

Supplemental Table 1: Primers list for Quantitative reverse transcriptase polymerase chain reaction (qPCR)

	Forward	Reverse	Note
<i>acta1b</i>	atgtgtgacgacgaggagac	tgctctgagcctcatcacct	*
<i>actb2</i>	ggtatcgtgatggactctgg	tctcctgctcaaagtcaagg	
<i>hm:zewp0073</i>	tattggaaatgagcgtttccgt	cagcgatacctggatacata	
<i>actc1a</i>	gtggctctggactttgagaat	gatccttgccgatatcaatg	*
<i>actc1b</i>	atgtgtgacgacgaggagac	tgctctgagcctcatcacct	†
<i>actn2</i>	cttccatgtcagctggaaggatgg	gcagtttcagcctgctcagctc	†
<i>atp2a2a</i>	atcggtaaagatccgtgatga	cacggcgatctgaagtgt	
<i>cmlc1</i>	aaagtggaaccaagaaac	tcatcacatcctccactgg	*
<i>gapdh</i>	ccacctatggaaagtacaag	ctctcttgcaccacctta	† *
<i>myh6</i>	tgaagacctgagaaggcaac	cagttcctcggttctctgaa	
<i>myh7ba</i>	gcctgaacttctgacatgc	ctccctctgcttctgttga	
<i>myh7bb</i>	gaactcaagacatgctgct	ttgaactcatgttgccaaa	
<i>myhc4</i>	tctgctgggtactcttgagg	ccaacttttctcggctca	
<i>myl1</i>	aacccaaacaaggcaacata	gtgttgacgaaagcctcat	†
<i>myl6</i>	atgtctgacttcaggagga	actgctcaaagtccagcatc	*
<i>mylz3</i>	actgctgaccagattgagga	caggaaagcctcaaagtcaa	†
<i>nppa</i>	gatgtacaagcgcacacgtt	tctgatgcctcttctgttgc	
<i>nppb</i>	catgggtgttttaaagttctcc	cttcaatattgccgcctttac	
<i>pcna</i>	aggcaacatcaagctctcac	atttgacgtgtcccatgtct	†
<i>pln-like</i>	aaggtgcagcacatgacac	ccgtggaaagagattagcaa	
<i>ryr2b</i>	cgagacaaagctcaggatgt	ttcgtgagggactctttcag	
<i>slc8a1a</i>	agaggcgtattgctgaaatg	tttcttggccacactcttc	
<i>tcap</i>	gggaggaaaacccaaataagag	tggagaggacgcacctgcca	† *
<i>tnnc2</i>	actgacgcgcaacagga	ctgccgtctcatcgacct	†
<i>tnnt2c</i>	gaccgaacgtgagaagaaga	aggacttctgtgtgttttc	*
<i>tpm4b</i>	acaacacagctggaaaacgag	tctgaatttccattttctcc	*
<i>ttna</i>	aaaactggcagaaatgctc	gtcgactttctcgaggttca	† *
<i>ttnb</i>	tgggaaatgcctcttattga	gatgacttcgccagaacta	† *
<i>tuba1b</i>	gagaaggcttaccatgagca	gttgatgccaaccttgaaac	†
<i>vmhc</i>	tcagatggcagagttggag	gcttcctttacagttacagctttc	†
<i>vmhcl</i>	gcgatgctgaaatgtctgtt	cagtcacagtcttgcctcct	†

† : Primers used in Supplemental Fig. 2 A

* : Primers used in Supplemental Fig. 2 B

Supplemental Table 2: Number of reads obtained from RNA-seq results

Sample	Embryonic heart-1	Embryonic heart-2	Embryonic heart-3	Adult heart-1	Adult heart-2	Adult heart-3	Adult muscle-1	Adult muscle-2	Adult muscle-3
Total Reads	74,573,872	78,329,760	86,943,448	114,487,262	130,464,794	140,988,744	159,924,332	154,395,064	132,226,076
Used Reads	74,572,136	78,328,939	86,942,220	114,485,019	130,463,951	140,986,424	159,921,302	154,394,110	132,224,272
Mapped Reads	62,600,036 (83.9%)	66,055,471 (84.3%)	73,763,903 (84.8%)	86,641,679 (75.7%)	98,868,892 (75.8%)	106,460,002 (75.5%)	140,647,303 (87.9%)	135,522,271 (87.8%)	116,239,320 (87.9%)
Mapped with Exons	52,833,743 (70.8%)	55,628,362 (71.0%)	61,581,273 (70.8%)	69,940,033 (61.1%)	81,883,617 (62.8%)	86,205,245 (61.1%)	107,495,382 (67.2%)	102,397,109 (66.3%)	88,805,249 (67.2%)
Mapped with Exon-Exon Junction	9,776,293 (13.1%)	10,427,109 (13.3%)	12,182,630 (14.0%)	16,701,646 (14.6%)	16,985,275 (13.0%)	120,254,757 (14.4%)	33,151,921 (20.7%)	33,125,162 (21.5%)	27,434,071 (20.7%)
Gene Count	40,950,818 (54.9%)	43,100,154 (55.0%)	49,459,154 (56.9%)	67,682,848 (59.1%)	70,432,766 (54.0%)	82,397,776 (58.4%)	119,792,094 (74.9%)	116,758,278 (75.6%)	98,720,406 (74.7%)

Supplemental Table 3. KEGG Pathway Analysis of Upregulated and Downregulated Pathways in Zebrafish Embryonic Heart

KEGG Pathway Term	Gene Count	<i>P</i> value*
Upregulated		
Cell cycle	60	7.50e-17
DNA replication	30	5.80e-17
Homologous recombination	18	1.10e-06
Mismatch repair	16	1.40e-06
Pyrimidine metabolism	36	1.20e-06
Nucleotide excision repair	21	1.90e-05
ECM-receptor interaction	30	6.10e-05
Purine metabolism	44	1.20e-04
Basal cell carcinoma	21	7.50e-04
Base excision repair	16	6.90e-04
Pathways in cancer	74	7.20e-04
p53 Signaling pathway	23	1.80e-03
Spliceosome	35	1.80e-03
TGF-beta signaling pathway	26	4.50e-03
Hedgehog signaling pathway	19	6.40e-03
Small cell lung cancer	24	1.40e-02
Bladder cancer	14	4.60e-02
Downregulated		
Glycolysis/gluconeogenesis	34	1.20e-11
Pyruvate metabolism	20	2.90e-05
Fatty acid metabolism	19	1.10e-04
Propanoate metabolism	16	3.20e-04

Supplemental Table 3 (continued)

KEGG Pathway Term	Gene Count	<i>P</i> value*
Insulin signaling pathway	39	3.50e-04
ABC transporters	18	1.20e-03
Fructose and mannose metabolism	14	9.50e-03
Calcium signaling pathway	42	1.00e-02
Drug metabolism	20	1.00e-02
Hypertrophic cardiomyopathy	24	1.80e-02
Vascular smooth muscle contraction	29	1.90e-02
Dilated cardiomyopathy	25	2.00e-02
Cardiac muscle contraction	22	2.40e-02
Valine, leucine, and isoleucine degradation	15	2.40e-02
Citrate cycle (TCA cycle)	12	2.50e-02
Renal cell carcinoma	20	2.90e-02
Arginine and proline metabolism	16	4.80e-02

Abbreviations: ECM, extracellular matrix; KEGG, Kyoto Encyclopedia of Genes and Genomes; TGF, transforming growth factor.

