

**SUPPLEMENTAL MATERIAL.**

**Evaluating pathogenicity of rare variants from dilated cardiomyopathy in the exome era**

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On behalf NHLBI GO Exome Sequencing Project

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**Supplemental methods.** The ESP2500 dataset is composed of individuals obtained from a number of large-scale NHLBI cohorts. It includes exome sequence data from individuals from the Women's Health Initiative, Framingham Heart Study, Jackson Heart Study, Multi-Ethnic Study of Atherosclerosis, Atherosclerosis Risk in Communities, Coronary Artery Risk Development in Young Adults, Cardiovascular Health Study, Genomic Research on Asthma in the African Diaspora, Lung Health Study, Pulmonary Arterial Hypertension population, Acute Lung Injury cohort, and the Cystic Fibrosis cohort. Subsets of samples were selected from these cohorts based on phenotypic criteria. Generally, individuals were selected as controls, or from extreme phenotypes. Extremes of lung phenotypes would include CF-Pseudomonas infection response, chronic obstructive pulmonary disease and pulmonary arterial hypertension. Other cardiovascular phenotypes include extremes of LDL levels, early onset stroke, and BMI/Type 2 diabetes status. Even though these samples were selected as extremes of specific phenotypes they are useful as controls for other unlinked phenotypes. Gender information was available for 2,422 of the total 2,439 individuals, of which 1,688, (69.7%) were female and 734, (30.3%) were male.

Exome sequencing was performed at the Broad Institute or the University of Washington. Single base variant data for these analyses are available on the ESP Exome Variant Server (EVS - [snp.gs.washington.edu/EVS/](http://snp.gs.washington.edu/EVS/)).

Legend supplemental table 1.

DCM variants reported in literature with genomic co-ordinates, hg19. Reference and variant nucleotides are reported on the positive strand for each position.

Legend supplemental table 2.

ESP dataset % sequence coverage >10x read depth for each DCM gene. \* RBM20 was not targeted for sequence capture in this ESP dataset. In fr del; in frame deletion. Genomic co-ordinates are hg19.

**Supplemental table 1.**

<b>Gene</b>	<b>Variant</b>	<b>Genomic co-ordinates</b>	<b>ref base (+)</b>	<b>variant base (+)</b>
ABCC9	Leu1524fs	chr12:21958186-21958188	TAA	ATTT
ABCC9	Ala1513Thr	chr12:21958221-21958221	C	T
ACTC1	Glu361Gly	chr15:35082659-35082659	T	C
ACTC1	Arg314His	chr15:35083364-35083364	C	T
ACTN2	Gln9Arg	chr1:236849999-236849999	A	G
ANKRD1	Ala276Val	chr10:92675321-92675321	C	T
ANKRD1	Leu199Arg	chr10:92675983-92675983	A	C
ANKRD1	Thr116Met	chr10:92678728-92678728	G	A
ANKRD1	Arg66Gln	chr10:92679936-92679936	C	T
ANKRD1	Glu57Gln	chr10:92679964-92679964	C	G
BAG3	Arg71Trp	chr10:121429393-121429393	C	T
BAG3	Arg90stop	chr10:121429450-121429450	C	T
BAG3	His109Arg	chr10:121429508-121429508	A	G
BAG3	Arg123stop	chr10:121429549-121429549	C	T
BAG3	Arg218GlyfsX89	chr10:121431911-121431911	C	-
BAG3	Gln251ArgfsX56	chr10:121432011-121432011	A	-
BAG3	Ala262Thr	chr10:121432043-121432043	G	A
BAG3	Arg309X	chr10:121435991-121435991	C	T
BAG3	Ser385GlnfsX56	chr10:121436219-121436226	TCTCCCC	-
BAG3	Arg395fs48	chr10:121436248-121436249	GA	-
BAG3	Glu455Lys	chr10:121436429-121436429	G	A
BAG3	Val468Met	chr10:121436468-121436468	G	A
BAG3	Arg477His	chr10:121436496-121436496	G	A
CRYAB	Arg157His	chr11:111779546-111779546	C	T
CSRP3	Lys69Arg	chr11:19209758-19209758	T	C
CSRP3	Trp4Arg	chr11:19213986-19213986	A	G
CSRP3	Gly72Arg	chr11:19209750-19209750	C	T
DES	Glu108Lys	chr2:220283506-220283506	G	A
DES	Ser298Leu	chr2:220285374-220285374	C	T
DES	Asp312Asn	chr2:220285586-220285586	G	A
DES	Arg350Trp	chr2:220286086-220286086	C	T
DES	Ile451Met	chr2:220290449-220290449	C	G
DES	Val459Ile	chr2:220290469-220290469	G	A
ILK	Ala262Val	chr11:6630799-6630799	C	T
LAMA4	Pro943Leu	chr6:112462089-112462089	G	A
LDB3	Ser196Leu	chr10:88441437-88441437	C	T
LDB3	Thr213Ile	chr10:88441488-88441488	C	T
LDB3	Asp117Asn	chr10:88446830-88446830	G	A

