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Supplementary Materials for

Decellularized zebrafish cardiac extracellular matrix induces mammalian heart regeneration

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SUPPLEMENTARY MATERIALS

Supplementary Materials and Methods

Ventricular amputation and procurement of zebrafish hearts. To obtain healing zebrafish hearts, ventricular resection surgeries were performed as described by Poss et al (*15*). Briefly, zebrafish were anesthetized in Tricaine (ethyl 3-aminobenzoate methanesulfonate, i.e. MS-222, tricaine methanesulfonate, A-5040; Sigma-Aldrich, St. Louis, MO, USA) and placed dorsally in a humid sponge. A small incision (scalpel 0.15mm, Fine Science Tools, Foster City, CA, USA) was made to expose the ventricle and approximately 20% of the ventricular apex was microscopically removed using iridectomy scissors (Fine Science Tools). After the surgery, fish were returned to water and stimulated to breathe with air bubbles. At 3 days post amputation (3 dpa), methylene blue (an anti-fungal/bacterial agent) was added to the fish tank 1 hr before harvesting. Amputated zebrafish and age-matched uninjured counterparts were lethally anesthetized with Tricaine. Zebrafish were then dipped 3 times in 70% ethanol immediately before harvesting. The whole hearts were extracted with sterile tools and placed on a sterile plate under the dissection microscope. To accentuate the regenerating ventricular apex, only two-thirds of the ventricle (including the apex) was collected for the decellularization. Normal zebrafish ventricles were collected in the same manner (only apical two-thirds). Tools were sterilized with 70% ethanol between each fish. Collected ventricles were immediately washed 3 times in 4% Penicillin/Streptomycin/Amphotericin-B with 1% Gentamycin (P/S/A/G) solution and transported back to the laboratory. Approximately 50 to 60 ventricles were pooled together per batch to obtain sufficient materials for decellularization. All ventricles were washed extensively in 4%, 2%, and 1% gradient P/S/A/G solutions (two times each) in the biosafety cabinet before being subjected to the decellularization process.

Procurement of adult mouse ventricular tissues. Mice were sacrificed, immersed in 70% ethanol for 30 seconds, and wiped clean before removing hearts with two sets of sterile tools (one set for cutting the skin and opening the chest and another set for removing the heart). Collected hearts were immediately washed 3 times in 4% P/S/A/G solution and transported back to the laboratory. Left ventricles were then dissected out and finely chopped to <1 mm^3 with sterile tools in the biosafety cabinet. All mouse ventricular pieces were washed extensively in 4%, 2%, and 1% gradient P/S/A/G solutions (two times each) before being subjected to the decellularization process.

Decellularization of cardiac ECM. Zebrafish ventricles and mouse ventricular pieces were carefully transferred to individually weighed, sterile 1.5 ml microcentrifuge tubes containing 1 ml 1% P/S/A/G solution. Tubes were centrifuged at 6,000 g for 3 minutes with careful removal of supernatants and then individually weighed to obtain the collective wet weights of samples. Tubes were subsequently replenished with 1 ml 1% P/S/A/G solution, vortexed to evenly distribute contents, parafilmed to seal caps, and subjected to three freeze-thaw cycles by submerging in liquid nitrogen for 10 minutes and then completely thawing at 37°C in water bath. Alternatively tubes can be chilled with dry ice for at least 30 minutes or at -80°C for at least 1 hour per cycle before being completely thawed at 37°C in water bath. Tubes were centrifuged at 6,000 g for 3 minutes with careful removal of supernatants and replenished with 1 ml 1% P/S/A/G solution between each freeze-thaw cycle and then vortexed to ensure even distribution of contents before starting the next cycle. After three cycles, erythrocyte lysis was performed twice by adding 1 ml erythrolysis buffer (ELB) to resuspend contents, incubating for 20-30 minutes at room temperature, and centrifuging at 6,000 g for 3 minutes. Samples were then subjected to two more freeze-thaw cycles as described above with 1 ml 1% P/S/A/G solution. Samples were subsequently incubated with 250 U/ml deoxyribonuclease I (DNase I, 18047-019) and 25 U/ml ribonuclease A (RNase A, AM2274) at 37 °C for at least 1 hour (both from Life Technologies, Grand Island, NY, USA). Treatment with DNase I and RNase A was repeated after centrifugation at 6,000 g for 3 minutes and careful removal of the supernatant. After 2 rounds of DNA/RNA lysis, samples were washed three times with sterile 0.9% normal saline (Baxter Healthcare, Deerfield, IL, USA) and frozen at -80°C for 1 hour. Samples were then washed with 0.9% normal saline, centrifuged at 6,000 g for 3 minutes with complete removal of supernatants, and subjected to lyophilization for 72 hours in original tubes in a sterilized chamber. Immediately after lyophilization, tubes were individually weighed to obtain the collective dry weights of lyophilized products. Lyophilized samples were finely crushed and ground for 15-20 minutes into fine powders in original tubes placed in a liquid nitrogen-cooled mini mortar (H37260-0100; Bel-Art Products, Wayne, NJ, USA). Lyophilized powders were stored at -80°C for future use.

Preparation of cardiac ECM suspension and particle size measurement. Prior to applications, lyophilized cardiac ECM powders were weighed in a sterile container, resuspended in 0.9% normal saline, and sonicated in cool water for 15 min. Large particles were then removed by centrifugation at 300 × *g*. Cardiac ECM suspension was collected for immediate use or stored on dry ice for later use. Cardiac ECM particle size was measured by Zetasizer Nano ZS90 (Malvern, Worcestershire, UK) and reported as the mean from 25 measurements. Results were then averaged from measurements of three independent samples. For in vivo administration, 0.5 mg of lyophilized zECM or mECM powders was resuspended in 30 μl of 0.9% normal saline, sonicated and centrifuged as described above, and transported on dry ice to the operating room prior to the administration.

Myocardial infarction model. The induction of myocardial infarction (MI) and intramyocardial injections have been performed as we previously reported (*59, 60*). In brief, after the induction of anesthesia with 4% isoflurane gas, mice were intubated and inhalationally anesthetized with 2% isoflurane gas throughout the surgery. MI was microscopically induced by permanent ligation of the left anterior descending coronary artery (LAD). Mice were then randomly assigned to one of the four groups: hzECM, nzECM, mECM, or saline control. Five minutes after the induction of infarction, 30 μl of zECM or mECM suspension was injected at three sites of the ischemic myocardium (center and two borders of the infarct; 10 μl for each site). Control mice received injections of 30 μl normal saline. The investigator who induced MI and performed injections was blinded to the content of the injectant. For ErbB2 inhibition in vivo, the ErbB2 inhibitor AG825 (sc-202045A; Santa Cruz Biotechnology, Dallas, TX, USA) was dissolved in dimethyl sulfoxide (DMSO) and intraperitoneally injected once at 5 mg/kg (20 to 25 μl in volume) immediately after the cardiac ECM administration (*40, 41*). Control mice received a sham injection or an intraperitoneal injection of 25 μl DMSO alone.

Echocardiography. Echocardiographic studies were performed by a blinded investigator repeatedly before surgery and at 5 days, 2 weeks, and 6 weeks after surgery to assess the cardiac function, as we previously described (*60, 61*). Briefly, mice were initially anesthetized with 2% isoflurane gas and subsequently maintained at 1-1.5% isoflurane gas throughout the echocardiographic study. Mice were then immobilized on a heated stage equipped with electrocardiography. Heart rate and respiratory rate were continuously monitored. The body temperature was maintained at 37°C. Echocardiographic parameters were measured using a high-frequency linear probe (MS400, 30 MHz) connected to a high-resolution ultrasound imaging system (Vevo 2100; FUJIFILM VisualSonics, Toronto, Ontario, Canada). M- and B-mode frames were acquired at a frame rate of 235 Hz during each scan. At least three independent M- and B-mode scans (300 frames per scan) were recorded respectively for each animal at each time point. End-systolic dimension (ESD) and end-diastolic dimensions (EDD) were determined from short axis images of the left ventricle using M-mode scan. Ten consecutive beats were measured from M-mode frames. Results were averaged. End-systolic area (ESA) and end-diastolic area (EDA) were measured from short-axis images of the LV using B-mode scan (minimum and maximum LV chamber area respectively). Functional parameters, including the LV fractional shortening (LVFS), LV fractional area change (LVFAC), and LV ejection fraction (LVEF), were determined as previously described (*62, 63*). Mice that died, displayed morphological/behavioral abnormality, or were sacrificed for histological analysis nefore 6 weeks post-injection were not included in echocardiographic studies.

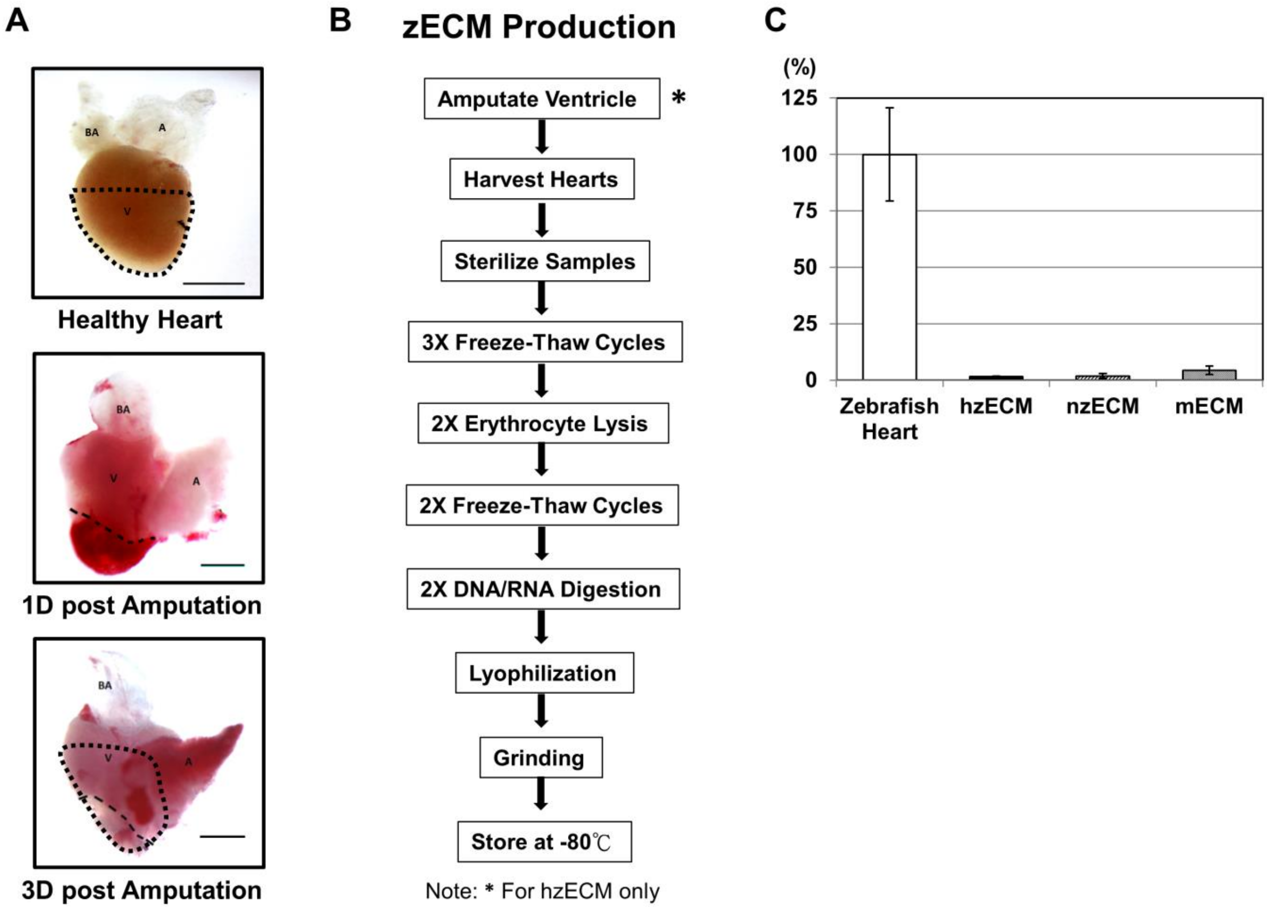

fig. S1. Amputated zebrafish hearts and decellularization processes. (**A**) Representative images of zebrafish hearts: (A) healthy, (B) 1-day, and (C) 3-day post amputation. Roughly 70% of the ventricular tissue (dotted lines), including the regenerating area in the amputated heart, is harvested. (**B**) The work flow of production of decellularized zebrafish heart ECM. (**C**) DNA assay shows residual DNA contents in decellularized ECM: hzECM, nzECM, and mECM; results are normalized to DNA contained in normal zebrafish hearts by unit dry weight.

