-value**
ADRB2	rs1042717	+252	G	A	L84L	x	x	0.2165	0.2133	0.7964	0.3318	0.3965	0.0144
	rs1042718	+523	C	A	R175R	x	x	0.2004	0.2020	0.9299	0.3442	0.3892	0.0950
	rs1042719	+1053	G	C	G351G	x	x	0.2995	0.2777	0.1716	0.3649	0.3851	0.4705
	rs1042720	+1239	G	A	L413L	x	x	0.3256	0.3134	0.4486	0.5625	0.5402	0.4169
HSPB7	rs945416	+57	C	T	S19S	x	x	0.5383	0.6057	**0.0001**	0.6556	0.6737	0.4917
	rs732286	+99	T	C	A33A	x	x	0.5171	0.5940	**< 0.0001**	0.6574	0.6639	0.8198
	rs1739840	+351	C	T	T117T	x	x	0.4735	0.3992	**< 0.0001**	0.3260	0.3096	0.5231
		+387	G	A	P129P	x	x	--	0.0008	--	0.0325	0.0526	0.1011

Common Non-synonymous SNPs that have no predicted functional significance								Caucasian			African American		
Gene	**dbSNP**	**Position**	**Major Allele**	**Minor Allele**	**Codon**	**SIFT**	**PolyPhen**	**Controls**	**Cases**	**p-value**	**Control**	**Cases**	**p-value**
ADRA1A	rs1048101	+1039	T	C	C347R	tolerated	benign	0.4317	0.4404	0.6436	0.7023	0.7590	0.0161
	rs2229126	+1395	A	T	E465D	tolerated	benign	0.0243	0.0345	0.1052	0.0226	0.0298	0.5170
ADRB2	rs1042714	+79	G	C	E27Q	tolerated	benign	0.5716	0.5484	0.2007	0.8165	0.8108	0.8360
	rs1800888	+491	C	T	T164I	tolerated	benign	0.0208	0.0135	0.1272	--	0.0023	-
	rs3729943	+659	C	G	S220C	tolerated	benign	--	0.0014	--	0.0330	0.0275	0.5247

Common Non-synonymous SNPs that have predicted functional significance								Caucasian			African American		
Gene	**dbSNP**	**Position**	**Major allele**	**Minor Allele**	**Codon**	**SIFT**	**PolyPhen**	**Controls**	**Cases**	**p-value**	**Controls**	**Cases**	**p-value**
ADRA1A	rs2229125	+599	T	G	I200S	affect function	probably damaging	0.022	0.027	0.426	0.002	0.004	0.681

Common Non-synonymous SNPs that have a mixed result from SIFT/PolyPhen								Caucasian			African American		
Gene	**dbSNP**	**Position**	**Major allele**	**Minor Allele**	**Codon**	**SIFT**	**PolyPhen**	**Controls**	**Cases**	**p-value**	**Controls**	**Cases**	**p-value**
ADRB2	rs1042713	+46	G	A	G16R	tolerated	possibly damaging	0.3985	0.3886	0.5631	0.4781	0.5032	0.3596

Supplemental Table 6 – Frequency comparison for rare non-synonymous SNPs in Caucasian and African Americans with systolic heart failure.

Rare Synonymous SNPs								Caucasian			African American		
Gene	**dbSNP**	**Position**	**Major Allele**	**Minor Allele**	**Codon**	**SIFT**	**PolyPhen**	**Control**	**HF**	**p-value**	**Control**	**HF**	**p-value**
ADRA1A	rs2229124	+462	C	G	S154S	x	x	0.0092	0.0062	0.2192	-	-	-
	rs7833704	+723	C	A	A241A	x	x	-	0.0006	-	0.0076	-	-
	rs61757007	+819	G	T	T273T	x	x	0.0012	0.0019	0.7068	-	-	-
		+996	G	A	E332E	x	x	-	-	-	-	0.0053	-
	rs56318220	+1074	C	T	Y358Y	x	x	0.0010	-	-	-	-	-
		+1173	G	A	T391T	x	x	-	-	-	0.0021	0.0026	0.6676
		+1203	T	G	S401S	x	x	-	0.0007	-	0.0026	-	-
ADRB2	rs35933628	+840	C	T	G280G	x	x	-	0.0006	-	0.0049	-	-
	rs41354346	+1098	T	C	Y366Y	x	x	0.0010	0.0030	0.5034	0.0017	-	-
COMBINED								0.0123	0.0129	0.8752	0.0189	0.0079	0.0667