LDB3	Lys136Met	chr10:88446888-88446888	A	T
LDB3	Lys204Arg	chr10:88451715-88451715	A	G
LDB3	Ile352Met	chr10:88466426-88466426	C	G
LDB3	Ala698Thr	chr10:88486007-88486007	G	A
LMNA	28insA	chr1:156084737-156084738	AC	AAC
LMNA	Ser22Leu	chr1:156084774-156084774	C	T
LMNA	Arg60Gly	chr1:156084887-156084887	C	G
LMNA	Leu85Arg	chr1:156084963-156084963	T	G
LMNA	Arg89Leu	chr1:156084975-156084975	G	T
LMNA	Lys97Glu	chr1:156084998-156084998	A	G
LMNA	Arg101Pro	chr1:156085011-156085011	G	C
LMNA	Glu111X	chr1:156085040-156085040	G	T
LMNA	splice site 357-1G>T	chr1:156100407-156100407	G	T
LMNA	Ala132Pro	chr1:156100445-156100445	G	C
LMNA	Ser143Pro	chr1:156100478-156100478	T	C
LMNA	Glu161Lys	chr1:156100532-156100532	G	A
LMNA	Arg166Pro	chr1:156100548-156100548	G	C
LMNA	Arg190Trp	chr1:156104248-156104248	C	T
LMNA	Arg190Gln	chr1:156104249-156104249	G	A
LMNA	Asp192Gly	chr1:156104255-156104255	A	G
LMNA	Asn195Lys	chr1:156104265-156104265	C	G
LMNA	Glu203Lys	chr1:156104287-156104287	G	A
LMNA	Glu203Gly	chr1:156104288-156104288	A	G
LMNA	Ile210Ser	chr1:156104309-156104309	T	G
LMNA	Leu215Pro	chr1:156104600-156104600	T	C
LMNA	Arg225X	chr1:156104629-156104629	C	T
LMNA	Gln234X	chr1:156104656-156104656	C	T
LMNA	delCT	chr1:156105075-156105076	CT	-
LMNA	Glu317Lys	chr1:156105704-156105704	G	A
LMNA	Ala318Thr	chr1:156105707-156105707	G	A
LMNA	frameshift	chr1:156105714-156105714	T	-
LMNA	Gln355Stop	chr1:156105818-156105818	C	T
LMNA	delT	chr1:156105840-156105840	T	-
LMNA	Glu372ArgfsX107	chr1:156105869-156105869	G	-
LMNA	Arg377His	chr1:156105885-156105885	G	A
LMNA	Arg388His	chr1:156106010-156106010	G	A
LMNA	Arg399Cys	chr1:156106042-156106042	C	T
LMNA	Ser437HisfsX1	chr1:156106154-156106155	CT	CGCACT
LMNA	Arg471His	chr1:156106743-156106743	G	A
LMNA	Gly474-Asp475insGlu	chr1:156106755-156106756	AT	AAGAT
LMNA	Tyr481Stop	chr1:156106774-156106774	C	G
LMNA	delG	chr1:156106908-156106908	G	-
LMNA	insCTGC	chr1:156106994-156106995	CG	CCTGCG

