Aberrant alternative splicing and extracellular matrix gene expression in mouse models of myotonic dystrophy.

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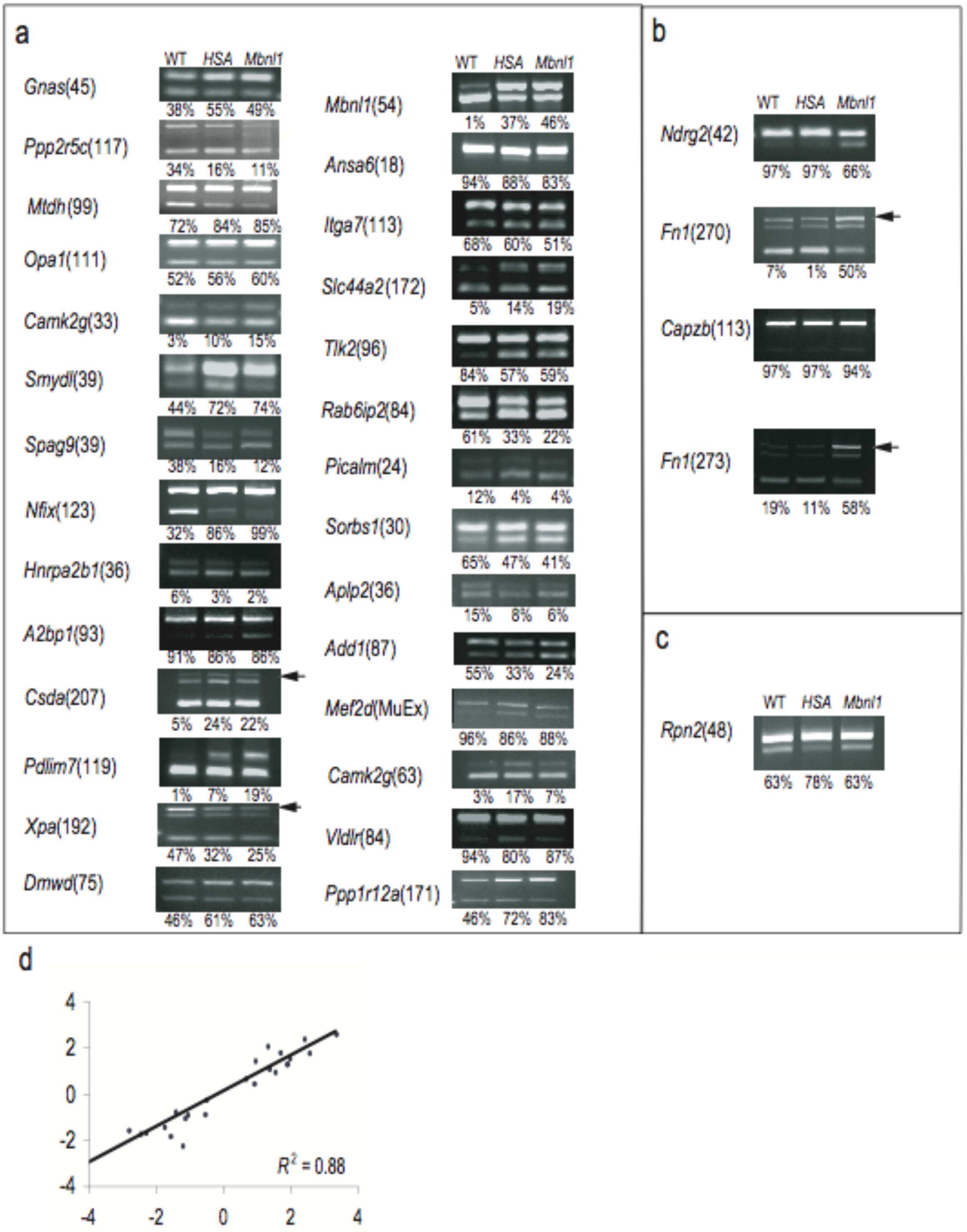
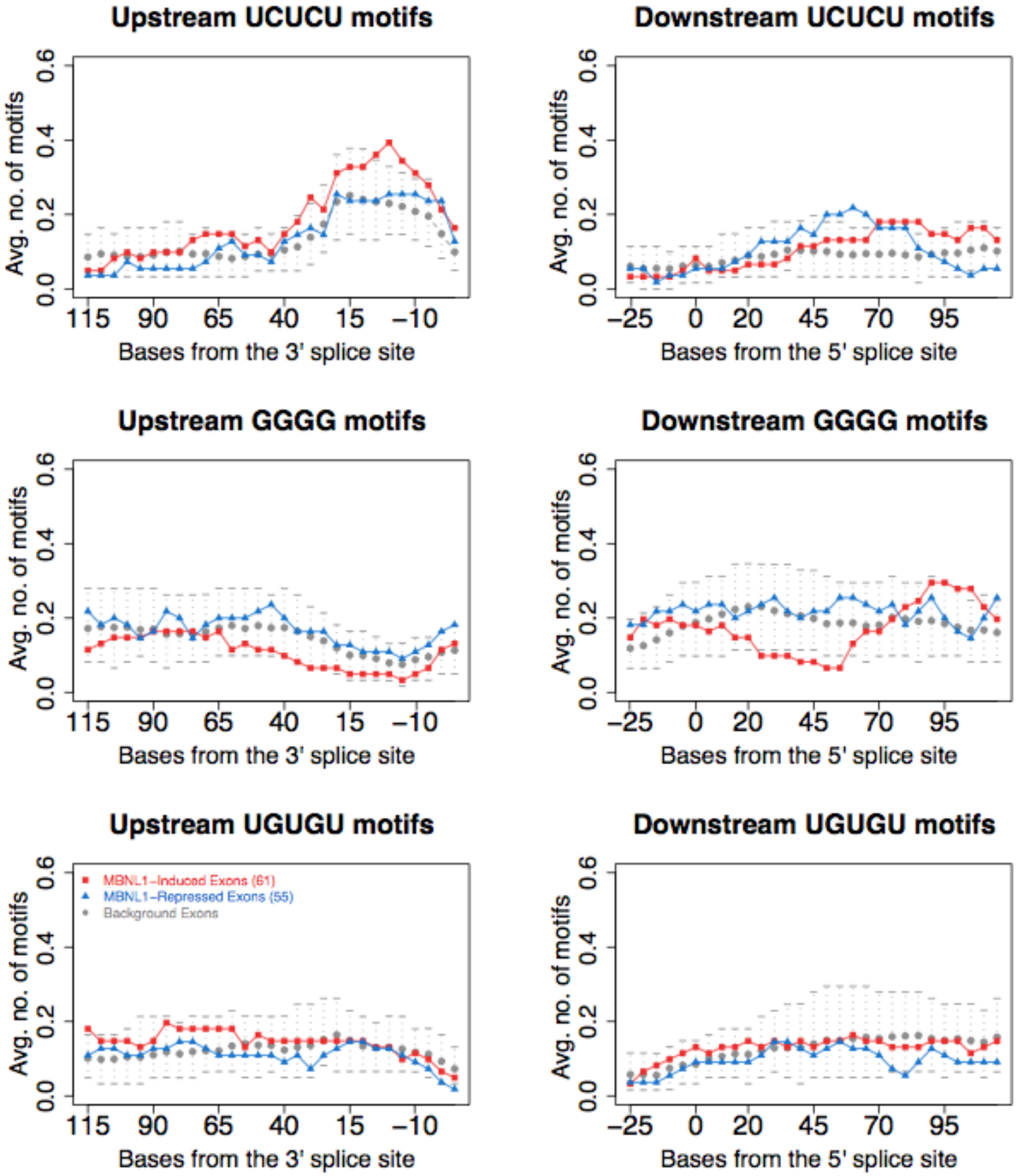
SUPPLEMENTARY FIGURES AND TABLES

Supplementary Figure 1



Supplementary Figure 1 Validation and comparison of mis-spliced events in quadriceps samples of HSA$^{\mathrm{LR}}$ and *MBNL1*$^{\Delta E3/\Delta E3}$ mice. RT-PCR fragments were separated on 2.5% agarose gel. The mis-splicing events validated by RT-PCR were classified (**a-c**): 28 RT-PCR validations of mis-splicing cassette exon events predicted by splicing microarray to be altered in both *HSA*^{LR} and *MBNL1*$^{\Delta E3/\Delta E3}$ mice (**a**); 4 mis-spliced cassette exon events altered only in *MBNL*$^{\Delta E3/\Delta E3}$ mice (**b**); 1 mis-splicing cassette exon event altered only in *HSA*^{LR} mice (**c**). (**d**) Comparison of separation score of altered splicing events predicted by RT-PCR in both *HSA*^{LR} mice and *MBNL1*$^{\Delta E3/\Delta E3}$ mice ($R^2 = 0.88$). Separation score for RT-PCR data were calculated using amounts determined by the Bioanalyzer.



