SUPPLEMENTAL MATERIAL

Burden Of Potentially Pathologic Copy Number Variants Is Higher In Children With Isolated Congenital Heart Disease And Significantly Impairs Covariate-Adjusted Transplant-Free Survival

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Supplemental Table S1. qPCR validation of 38 CNVs identified in 38 unique CHD participants with available DNA.

Group	CNV Region	Size	CNV Type	Validate
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr7:4102511-4867717	765,206	Duplication, 1 copy	1
CHD	chr18:13417800-15112502	1,694,702	Duplication, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr15:20306549-20685685	379,136	Deletion, 1 copy	1
CHD	chr22:21122400-21554058	431,658	Deletion, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr15:20306549-20685685	379,136	Deletion, 1 copy	1
CHD	chr22:21011312-21554058	542,746	Deletion, 1 copy	1
CHD	chr7:143056311-143505123	448,812	Duplication, 1 copy	1
CHD	chr16:15032942-16197033	1,164,091	Duplication, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr15:20306549-20685685	379,136	Deletion, 1 copy	1
CHD	chr15:20306549-20685685	379,136	Deletion, 1 copy	1
CHD	chr10:133136594-133608348	471,754	Duplication, 1 copy	1
CHD	chr10:46410734-47173619	762,885	Duplication, 1 copy	1
CHD	chr22:17257787-19726528	2,468,741	Deletion, 1 copy	1
CHD	chr22:21024486-21441861	417,375	Deletion, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr3:95067163-95989113	921,950	Duplication, 1 copy	1
CHD	chr10:2682656-3123648	440,992	Duplication, 1 copy	1
CHD	chr1:239320770-240023059	702,289	Duplication, 1 copy	1
CHD	chr12:33415349-34669982	1,254,633	Duplication, 1 copy	1
CHD	chr22:21024486-21554058	529,572	Deletion, 1 copy	1
CHD	chr13:102725899-103348161	622,262	Duplication, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr22:17257787-19790220	2,532,433	Deletion, 1 copy	1
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	1
CHD	chr15:20306549-20778963	472,414	Deletion, 1 copy	1
CHD	chr22:20885078-21401228	516,150	Deletion, 1 copy	1
CHD	chr22:17257787-18686993	1,429,206	Deletion, 1 copy	1
CHD	chr8:11620338-11935618	315,280	Duplication, 1 copy	0
CHD	chr2:111303487-111617069	313,582	Duplication, 1 copy	0
CHD	chr9:194201-589666	395,465	Duplication, 1 copy	NA*

CHD	chr22:21100917-21554058	453,141	Deletion, 1 copy	-
CHD	chr15:20306549-20685685	379,136	Deletion, 1 copy	-
CHD	chr6:65228140-66383666	1,155,526	Deletion, 1 copy	-
CHD	chr16:15032942-16197033	1,164,091	Deletion, 1 copy	-
CHD	chr7:158059922-158621330	561,408	Duplication, 1 copy	-
CHD	chr7:57212608-57593745	381,137	Duplication, 1 copy	-
CHD	chr16:21892987-22331199	438,212	Duplication, 1 copy	-
CHD	chr15:20306549-20685685	379,136	Deletion, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	-
CHD	chr15:20306549-20685684	329,335	Deletion, 1 copy	-
CHD	chr22:17257787-19729278	2,471,491	Deletion, 1 copy	-
CHD	chr22:21024486-21554058	529,572	Deletion, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	-
CHD	chr22:20784580-21330892	546,312	Deletion, 1 copy	-
CHD	chr22:21100917-21554058	453,141	Deletion, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Duplication, 1 copy	-
CHD	chr1:244544759-244871447	326,688	Duplication, 1 copy	-
CHD	chr3:11622173-11958591	336,418	Duplication, 1 copy	-
CHD	chr22:21328337-21979242	650,905	Deletion, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	-
CHD	chr22:21046568-21401228	354,660	Deletion, 1 copy	-
CHD	chr6:162521711-162900893	379,182	Duplication, 1 copy	-
CHD	chr12:24803300-25155526	352,226	Duplication, 1 copy	-
CHD	chr15:20306549-20685684	329,335	Duplication, 1 copy	-
CHD	chr22:21328337-21979242	650,905	Deletion, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Duplication, 1 copy	-
CHD	chr22:19066315-19792353	726,038	Duplication, 1 copy	-
CHD	chr3:1394026-1975594	581,568	Duplication, 1 copy	-
CHD	chr12:33415349-34565140	1,149,791	Duplication, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	-
CHD	chr9:4117491-4537288	419,797	Duplication, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	-
CHD	chr3:832325-1403635	571,310	Duplication, 1 copy	-
CHD	chr22:17257787-19792353	2,534,566	Deletion, 1 copy	-
CHD	chr9:36587-360439	323,852	Deletion, 1 copy	-
CHD	chr3:133579573-133940085	360,512	Deletion, 1 copy	-
Control	chr22:19420148-19792353	372,205	Duplication, 1 copy	-
Control	chr18:1070791-1767013	696,222	Duplication, 1 copy	-
Control	chr4:117695261-118972510	1,277,249	Deletion, 1 copy	-