LMNA	Arg541Ser	chr1:156107457-156107457	C	A
LMNA	Arg571Ser	chr1:156107547-156107547	C	A
LMNA	Ser573Leu	chr1:156108298-156108298	C	T
LMNA	Arg654X	chr1:156108540-156108540	C	T
MYBPC3	Asn948Thr	chr11:47356655-47356655	T	G
MYBPC3	Glu619Lys	chr11:47362731-47362731	C	T
MYBPC3	Thr494Ile	chr11:47364272-47364272	G	A
MYBPC3	Arg326Gln	chr11:47367871-47367871	C	T
MYBPC3	Cys1264Phe	chr11:47353646-47353646	C	A
MYBPC3	Gly1260Asp	chr11:47353658-47353658	C	T
MYBPC3	Splice site 31+1	chr11:47354364-47354364	C	A
MYBPC3	Splice site 29+1	chr11:47355107-47355107	C	T
MYBPC3	Pro910Thr	chr11:47357437-47357437	G	T
MYBPC3	Ala833Thr	chr11:47359047-47359047	C	T
MYBPC3	Asp605Gly	chr11:47362772-47362772	T	C
MYBPC3	Met555Thr	chr11:47363668-47363668	A	G
MYBPC3	Gly490Arg	chr11:47364285-47364285	C	T
MYBPC3	Arg272Cys	chr11:47369415-47369415	G	A
MYBPC3	Lys202Gln	chr11:47371375-47371375	T	G
MYBPC3	Gly5Arg	chr11:47374186-47374186	C	G
MYH6	Glu1457Lys	chr14:23857123-23857123	C	T
MYH6	Ala1004Ser	chr14:23862646-23862646	C	A
MYH6	Pro830Leu	chr14:23863473-23863473	G	A
MYH6	Gly1826Asn	chr14:23853739-23853739	C	T
MYH6	Arg1502Gln	chr14:23856987-23856987	C	T
MYH6	Ala1440Pro	chr14:23857405-23857405	C	G
MYH6	Arg1177Trp	chr14:23859469-23859469	T	C
MYH6	Arg568Cys	chr14:23868126-23868126	G	A
MYH6	Ile275Asn	chr14:23872631-23872631	A	T
MYH7	Arg1832Cys	chr14:23884269-23884269	G	A
MYH7	Arg1634Cys	chr14:23885266-23885266	G	A
MYH7	Glu1426Lys	chr14:23886789-23886789	C	T
MYH7	Arg1193Ser	chr14:23889203-23889203	G	T
MYH7	Leu1038Pro	chr14:23892756-23892756	A	G
MYH7	Thr1019Asn	chr14:23892799-23892799	G	T
MYH7	Phe764Leu	chr14:23894622-23894622	G	C
MYH7	Ser642Leu	chr14:23896480-23896480	G	A
MYH7	Lys637Glu	chr14:23896496-23896496	T	C
MYH7	Ala550Val	chr14:23897033-23897033	G	A
MYH7	Ser532Pro	chr14:23897088-23897088	A	G
MYH7	Arg442His	chr14:23898246-23898246	C	T
MYH7	Thr412Asn	chr14:23898460-23898460	G	T
MYH7	Ala223Thr	chr14:23900859-23900859	C	T

MYH7	Ile201Thr	chr14:23901007-23901007	A	G
MYH7	His1901Gln	chr14:23883054-23883054	G	C
MYH7	Arg1863Gln	chr14:23883282-23883282	A	G
MYH7	Gly1808Ala	chr14:23884339-23884339	C	G
MYH7	Val1691Met	chr14:23884923-23884923	C	T
MYH7	Glu1619Lys	chr14:23885310-23885310	C	T
MYH7	Arg1500Trp	chr14:23886383-23886383	G	A
MYH7	Arg1359Cys	chr14:23887512-23887512	G	A
MYH7	Asp1096Tyr	chr14:23890217-23890217	C	A
MYH7	Arg1045Cys	chr14:23891501-23891501	G	A
MYH7	Ala970Val	chr14:23893129-23893129	G	A
MYH7	Val964Leu	chr14:23893148-23893148	C	G
MYH7	Arg237Trp	chr14:23900817-23900817	G	A
MYPN	Ile83fsX105	chr10:69881443-69881443	T	-
MYPN	Arg1088His	chr10:69957213-69957213	G	A
MYPN	Pro1112Leu	chr10:69959174-69959174	C	T
MYPN	Val1195Met	chr10:69961675-69961675	G	A
PLN	Arg9Cys	chr6:118880109-118880109	C	T
PLN	Arg14del	chr6:118880124-118880126	AGA	-
PLN	L39stop	chr6:118880200-118880200	T	G
PSEN1	Asp333Gly	chr14:73678519-73678519	A	G
PSEN2	Ser130Leu	chr1:227073271-227073271	C	T
SCN5A	Asp1595His	chr3:38595800-38595800	C	G
SCN5A	Asp1275Asn	chr3:38607917-38607917	C	T
SCN5A	insTG	chr3:38627417-38627418	TT	TCAT
SCN5A	Arg814Trp	chr3:38627529-38627529	G	A
SCN5A	Thr220Ile	chr3:38655278-38655278	G	A
SCN5A	Pro2005Ala	chr3:38591847-38591847	G	C
SCN5A	Ile1835Thr	chr3:38592356-38592356	A	G
SCN5A	Pro648Leu	chr3:38640489-38640489	G	A
SCN5A	Arg222Gln	chr3:38655272-38655272	C	T
SCN5A	Ser216Leu	chr3:38655290-38655290	G	A
SGCD	Arg71Thr	chr5:155935630-155935630	G	C
SGCD	Lys238 del	chr5:156184728-156184730	AAG	-
TCAP	Glu132Gln	chr17:37822252-37822252	G	C
TCAP	Arg18Gln	chr17:37821665-37821665	G	C
TCAP	Glu49Lys	chr17:37822003-37822003	G	A
TMPO	Arg690Cys	chr12:98928103-98928103	C	T
TNNC1	Gly159Asp	chr3:52485301-52485301	C	T
TNNC1	Ile148Val	chr3:52485419-52485419	T	C
TNNC1	Asp145Glu	chr3:52485426-52485426	G	T
TNNC1	Met103Ile	chr3:52485768-52485768	C	T
TNNC1	Tyr5His	chr3:52488019-52488019	A	G