Supplementary Figure 2 Mapping binding motifs for other splicing factors. (**a**) PTB/nPTB, UCUCU (**b**) hnRNP H, GGGG (**c**) CUGBP1, UGUGU. Each point represents the average frequency of the motif element for the 55 MBNL1-repressed exons (blue triangles), or 66 MBNL1-activated exons (red squares) or 790 background exons expressed but showing no significant splicing change (grey circles), in each window. Error bars indicate plus and minus two standard deviations.

All mis-splicing events grouped by separation score>0.3

Group (sepscore>0.3	Functional category	gene name	Splicing mode	Coordinates in 2006 mouse genome brov	Function in Aceview	mbnl1-has-sepscore	mbnl1wt-sepscore	has-wt-sepscore	validation
HSALR and MBNL1 Knockout	Ion channel and ion transportation	Camk2g(63)	altCassette	chr14:19544243-19548708	calcium ion transport	NA	-1.2322	-1.1488	O
		Camk2g(33)	altCassette	chr14:19534402-19544224	calcium ion transport	NA	-1.0091	-1.1432	O
		Anxa6(18)	altCassette	chr11:54829628-54834827	calcium ion transport, regulatic	NA	0.6118	0.4799	O
		Slc38a4(78)	altTxStart	chr15:96827612-96877998	amino acid transport, ion trans	NA	-1.4766	-0.9866	ND
		Slc38a4(92)	altTxStart	chr15:96827612-96877998	amino acid transport, ion trans	0.7731	-0.7721	-0.6515	ND
		Tnfaip1(118)	altTxStart	chr11:78344646-78352277	embryonic development, potas	NA	0.3353	-0.3421	ND
		Slc6a8(1533)	alt5Prime	chrX:69928384-69933692	creatine transporter activity, cr	0.2312	-0.551	-0.6215	ND
	Cytoskeleton and muscle contraction	Pdlim7(119)	altCassette	chr13:55517492-55518416	actin cytoskeleton organizatior	1.3834	-3.6338	-2.3723	O
		Pdlim7(305)	altCassette	chr13:55515974-55516966	actin cytoskeleton organizatior	-0.7375	2.3549	1.7066	ND
		Pdlim3(144)	altMutEx	chr8:47407462-47413958	actin filament organization	NA	1.7503	1.5867	ND
		Lmo7(49)	altTxStart	chr14:100802337-100812860	actinin binding, metal ion bindi	NA	0.4206	0.5186	ND
		Vcl(125)	altTxEnd	chr14:19809157-19815707	oxidoreductase activity, proteir	0.2804	-0.3098	0.5636	ND
	Metabolism	Sorbs1(30)	altCassette	chr19:40418465-40426798	glucose transport, insulin rece	-0.3774	0.8141	0.442	O
		Eno3(112)	alt3Prime	chr11:70473452-70474080	Glycolysis / Gluconeogenesis,	NA	-0.5805	-0.514	ND
		Eif4el3(645)	altTxEnd	chr1:89057295-89069027	Insulin signaling pathway, mT(	NA	-0.8702	-0.8005	ND
		Acas2(204)	altTxEnd	chr2:155209938-155213457	acetyl-CoA biosynthetic proces	NA	-0.6283	-0.7412	ND
		Pfkfb3(42)	altTxStart	chr2:11411837-11416201	fructose 2,6-bisphosphate met	NA	-1.4239	-1.937	ND
		Siat6(491)	altTxStart	chr4:117430573-117632332	Glycan structures - biosynthes	-1.7289	-0.496	-1.8899	ND
		Lpin1(3344)	altTxStart	chr12:16574470-16599189	lipid metabolic process, regula	NA	-0.7281	-0.841	ND
		Plcd4(275)	altTxStart	chr1:74477671-74481378	acrosome reaction, intracellula	NA	-0.6438	-0.8284	ND
		Lpin1(42)	altTxStart	chr12:16599165-16615207	lipid metabolic process, regula	0.3568	-0.8435	-0.7979	ND
		Mknk2(112)	altTxStart	chr10:80069111-80075313	Insulin signaling pathway, MAF	NA	0.4487	0.389	ND
		Atp9a(165)	altTxStart	chr2:168331123-168403964	metabolic process, phospholip	NA	0.7914	0.7845	ND
		Cast(365)	altTxStart	chr13:75170103-75274448	protein catabolic process	NA	0.3603	1.0335	ND
	Signaling transduction	Gnas(45)	altCassette	chr2:173977210-173984604	GTPase activity, signal transdu	NA	-0.6722	-0.8036	O