* A modified Fisher Exact *P* Value. Usually *P* Value is equal or smaller than 0.05 to be considered strongly enriched in the annotation categories.

Supplemental Table 4: List of downregulated genes in calcium signaling pathway in embryonic heart

Ensembl Gene ID	Gene Name	Fold change	P value
ENSDARG00000069419	<i>adcy9</i> adenylate cyclase 9	-2.01	1.50E-03
ENSDARG00000058488	<i>adora2ab</i> adenosine A2a receptor	-2.60	3.92E-04
ENSDARG00000041173	<i>adra1bb</i> adrenergic, alpha-1B-, receptor	-10.75	9.65E-03
ENSDARG00000054510	<i>adrb2b</i> adrenergic, beta-2-, receptor, surface	-18.46	8.77E-04
ENSDARG00000029439	<i>atp2a2a</i> ATPase, Ca ⁺⁺ transporting, cardiac muscle, slow twitch 2	-3.57	1.87E-10
ENSDARG00000012684	<i>atp2b1b</i> ATPase, Ca ⁺⁺ transporting, plasma membrane 1	-3.22	2.53E-03
ENSDARG00000077083	<i>AVPR1A</i> arginine vasopressin receptor 1A	-3.04	1.24E-07
ENSDARG00000037619	<i>BX569798.1</i> GNAS complex locus	-5.23	8.03E-06
ENSDARG00000006923	<i>cacna1ab</i> calcium channel, voltage-dependent, P/Q type, alpha 1A subunit	-19.04	4.72E-35
ENSDARG00000008398	<i>cacna1c</i> calcium channel, voltage-dependent, L type, alpha 1C subunit	-2.92	1.46E-07
ENSDARG000000089913	<i>cacna1g</i> calcium channel, voltage-dependent, T type, alpha 1G subunit	-3.29	2.48E-09
ENSDARG00000015050	<i>calm2a</i> calmodulin 2a (phosphorylase kinase, delta)	-2.47	7.80E-06
ENSDARG00000014273	<i>camk2d2</i> calcium/calmodulin-dependent protein kinase II delta	-9.08	4.04E-26
ENSDARG00000055577	<i>chrm2a</i> cholinergic receptor, muscarinic 2	-2.09	6.32E-03
ENSDARG00000062262	<i>ednrab</i> endothelin receptor type Ab	-7.25	4.47E-22
ENSDARG00000089334	<i>ednrb1a</i> endothelin receptor B1a	-3.16	7.77E-03
ENSDARG00000086207	<i>grin2da</i> glutamate receptor, ionotropic, N-methyl D-aspartate 2D	-5.97	3.04E-11
ENSDARG000000052425	<i>hrh1</i> histamine receptor H1	-10.38	1.12E-03
ENSDARG00000016095	<i>htr6</i> 5-hydroxytryptamine (serotonin) receptor 6	-3.60	3.37E-03
ENSDARG00000074149	<i>ITPR1</i> inositol 1,4,5-triphosphate receptor, type 1	-4.48	1.73E-10
ENSDARG00000026081	<i>lhcg</i> luteinizing hormone/choriogonadotropin receptor	-335.67	2.45E-26
ENSDARG00000031698	<i>mylk2</i> myosin light chain kinase 2	-4.18	3.94E-06
ENSDARG00000076348	<i>mylk3</i> myosin light chain kinase 3	-5.33	9.61E-03
ENSDARG00000026925	<i>nos2a</i> nitric oxide synthase 2, inducible	-4.13	4.22E-11
ENSDARG00000044175	<i>oxtrl</i> oxytocin receptor like	-4.20	2.74E-03
ENSDARG00000004455	<i>p2rx5</i> purinergic receptor P2X, ligand-gated ion channel, 5	-3.77	9.39E-05
ENSDARG000000060875	<i>PDE1A</i> phosphodiesterase 1A, calmodulin-dependent	-9.37	3.71E-27
ENSDARG000000067683	<i>PDE1C</i> phosphodiesterase 1C, calmodulin-dependent 70kDa	-70.97	3.82E-10
ENSDARG00000030604	<i>phkg1a</i> phosphorylase kinase, gamma 1a (muscle)	-2.49	2.41E-05
ENSDARG00000069498	<i>phkg1b</i> phosphorylase kinase, gamma 1b (muscle)	-3.71	1.63E-10
ENSDARG00000090381	<i>PLCB2</i> phospholipase C, beta 2	-4.79	5.59E-08
ENSDARG00000068763	<i>plcg2</i> phospholipase C, gamma 2 (phosphatidylinositol-specific)	-4.37	6.06E-09
ENSDARG00000069404	<i>pln-like</i> cardiac phospholamban-like	-3.66	7.15E-11
ENSDARG00000086250	<i>PRKCA</i> protein kinase C, alpha	-6.44	1.22E-05
ENSDARG00000060716	<i>prkx</i> protein kinase, X-linked	-2.09	5.54E-03
ENSDARG00000023797	<i>ryr1b</i> ryanodine receptor 1 (skeletal)	-7.15	7.49E-22
ENSDARG00000003706	<i>ryr2b</i> ryanodine receptor 2b	-3.35	3.44E-09
ENSDARG00000071331	<i>ryr3</i> ryanodine receptor 3	-3.08	3.35E-08
ENSDARG00000027355	<i>slc25a4</i> solute carrier family 25, member 4	-5.30	2.93E-15
ENSDARG00000092553	<i>slc25a5</i> solute carrier family 25 alpha, member 5	-2.82	9.77E-07
ENSDARG00000013422	<i>slc8a1a</i> solute carrier family 8 (sodium/calcium exchanger), member 1a	-2.47	8.02E-06
ENSDARG00000008912	<i>slc8a2a</i> solute carrier family 8 (sodium/calcium exchanger), member 2a	-5.62	1.41E-11
ENSDARG00000011400	<i>tnnc1a</i> troponin C type 1 (slow)	-2.52	6.07E-06
ENSDARG00000037539	<i>tnnc1b</i> troponin C type 1b (slow)	-3.11	1.12E-07
ENSDARG00000021564	<i>VDAC3</i> voltage-dependent anion channel 3	-2.20	2.46E-04

The fold change and adjusted *P* value were calculated by the R package DESeq in embryonic heart over that in adult heart.