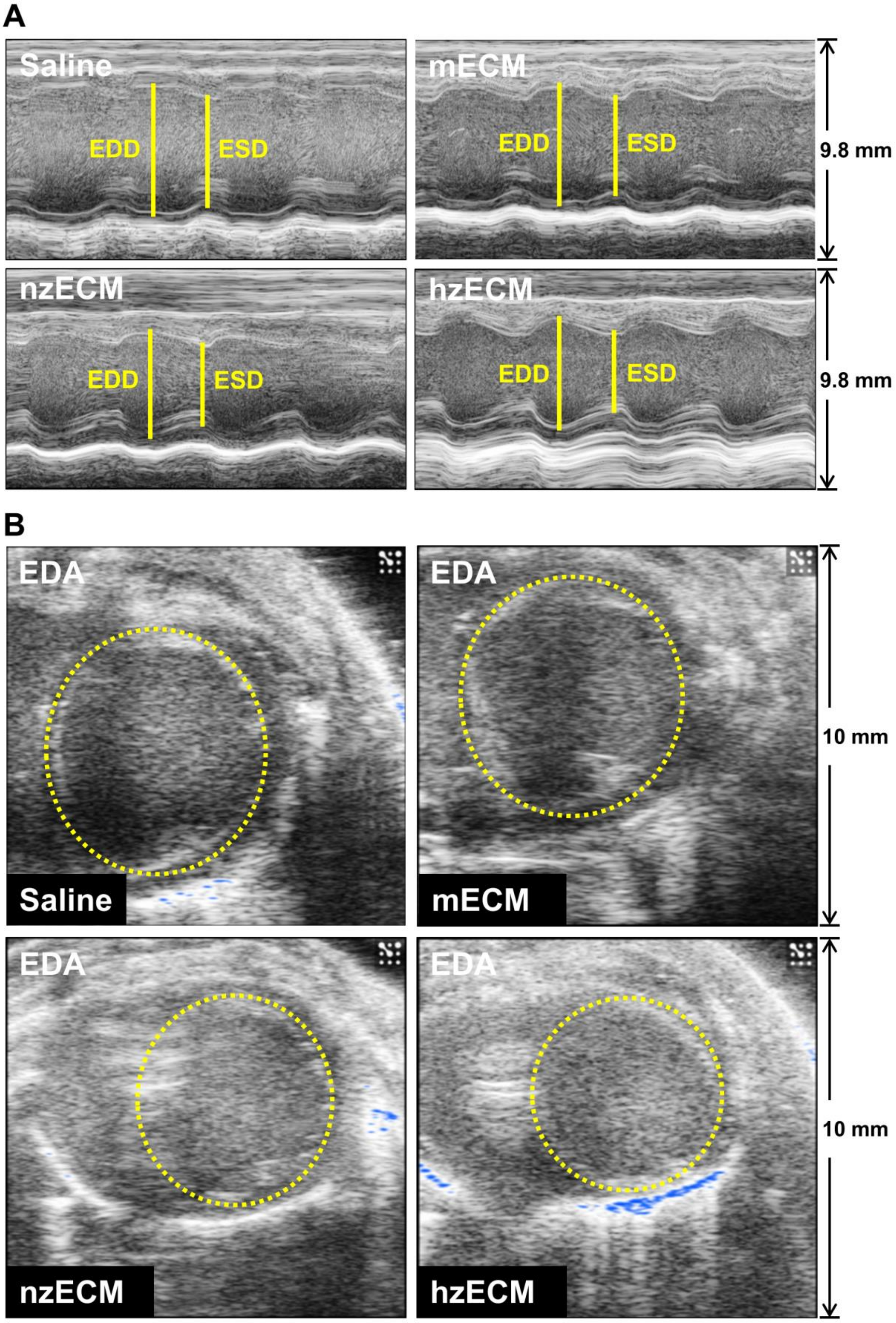

fig. S2. Representative LV images of M- and B-mode echocardiography. End-systolic dimension (ESD) and end-diastolic dimension (EDD) are indicated by yellow lines in (**A**). Dotted circles in (**B**) approximate the left ventricular wall at the end-diastole.

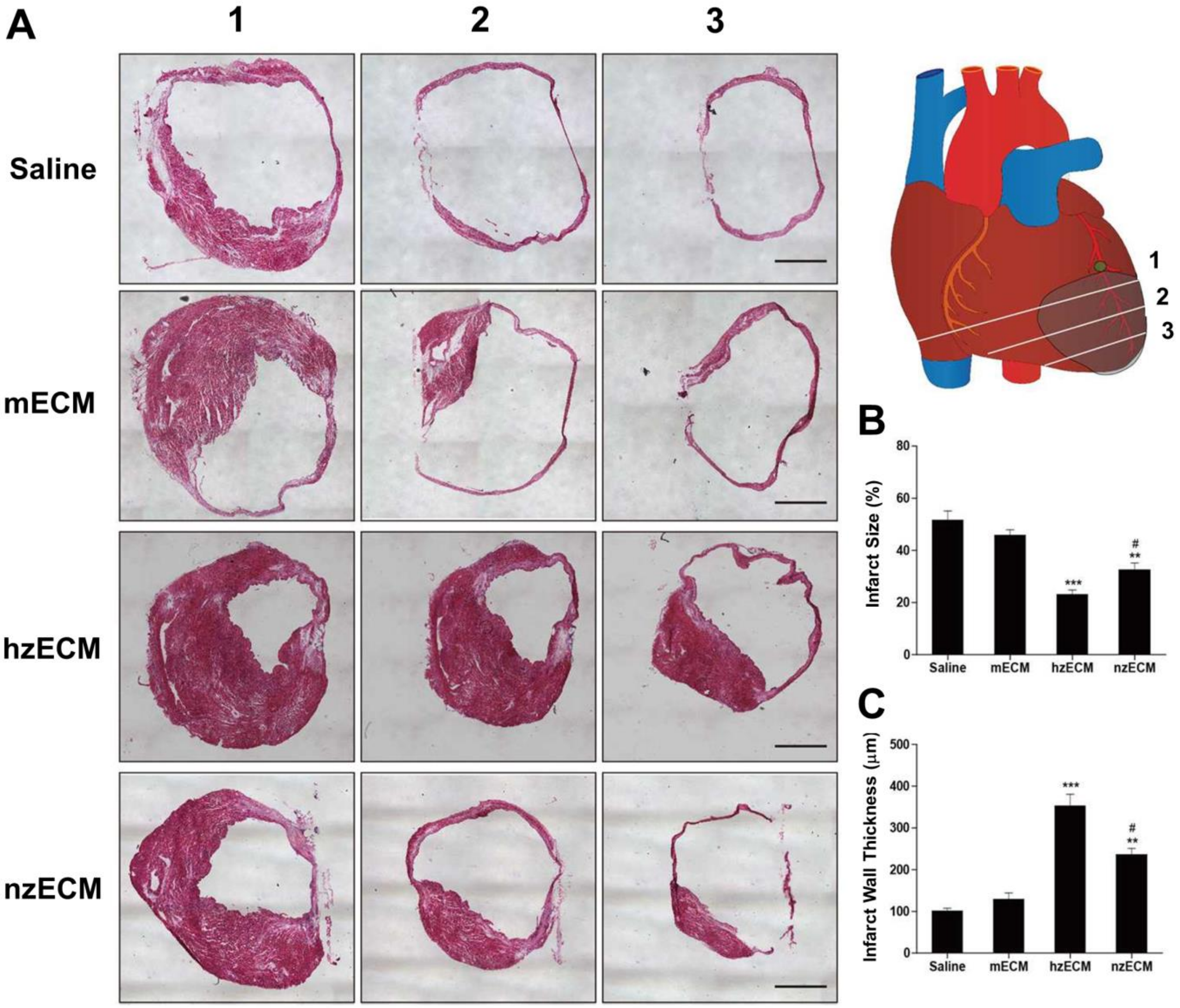

fig. S3. Histological analysis of mouse hearts after zECM treatment. (**A**) Representative H&E staining images of serially sectioned mouse hearts at 6 weeks post-MI. 1, 2, and 3 approximate the section level in the model heart (scale bars = 1 mm). (**B**) Analysis of the infarct size with H&E stained sections at level 1 (N = 4 per group). (**C**) Analysis of the left ventricular wall thickness with H&E stained sections at level 1 (N = 4 per group). ***p*<0.01, ****p*<0.001 compared to mECM and saline; $^{\#}$*p*<0.05 hzECM vs nzECM). All quantitative data represent means ± SD.

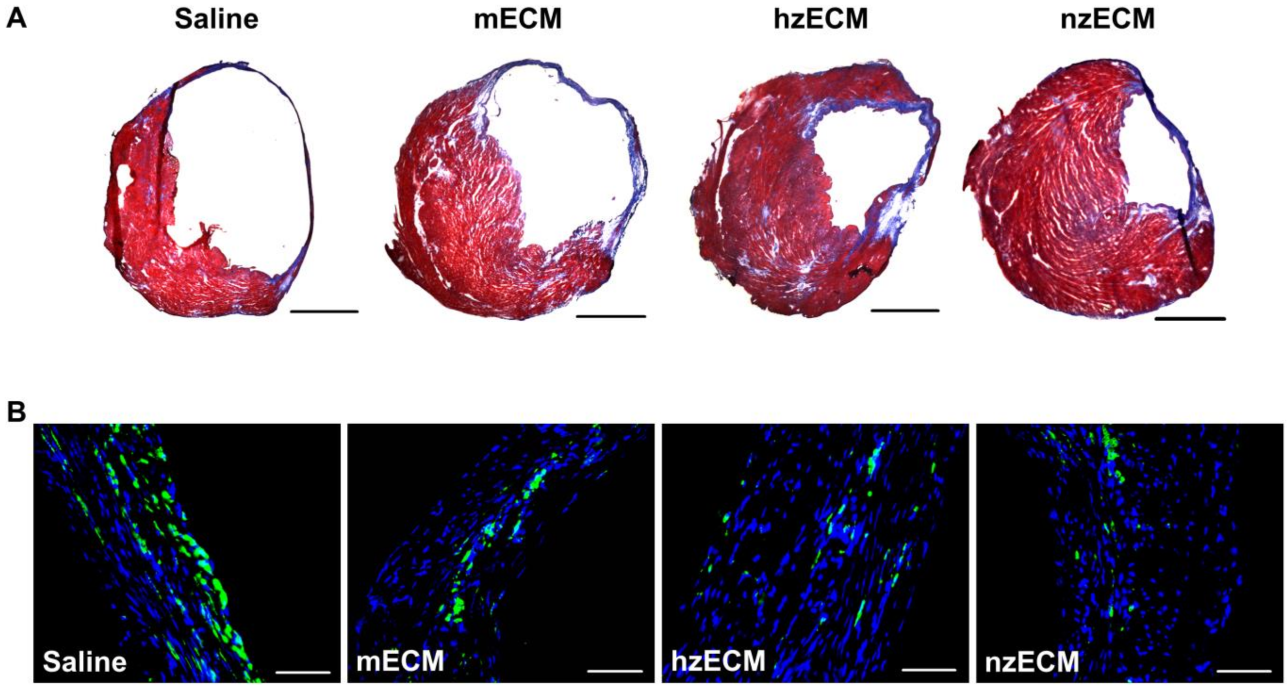

fig. S4. Fibrosis and chronic inflammation. (**A**) Myocardial fibrosis at 6 weeks post-MI is revealed by Masson's trichrome stain in transverse sections of hearts injected with saline, mECM, nzECM, or hzECM (collagen in blue/purple, cardiac muscle in red; scale bars = 1 mm). (**B**) Detection of chronic phagocytic cell infiltration by anti-mouse CD68 immunohistochemistry at 6 weeks post-MI in transverse sections of hearts injected with saline, mECM, nzECM, or hzECM (CD68 in green; scale bars = 50 μm).