Control	chr3:2721456-3035501	314,045	Duplication, 1 copy	-
Control	chr6:93770526-94218919	448,393	Duplication, 1 copy	-
Control	chr8:13592327-14702986	1,110,659	Duplication, 2 copies	-
Control	chr4:189370201-189766567	396,366	Deletion, 1 copy	-
Control	chr21:46289633-46909417	619,784	Duplication, 1 copy	-
Control	chr21:46192812-46909417	716,605	Duplication, 1 copy	-
Control	chr21:46391256-46909417	518,161	Duplication, 1 copy	-
Control	chr3:832325-1403635	571,310	Duplication, 1 copy	-
Control	chr15:20314760-20635884	321,124	Duplication, 1 copy	-
Control	chr21:46086792-46909417	822,625	Duplication, 1 copy	-
Control	chr1:246136535-246563486	426,951	Duplication, 1 copy	-
Control	chr7:71532565-71921501	388,936	Deletion, 1 copy	-
Control	chr15:20321135-20778963	457,828	Deletion, 1 copy	-
Control	chr19:47975960-48387680	411,720	Duplication, 1 copy	-
Control	chr15:20314760-20635884	321,124	Duplication, 1 copy	-
Control	chr2:78591176-79811160	1,219,984	Deletion, 1 copy	-
Control	chr3:540961-1325458	784,497	Duplication, 1 copy	-
Control	chr21:46449972-46909417	459,445	Duplication, 1 copy	-
Control	chr3:832325-1415351	583,026	Duplication, 1 copy	-
Control	chr12:1142624-1461019	318,395	Duplication, 1 copy	-
Control	chr15:29807358-30302218	494,860	Duplication, 1 copy	-
Control	chr21:20828763-21672012	843,249	Duplication, 1 copy	-
Total CNVs qPCR validated: 35/37 (94.6%) (Excluding 1 Sample Failure)*				

Positions based on hg18 genome build.

*Sample failure did not amplify tested CNV regions or control CNV regions, indicating poor DNA quality; denoted by “NA”.

Supplemental Table S2. Primer design for qPCR validation of CNVs in the CHD cohort.

Please see the Microsoft Excel Worksheet separately included with the online materials.

Supplemental Table S3. Sensitivity analyses from Cox proportional hazards regression by diagnostic class for the outcome of covariate-adjusted transplant-free survival.

	Total N	N Events	CNV Burden Hazard Ratio (HR)	P-Value
Diagnostic Class 1	204	9	16.54 (1.71-159.80)	0.015
Diagnostic Class 2	41	2	60.47 (0.15-2.45x10^{9})	0.646
Diagnostic Class 3	46	5	6.64 (0.51-86.33)	0.148
Diagnostic Class 4	131	31	2.47 (9.67-6.31)	0.059

Cox proportional hazards regression analyses reported adjusted for all variables reported in the "Statistical Analyses" section of the Methods with the exception of Diagnostic Class (which was singular in each sensitivity analysis).