Supplemental Table 5: List of upregulated sarcomeric genes in a zebrafish embryonic and an adult heart

A

Ensembl Gene ID	Gene Name	Embryonic heart	Adult heart	Fold change	P value	
ENSDARG00000037840	<i>actc1b</i>	<i>actin, alpha, cardiac muscle 1b</i>	134.43	6.89	16.12	1.28E-09
ENSDARG00000001431	<i>actn3b</i>	<i>actinin, alpha 3b</i>	1.27	0.37	2.85	3.04E-03
ENSDARG00000014196	<i>myl1</i>	<i>myosin, light chain 1, alkali; skeletal, fast</i>	33.91	0.40	70.16	2.33E-06
ENSDARG00000008494	<i>myl6</i>	<i>myosin, light chain 6, smooth muscle and non-muscle</i>	9.19	2.74	2.74	1.13E-06
ENSDARG000000062592	<i>myl10</i>	<i>myosin, light chain 10, regulatory</i>	4.83	0.12	35.26	4.18E-05
ENSDARG00000017441	<i>mylz3</i>	<i>myosin, light polypeptide 3, skeletal muscle</i>	95.64	3.36	23.79	1.99E-05
ENSDARG00000079564	<i>vmhc</i>	<i>ventricular myosin heavy chain</i>	283.63	24.75	9.51	8.55E-20
ENSDARG00000009782	<i>myh11a</i>	<i>myosin, heavy polypeptide 11, smooth muscle a</i>	5.96	2.02	2.39	1.52E-05
ENSDARG000000093467	<i>MYH13</i>	<i>myosin, heavy polypeptide 13</i>	0.67	0.02	25.21	1.20E-04
ENSDARG000000071433	<i>smyhc2</i>	<i>slow myosin heavy chain 2</i>	0.54	0.02	25.22	1.51E-09
ENSDARG000000067990	<i>myhz1.1</i>	<i>myosin, heavy polypeptide 1.1, skeletal muscle</i>	6.00	0.02	318.08	1.61E-12
ENSDARG000000067995	<i>myhz1.2</i>	<i>myosin, heavy polypeptide 1.2, skeletal muscle</i>	3.60	0.05	63.88	3.50E-11
ENSDARG00000012944	<i>myhz2</i>	<i>myosin, heavy polypeptide 2, fast muscle specific</i>	1.65	0.08	17.82	4.03E-08
ENSDARG000000087402	<i>tpm1</i>	<i>tropomyosin 1 (alpha)</i>	16.84	1.64	8.56	3.80E-05
ENSDARG000000005162	<i>tpm3</i>	<i>tropomyosin 3</i>	22.46	5.70	3.23	4.99E-09
ENSDARG000000019128	<i>tpm4b</i>	<i>tropomyosin 4b</i>	20.71	0.20	86.68	9.23E-40
ENSDARG000000033683	<i>tpma</i>	<i>alpha-tropomyosin</i>	39.37	2.55	12.94	1.65E-03
ENSDARG000000045822	<i>tnnt2e</i>	<i>troponin T2e, cardiac</i>	0.78	0.14	4.68	3.03E-05
ENSDARG000000030270	<i>tnnt3a</i>	<i>troponin T3a, skeletal, fast</i>	3.62	0.00	760.73	1.54E-12
ENSDARG000000068457	<i>tnnt3b</i>	<i>troponin T3b, skeletal, fast</i>	22.82	1.82	10.48	1.00E-04
ENSDARG000000070835	<i>tnnc2</i>	<i>troponin C type 2 (fast)</i>	53.91	1.15	39.11	7.99E-11
ENSDARG000000045592	<i>tnni2a.1</i>	<i>troponin I, skeletal, fast 2a, tandem duplicate 1</i>	2.74	0.15	15.00	2.44E-03
ENSDARG000000029069	<i>tnni2a.4</i>	<i>troponin I, skeletal, fast 2a, tandem duplicate 4</i>	11.02	0.04	221.21	1.08E-11
ENSDARG000000035958	<i>tnni2b.1</i>	<i>troponin I, skeletal, fast 2b, tandem duplicate 1</i>	2.44	0.00	866.94	2.47E-12
ENSDARG000000029995	<i>tnni2b.2</i>	<i>troponin I, skeletal, fast 2b, tandem duplicate 2</i>	8.08	0.75	8.73	9.09E-07

B

Ensembl Gene ID	Gene Name	Embryonic heart	Adult heart	Fold change	P value	
ENSDARG000000071090	<i>actn2</i>	<i>actinin, alpha 2</i>	168.80	547.77	3.99	7.26E-12
ENSDARG000000028213	<i>ttna</i>	<i>titin a</i>	4.24	20.39	5.88	1.24E-12
ENSDARG000000000563	<i>ttnb</i>	<i>titin b</i>	3.33	14.85	5.45	1.75E-17
ENSDARG000000032976	<i>cmlc1</i>	<i>cardiac myosin light chain-1</i>	2755.59	8777.13	3.94	8.20E-09
ENSDARG00000019096	<i>myl7</i>	<i>myosin, light polypeptide 7, regulatory (cmlc2)</i>	1494.78	4660.26	3.83	1.97E-11
ENSDARG000000038123	<i>myl9a</i>	<i>myosin, light chain 9a, regulatory</i>	48.49	124.94	3.16	1.27E-08
ENSDARG000000008030	<i>myl9b</i>	<i>myosin, light chain 9b, regulatory</i>	80.53	144.39	2.20	1.60E-04
ENSDARG000000007344	<i>tcap</i>	<i>titin-cap (telethonin)</i>	0.35	141.31	501.41	4.41E-20
ENSDARG000000079782	<i>vmhcl</i>	<i>ventricular myosin heavy chain-like</i>	482.68	1975.71	5.00	5.30E-16
ENSDARG000000076075	<i>myh7ba</i>	<i>myosin, heavy chain 7B, cardiac muscle, beta a</i>	20.01	67.46	4.03	8.54E-04
ENSDARG000000073732	<i>myh14</i>	<i>myosin, heavy chain 14, non-muscle</i>	1.45	5.77	4.86	3.15E-15
ENSDARG000000023963	<i>tpm4a</i>	<i>tropomyosin 4a</i>	1024.14	1683.55	2.01	8.24E-04
ENSDARG000000020610	<i>tnnt2a</i>	<i>troponin T2a, cardiac</i>	947.36	1859.01	2.41	1.96E-05
ENSDARG000000011400	<i>tnnc1a</i>	<i>troponin C type 1a (slow)</i>	546.73	1125.60	2.52	6.07E-06
ENSDARG000000037539	<i>tnnc1b</i>	<i>troponin C type 1b (slow)</i>	54.00	136.23	3.11	1.12E-07
ENSDARG000000070827	<i>zgc:112242</i>		0.16	14.59	116.57	1.33E-03
ENSDARG000000028343	<i>zgc:101560</i>		31.83	128.18	4.92	1.81E-15