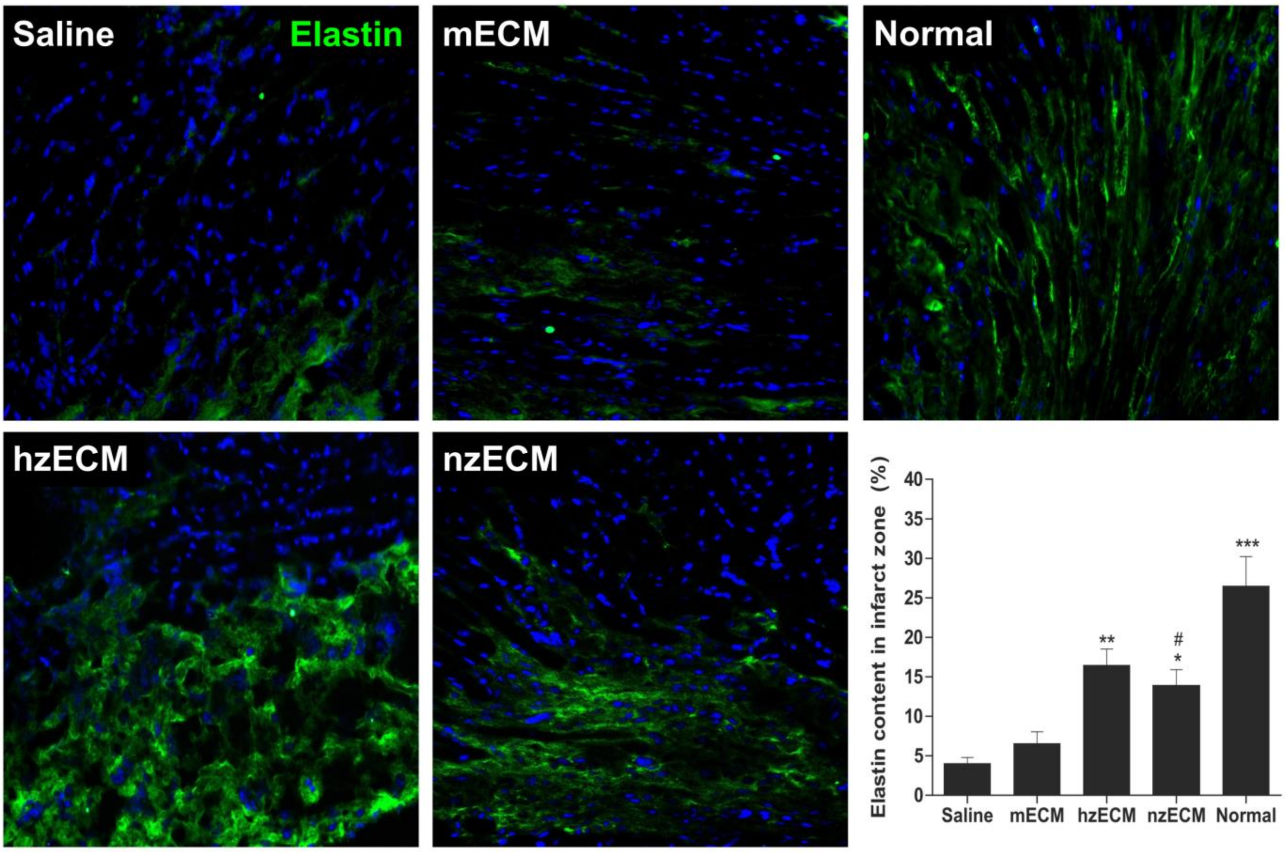

fig. S5. Analysis of elastin within the infarct zone in zECM-treated hearts. Representative images show anti-elastin immunostaining (elastin in green and DAPI in blue) at the infarct zone in normal, saline control, mECM-, hzECM-, and nzECM-treated hearts. Quantification of the elastin content at the infarct zone indicates significantly more elastin is preserved in both hzECM- and nzECM-treated hearts. *p<0.05, **p<0.01, ***p<0.001, compared to saline and mECM. All quantitative data represent means ± SD.

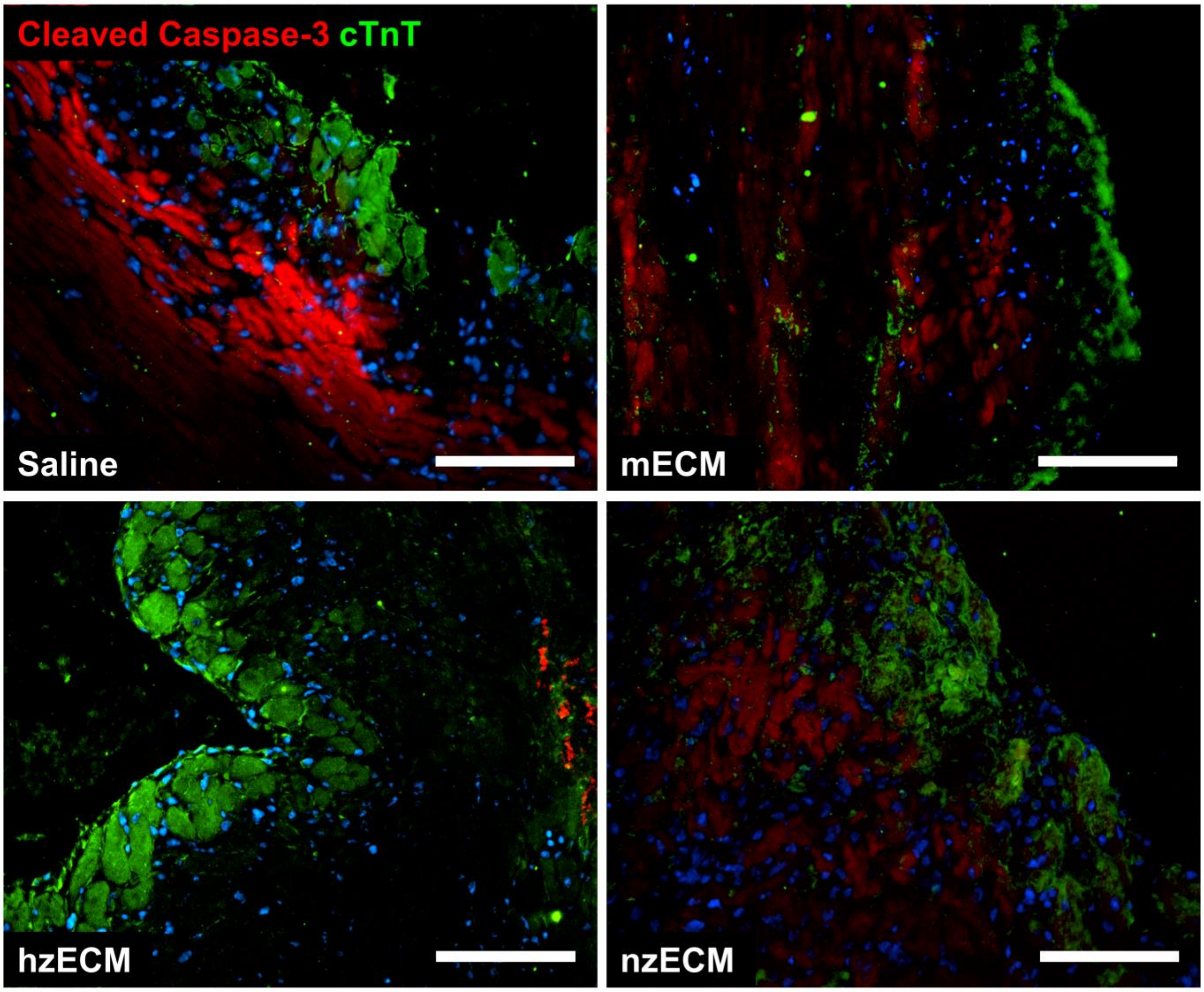

fig. S6. Cardiomyocyte apoptosis. Dual immunofluorescent detection of cleaved caspase-3+/cTnT+ apoptotic cardiomyocytes at 3 days post-MI at the infarct area (cleaved caspase-3 in red, cTnT in green, and DAPI in blue; scale bars = 100 μm).

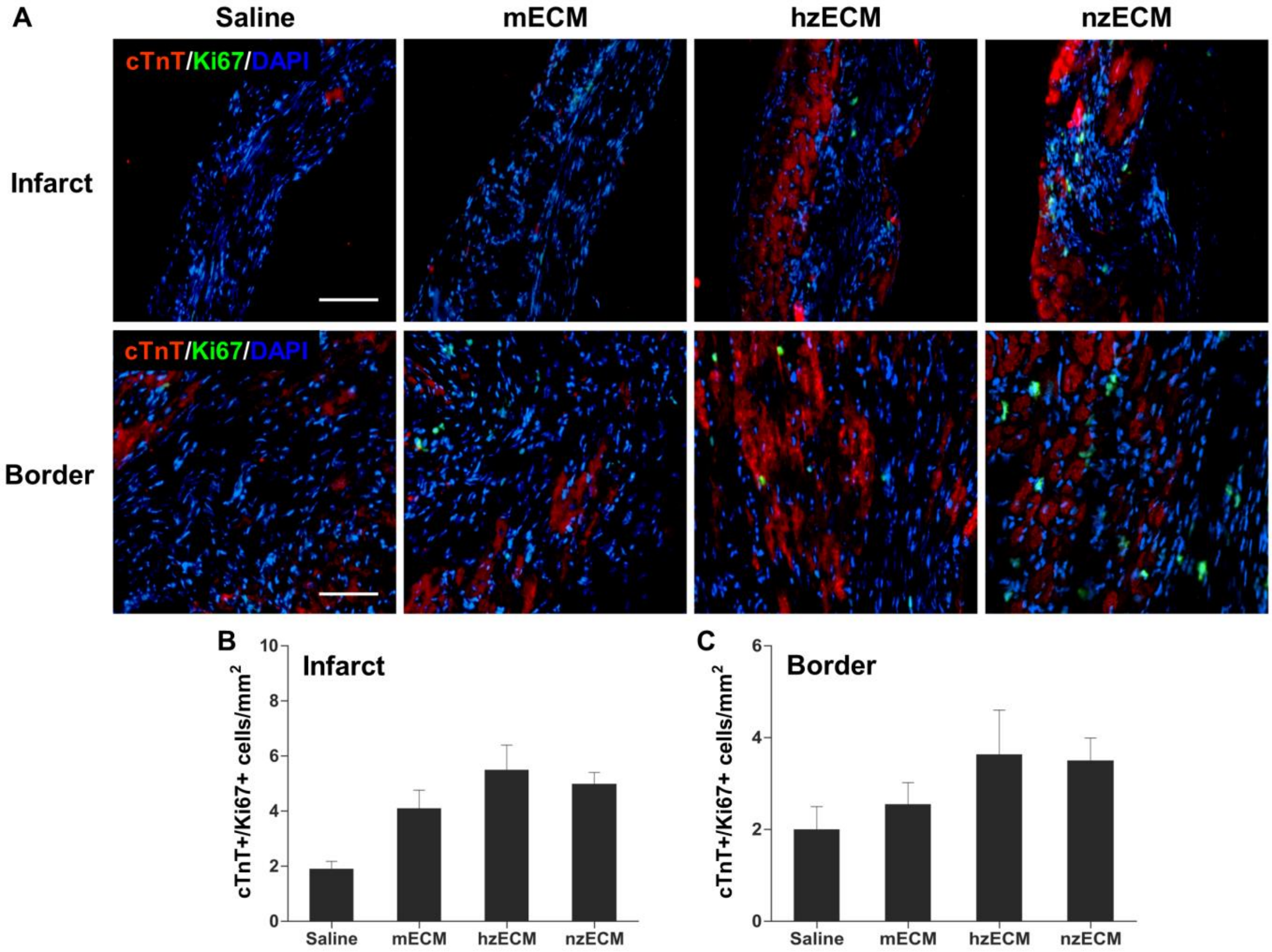

fig. S7. Cardiomyocyte proliferation at 6 weeks after MI. (**A**) Dual immunofluorescent detection of cTnT+/Ki67+ cardiomyocytes at 6 weeks post-MI at the mid-infarct level of mouse left ventricles (scale bars = 50 μm). Quantification of cTnT+/Ki67+ cardiomyocytes at the (**B**) infarct and (**C**) peri-infarct border zone. All $p>0.05$. All quantitative data represent means ± SD.