Number of Subjects	Targeted Region(s)	Amplicon Position (hg18)	Amplicon Sequence	UPL Probe	Left Primer Sequence	Rig
1	chr1:239320770-240023059	chr1:239824508-239824631	tcacaatgggtctgatctgcatttcacttccagctgctggtaggtctttagcaggcctctggcacctcagcagtcggaggcacagaagctgcaaaagggatcttcgaaactgggcagagaaaaa	11	tcacaatgggtctgatctgc	tttt
1	chr2:111303487-111617069	chr2:111461205-111461304	aaccactctttggcctgctccaaaactgggctgaatctgtgggggacaagctgagaaccaggtacgtattactcaggccatcatcatctgccttcagtgg	26	aaccactctttggcctgct	cca
1	chr3:95067163-95989113	chr3:95285939-95285998	gctcctggagggaaatcaatagctctgctgcagtgtgcttgtccaggtagtgtgctttcc	84	gctcctggagggaaatcaat	gga
1	chr7:4102511-4867717	chr7:4214233-4214299	ccaacctcttgctgttcctaacagatttactactgggaggcagacagccagaacgaaacggagaaaa	16	ccaacctcttgctgttcctaa	tttt
1	chr7:143056311-143505123	chr7:143297051-143297125	caaacttctctgcttcactcttgtgtcccagcagtcagagggaaccctttaaaatataactcagctttgggaggc	3	caaacttctctgcttcactcttgt	gcc
1	chr8:11620338-11935618	chr8:11748292-11748409	cgacaggggatggaaagagggcctgctccgggcattggccaacaccagcaggcagcagagggaggcccagagctgccacatgttggaagccggatcctagatccacctggagaggaca	27	cgacaggggatggaaagag	tgt
1	chr9:194201-589666	chr9:460625-460697	caagaaagcaccgccactccagtgggaacggacacgcgtgcacacagccacgagtgaggtttgaaagaggccc	76	caagaaagcaccgccact	ggg
1	chr10:2682656-3123648	chr10:2822646-2822705	cccgctcctctgatttactgtgaatcctggctgtgtgcagatgatggctgagagcaaagg	76	cccgctcctctgatttactg	cct
1	chr10:46410734-47173619	chr10:47128596-47128719	ggtaccatggacctgactggagaatatttcaccgcctggccctgggctccaggagagcccaccaccaccatggcccaggatggaggcagcactggcgccaggggcaagcaggtcacagatgcca	58	ggtaccatggacctgactgg	tgg
1	chr10:133136594-133608348	chr10:133261877-133261938	cttggtaaccgccagacgggatcccatccagccattcagctgccatcctgggaaagggagac	42	cttggtaaccgccagacg	gtc
1	chr12:33415349-34669982	chr12:33644954-33645013	aatccccaggacggtgtttgtacttggggagcagccttagtagcagcaagccactgagtg	32	aatccccaggacggtgtt	cac
1	chr13:102725899-103348161	chr13:102965076-102965136	tcacctatccctggtgcattaggcttttaaactctgccttcaggttgattgggaattgcat	13	tcacctatccctggtgcatt	atg
5	chr15:20306549-20685685	chr15:20415639-20415748	acttgcaagctatgaggaatttttcttaatggaaggaggagataccatgtatgacttctacacgtcaatttttgataaaataagagaaaaggaaacatggcagaatgtg	12	acttgcaagctatgaggaattttt	cac
1	chr16:15032942-16197033	chr16:16045782-16045846	aacggcttcacctccttgtgttccaggcagccggtgaaggttgtgtactcctccaaggatcctgc	27	aacggcttcacctccttgt	gca
1	chr18:13417800-15112502	chr18:13731942-13732020	caggcacagagatgaaccagctgtcatgagagtgatacctacttccagcttaattttattggtgtgactgttggtgatc	11	caggcacagagatgaaccag	gat
14	chr22:17257787-19792353, chr22:17257787-19726528, chr22:17257787-19790220, chr22:17257787-18686993	chr22:17729380-17729493	ttctcatcgctgtcactgctgctctccaggaggtctcggggcctcagctctttcacaaggttctgctcttttaacctgcacaaaaacattacatcacacttcccttcagaaacc	79	ttctcatcgctgtcactgct	ggt
5	chr22:20885078-21401228, chr22:21011312-21554058, chr22:21024486-21441861, chr22:21024486-21554058, chr22:21122400-21554058	chr22:21222566-21222627	cgagcacctctactggaatgaagggctgctctgcctctgtgctcaaaccatctacttttcgc	13	cgagcacctctactggaatga	gcg
	SNCA Control	chr4:90962489-90962560	gctgagaagaccaaagagcaagtgacaaatgttggaggagcagtggtgacgggtgtgacagcagtagcccag	68	gctgagaagaccaaagagcaa	ctg
	GAPDH Control	chr12:6515824-6515886	gctgcattcgccctcttaatggggaggtggcctagggctgctcacatattctggaggagcctc	10	gctgcattcgccctctta	gag