TNNI3	Asn185Lys	chr19:55663280-55663280	G	C
TNNI3	Lys36Gln	chr19:55668420-55668420	T	G
TNNI3	Ala2Val	chr19:55668953-55668953	G	A
TNNI3	Asp180Gly	chr19:55665408-55665408	T	C
TNNT2	Asp270Asn	chr1:201328764-201328764	C	T
TNNT2	Lys247Arg	chr1:201330447-201330447	T	C
TNNT2	Lys210del	chr1:201331099-201331101	CTC	-
TNNT2	Arg205Leu	chr1:201331116-201331116	C	A
TNNT2	Ala172Ser	chr1:201332480-201332480	C	A
TNNT2	Arg141Trp	chr1:201333464-201333464	G	A
TNNT2	Arg131Trp	chr1:201333494-201333494	G	A
TNNT2	Glu244Asp	chr1:201330455-201330455	C	A
TNNT2	Arg205Trp	chr1:201331117-201331117	G	A
TNNT2	Arg159Gln	chr1:201332518-201332518	C	T
TNNT2	Arg151Cys	chr1:201333434-201333434	G	A
TNNT2	Arg134Gly	chr1:201333485-201333485	G	C
TPM1	Glu40Lys	chr15:63336229-63336229	G	A
TPM1	Glu54Lys	chr15:63336271-63336271	G	A
TPM1	Asp230Asn	chr15:63354462-63354462	G	A
TPM1	Lys15Asn	chr15:63335073-63335073	G	T
TPM1	Glu23Gln	chr15:63335095-63335095	G	C
TPM1	Ser16Ile	chr15:63340821-63340821	G	T
TPM1	Ile92Thr	chr15:63349218-63349218	T	C
TPM1	Ala239Thr	chr15:63354787-63354787	G	A
TPM1	Ala277Val	chr15:63356320-63356320	C	T
TTN	Glu20963LysfsX10	chr2:179417542-179417542	C	-
TTN	Trp930Arg	chr2:179647707-179647707	A	G
VCL	Ala934Val	chr10:75871722-75871722	C	T
VCL	Leu954del	chr10:75871783-75871785	GTT	-
VCL	Arg975Trp	chr10:75871844-75871844	C	T



Supplemental table 2.

Gene	Chr	Start	Stop	Targets(bp)	Coverage(bp)	Coverage%
<i>ABCC9</i>	12	21950323	22089628	8698	8905	100
<i>ACTC1</i>	15	35080297	35087927	1753	1751	99.89
<i>ACTN2</i>	1	236849770	236927558	4878	4877	99.98
<i>ANKRD1</i>	10	92671857	92681032	1947	1946	99.95
<i>BAG3</i>	10	121410882	121437331	2140	2132	99.63
<i>CRYAB</i>	11	111779350	111782473	562	808	100
<i>CSRP3</i>	11	19203578	19223589	1108	1108	100
<i>DES</i>	2	220283099	220291461	2413	2343	97.1
<i>ILK</i>	11	6625207	6632101	2560	2561	100
<i>LAMA4</i>	6	112429134	112575828	11122	10066	90.51
<i>LDB3</i>	10	88428426	88495825	4012	4168	100
<i>LMNA</i>	1	156084461	156109878	3828	3782	98.8
<i>MYBPC3</i>	11	47352957	47374253	7206	7128	98.92
<i>MYH6</i>	14	23851199	23877482	9739	9887	100
<i>MYH7</i>	14	23881947	23904870	10095	10095	100
<i>MYPN</i>	10	69869250	69971774	6024	6019	99.92
<i>PLN</i>	6	118869442	118881587	263	263	100
<i>PSEN1</i>	14	73603143	73690399	2451	2448	99.88
<i>PSEN2</i>	1	227058273	227083804	2573	2573	100
<i>RBM20*</i>	10	112394203	112589217			
<i>SCN5A</i>	3	38589553	38691163	9003	8987	99.82
<i>SGCD</i>	5	155753767	156194799	1751	1742	99.49
<i>TCAP</i>	17	37821599	37822807	498	671	100
<i>TMPO</i>	12	98909409	98942735	3900	3811	97.72
<i>TNNC1</i>	3	52485107	52488057	1063	1156	100
<i>TNNI3</i>	19	55663135	55669100	1453	1433	98.62
<i>TNNT2</i>	1	201328142	201346805	3177	2979	93.77
<i>TPM1</i>	15	63334838	63364114	2937	2903	98.84
<i>TTN</i>	2	179390716	179672150	147177	146906	99.82
<i>VCL</i>	10	75757872	75879918	5693	5684	99.84