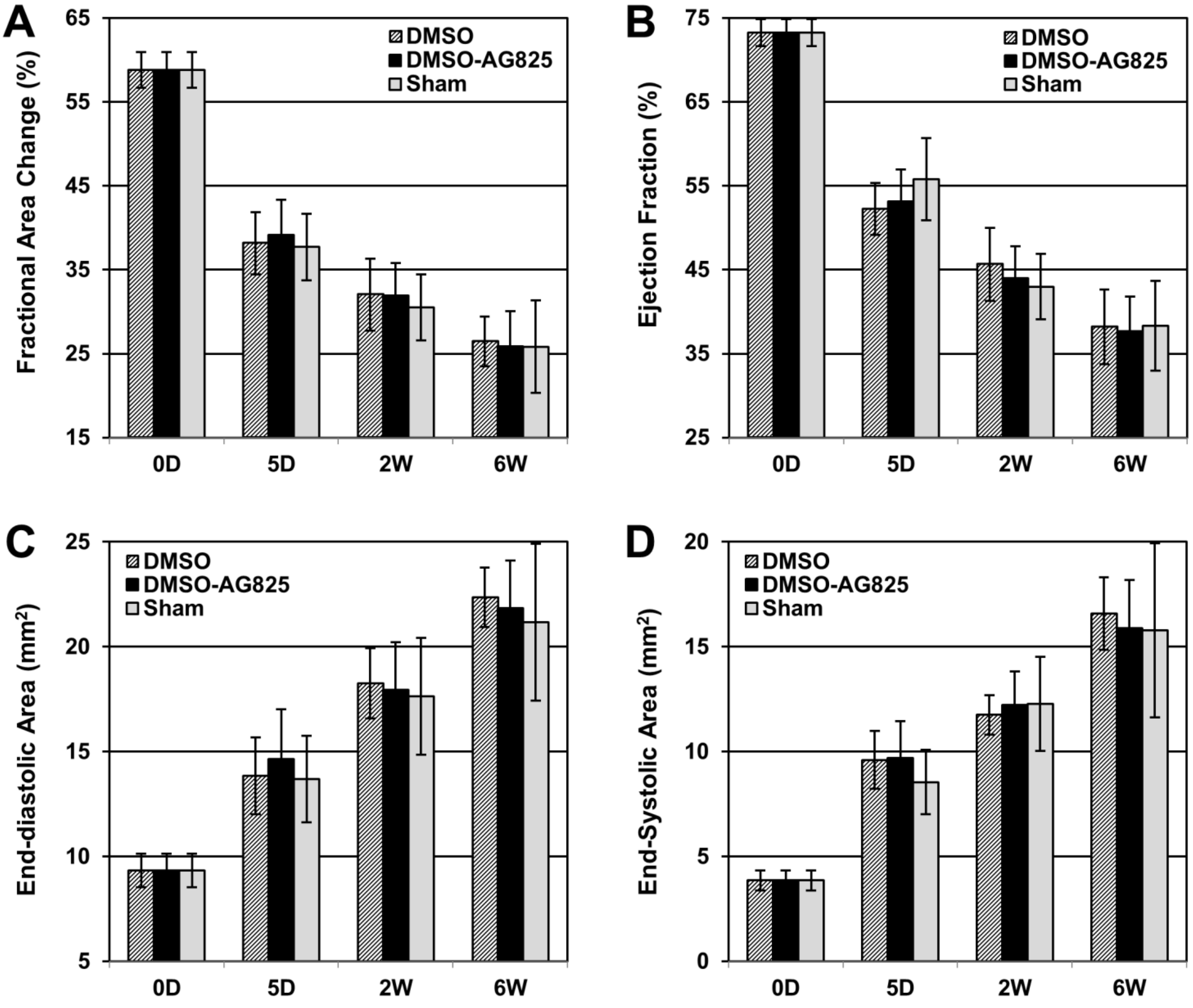

fig. S8. Echocardiographic analysis of cardiac function in control mice receiving myocardial saline injections and an intraperitoneal sham or DMSO injection with or without the ErbB2 inhibitor AG825 after AMI. When compared with the DMSO-AG825 or sham group, the DMSO group exhibited no significant difference at all time points over the course of 6 weeks in (**A**) fractional area change, (**B**) ejection fraction, (**C**) end-diastolic area, and (**D**) end-systolic area (N=4 per group, all $p>0.05$). Please note that the DMSO-AG825 group is equivalent to the Saline control group in Fig. 8.

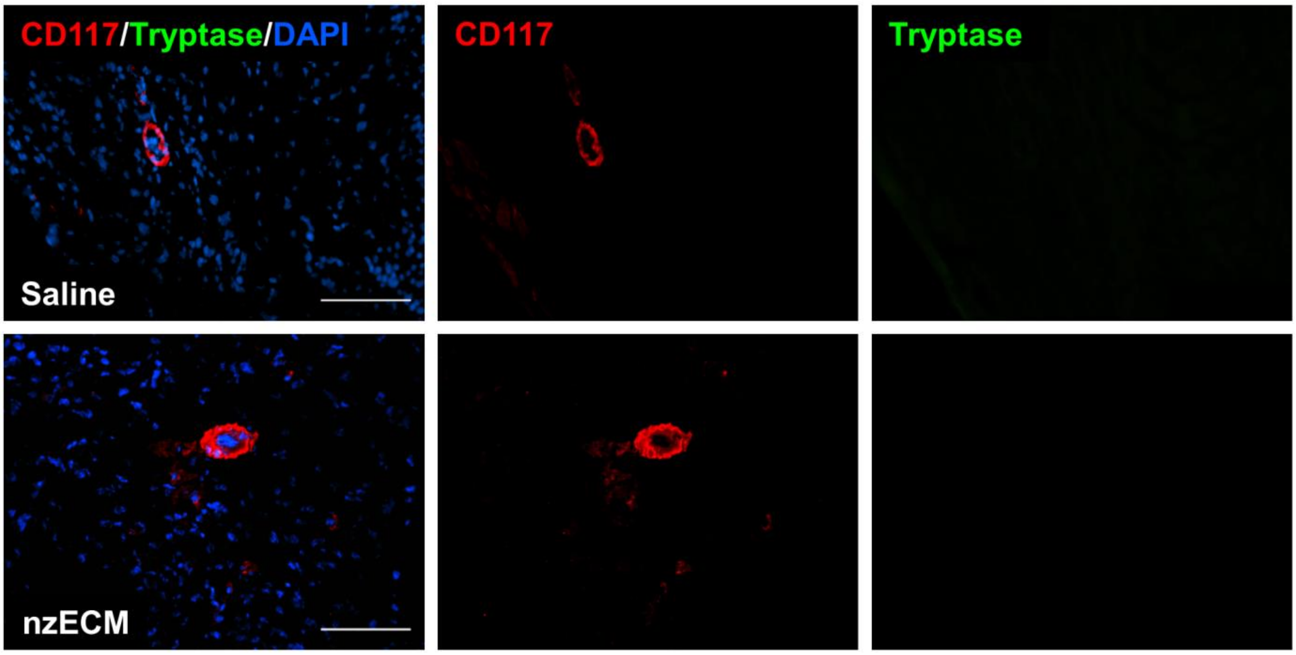

fig. S9. c-kit$^+$ cells do not express mast cell marker tryptase. Dual immunofluorescent detection of c-kit (CD117) and tryptase at 3 days post-MI showed no c-kit+ cells expressing tryptase in zECM and control groups (CD117 in red, tryptase in green, and DAPI in blue; scale bars = 100 μm).

Supplemental Table S1_Danre

Identified Protein	Gene Name	Accession #	MW	nzEC M-1	nzEC M-2	hzEC M-1	hzEC M-2
143BA_DANRE 14-3-3 protein beta/alpha-A GN=ywhaba	ywhaba	Q5PRD0	28 kDa	88% (88%)		64% (64%)	100% (100%)
A2ARG7_DANRE Uncharacterized protein OS=Danio rerio GN=atp5ib PE=4 SV=2	atp5ib	A2ARG7	8 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
A3KPR4_DANRE Histone H4 OS=Danio rerio GN=wu:fe37d09 PE=3 SV=1	wu:fe37d09	A3KPR4 (+2)	11 kDa	100% (100%)	100% (100%)	100% (100%)	62% (62%)
A4VAK4_DANRE Heat shock protein 1 OS=Danio rerio GN=hspb1 PE=2 SV=1	GN=hspb1	A4VAK4 (+1)	22 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
A8BBI6_DANRE Lrrc15 (Fragment) OS=Danio rerio GN=lrrc15 PE=2 SV=1	GN=lrrc15	A8BBI6	58 kDa	91% (91%)	81% (81%)	100% (100%)	52% (52%)
A8E5I7_DANRE Voltage-dependent anion channel 3 OS=Danio rerio GN=vdac3 PE=2 SV=1	vdac3	A8E5I7 (+2)	30 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
A8WG85_DANRE Ckmt2 protein OS=Danio rerio GN=ckmt2 PE=2 SV=1	ckmt2	A8WG85 (+1)	46 kDa	96% (96%)	66% (66%)	100% (100%)	68% (68%)
A8WGC6_DANRE ATP synthase subunit beta OS=Danio rerio GN=atp5b PE=2 SV=1	atp5b	A8WGC6	55 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
A9C3Q4_DANRE Uncharacterized protein OS=Danio rerio GN=atp2a2a PE=2 SV=1	atp2a2a	A9C3Q4 (+2)	115 kDa	100% (100%)			76% (76%)
A9JT52_DANRE Acadvl protein OS=Danio rerio GN=acadvl PE=2 SV=1	acadvl	A9JT52 (+2)	71 kDa	98% (98%)	100% (100%)	56% (56%)	80% (80%)
B0R0F7_DANRE Uncharacterized protein OS=Danio rerio GN=cmlc1 PE=2 SV=1	cmlc1	B0R0F7	22 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
B0R0K9_DANRE Uncharacterized protein OS=Danio rerio GN=si:ch211-103n10.5 PE=4 SV=1	si:ch211-103n10.5	B0R0K9	19 kDa			99% (99%)	81% (81%)
B3DFS9_DANRE Myosin, heavy polypeptide 11, smooth muscle OS=Danio rerio GN=myh11a PE=2 SV=1	myh11a	B3DFS9 (+1)	228 kDa				99% (99%)
B3DJP9_DANRE Myosin, heavy polypeptide 6, cardiac muscle, alpha OS=Danio rerio GN=myh6 PE=2 SV=1	myh6	B3DJP9	223 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
CHCH6_DANRE Coiled-coil-helix-coiled-coil-helix domain-containing protein 6, mitochondrial OS=Danio rerio GN=chchd6 PE=2 SV=1	chchd6	Q63ZW2	28 kDa	100% (100%)	100% (100%)	98% (98%)	100% (100%)
COX2_DANRE Cytochrome c oxidase subunit 2 OS=Danio rerio GN=mt-co2 PE=3 SV=1	mt-co2	Q9MIY7	26 kDa	100% (100%)	100% (100%)	70% (70%)	100% (100%)
E7EZX1_DANRE Histone H2A OS=Danio rerio GN=CR762436.4 PE=3 SV=1	CR762436.4	E7EZX1 (+4)	14 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
E7F1L7_DANRE Uncharacterized protein OS=Danio rerio GN=CU302436.1 PE=4 SV=1	CU302436.1	E7F1L7	292 kDa		51% (51%)	100% (100%)	100% (100%)

E7F5J9_DANRE Uncharacterized protein OS=Danio rerio GN=tnni1b PE=4 SV=1	tnni1b	E7F5J9 (+2)	21 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
E7FAV6_DANRE Uncharacterized protein OS=Danio rerio GN=LOC564077 PE=4 SV=1	LOC564077	E7FAV6	57 kDa	100% (100%)	100% (100%)	54% (54%)	100% (100%)
E7FES0_DANRE Uncharacterized protein OS=Danio rerio PE=4 SV=1		E7FES0	30 kDa	100% (100%)		98% (98%)	97% (97%)
E9QCD1_DANRE Uncharacterized protein OS=Danio rerio GN=fga PE=2 SV=1	fga	E9QCD1	50 kDa			100% (100%)	100% (100%)
E9QCG6_DANRE Uncharacterized protein OS=Danio rerio GN=col1a2 PE=2 SV=1	colla2	E9QCG6 (+1)	127 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
E9QG44_DANRE Uncharacterized protein OS=Danio rerio PE=3 SV=1		E9QG44	17 kDa		73% (73%)	78% (78%)	100% (100%)
E9QGR6_DANRE Uncharacterized protein OS=Danio rerio GN=tmod1 PE=4 SV=1	tmod1	E9QGR6	40 kDa		100% (100%)		
F1Q615_DANRE Uncharacterized protein OS=Danio rerio GN=mybpc3 PE=2 SV=1	mybpc3	F1Q615	144 kDa	55% (55%)	100% (100%)		99% (99%)
F1Q766_DANRE Uncharacterized protein OS=Danio rerio GN=zgc:56085 PE=2 SV=1	zgc:56085	F1Q766	47 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
F1Q9A0_DANRE Uncharacterized protein (Fragment) OS=Danio rerio GN=sorbs2a PE=4 SV=1	sorbs2a	F1Q9A0	141 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
F1QBP1_DANRE Uncharacterized protein OS=Danio rerio GN=myoz2b PE=4 SV=1	myoz2b	F1QBP1	29 kDa	100% (100%)	89% (89%)	100% (100%)	100% (100%)
F1QDL1_DANRE Uncharacterized protein OS=Danio rerio GN=col1a1b PE=4 SV=1	col1a1b	F1QDL1 (+1)	137 kDa	100% (100%)	76% (76%)	95% (95%)	100% (100%)
F1QG64_DANRE Histone H2B OS=Danio rerio GN=zgc:112234 PE=3 SV=1	zgc:112234	F1QG64	15 kDa	100% (100%)	98% (98%)	100% (100%)	100% (100%)
F1QJ99_DANRE Uncharacterized protein (Fragment) OS=Danio rerio GN=cox5ab PE=2 SV=1	cox5ab	F1QJ99 (+1)	17 kDa	100% (100%)	100% (100%)	100% (100%)	61% (61%)
F1QJK4_DANRE Uncharacterized protein OS=Danio rerio GN=si:ch211-150d5.2 PE=4 SV=2	si:ch211-150d5.2	F1QJK4	196 kDa				100% (100%)
F1QKG7_DANRE Uncharacterized protein OS=Danio rerio GN=tpm4a PE=2 SV=1	tpm4a	F1QKG7	33 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
F1QSE1_DANRE Uncharacterized protein OS=Danio rerio GN=vmhcl PE=2 SV=1	vmhcl	F1QSE1 (+1)	223 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
F1R3F7_DANRE Uncharacterized protein OS=Danio rerio GN=si:ch1073-329n19.2 PE=4 SV=1	si:ch1073-329n19.2	F1R3F7 (+1)	30 kDa	100% (100%)	100% (100%)	68% (68%)	85% (85%)
F1R446_DANRE Uncharacterized protein OS=Danio rerio GN=spna2 PE=2 SV=1	spna2	F1R446	285 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
F1R6I1_DANRE Uncharacterized protein (Fragment) OS=Danio rerio	LOC402880	F1R6I1	20	100%	100%	100%	100%