Rare Non-synonymous SNPs that have no predicted functional significance								Caucasian			African American		
Gene	**dbSNP**	**Position**	**Major Allele**	**Minor Allele**	**Codon**	**SIFT**	**PolyPhen**	**Control**	**HF**	**p-value**	**Control**	**HF**	**p-value**
ADRA1A		+226	A	C	T76P	tolerated	benign	0.0006	-	-	-	0.0010	-
		+435	G	T	M145I	tolerated	benign	-	-	-	0.0028	-	-
	rs61757009	+460	T	G	S154A	tolerated	benign	0.0046	0.0109	0.0602	-	-	-
		+475	A	G	I159V	tolerated	benign	-	0.0004	-	-	-	-
	rs56233953	+497	G	A	R166K	tolerated	benign	0.0048	0.0010	0.0783	-	-	-
	rs3730287	+739	G	A	G247R	tolerated	benign	-	-	-	-	0.0009	-
		+746	C	A	A249D	tolerated	benign	-	-	-	0.0027	-	-
	rs61731555	+1123	G	T	V375L	tolerated	benign	-	-	-	0.0017	0.0017	1.0000
		+1124	T	G	V375G	tolerated	benign	0.0016	-	-	-	-	-
ADRB2	rs33973603	+44	A	G	N15S	tolerated	benign	-	-	-	0.0041	-	-
		+1108	C	A	Q370K	tolerated	benign	0.0008	0.0005	0.5573	-	-	-
HSPB7		+151	G	A	D51N	tolerated	benign	-	-	-	0.0085	0.0027	0.2251
		+478	G	A	V160I	tolerated	benign	-	-	-	-	0.0012	-
COMBINED								0.0124	0.0128	1	0.0198	0.0075	0.0575

Rare Non-synonymous SNPs that have predicted functional significance								Caucasian			African American		
Gene	**dbSNP**	**Position**	**Major Allele**	**Minor Allele**	**Codon**	**SIFT**	**PolyPhen**	**Control**	**HF**	**p-value**	**Control**	**HF**	**p-value**
ADRA1A		+320	T	G	V107G	affect function	probably damaging	0.002	-	-	0.008	-	-
	rs61757010	+367	G	T	D123Y	affect function	probably damaging	-	0.001	-	-	-	-
		+581	A	C	Y194S	affect function	probably damaging	0.001	-	-	-	-	-
ADRB2		+328	A	C	T110P	affect function	probably damaging	0.001	-	-	-	-	-
		+328	A	C	T110P	affect function	probably damaging	0.001	-	-	-	-	-
		+379	A	G	I127V	affect function	possibly damaging	-	0.001	-	-	-	-
		+587	A	C	N196T	affect function	probably damaging	0.001	-	-	-	-	-
		+626	A	C	Y209S	affect function	probably damaging	-	-	-	-	0.001	0.472
		+847	A	C	T283P	affect function	probably damaging	0.001	-	-	-	-	-
		+1062	C	A	Y354-Stop	N/A	N/A	0.002	0.005	0.282	-	-	-
COMBINED								0.009	0.006	0.4078	0.008	0.001	0.0216