List of sarcomeric genes upregulated in a zebrafish embryonic (A) and an adult heart (B). The average normalized expression level of each gene (using the R Package DESeq) in embryonic and adult heart. The fold change and adjusted *P* value were calculated by the R package DESeq in embryonic heart over that in adult heart (A) and vice versa (B).

Supplemental Table 6. 19 Human DCM - Associated Genes With Multiple Zebrafish Homologues

Human DCM-Associated Gene		Zebrafish			mRNA Expression, RPKM			
		Orthologue	Ensembl Gene ID	Identity	Type*	Embryo Heart	Adult Heart	Adult Muscle
<i>ACTC1</i>	Cardiac actin	<i>acta1a</i>	ENSDARG00000036371	99.00%	M	29.14	78.48	0.41
		<i>acta1b</i>	ENSDARG00000055618	98.00%	M	710.50	1200.72	3.10
		<i>hm:zewp0073</i>	ENSDARG00000076126	99.00%	M	134.07	224.02	0.90
		<i>actc1a</i>	ENSDARG00000042535	99.00%	M	2860.02	4429.03	15.66
		<i>actc1b</i>	ENSDARG00000037840	99.00%	M	134.43	6.89	9490.87
<i>ACTN2</i>	?-Actinin-2	<i>actn2</i>	ENSDARG00000071090	85.01%	1	168.80	547.77	1.28
		<i>CABZ01111872.1</i>	ENSDARG00000090343	75.57%	1	0.28	1.85	16.05
<i>ANKRD1</i>	Ankyrin repeat domain-containing protein 1	<i>ankrd1a</i>	ENSDARG00000075263	54.86%	1	1.13	0.12	0.93
		<i>ankrd1b</i>	ENSDARG00000076192	45.14%	1	0.05	0.09	0.01
<i>CRYAB</i>	Alpha B crystallin	<i>cryaba</i>	ENSDARG00000042621	59.43%	1	0.00	0.00	0.00
		<i>cryabb</i>	ENSDARG00000052447	58.86%	1	0.02	2.05	1.31
<i>DES</i>	Desmin	<i>desma</i>	ENSDARG00000058656	71.91%	1	162.66	248.08	56.60
		<i>desmb</i>	ENSDARG00000005221	71.06%	1	0.88	0.09	0.02

Supplemental Table 6 (continued)

Human DCM-Associated Gene		Zebrafish		Identity	Type*	mRNA Expression, RPKM		
		Orthologue	Ensembl Gene ID			Embryo Heart	Adult Heart	Adult Muscle
<i>DSP</i>	Desmoplakin	<i>dspe</i>	ENSDARG00000022309	47.76%	1	4.95	5.79	5.75
		<i>dspe</i>	ENSDARG00000076673	22.32%	1	8.31	10.49	2.26
<i>FHL2</i>	Four and a half LIM domains 2	<i>fhl2a</i>	ENSDARG00000042018	82.44%	1	115.64	27.84	2.12
		<i>fhl2b</i>	ENSDARG00000003991	81.36%	1	2.30	10.73	0.70
<i>LDB3</i>	LIM domain binding 3	<i>ldb3a</i>	ENSDARG00000056322	45.80%	M	46.17	65.76	107.66
		<i>ldb3b</i>	ENSDARG00000019202	22.97%	M	32.19	232.01	381.76
<i>MYH6</i>	?-Myosin heavy chain	<i>myh6</i>	ENSDARG00000090637	82.98%	M	109.73	173.77	0.10
		<i>vmhc</i>	ENSDARG00000079564	86.00%	M	283.63	24.75	0.66
		<i>vmhcl</i>	ENSDARG00000079782	86.00%	M	482.68	1975.71	0.66
		<i>CR450736.2</i>	ENSDARG00000092902	86.00%	M	0.02	0.01	1.59
		<i>CU633479.5</i>	ENSDARG00000092357	86.00%	M	0.01	0.03	1.29
		<i>CU633479.6</i>	ENSDARG00000093148	86.00%	M	0.08	0.01	4.78
		<i>si:ch211-24n20.3</i>	ENSDARG00000093715	86.00%	M	0.07	0.00	5.19

Supplemental Table 6 (continued)

Human DCM-Associated Gene		Zebrafish		Identity	Type*	mRNA Expression, RPKM		
		Orthologue	Ensembl Gene ID			Embryo Heart	Adult Heart	Adult Muscle
<i>MYH7</i>	?-Myosin heavy chain	<i>myh7ba</i>	ENSDARG00000076075	67.44%	M	20.01	67.46	3.75
		<i>myh7bb</i>	ENSDARG00000035322	66.25%	M	8.31	6.64	0.45
		<i>vmhc</i>	ENSDARG00000079564	85.99%	M	283.63	24.75	0.66
		<i>vmhcl</i>	ENSDARG00000079782	85.89%	M	482.68	1975.71	0.66
		<i>CR450736.2</i>	ENSDARG00000092902	87.00%	M	0.02	0.01	1.59
		<i>CU633479.5</i>	ENSDARG00000092357	86.00%	M	0.01	0.03	1.29
		<i>CU633479.6</i>	ENSDARG00000093148	86.00%	M	0.08	0.01	4.78
		<i>si:ch211-24n20.3</i>	ENSDARG00000093715	86.00%	M	0.07	0.00	5.19
<i>PDLIM3</i>	PDZ LIM domain protein 3	<i>pdlim3a</i>	ENSDARG00000011023	57.59%	1	1.50	1.98	0.09
		<i>pdlim3b</i>	ENSDARG00000014248	58.23%	1	5.88	9.47	0.95
<i>SCN5A</i>	Sodium channel	<i>scn12aa</i>	ENSDARG00000059692	64.00%	M	0.00	0.01	0.00
		<i>scn12ab</i>	ENSDARG00000078758	65.00%	M	1.43	7.11	0.04
<i>SYNE1</i>	Spectrin repeat containing, nuclear envelope 1	<i>syne1a</i>	ENSDARG00000009499	49.42%	1	1.39	2.48	0.45
		<i>syne1b</i>	ENSDARG00000063068	55.39%	1	0.75	1.06	0.55