GN=LOC402880 PE=4 SV=1		(+1)	kDa	(100%)	(100%)	(100%)	(100%)
F1R8U0_DANRE Uncharacterized protein OS=Danio rerio GN=zgc:153629 PE=3 SV=1	zgc:153629	F1R8U0 (+1)	48 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
F1R8W3_DANRE Uncharacterized protein OS=Danio rerio GN=desma PE=2 SV=1	desma	F1R8W3	56 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
F1RBH3_DANRE Uncharacterized protein OS=Danio rerio GN=chchd6b PE=4 SV=1	chchd6b	F1RBH3 (+1)	26 kDa	100% (100%)			51% (51%)
H9GYI1_DANRE Uncharacterized protein (Fragment) OS=Danio rerio GN=zgc:101560 PE=4 SV=1	zgc:101560	H9GYI1	21 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
HBB2_DANRE Hemoglobin subunit beta-2 OS=Danio rerio GN=ba2 PE=1 SV=3	ba2	Q90485	16 kDa	60% (60%)		100% (100%)	100% (100%)
K2C8_DANRE Keratin, type II cytoskeletal 8 OS=Danio rerio GN=krt8 PE=1 SV=1	krt8	Q6NWF6	58 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
LAMC1_DANRE Laminin subunit gamma-1 OS=Danio rerio GN=lamc1 PE=2 SV=2	lamc1	Q1LVF0	176 kDa	100% (100%)	100% (100%)	88% (88%)	100% (100%)
MYG_DANRE Myoglobin OS=Danio rerio GN=mb PE=2 SV=3	mb	Q6VN46	16 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q08BA1_DANRE ATP synthase subunit alpha OS=Danio rerio GN=atp5a1 PE=2 SV=1	atp5a1	Q08BA1	60 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q1RLV5_DANRE Uncharacterized protein (Fragment) OS=Danio rerio GN=slmapa PE=2 SV=1	slmapa	Q1RLV5	50 kDa			64% (64%)	100% (100%)
Q2YDR5_DANRE Actinin, alpha 2 OS=Danio rerio GN=actn2 PE=2 SV=1	actn2	Q2YDR5	103 kDa	100% (100%)			47% (47%)
Q3YAA0_DANRE Integrin beta OS=Danio rerio GN=itgb1b PE=2 SV=1	itgb1b	Q3YAA0	88 kDa	100% (100%)	75% (75%)		100% (100%)
Q4JHL7_DANRE Voltage-dependent anion channel 2 OS=Danio rerio GN=vdac2 PE=2 SV=1	vdac2	Q4JHL7 (+1)	30 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q4VBU7_DANRE Cytochrome c oxidase subunit Vaa OS=Danio rerio GN=cox5aa PE=2 SV=1	cox5aa	Q4VBU7	16 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q4VBV1_DANRE Cytochrome b-c1 complex subunit 7 OS=Danio rerio GN=uqcrb PE=3 SV=1	uqcrb	Q4VBV1	13 kDa	100% (100%)	100% (100%)	99% (99%)	80% (80%)
Q58XP5_DANRE Fibronectin 1b OS=Danio rerio GN=fn1b PE=2 SV=1	fn1b	Q58XP5	276 kDa				100% (100%)
Q5BJA2_DANRE Uncharacterized protein OS=Danio rerio GN=ndufa5 PE=4 SV=1	ndufa5	Q5BJA2	13 kDa	100% (100%)	51% (51%)	100% (100%)	100% (100%)
Q68EI6_DANRE Cyc1 protein (Fragment) OS=Danio rerio GN=cyc1 PE=2 SV=1	cyc1	Q68EI6	33 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q6DEH8_DANRE Uncharacterized protein OS=Danio rerio GN=sh3bgr PE=2 SV=1	sh3bgr	Q6DEH8	21 kDa	98% (98%)	94% (94%)		100% (100%)

Q6DGK4_DANRE Zgc:92880 OS=Danio rerio GN=zgc:92880 PE=2 SV=1	zgc:92880	Q6DGK4 (+1)	16 kDa			95% (95%)	100% (100%)
Q6DRD1_DANRE ATP synthase oligomycin sensitivity conferral protein OS=Danio rerio GN=atp5o PE=2 SV=1	atp5o	Q6DRD1	22 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q6IQ59_DANRE Ubiquinol-cytochrome c reductase core protein II OS=Danio rerio GN=uqcrc2b PE=2 SV=1	uqcrc2b	Q6IQ59	48 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q6IQR3_DANRE Actin, alpha, cardiac muscle 1a OS=Danio rerio GN=actc1a PE=2 SV=1	actc1a	Q6IQR3	42 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q6NSN3_DANRE Ubiquinol-cytochrome c reductase core protein I OS=Danio rerio GN=uqcrc1 PE=2 SV=1	uqcrc1	Q6NSN3 (+1)	52 kDa	98% (98%)	98% (98%)	98% (98%)	100% (100%)
Q6NYE1_DANRE Fibrinogen, B beta polypeptide OS=Danio rerio GN=fgb PE=2 SV=1	fgb	Q6NYE1	54 kDa			100% (100%)	100% (100%)
Q6NYV3_DANRE Uncharacterized protein OS=Danio rerio GN=h1f0 PE=2 SV=1	h1f0	Q6NYV3	21 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q6P0T0_DANRE NADH dehydrogenase (Ubiquinone) Fe-S protein 8, (NADH-coenzyme Q reductase) OS=Danio rerio GN=ndufs8a PE=2 SV=1	ndufs8a	Q6P0T0	24 kDa	100% (100%)	100% (100%)	84% (84%)	92% (92%)
Q6PC77_DANRE ATP synthase, H+ transporting, mitochondrial F0 complex, subunit d OS=Danio rerio GN=atp5h PE=2 SV=1	atp5h	Q6PC77	18 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q6PEI6_DANRE Aconitase 2, mitochondrial OS=Danio rerio GN=aco2 PE=2 SV=1	aco2	Q6PEI6	85 kDa	100% (100%)	100% (100%)	81% (81%)	100% (100%)
Q6PFS4_DANRE Inner membrane protein, mitochondrial (Mitofilin) OS=Danio rerio GN=immt PE=2 SV=1	immt	Q6PFS4	83 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q6TNQ9_DANRE Succinate dehydrogenase complex, subunit A, flavoprotein (Fp) OS=Danio rerio GN=sdha PE=2 SV=1	sdha	Q6TNQ9	73 kDa	54% (54%)	100% (100%)	73% (73%)	97% (97%)
Q6VYM3_DANRE Natriuretic peptide OS=Danio rerio GN=nppa PE=3 SV=1	nppa	Q6VYM3	12 kDa			79% (79%)	100% (100%)
Q6ZM23_DANRE Uncharacterized protein OS=Danio rerio GN=cox6c PE=2 SV=1	cox6c	Q6ZM23	8 kDa	98% (98%)	100% (100%)	100% (100%)	100% (100%)
Q7T3F0_DANRE Tropomyosin 4 OS=Danio rerio GN=tpm4a PE=2 SV=1	tpm4a	Q7T3F0	29 kDa	57% (57%)	85% (85%)		100% (100%)
Q7ZSY4_DANRE Cardiac troponin T OS=Danio rerio GN=tnnt2a PE=2 SV=1	tnnt2a	Q7ZSY4 (+2)	34 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q7ZUP6_DANRE Isocitrate dehydrogenase [NADP] OS=Danio rerio GN=idh2 PE=2 SV=1	idh2	Q7ZUP6	50 kDa	100% (100%)	100% (100%)	61% (61%)	100% (100%)
Q7ZVG7_DANRE Fibrinogen, gamma polypeptide OS=Danio rerio GN=fgg PE=2 SV=1	fgg	Q7ZVG7	49 kDa			100% (100%)	100% (100%)
Q7ZVX2_DANRE ATPase, Na+\/K+ transporting, beta 1a polypeptide OS=Danio rerio GN=atp1b1a PE=2 SV=1	atp1b1a	Q7ZVX2	35 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q7ZYY3_DANRE Heat shock protein 9 OS=Danio rerio GN=hspa9 PE=2	hspa9	Q7ZYY3	74	91%			100%

SV=1			kDa	(91%)			(100%)
Q800V7_DANRE Cardiac troponin C OS=Danio rerio GN=tnnc1a PE=2 SV=1	tnnc1a	Q800V7	18 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q801M3_DANRE Myosin light chain 2 Mlc2a OS=Danio rerio GN=myl7 PE=2 SV=1	myl7	Q801M3	19 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q803B0_DANRE Heat shock 60kD protein 1 (Chaperonin) OS=Danio rerio GN=hspd1 PE=2 SV=1	hspd1	Q803B0	61 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q804G9_DANRE Annexin OS=Danio rerio GN=anxa2a PE=2 SV=1	anxa2a	Q804G9	38 kDa			100% (100%)	100% (100%)
Q8JHI0_DANRE Solute carrier family 25 alpha, member 5 OS=Danio rerio GN=slc25a5 PE=2 SV=1	slc25a5	Q8JHI0	33 kDa	100% (100%)	100% (100%)	100% (100%)	100% (100%)
Q9DGL6_DANRE ATPase, Na+/K+ transporting, alpha 1 polypeptide OS=Danio rerio GN=atp1a1 PE=2 SV=1	atp1a1	Q9DGL6	113 kDa	97% (97%)	100% (100%)		100% (100%)
Q9PTR4_DANRE Alpha-cardiac actin OS=Danio rerio GN=actc1a PE=2 SV=1	actc1a	Q9PTR4	42 kDa			100% (100%)	
Q9W6T5_DANRE Lamin B2 OS=Danio rerio GN=lmnb2 PE=2 SV=1	lmnb2	Q9W6T5	66 kDa		99% (99%)	100% (100%)	100% (100%)

Note: The percentage in the table indicates the identification probability of the specified protein.