Non-synonymous SNPs that have a mixed result from SIFT/PolyPhen								Caucasian			African American		
Gene	**dbSNP**	**Position**	**Major allele**	**Minor allele**	**Codon**	**SIFT**	**PolyPhen**	**Control**	**HF**	**p-value**	**Control**	**HF**	**p-value**
ADRA1A		+404	C	T	P135L	tolerated	probably damaging	-	0.0005	-	-	-	-
		+679	T	C	S227P	tolerated	possibly damaging	-	0.0015	-	-	-	-
		+695	T	G	V232G	tolerated	probably damaging	0.0008	-	-	-	-	-
		+1172	C	T	T391M	affect function	benign	-	0.0005	-	-	-	-
HSPB7		+152	A	G	D51G	tolerated	possibly damaging	-	-	-	0.0115	0.0023	0.0156
		+485	A	C	Q162P	tolerated	possibly damaging	-	-	-	0.0089	0.0030	0.0690
COMBINED								0.0008	0.0026	0.4332	0.0204	0.0053	0.0103

Supplemental Table 7. Odds ratios of *HSPB7* SNPs in Caucasian heart failure.

Gene	dbSNP	Position	Type	Major Allele	Minor Allele	Codon	Odds ratio	95% CI	P-value
HSPB7	rs945416	57	Coding S	C	T	S19S	1.46	1.20 to 1.78	< 0.0001
	rs732286	99	Coding S	T	C	A33A	1.54	1.28 to 1.87	< 0.0001
	rs1763596	I1-133	intronic	G	A		1.51	1.24 to 1.83	< 0.0001
	rs1739844	I2+247	intronic	A	G		1.56	1.30 to 1.89	< 0.0001
	rs1763597	I2+272	intronic	G	A		1.53	1.26 to 1.86	< 0.0001
	rs1739843	I2+315	intronic	A	G		1.58	1.30 to 1.92	< 0.0001
	rs1739842	I2-594	intronic	A	C		1.62	1.33 to 1.96	< 0.0001
	rs1739841	I2-473	intronic	T	C		1.63	1.36 to 1.95	< 0.0001
	rs1763599	I2-348	intronic	G	A		1.50	1.21 to 1.86	0.0002
	rs761760	I2-165	intronic	T	C		1.48	1.22 to 1.79	0.0001
	rs761759	I2-96	intronic	T	A		1.67	1.37 to 2.03	< 0.0001
	rs1739840	351	Coding S	C	T	T117T	0.65	0.54 to 0.77	< 0.0001

The allele frequencies of twelve associated *HSPB7* SNPs (see Table 4) were used to estimate numbers of wild-type homozygous and SNP carriers under the assumptions of Hardy-Weinberg equilibrium. Odds ratios, 95% confidence intervals, and p-values from the z-statistic were calculated for all cases (primary and secondary cohorts combined, n=1974) versus all controls (n=936).

Supplemental Table 8 - PCR primer sequences and positions

Gene	Primer Sequence	Primer Position	Amplicon size
ADRA1A #1 R	TTT TGG TTT GAG GGA GAG ACT GGC G	I1+80	1434 bp
ADRA1A #1 F	CGG ACT GGG AGT CTG GGG TAA CAG A	-471	
ADRA1A #2 R	CCA ATT GGC TTG CTG GCT TTC AA	+1897	1070 bp
ADRA1A #2 F	TGT CTG GAT CTC GGC CAC CAT CTT A	I1-56	
ADRB2 F	ATT GGC CGA AAG TTC CCG TAC GTC	-293	2129 bp
ADRB2 R	AGC ACT CCA GTC AAG GGG TTT TGG A	+1836	
HSPB7 R	CAC ACC CTC TCC TGT CCA GCC CT	+613	2541 bp
HSPB7 F	GAA CCT GGG CTG AGA TGT CCT GGA G	-57	
PLN F	ACA AAT GAG ACG GTC ATG GTG TGC C	I1-274	2215 bp
PLN R	GGA AGA TGT TCT GAA ATG GTC AGA GG	+1818	

Primer sequences, given in 5' to 3' orientation. Primer position uses the same nomenclature and numbering as SNP identification. F = Forward primer; R = Reverse primer (*ADRA1A* and *HSPB7* are on the complementary strand).