Supplemental Table 6 (continued)

Human DCM-Associated Gene		Zebrafish			mRNA Expression, RPKM			
		Orthologue	Ensembl Gene ID	Identity	Type*	Embryo Heart	Adult Heart	Adult Muscle
<i>SYNE2</i>	Spectrin repeat containing, nuclear	<i>syne2a</i>	ENSDARG00000030107	17.03%	1	0.13	0.08	2.09
	envelope 2	<i>syne2b</i>	ENSDARG00000053484	24.97%	1	2.69	10.39	2.80
<i>TMPO</i>	Thymopoietin	<i>Tmpoa</i>	ENSDARG00000007315	47.98%	1	7.24	1.32	0.70
		<i>Tmpob</i>	ENSDARG00000022978	46.37%	1	2.71	1.04	1.12
<i>TNNC1</i>	Cardiac troponin C	<i>tnnc1a</i>	ENSDARG00000011400	89.44%	1	546.73	1125.60	0.41
		<i>tnnc1b</i>	ENSDARG00000037539	88.20%	1	54.00	136.23	54.31
<i>TNNI3</i>	Cardiac troponin I	<i>tnni1a</i>	ENSDARG00000000474	49.00%	M	0.17	0.23	0.26
		<i>tnni1al</i>	ENSDARG00000036671	49.00%	M	0.06	0.07	4.12
		<i>tnni1b</i>	ENSDARG00000052708	54.00%	M	280.29	334.69	1.33
		<i>tnni1c</i>	ENSDARG00000042559	53.00%	M	1.35	1.45	25.31
		<i>tnni1d</i>	ENSDARG00000073766	50.00%	M	0.06	1.14	3.23
		<i>tnni2a.1</i>	ENSDARG00000045592	48.00%	M	2.74	0.15	0.88
		<i>tnni2a.2</i>	ENSDARG00000005841	34.00%	M	2.40	5.84	15.76
<i>tnni2a.3</i>	ENSDARG00000013752	37.00%	M	1.13	0.89	1385.45		

Supplemental Table 6 (continued)

Human DCM-Associated Gene		Zebrafish			mRNA Expression, RPKM			
		Orthologue	Ensembl Gene ID	Identity	Type*	Embryo Heart	Adult Heart	Adult Muscle
		<i>tnni2a.4</i>	ENSDARG00000029069	40.00%	M	11.02	0.04	58.12
		<i>tnni2b.1</i>	ENSDARG00000035958	47.00%	M	2.44	0.00	0.19
		<i>tnni2b.2</i>	ENSDARG00000029995	43.00%	M	8.08	0.75	1135.97
		<i>zgc:112242</i>	ENSDARG00000070827	49.00%	M	0.16	14.59	5.87
		<i>zgc:101560</i>	ENSDARG00000028343	37.00%	M	31.83	128.18	1.27
		<i>si:dkey-206m15.8</i>	ENSDARG00000092999	34.00%	M	0.14	0.05	5.24
<i>TNNT2</i>	Cardiac troponin T	<i>tnnt2a</i>	ENSDARG00000020610	54.24%	M	947.36	1859.01	0.78
		<i>tnnt2b</i>	ENSDARG00000031920	47.46%	M	1.73	1.12	2.27
		<i>tnnt2c</i>	ENSDARG00000032242	48.00%	M	0.36	0.44	0.25
<i>TTN</i>	Titin	<i>ttna</i>	ENSDARG00000028213	58.10%	M	4.24	20.39	48.00
		<i>ttnb</i>	ENSDARG00000000563	59.88%	M	3.33	14.85	53.11

Abbreviations: DCM, dilated cardiomyopathy; RPKM, reads per kilobase per million reads.

* Human and zebrafish genes were either many-to-many orthologues (“M”) or 1 human to many zebrafish orthologues (“1”).

Supplemental Table 7: List of upregulated genes in Hedgehog signaling pathway in embryonic heart

Ensembl Gene ID	Gene Name	Fold change	P value
ENSDARG00000025641	<i>gli2a</i> <i>GLI family zinc finger 2a</i>	5.71E+00	8.90E-13
ENSDARG00000041430	<i>bmp2b</i> <i>bone morphogenetic protein 2b</i>	7.69E+00	1.35E-10
ENSDARG00000019995	<i>bmp4</i> <i>bone morphogenetic protein 4</i>	1.35E+01	1.43E-25
ENSDARG00000004965	<i>bmp5</i> <i>bone morphogenetic protein 5</i>	1.72E+01	2.03E-33
ENSDARG00000063230	<i>bmp7b</i> <i>bone morphogenetic protein 7b</i>	5.79E+00	7.64E-10
ENSDARG00000077298	<i>gas1a</i> <i>growth arrest-specific 1a</i>	5.71E+00	4.26E-15
ENSDARG00000060397	<i>hhip</i> <i>hedgehog interacting protein</i>	5.76E+00	2.11E-11
ENSDARG00000060649	<i>lrp2a</i> <i>low density lipoprotein receptor-related protein 2a</i>	3.36E+00	3.59E-04
ENSDARG00000055026	<i>ptch2</i> <i>patched 2</i>	2.76E+00	5.20E-06
ENSDARG00000002952	<i>smo</i> <i>smoothened, frizzled class receptor</i>	3.10E+00	2.16E-07
ENSDARG00000068567	<i>shha</i> <i>sonic hedgehog a</i>	1.19E+01	7.08E-04
ENSDARG00000014796	<i>wnt11r</i> <i>wingless-type MMTV integration site family, member 11, related</i>	3.38E+00	3.45E-10
ENSDARG00000032234	<i>wnt2bb</i> <i>wingless-type MMTV integration site family, member 2Bb</i>	2.16E+00	1.31E-03
ENSDARG00000034894	<i>wnt5b</i> <i>wingless-type MMTV integration site family, member 5b</i>	2.24E+00	1.88E-04
ENSDARG00000073935	<i>wnt6b</i> <i>wingless-type MMTV integration site family, member 6b</i>	3.20E+00	9.68E-03
ENSDARG00000044827	<i>wnt7aa</i> <i>wingless-type MMTV integration site family, member 7Aa</i>	7.29E+00	8.23E-10
ENSDARG00000071107	<i>wnt7bb</i> <i>wingless-type MMTV integration site family, member 7Bb</i>	3.52E+01	2.55E-03
ENSDARG00000063437	<i>wnt9a</i> <i>wingless-type MMTV integration site family, member 9A</i>	1.30E+01	1.22E-06
ENSDARG00000037889	<i>wnt9b</i> <i>wingless-type MMTV integration site family, member 9B</i>	3.21E+01	3.01E-08

The fold change and adjusted *P* value were calculated by the R package DESeq in embryonic heart over that in adult heart.