Supplemental Table S2_Mouse

Identified Protein	Gene Name	Accession #	MW	mECM-1	mECM-2
A2A513_MOUSE Keratin, type I cytoskeletal 10 OS=Mus musculus GN=Krt10 PE=3 SV=1	Krt10	A2A513 (+3)	57 kDa	100% (100%)	100% (100%)
A3KGU7_MOUSE Spectrin alpha chain, non-erythrocytic 1 OS=Mus musculus GN=Sptan1 PE=2 SV=1	Sptan1	A3KGU7 (+1)	285 kDa	100% (100%)	48% (48%)
ACADV_MOUSE Very long-chain specific acyl-CoA dehydrogenase, mitochondrial OS=Mus musculus GN=Acadvl PE=1 SV=3	Acadvl	P50544	71 kDa	67% (67%)	100% (100%)
ACON_MOUSE Aconitate hydratase, mitochondrial OS=Mus musculus GN=Aco2 PE=1 SV=1	Aco2	Q99KI0	85 kDa		100% (100%)
ACTN2_MOUSE Alpha-actinin-2 OS=Mus musculus GN=Actn2 PE=1 SV=2	Actn2	Q9JI91	104 kDa	100% (100%)	100% (100%)
ACTS_MOUSE Actin, alpha skeletal muscle OS=Mus musculus GN=Acta1 PE=1 SV=1	Acta1	P68134	42 kDa	100% (100%)	95% (95%)
ADT1_MOUSE ADP/ATP translocase 1 OS=Mus musculus GN=Slc25a4 PE=1 SV=4	Slc25a4	P48962	33 kDa	100% (100%)	100% (100%)
ALBU_MOUSE Serum albumin OS=Mus musculus GN=Alb PE=1 SV=3	Alb	P07724	69 kDa	100% (100%)	100% (100%)
ANXA2_MOUSE Annexin A2 OS=Mus musculus GN=Anxa2 PE=1 SV=2	Anxa2	P07356	39 kDa		100% (100%)
AT1A1_MOUSE Sodium/potassium-transporting ATPase subunit alpha-1 OS=Mus musculus GN=Atp1a1 PE=1 SV=1	Atp1a1	Q8VDN2	113 kDa	100% (100%)	100% (100%)
AT1B1_MOUSE Sodium/potassium-transporting ATPase subunit beta-1 OS=Mus musculus GN=Atp1b1 PE=1 SV=1	Atp1b1	P14094	35 kDa	84% (84%)	100% (100%)
ATP5I_MOUSE ATP synthase subunit e, mitochondrial OS=Mus musculus GN=Atp5i PE=1 SV=2	Atp5i	Q06185	8 kDa	91% (91%)	100% (100%)
ATPA_MOUSE ATP synthase subunit alpha, mitochondrial OS=Mus musculus GN=Atp5a1 PE=1 SV=1	Atp5a1	Q03265	60 kDa	100% (100%)	100% (100%)
ATPB_MOUSE ATP synthase subunit beta, mitochondrial OS=Mus musculus GN=Atp5b PE=1 SV=2	Atp5b	P56480	56 kDa	100% (100%)	100% (100%)

ATPD_MOUSE ATP synthase subunit delta, mitochondrial OS=Mus musculus GN=Atp5d PE=1 SV=1	Atp5d	Q9D3D9	18 kDa	96% (96%)	100% (100%)
ATPO_MOUSE ATP synthase subunit O, mitochondrial OS=Mus musculus GN=Atp5o PE=1 SV=1	Atp5o	Q9DB20	23 kDa	100% (100%)	100% (100%)
B1ASQ2_MOUSE Apolipoprotein O OS=Mus musculus GN=Apoo PE=4 SV=1	Apoo	B1ASQ2 (+1)	23 kDa	38% (38%)	100% (100%)
B1B0C7_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein OS=Mus musculus GN=Hspg2 PE=2 SV=1	Hspg2	B1B0C7 (+1)	469 kDa	49% (49%)	100% (100%)
CALX_MOUSE Calnexin OS=Mus musculus GN=Canx PE=1 SV=1	Canx	P35564	67 kDa		100% (100%)
CAV1_MOUSE Caveolin-1 OS=Mus musculus GN=Cav1 PE=1 SV=1	Cav1	P49817	21 kDa	100% (100%)	100% (100%)
CD36_MOUSE Platelet glycoprotein 4 OS=Mus musculus GN=Cd36 PE=1 SV=2	Cd36	Q08857	53 kDa	100% (100%)	100% (100%)
CH60_MOUSE 60 kDa heat shock protein, mitochondrial OS=Mus musculus GN=Hspd1 PE=1 SV=1	Hspd1	P63038	61 kDa		100% (100%)
CHCH3_MOUSE Coiled-coil-helix-coiled-coil-helix domain-containing protein 3, mitochondrial OS=Mus musculus GN=Chchd3 PE=1 SV=1	Chchd3	Q9CRB9	26 kDa	100% (100%)	100% (100%)
CISY_MOUSE Citrate synthase, mitochondrial OS=Mus musculus GN=Cs PE=1 SV=1	Cs	Q9CZU6	52 kDa	41% (41%)	100% (100%)
CO1A1_MOUSE Collagen alpha-1(I) chain OS=Mus musculus GN=Col1a1 PE=1 SV=4	Col1a1	P11087	138 kDa	100% (100%)	100% (100%)
CO1A2_MOUSE Collagen alpha-2(I) chain OS=Mus musculus GN=Col1a2 PE=2 SV=2	Col1a2	Q01149	130 kDa	100% (100%)	100% (100%)
CO6A2_MOUSE Collagen alpha-2(VI) chain OS=Mus musculus GN=Col6a2 PE=2 SV=3	Col6a2	Q02788	110 kDa	100% (100%)	54% (54%)
COX2_MOUSE Cytochrome c oxidase subunit 2 OS=Mus musculus GN=Mtco2 PE=1 SV=1	Mtco2	P00405 (+1)	26 kDa	100% (100%)	100% (100%)
COX41_MOUSE Cytochrome c oxidase subunit 4 isoform 1, mitochondrial OS=Mus musculus GN=Cox4i1 PE=1 SV=2	Cox4i1	P19783	20 kDa	100% (100%)	100% (100%)

COX5A_MOUSE Cytochrome c oxidase subunit 5A, mitochondrial OS=Mus musculus GN=Cox5a PE=1 SV=2	Cox5a	P12787	16 kDa	100% (100%)	100% (100%)
CRYAB_MOUSE Alpha-crystallin B chain OS=Mus musculus GN=Cryab PE=1 SV=2	Cryab	P23927	20 kDa	100% (100%)	100% (100%)
CX6B1_MOUSE Cytochrome c oxidase subunit 6B1 OS=Mus musculus GN=Cox6b1 PE=1 SV=2	Cox6b1	P56391	10 kDa	100% (100%)	95% (95%)
CY1_MOUSE Cytochrome c1, heme protein, mitochondrial OS=Mus musculus GN=Cyc1 PE=1 SV=1	Cyc1	Q9D0M3	35 kDa	100% (100%)	100% (100%)
D3YYT0_MOUSE Cadherin-2 OS=Mus musculus GN=Cdh2 PE=2 SV=1	Cdh2	D3YYT0 (+1)	94 kDa	100% (100%)	100% (100%)
DESM_MOUSE Desmin OS=Mus musculus GN=Des PE=1 SV=3	Des	P31001	53 kDa	100% (100%)	100% (100%)
DHSA_MOUSE Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial OS=Mus musculus GN=Sdha PE=1 SV=1	Sdha	Q8K2B3	73 kDa	100% (100%)	100% (100%)
DHSB_MOUSE Succinate dehydrogenase [ubiquinone] iron-sulfur subunit, mitochondrial OS=Mus musculus GN=Sdhb PE=1 SV=1	Sdhb	Q9CQA3	32 kDa	100% (100%)	100% (100%)
DPEP1_MOUSE Dipeptidase 1 OS=Mus musculus GN=Dpep1 PE=1 SV=2	Dpep1	P31428	46 kDa	39% (39%)	100% (100%)
E9Q1X8_MOUSE Voltage-dependent calcium channel subunit alpha-2/delta-1 OS=Mus musculus GN=Cacna2d1 PE=2 SV=2	Cacna2d1	E9Q1X8 (+5)	123 kDa	100% (100%)	76% (76%)
E9Q800_MOUSE Mitochondrial inner membrane protein OS=Mus musculus GN=Immt PE=2 SV=1	Immt	E9Q800	76 kDa	100% (100%)	100% (100%)
ECHA_MOUSE Trifunctional enzyme subunit alpha, mitochondrial OS=Mus musculus GN=Hadha PE=1 SV=1	Hadha	Q8BMS1	83 kDa	100% (100%)	100% (100%)
ECHB_MOUSE Trifunctional enzyme subunit beta, mitochondrial OS=Mus musculus GN=Hadhb PE=1 SV=1	Hadhb	Q99JY0	51 kDa	100% (100%)	100% (100%)
F6QYE1_MOUSE Calsequestrin OS=Mus musculus GN=Casq2 PE=2 SV=1	Casq2	F6QYE1 (+1)	48 kDa	100% (100%)	100% (100%)
F8VQJ3_MOUSE Laminin subunit gamma-1 OS=Mus musculus GN=Lamc1 PE=2 SV=1	Lamc1	F8VQJ3	177 kDa	100% (100%)	100% (100%)

F8WHP8_MOUSE ATP synthase subunit f, mitochondrial OS=Mus musculus GN=Atp5j2 PE=2 SV=1	Atp5j2	F8WHP8	9 kDa	100% (100%)	69% (69%)
F8WIT2_MOUSE Annexin OS=Mus musculus GN=Anxa6 PE=2 SV=1	Anxa6	F8WIT2 (+1)	75 kDa	100% (100%)	100% (100%)
G3UX26_MOUSE Voltage-dependent anion-selective channel protein 2 (Fragment) OS=Mus musculus GN=Vdac2 PE=4 SV=1	Vdac2	G3UX26 (+1)	30 kDa		100% (100%)
G3X8R0_MOUSE Receptor accessory protein 5, isoform CRA_a OS=Mus musculus GN=Reep5 PE=4 SV=1	Reep5	G3X8R0	21 kDa	57% (57%)	100% (100%)
G3X9L6_MOUSE MCG55033 OS=Mus musculus GN=Gm10250 PE=4 SV=1	Gm10250	G3X9L6 (+1)	19 kDa	100% (100%)	100% (100%)
H14_MOUSE Histone H1.4 OS=Mus musculus GN=Hist1h1e PE=1 SV=2	Hist1h1e	P43274	22 kDa	100% (100%)	100% (100%)
HBB1_MOUSE Hemoglobin subunit beta-1 OS=Mus musculus GN=Hbb-b1 PE=1 SV=2	Hbb-b1	P02088	16 kDa	100% (100%)	100% (100%)
HSPB1_MOUSE Heat shock protein beta-1 OS=Mus musculus GN=Hspb1 PE=1 SV=3	Hspb1	P14602 (+1)	23 kDa	100% (100%)	67% (67%)
IDH3A_MOUSE Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial OS=Mus musculus GN=Idh3a PE=1 SV=1	Idh3a	Q9D6R2	40 kDa	40% (40%)	100% (100%)
ITB1_MOUSE Integrin beta-1 OS=Mus musculus GN=Itgb1 PE=1 SV=1	Itgb1	P09055	88 kDa	100% (100%)	100% (100%)
J3QQ13_MOUSE Troponin T, cardiac muscle OS=Mus musculus GN=Tnnt2 PE=2 SV=1	Tnnt2	J3QQ13 (+7)	36 kDa	100% (100%)	100% (100%)
K1C42_MOUSE Keratin, type I cytoskeletal 42 OS=Mus musculus GN=Krt42 PE=1 SV=1	Krt42	Q6IFX2	50 kDa	100% (100%)	100% (100%)
K22E_MOUSE Keratin, type II cytoskeletal 2 epidermal OS=Mus musculus GN=Krt2 PE=1 SV=1	Krt2	Q3TTY5	71 kDa	100% (100%)	100% (100%)
K2C1_MOUSE Keratin, type II cytoskeletal 1 OS=Mus musculus GN=Krt1 PE=1 SV=4	Krt1	P04104	66 kDa	100% (100%)	100% (100%)
K2C5_MOUSE Keratin, type II cytoskeletal 5 OS=Mus musculus GN=Krt5 PE=1 SV=1	Krt5	Q922U2	62 kDa	100% (100%)	100% (100%)
K2C8_MOUSE Keratin, type II cytoskeletal 8 OS=Mus musculus GN=Krt8 PE=1 SV=4	Krt8	P11679	55 kDa	96% (96%)	100% (100%)