Supplemental Table 8: List of upregulated genes in TGF-beta signaling pathway in embryonic heart

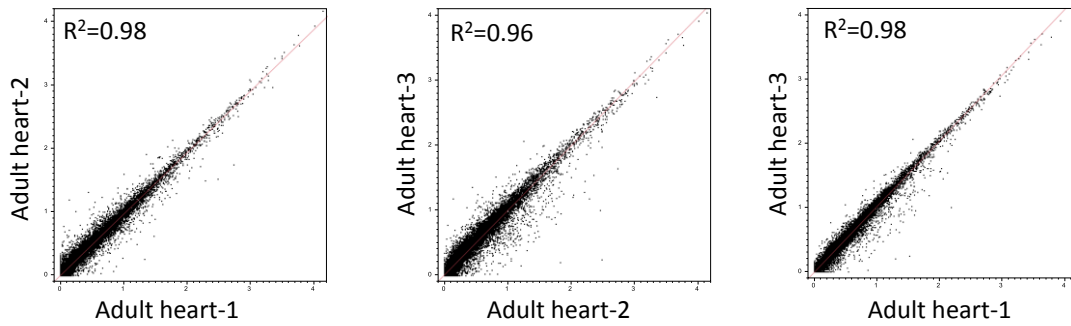
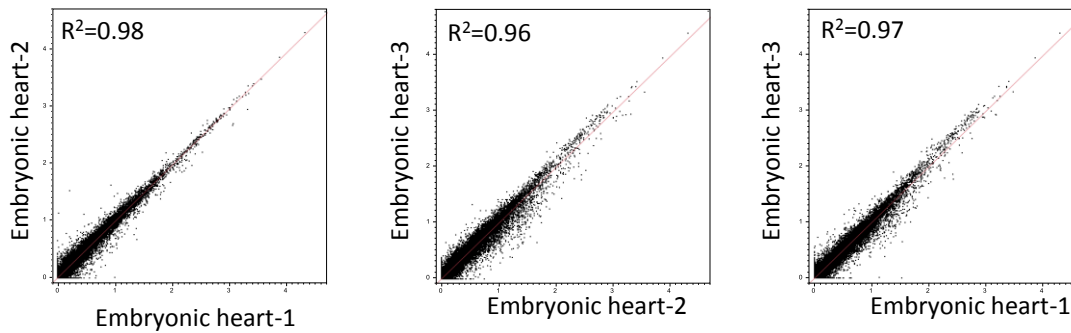
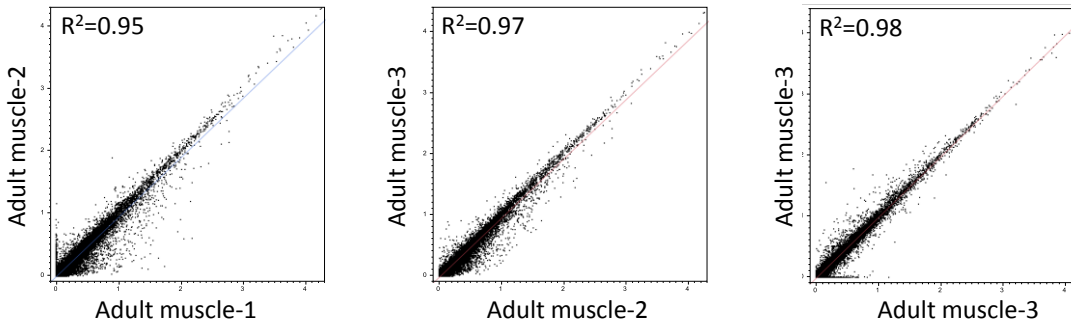
Ensembl Gene ID	Gene Name	Fold change	P value
ENSDARG00000029358	<i>e2f4</i> E2F transcription factor 4	2.23E+00	5.50E-04
ENSDARG00000070428	<i>smad4a</i> SMAD family member 4a	3.46E+00	1.64E-08
ENSDARG00000053209	<i>smad6a</i> SMAD family member 6a	2.78E+00	6.39E-07
ENSDARG00000021938	<i>smad9</i> SMAD family member 9	2.35E+00	2.45E-04
ENSDARG00000041516	<i>acvr2b</i> activin A receptor, type IIB	2.73E+00	1.53E-03
ENSDARG00000041430	<i>bmp2b</i> bone morphogenetic protein 2	7.69E+00	1.35E-10
ENSDARG00000019995	<i>bmp4</i> bone morphogenetic protein 4	1.35E+01	1.43E-25
ENSDARG00000004965	<i>bmp5</i> bone morphogenetic protein 5	1.72E+01	2.03E-33
ENSDARG00000063230	<i>bmp7b</i> bone morphogenetic protein 7	5.79E+00	7.64E-10
ENSDARG00000052846	<i>fsta</i> follistatin a	4.86E+00	5.26E-06
ENSDARG00000053479	<i>gdf6a</i> growth differentiation factor 6a	2.36E+01	1.06E-22
ENSDARG00000040764	<i>id1</i> inhibitor of DNA binding 1	7.29E+00	2.33E-22
ENSDARG00000055283	<i>id2a</i> inhibitor of DNA binding 2, dominant negative helix-loop-helix protein, a	2.82E+00	9.99E-07
ENSDARG00000054823	<i>id3</i> inhibitor of DNA binding 3	2.99E+00	2.13E-07
ENSDARG00000045131	<i>id4</i> inhibitor of DNA binding 4	3.96E+00	1.06E-07
ENSDARG00000056922	<i>ltbp1</i> latent transforming growth factor beta binding protein 1	3.93E+00	1.13E-10
ENSDARG00000044059	<i>lft2</i> lefty2	7.83E+01	2.16E-12
ENSDARG00000058819	<i>nog1</i> noggin 1	7.37E+00	6.85E-04
ENSDARG00000036194	<i>pitx2</i> paired-like homeodomain 2	1.56E+01	4.99E-28
ENSDARG00000032430	<i>ppp2r1b</i> protein phosphatase 2, regulatory subunit A, beta	2.14E+00	2.05E-04
ENSDARG00000008141	<i>rbl1</i> retinoblastoma-like 1 (p107)	2.69E+00	9.33E-06
ENSDARG00000010785	<i>thbs1b</i> thrombospondin 1b	2.65E+00	3.86E-04
ENSDARG00000073810	<i>thbs2b</i> thrombospondin 2b	5.24E+00	5.44E-14
ENSDARG00000012060	<i>thbs3b</i> thrombospondin 3b	4.47E+00	3.72E-03
ENSDARG00000020072	<i>thbs4b</i> thrombospondin 4b	3.45E+00	5.63E-03
ENSDARG00000077473	<i>mych</i> myelocytomatosis oncogene homolog	4.86E+00	7.49E-13

The fold change and adjusted *P* value were calculated by the R package DESeq in embryonic heart over that in adult heart.

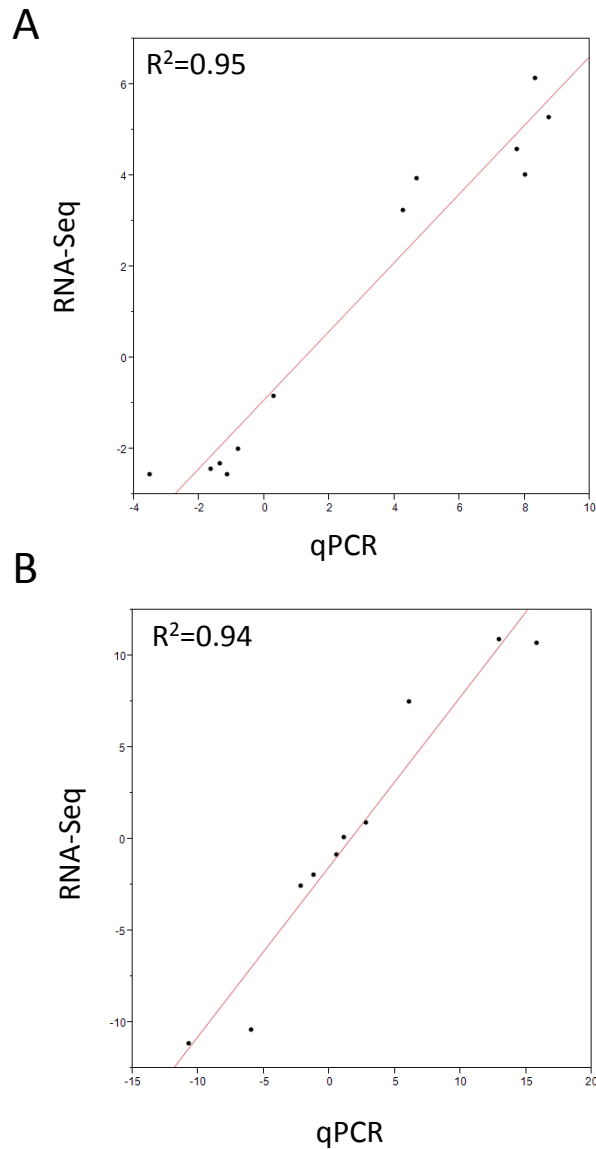
Supplemental Table 9. Differential expression of zebrafish homologues of DCM-causative genes with multiple homologues in hearts and in muscles.

Zebrafish orthologues	Fold Change	P value
Cardiac-Enriched		
<i>vmhcl</i>	1784.02	2.98E-138
<i>tnnc1a</i>	1639.25	1.36E-133
<i>tnnt2a</i>	1427.04	4.45E-132
<i>myh6</i>	1082.61	9.92E-69
<i>actn2</i>	258.31	7.62E-94
<i>acta1b</i>	248.67	2.74E-04
<i>actc1a</i>	178.41	1.13E-15
<i>hm:zewp0073</i>	157.02	6.83E-15
<i>tnni1b</i>	152.79	6.50E-82
<i>scn12ab</i>	111.39	5.89E-36
<i>zgc:101560</i>	60.47	1.18E-61
<i>vmhc</i>	22.40	9.47E-12
<i>pdlim3a</i>	13.16	2.15E-13
<i>myh7ba</i>	10.62	3.21E-07
<i>fhl2b</i>	9.28	2.30E-22
<i>myh7bb</i>	8.73	3.13E-07
<i>fhl2a</i>	7.99	2.39E-20
<i>pdlim3b</i>	6.19	4.14E-11
<i>syne1a</i>	3.38	2.88E-08
<i>dspb</i>	2.88	1.99E-04
<i>desma</i>	2.68	9.31E-06
<i>syne2b</i>	2.28	3.06E-04
Skeletal-Muscle Enriched		
<i>si:ch211-24n20.3</i>	3391.34	5.92E-15
<i>tnni2a.3</i>	2602.91	2.90E-141
<i>tnni2b.2</i>	2418.42	2.36E-30
<i>tnni2a.4</i>	2328.37	4.86E-30
<i>actc1b</i>	2251.67	2.20E-140
<i>CU633479.6</i>	1069.78	4.56E-12
<i>CR450736.2</i>	208.05	2.56E-17
<i>si:dkey-206m15.8</i>	172.99	1.08E-06
<i>tnni2b.1</i>	139.03	3.40E-06
<i>tnni1al</i>	96.12	1.70E-06
<i>CU633479.5</i>	66.04	6.62E-08
<i>syne2a</i>	40.48	4.49E-34
<i>zgc:153662(tnni1c)</i>	30.52	2.95E-04
<i>ankrd1a</i>	12.18	1.72E-03
<i>ttnb</i>	5.89	1.01E-15
<i>ttna</i>	3.86	7.75E-10
<i>ldb3b</i>	2.69	8.66E-06
<i>ldb3a</i>	2.66	9.63E-06

The average normalized expression level of each gene (using the R Package DESeq) in adult heart and muscle. The fold change and adjusted *P* value were calculated by the R package DESeq in adult heart over that in adult muscle (A) and vice versa (B).