K3W4Q8_MOUSE Basigin OS=Mus musculus GN=Bsg PE=4 SV=1	Bsg	K3W4Q8 (+2)	24 kDa	100% (100%)	100% (100%)
KCRM_MOUSE Creatine kinase M-type OS=Mus musculus GN=Ckm PE=1 SV=1	Ckm	P07310	43 kDa	100% (100%)	100% (100%)
KCRS_MOUSE Creatine kinase S-type, mitochondrial OS=Mus musculus GN=Ckmt2 PE=1 SV=1	Ckmt2	Q6P8J7	47 kDa	100% (100%)	100% (100%)
KRT85_MOUSE Keratin, type II cuticular Hb5 OS=Mus musculus GN=Krt85 PE=2 SV=2	Krt85	Q9Z2T6	56 kDa	100% (100%)	
KT33B_MOUSE Keratin, type I cuticular Ha3-II OS=Mus musculus GN=Krt33b PE=2 SV=2	Krt33b	Q61897	46 kDa	100% (100%)	
LAMA2_MOUSE Laminin subunit alpha-2 OS=Mus musculus GN=Lama2 PE=1 SV=2	Lama2	Q60675	344 kDa	100% (100%)	
LAMB1_MOUSE Laminin subunit beta-1 OS=Mus musculus GN=Lamb1 PE=1 SV=3	Lamb1	P02469	197 kDa	100% (100%)	100% (100%)
LMNA_MOUSE Prelamin-A/C OS=Mus musculus GN=Lmna PE=1 SV=2	Lmna	P48678 (+1)	74 kDa	96% (96%)	100% (100%)
MLRV_MOUSE Myosin regulatory light chain 2, ventricular/cardiac muscle isoform OS=Mus musculus GN=Myl2 PE=1 SV=3	Myl2	P51667	19 kDa	100% (100%)	100% (100%)
MYH6_MOUSE Myosin-6 OS=Mus musculus GN=Myh6 PE=1 SV=2	Myh6	Q02566	224 kDa	100% (100%)	100% (100%)
MYH7_MOUSE Myosin-7 OS=Mus musculus GN=Myh7 PE=1 SV=1	Myh7	Q91Z83	223 kDa	100% (100%)	100% (100%)
MYH9_MOUSE Myosin-9 OS=Mus musculus GN=Myh9 PE=1 SV=4	Myh9	Q8VDD5	226 kDa	100% (100%)	100% (100%)
MYL3_MOUSE Myosin light chain 3 OS=Mus musculus GN=Myl3 PE=1 SV=4	Myl3	P09542	22 kDa	100% (100%)	100% (100%)
MYOZ2_MOUSE Myozenin-2 OS=Mus musculus GN=Myoz2 PE=1 SV=1	Myoz2	Q9JJW5	30 kDa	37% (37%)	100% (100%)
NDUA5_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 5 OS=Mus musculus GN=Ndufa5 PE=1 SV=3	Ndufa5	Q9CPP6	13 kDa	100% (100%)	

NDUB7_MOUSE NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 7 OS=Mus musculus GN=Ndufb7 PE=1 SV=3	Ndufb7	Q9CR61	16 kDa	74% (74%)	100% (100%)
NDUBA_MOUSE NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 10 OS=Mus musculus GN=Ndufb10 PE=1 SV=3	Ndufb10	Q9DCS9	21 kDa	100% (100%)	100% (100%)
NDUS1_MOUSE NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial OS=Mus musculus GN=Ndufs1 PE=1 SV=2	Ndufs1	Q91VD9	80 kDa	100% (100%)	100% (100%)
NDUS8_MOUSE NADH dehydrogenase [ubiquinone] iron-sulfur protein 8, mitochondrial OS=Mus musculus GN=Ndufs8 PE=1 SV=1	Ndufs8	Q8K3J1	24 kDa	100% (100%)	100% (100%)
NIPS2_MOUSE Protein NipSnap homolog 2 OS=Mus musculus GN=Gbas PE=2 SV=1	Gbas	O55126 (+1)	33 kDa		100% (100%)
PGS2_MOUSE Decorin OS=Mus musculus GN=Dcn PE=2 SV=1	Dcn	P28654	40 kDa	100% (100%)	100% (100%)
PHB_MOUSE Prohibitin OS=Mus musculus GN=Phb PE=1 SV=1	Phb	P67778	30 kDa	100% (100%)	100% (100%)
PTRF_MOUSE Polymerase I and transcript release factor OS=Mus musculus GN=Ptrf PE=1 SV=1	Ptrf	O54724	44 kDa	100% (100%)	100% (100%)
Q8R5L1_MOUSE Complement component 1 Q subcomponent-binding protein, mitochondrial OS=Mus musculus GN=C1qbp PE=2 SV=1	C1qbp	Q8R5L1	31 kDa	83% (83%)	100% (100%)
Q9CQB4_MOUSE Cytochrome b-c1 complex subunit 7 OS=Mus musculus GN=Uqcrb PE=3 SV=1	Uqcrb	Q9CQB4 (+1)	14 kDa	100% (100%)	100% (100%)
QCR1_MOUSE Cytochrome b-c1 complex subunit 1, mitochondrial OS=Mus musculus GN=Uqcrc1 PE=1 SV=2	Uqcrc1	Q9CZ13	53 kDa	100% (100%)	100% (100%)
QCR2_MOUSE Cytochrome b-c1 complex subunit 2, mitochondrial OS=Mus musculus GN=Uqcrc2 PE=1 SV=1	Uqcrc2	Q9DB77	48 kDa	100% (100%)	100% (100%)
SPTB2_MOUSE Spectrin beta chain, non-erythrocytic 1 OS=Mus musculus GN=Sptbn1 PE=1 SV=2	Sptbn1	Q62261	274 kDa		100% (100%)
TBB4B_MOUSE Tubulin beta-4B chain OS=Mus musculus GN=Tubb4b PE=1 SV=1	Tubb4b	P68372	50 kDa	100% (100%)	

THIM_MOUSE 3-ketoacyl-CoA thiolase, mitochondrial OS=Mus musculus GN=Acaa2 PE=1 SV=3	Acaa2	Q8BWT1	42 kDa	86% (86%)	100% (100%)
TNNC1_MOUSE Troponin C, slow skeletal and cardiac muscles OS=Mus musculus GN=Tnnc1 PE=2 SV=1	Tnnc1	P19123	18 kDa	100% (100%)	100% (100%)
TNNI3_MOUSE Troponin I, cardiac muscle OS=Mus musculus GN=Tnni3 PE=1 SV=2	Tnni3	P48787	24 kDa	100% (100%)	100% (100%)
TPM1_MOUSE Tropomyosin alpha-1 chain OS=Mus musculus GN=Tpm1 PE=1 SV=1	Tpm1	P58771	33 kDa	100% (100%)	100% (100%)
USMG5_MOUSE Up-regulated during skeletal muscle growth protein 5 OS=Mus musculus GN=Usmg5 PE=1 SV=1	Usmg5	Q78IK2	6 kDa	100% (100%)	100% (100%)
VDAC1_MOUSE Isoform Mt-VDAC1 of Voltage-dependent anion-selective channel protein 1 OS=Mus musculus GN=Vdac1	OS	Q60932-2	31 kDa	100% (100%)	100% (100%)
VIME_MOUSE Vimentin OS=Mus musculus GN=Vim PE=1 SV=3	Vim	P20152	54 kDa	100% (100%)	100% (100%)
VINC_MOUSE Vinculin OS=Mus musculus GN=Vcl PE=1 SV=4	Vcl	Q64727	117 kDa	100% (100%)	100% (100%)

Note: The percentage in the table indicates the identification probability of the specified protein.

Supplemental Table S3

Proteins in common

mECM	**nzECM**	**hzECM**
Mouse gene (accession #, MW)	**Zfish gene (accession #, MW)**	**Zfish gene (accession #, MW)**
acadvl (P50544, 71 kDa)	acadvl (A9JT52 (+2), 71 kDa)	acadvl (A9JT52 (+2), 71 kDa)
Aco2 (Q99KI0, 85 kDa)	aco2 (Q6PEI6, 85 kDa)	aco2 (Q6PEI6, 85 kDa)
Actn2 (Q9JI91, 104 kDa)	actn2 (Q2YDR5, 103 kDa)	actn2 (Q2YDR5, 103 kDa)
Anxa2 (P07356, 39 kDa)		**anxa2a (Q804G9, 38 kDa)**
Atp1a1 (Q8VDN2, 113 kDa)	atp1a1 (Q9DGL6, 113 kDa)	atp1a1 (Q9DGL6, 113 kDa)
Atp1b1 (P14094, 35 kDa)	atp1b1a (Q7ZVX2, 35 kDa)	atp1b1a (Q7ZVX2, 35 kDa)
Atp5a1 (Q03265, 60 kDa)	atp5a1 (Q08BA1, 60 kDa)	atp5a1 (Q08BA1, 60 kDa)
Atp5b (P56480, 56 kDa)	atp5b (A8WGC6, 55 kDa)	atp5b (A8WGC6, 55 kDa)
Atp5o (Q9DB20, 23 kDa)	atp5o (Q6DRD1, 22 kDa)	atp5o (Q6DRD1, 22 kDa)
Ckmt2 (Q6P8J7, 47 kDa)	ckmt2 (A8WG85 (+1), 46 kDa)	ckmt2 (A8WG85 (+1), 46 kDa)
Col1a1 (P11087, 138 kDa)	col1a1b (F1QDL1 (+1), 137 kDa)	col1a1b (F1QDL1 (+1), 137 kDa)
Col1a2 (Q01149, 130 kDa)	col1a2 (E9QCG6 (+1), 127 kDa)	col1a2 (E9QCG6 (+1), 127 kDa)
Cox5a (P12787, 16 kDa)	cox5aa (Q4VBU7, 16 kDa)	cox5aa (Q4VBU7, 16 kDa)
	cox5ab (F1QJ99 (+1), 17 kDa)	cox5ab (F1QJ99 (+1), 17 kDa)
Cyc1 (Q9D0M3, 35 kDa)	cyc1 (Q68EI6, 33 kDa)	cyc1 (Q68EI6, 33 kDa)
Des (P31001, 53 kDa)	desma (F1R8W3, 56 kDa)	desma (F1R8W3, 56 kDa)

Hspb1 (P14602 (+1), 23 kDa)	hspb1 (A4VAK4 (+1), 22 kDa)	hspb1 (A4VAK4 (+1), 22 kDa)
Hspd1 (P63038, 61 kDa)	hspd1 (Q803B0, 61 kDa)	hspd1 (Q803B0, 61 kDa)
Immt (E9Q800, 76 kDa)	immt (Q6PFS4, 83 kDa)	immt (Q6PFS4, 83 kDa)
Itgb1 (P09055, 88 kDa)	itgb1b (Q3YAA0, 88 kDa)	itgb1b (Q3YAA0, 88 kDa)
Krt8 (P11679, 55 kDa)	krt8 (Q6NWF6, 58 kDa)	krt8 (Q6NWF6, 58 kDa)
Lamc1 (F8VQJ3, 177 kDa)	lamc1 (Q1LVF0, 176 kDa)	lamc1 (Q1LVF0, 176 kDa)
Mtco2 (P00405 (+1), 26 kDa)	mt-co2 (Q9MIY7, 26 kDa)	mt-co2 (Q9MIY7, 26 kDa)
Myh6 (Q02566, 224 kDa)	myh6 (B3DJP9, 223 kDa)	myh6 (B3DJP9, 223 kDa)
Myh7 (Q91Z83, 223 kDa)	myl7 (Q801M3, 19 kDa)	myl7 (Q801M3, 19 kDa)
Myoz2 (Q9JJW5, 30 kDa)	myoz2b (F1QBP1, 29 kDa)	myoz2b (F1QBP1, 29 kDa)
Ndufa5 (Q9CPP6, 13 kDa)	ndufa5 (Q5BJA2, 13 kDa)	ndufa5 (Q5BJA2, 13 kDa)
Ndufs8 (Q8K3J1, 24 kDa)	ndufs8a (Q6P0T0, 24 kDa)	ndufs8a (Q6P0T0, 24 kDa)
Sdha (Q8K2B3, 73 kDa)	sdha (Q6TNQ9, 73 kDa)	sdha (Q6TNQ9, 73 kDa)
Tnnc1 (P19123, 18 kDa)	tnnc1a (Q800V7, 18 kDa)	tnnc1a (Q800V7, 18 kDa)
Tnnt2 (J3QQ13 (+7), 36 kDa)	tnnt2a (Q7ZSY4 (+2), 34 kDa)	tnnt2a (Q7ZSY4 (+2), 34 kDa)
Uqcrb (Q9CQB4 (+1), 14 kDa)	uqcrb (Q4VBV1, 13 kDa)	uqcrb (Q4VBV1, 13 kDa)
Uqcrc1 (Q9CZ13, 53 kDa)	uqcrc1 (Q6NSN3 (+1), 52 kDa)	uqcrc1 (Q6NSN3 (+1), 52 kDa)
Uqcrc2 (Q9DB77, 48 kDa)	uqcrc2b (Q6IQ59, 48 kDa)	uqcrc2b (Q6IQ59, 48 kDa)
Vdac2 (G3UX26 (+1), 30 kDa)	vdac2 (Q4JHL7 (+1), 30 kDa)	vdac2 (Q4JHL7 (+1), 30 kDa)