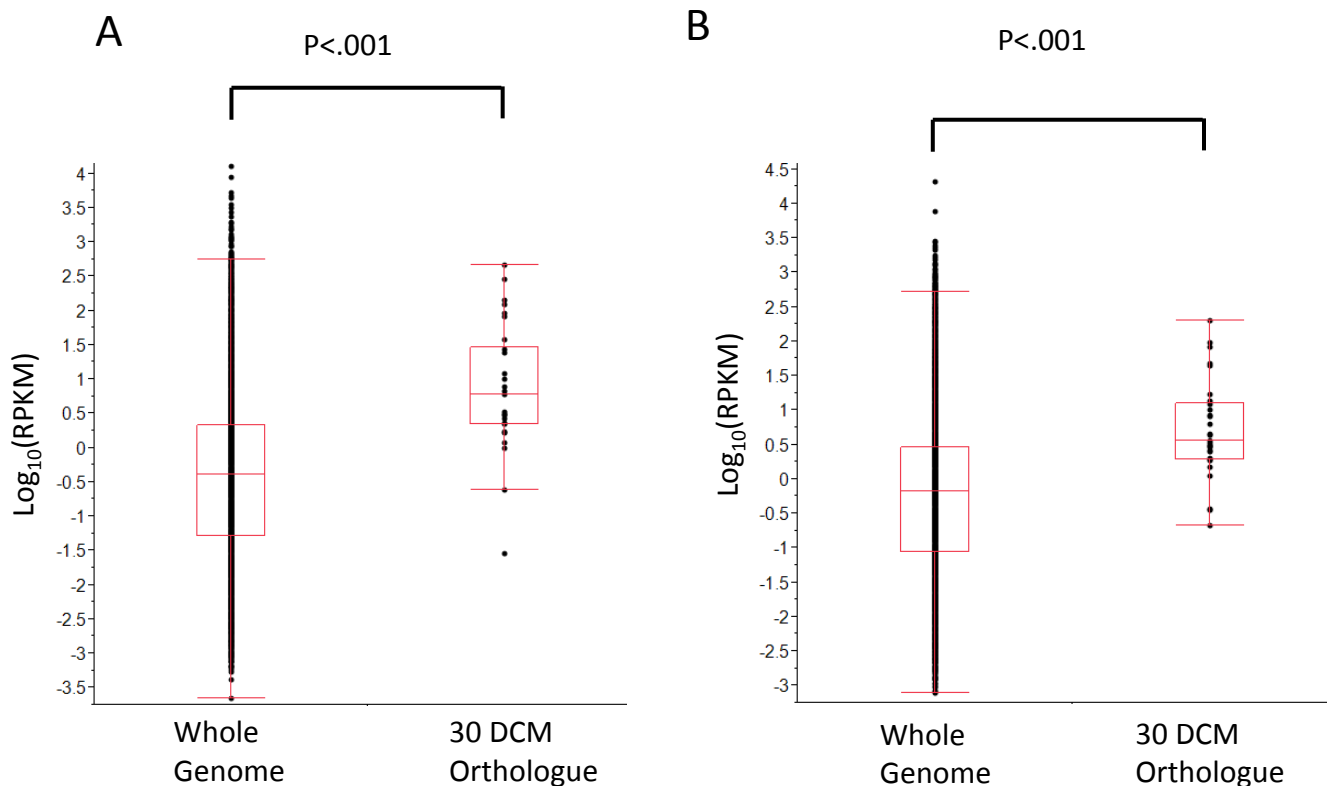
A**B****C****Supplemental Fig. 1 Biological repeats of RNA-seq analysis.**

Scatter plots of Log₁₀(RPKM+1) values between individual samples of three biological repeats for RNA-seq analysis of adult heart (A), embryonic heart (B) and adult muscle (C). The Pearson correlation coefficient (R²) is shown in each comparison. RPKM indicates reads per kilobase per million reads.



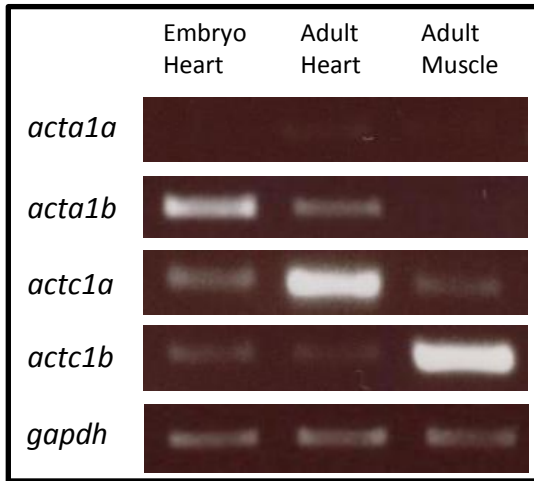
Supplemental Fig. 2 qPCR validation of gene expression level estimated by RNA-seq

X axis is the $\Delta\Delta C_t$ values of qPCR comparing different samples normalized by the expression level of *gapdh*. Y axis is the Log₂ of fold change of the RPKM between the samples. Scatter plots based on examined genes shown in comparison of (A) adult heart and embryo heart and (B) adult heart and muscle. The Pearson correlation coefficient (R^2) is shown in each comparison.

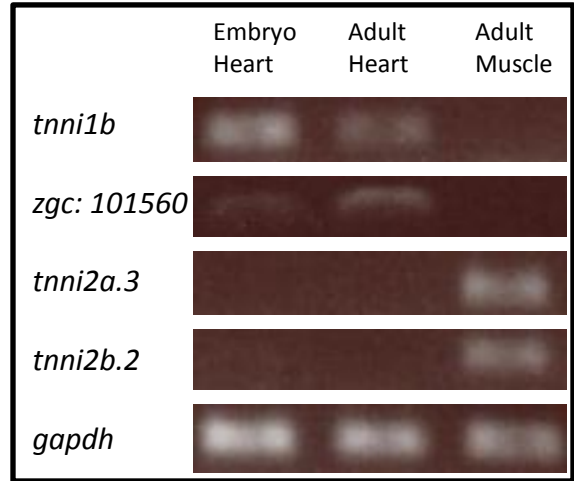


Supplemental Figure 3. Expressional Analysis of Zebrafish Orthologues of 30 Dilated Cardiomyopathy–Causative Genes. Box and whisker plots comparing expression levels of all genes in \log_{10} (reads per kilobase per million reads [RPKM]) between the whole zebrafish genome and 30 orthologues in adult heart (A) and embryonic heart (B).

A



B



Supplemental Fig 4. Validation of RNA-seq data with semi-Quantitative reverse transcriptase polymerase chain reaction (semi-qPCR). Shown are semi-qPCR using cDNA extracted from embryonic hearts, adult hearts and adult muscles. Expression of genes within *actin* family (A) and *tnni* family (B) were assessed. *gapdh* was used as a loading control.