	Note:	Pink color = uncharacterized protein
		Bold = protein detected only in hzECM
Proteins not in common		
mECM	**nzECM**	**hzECM**
Mouse gene (accession #, MW)	**Zfish gene (accession #, MW)**	**Zfish gene (accession #, MW)**
Acaa2 (Q8BWT1, 42 kDa)	actc1a (Q6IQR3, 42 kDa)	actc1a (Q6IQR3, 42 kDa)
Acta1 (P68134, 42 kDa)	actc1a (Q9PTR4, 42 kDa)	actc1a (Q9PTR4, 42 kDa)
Alb (P07724, 69 kDa)	atp2a2a (A9C3Q4 (+2), 115 kDa)	atp2a2a (A9C3Q4 (+2), 115 kDa)
Anxa6 (F8WIT2 (+1), 75 kDa)	atp5h (Q6PC77, 18 kDa)	atp5h (Q6PC77, 18 kDa)
Apoo (B1ASQ2 (+1), 23 kDa)	atp5ib (A2ARG7, 8 kDa)	atp5ib (A2ARG7, 8 kDa)
Atp5d (Q9D3D9, 18 kDa)	ba2 (Q90485, 16 kDa)	ba2 (Q90485, 16 kDa)
Atp5i (Q06185, 8 kDa)	chchd6 (Q63ZW2, 28 kDa)	chchd6 (Q63ZW2, 28 kDa)
Atp5j2 (F8WHP8, 9 kDa)	chchd6b (F1RBH3 (+1), 26 kDa)	chchd6b (F1RBH3 (+1), 26 kDa)
Bsg (K3W4Q8 (+2), 24 kDa)	cmlc1 (B0R0F7, 22 kDa)	cmlc1 (B0R0F7, 22 kDa)
C1qbp (Q8R5L1, 31 kDa)	cox6c (Q6ZM23, 8 kDa)	cox6c (Q6ZM23, 8 kDa)
Cacna2d1 (E9Q1X8 (+5), 123 kDa)	CR762436.4 (E7EZX1 (+4), 14 kDa)	CR762436.4 (E7EZX1 (+4), 14 kDa)
Canx (P35564, 67 kDa)	CU302436.1 (E7F1L7, 292 kDa)	CU302436.1 (E7F1L7, 292 kDa)

Casq2 (F6QYE1 (+1), 48 kDa)		**fga (E9QCD1, 50 kDa)**
Cav1 (P49817, 21 kDa)		**fgb (Q6NYE1, 54 kDa)**
Cd36 (Q08857, 53 kDa)		**fgg (Q7ZVG7, 49 kDa)**
Cdh2 (D3YYT0 (+1), 94 kDa)	fn1b (Q58XP5, 276 kDa)	fn1b (Q58XP5, 276 kDa)
Chchd3 (Q9CRB9, 26 kDa)	hlf0 (Q6NYV3, 21 kDa)	hlf0 (Q6NYV3, 21 kDa)
Ckm (P07310, 43 kDa)	hspa9 (Q7ZYY3, 74 kDa)	hspa9 (Q7ZYY3, 74 kDa)
Col6a2 (Q02788, 110 kDa)	idh2 (Q7ZUP6, 50 kDa)	idh2 (Q7ZUP6, 50 kDa)
Cox4i1 (P19783, 20 kDa)	lmnb2 (Q9W6T5, 66 kDa)	lmnb2 (Q9W6T5, 66 kDa)
Cox6b1 (P56391, 10 kDa)	LOC402880 (F1R6I1 (+1), 20 kDa)	LOC402880 (F1R6I1 (+1), 20 kDa)
Cryab (P23927, 20 kDa)	LOC564077 (E7FAV6, 57 kDa)	LOC564077 (E7FAV6, 57 kDa)
Cs (Q9CZU6, 52 kDa)	lrrc15 (A8BBI6, 58 kDa)	lrrc15 (A8BBI6, 58 kDa)
Dcn (P28654, 40 kDa)	mb (Q6VN46, 16 kDa)	mb (Q6VN46, 16 kDa)
Dpep1 (P31428, 46 kDa)	mybpc3 (F1Q615, 144 kDa)	mybpc3 (F1Q615, 144 kDa)
Gbas (O55126 (+1), 33 kDa)	myh11a (B3DFS9 (+1), 228 kDa)	myh11a (B3DFS9 (+1), 228 kDa)
Gm10250 (G3X9L6 (+1), 19 kDa)		**nppa (Q6VYM3, 12 kDa)**
Hadha (Q8BMS1, 83 kDa)	sh3bgr (Q6DEH8, 21 kDa)	sh3bgr (Q6DEH8, 21 kDa)
Hadhb (Q99JY0, 51 kDa)	si:ch1073-329n19.2 (F1R3F7 (+1), 30 kDa)	si:ch1073-329n19.2 (F1R3F7 (+1), 30 kDa)
Hbb-b1 (P02088, 16 kDa)		**si:ch211-103n10.5 (B0R0K9, 19 kDa)**
Hist1h1e (P43274, 22 kDa)	si:ch211-150d5.2 (F1QJK4, 196 kDa)	si:ch211-150d5.2 (F1QJK4, 196 kDa)

Hspg2 (B1B0C7 (+1), 469 kDa)	slc25a5 (Q8JHI0, 33 kDa)	slc25a5 (Q8JHI0, 33 kDa)
Idh3a (Q9D6R2, 40 kDa)		**slmapa (Q1RLV5, 50 kDa)**
Krt1 (P04104, 66 kDa)	sorbs2a (F1Q9A0, 141 kDa)	sorbs2a (F1Q9A0, 141 kDa)
Krt10 (A2A513 (+3), 57 kDa)	spna2 (F1R446, 285 kDa)	spna2 (F1R446, 285 kDa)
Krt2 (Q3TTY5, 71 kDa)	tmod1 (E9QGR6, 40 kDa)	tmod1 (E9QGR6, 40 kDa)
Krt33b (Q61897, 46 kDa)	tnni1b (E7F5J9 (+2), 21 kDa)	tnni1b (E7F5J9 (+2), 21 kDa)
Krt42 (Q6IFX2, 50 kDa)	tpm4a (F1QKG7, 33 kDa)	tpm4a (F1QKG7, 33 kDa)
Krt5 (Q922U2, 62 kDa)	tpm4a (Q7T3F0, 29 kDa)	tpm4a (Q7T3F0, 29 kDa)
Krt85 (Q9Z2T6, 56 kDa)	vdac3 (A8E5I7 (+2), 30 kDa)	vdac3 (A8E5I7 (+2), 30 kDa)
Lama2 (Q60675, 344 kDa)	vmhcl (F1QSE1 (+1), 223 kDa)	vmhcl (F1QSE1 (+1), 223 kDa)
Lamb1 (P02469, 197 kDa)	wu:fe37d09 (A3KPR4 (+2), 11 kDa)	wu:fe37d09 (A3KPR4 (+2), 11 kDa)
Lmna (P48678 (+1), 74 kDa)	ywhaba (Q5PRD0, 28 kDa)	ywhaba (Q5PRD0, 28 kDa)
Myh9 (Q8VDD5, 226 kDa)	zgc:101560 (H9GYI1, 21 kDa)	zgc:101560 (H9GYI1, 21 kDa)
Myl2 (P51667, 19 kDa)	zgc:112234 (F1QG64, 15 kDa)	zgc:112234 (F1QG64, 15 kDa)
Myl3 (P09542, 22 kDa)	zgc:153629 (F1R8U0 (+1), 48 kDa)	zgc:153629 (F1R8U0 (+1), 48 kDa)
Ndufb10 (Q9DCS9, 21 kDa)	zgc:56085 (F1Q766, 47 kDa)	zgc:56085 (F1Q766, 47 kDa)
Ndufb7 (Q9CR61, 16 kDa)		**zgc:92880 (Q6DGK4 (+1), 16 kDa)**
Ndufs1 (Q91VD9, 80 kDa)		
OS (Q60932-2, 31 kDa)		
Phb (P67778, 30 kDa)		

Ptrf (O54724, 44 kDa)	**Note:**	Pink color = uncharacterized protein
Reep5 (G3X8R0, 21 kDa)		**Bold = protein detected only in hzECM**
Sdhb (Q9CQA3, 32 kDa)		
Slc25a4 (P48962, 33 kDa)		
Sptan1 (A3KGU7 (+1), 285 kDa)		
Sptbn1 (Q62261, 274 kDa)		
Tnni3 (P48787, 24 kDa)		
Tpm1 (P58771, 33 kDa)		
Tubb4b (P68372, 50 kDa)		
Usmg5 (Q78IK2, 6 kDa)		
Vcl (Q64727, 117 kDa)		
Vim (P20152, 54 kDa)		

Supplemental Table T4. Echocardiographic parameters of infarcted mouse hearts following ECM treatment

Fractional Area Change

Mean ± SD (%)	0D	5D	2W	6W
hzECM	57.12 ± 3.53	54.35 ± 4.83	47.47 ± 4.74	45.29 ± 4.40
nzECM	57.12 ± 3.53	43.80 ± 7.35	45.13 ± 5.67	37.88 ± 2.44
mECM	57.12 ± 3.53	45.39 ± 3.21	36.13 ± 3.50	29.97 ± 2.77
Saline	57.12 ± 3.53	40.05 ± 5.28	32.27 ± 4.43	25.23 ± 4.72

Ejection Fraction

Mean ± SD (%)	0D	5D	2W	6W
hzECM	72.36 ± 2.24	68.24 ± 3.84	62.75 ± 5.62	59.83 ± 4.58
nzECM	72.36 ± 2.24	59.64 ± 5.87	60.33 ± 5.54	51.31 ± 2.39
mECM	72.36 ± 2.24	60.32 ± 3.02	50.03 ± 3.14	43.61 ± 3.46
Saline	72.36 ± 2.24	57.21 ± 4.88	45.57 ± 5.47	38.02 ± 4.56

End-Diastolic Area

Mean ± SD (mm^2)	0D	5D	2W	6W
hzECM	9.83 ± 1.08	11.89 ± 0.77	14.65 ± 1.90	17.08 ± 1.38
nzECM	9.83 ± 1.08	11.60 ± 1.04	13.72 ± 1.19	17.61 ± 1.80
mECM	9.83 ± 1.08	13.73 ± 1.21	16.65 ± 1.07	20.95 ± 1.20
Saline	9.83 ± 1.08	13.37 ± 1.77	16.88 ± 2.62	20.07 ± 4.36

End-Systolic Area

Mean ± SD (mm^2)	0D	5D	2W	6W
hzECM	4.24 ± 0.79	5.41 ± 0.39	7.72 ± 1.41	9.33 ± 0.90
nzECM	4.24 ± 0.79	6.49 ± 0.76	7.51 ± 0.84	10.96 ± 1.40
mECM	4.24 ± 0.79	7.48 ± 0.55	10.64 ± 0.94	14.67 ± 1.03
Saline	4.24 ± 0.79	8.05 ± 1.52	11.48 ± 2.29	15.04 ± 3.62

Supplemental Table T5. Echocardiographic parameters of infarcted mouse hearts following ECM treatment and ErbB2 inhibitor administration

Fractional Area Change

Mean ± SD (%)	0D	5D	2W	6W
hzECM	57.12 ± 3.53	46.11 ± 4.21	38.16 ± 4.52	30.14 ± 4.55
nzECM	57.12 ± 3.53	44.37 ± 5.24	36.46 ± 6.71	29.18 ± 4.38
mECM	57.12 ± 3.53	42.37± 3.30	35.02 ± 3.47	27.45 ± 2.50
Saline	57.12 ± 3.53	39.48 ± 4.76	31.87 ± 3.68	25.16 ± 4.91

Ejection Fraction

Mean ± SD (%)	0D	5D	2W	6W
hzECM	72.36 ± 2.24	60.44 ± 5.13	51.37 ± 5.95	43.49 ± 5.21
nzECM	72.36 ± 2.24	58.51 ± 5.32	49.35 ± 4.98	41.29 ± 2.83
mECM	72.36 ± 2.24	56.24 ± 2.11	47.63 ± 3.34	39.21 ± 3.44
Saline	72.36 ± 2.24	53.37 ± 4.33	43.76 ± 4.12	37.22 ± 5.65

End-Diastolic Area

Mean ± SD (mm^2)	0D	5D	2W	6W
hzECM	9.83 ± 1.08	13.39 ± 0.84	16.35 ± 1.28	19.50 ± 1.43
nzECM	9.83 ± 1.08	13.99 ± 1.12	16.71 ± 1.41	19.91 ± 1.95
mECM	9.83 ± 1.08	14.72 ± 1.04	17.45 ± 1.50	21.05 ± 1.17
Saline	9.83 ± 1.08	14.38 ± 1.58	17.85 ± 1.92	21.96 ± 2.25

End-Systolic Area

Mean ± SD (mm^2)	0D	5D	2W	6W
hzECM	4.24 ± 0.79	7.21 ± 0.43	10.11 ± 0.94	13.32 ± 1.10
nzECM	4.24 ± 0.79	7.78 ± 0.61	10.62 ± 1.41	13.96 ± 1.01
mECM	4.24 ± 0.79	8.49 ± 0.48	11.33 ± 0.53	15.27 ± 1.53
Saline	4.24 ± 0.79	9.13 ± 1.23	12.18 ± 1.72	15.93 ± 2.21