		Opa1(111)	altCassette	chr16:29509485-29521972	GTP binding, GTPase activity,	NA	-0.6566	-0.5233	O
		Ppp2r5c(117)	altCassette	chr12:111018563-111028221	signal transduction	-0.6415	1.4235	0.8097	O
		Spag9(39)	altCassette	chr11:93928226-93930276	activation of MAPK activity	-0.3095	1.3689	1.127	O
		Tlk2(96)	altCassette	chr11:105025917-105037289	protein kinase activity, ATP bir	NA	1.3896	1.4781	O
		Mef2d(3)	altMutEx	chr3:88242437-88245061	DNA binding, transcription acti	NA	-1.5532	-1.9849	O
		Mfn2(83)	altCassette	chr4:146742429-146747166	protein binding, GTP binding, (	0.7192	0.9218	1.65	S
		Akt2(163)	altCassette	chr7:27314682-27317393	regulation of JNK cascade, prc	-0.292	-0.784	-1.2716	ND
		Homer1(36)	altCassette	chr13:94456821-94488291	metabotropic glutamate recept	NA	-1.3421	-1.1826	ND
		Mtmr3(111)	altCassette	chr11:4385440-4387246	dephosphorylation, phospholip	NA	0.6044	0.6524	ND
		Mgrn1(66)	altCassette	chr16:4839750-4842916	kinase activity, protein serine/t	NA	0.6357	0.7642	ND
		Col4a3bp(78)	altCassette	chr13:97717236-97725405	kinase activity, protein serine/t	NA	1.3444	0.8518	ND
		2810004N20Rik(58)	altCassette	chr2:90714999-90718278	phosphatidylinositol metabolic	NA	0.9864	1.1145	ND
		Tbc1d9b(1193)	altTxEnd	chr11:49993305-50001850	calcium ion binding, GTPase a	NA	-0.4603	-0.455	ND
		Tbc1d1(316)	altTxEnd	chr5:64554531-64590310	regulation of Rab GTPase acti	NA	-0.3118	-0.3023	ND
		Mapbpip(138)	altTxStart	chr3:88638429-88638793	activation of MAPKK activity	-1.6115	-0.7463	-1.4874	ND
		Uaca(526)	altTxStart	chr9:60635835-60638958	DNA damage response, signal	NA	-0.839	-0.8496	ND
		Ptprm(1011)	altTxStart	chr17:66719431-66967998	cell adhesion, dephosphorylati	0.1631	-0.3569	-0.5016	ND
		Rab24(414)	altTxStart	chr13:55330750-55331546	autophagy, protein transport, s	NA	-0.4708	-0.3014	ND
		Cd36(177)	altTxStart	chr5:17332364-17361494	cell adhesion, transport	NA	0.5423	0.4224	ND
		Eef2k(172)	altTxStart	chr7:120634891-120677813	protein amino acid phosphoryl	0.3175	0.5014	0.7903	ND
		Dgkz(301)	altTxStart	chr2:91741822-91764136	intracellular signaling cascade	0.5465	0.3799	0.8831	ND
		Map2k6(387)	altTxStart	chr11:110295431-110306892	activation of MAPK activity, ca	NA	-0.7474	0.3532	ND
		Jag2(114)	altCassette	chr12:113363313-113363700	growth factor activity, Notch bi	NA	-1.1206	-1.091	ND
	DNA transcription and mRNA processing	Mbnl1(54)	altCassette	chr3:60701440-60703563	metal ion binding, nucleic acid	0.6094	-2.6249	-1.8331	O
		Nfix(123)	altCassette	chr8:87611908-87616588	DNA binding, transcription fact	NA	-1.5055	-1.3985	O
		Smyd1(39)	altCassette	chr6:71155087-71166950	protein binding, transcription c	NA	-1.0493	-1.025	O
		Csda(207)	altCassette	chr6:131336094-131345063	regulation of transcription, DN/	NA	-0.4813	-0.605	O
		Mtdh(99)	altCassette	chr15:34062686-34075763	regulation of transcription, DN/	NA	-0.4974	-0.4957	O
		Hnrpa2b1(36)	altCassette	chr6:51396863-51399268	mRNA processing, RNA splicir	NA	1.0445	0.9699	O
		Mlf1(45)	altCassette	chr3:67472617-67480834	myeloid progenitor cell differer	1.7853	-3.5681	-1.6473	ND
		Ncoa2(207)	altCassette	chr1:13147490-13152122	negative regulation of transcrip	NA	0.7276	0.6631	ND
		Tcea1(32)	altCassette	chr1:4798050-4818675	positive regulation of transcript	-0.3291	0.9891	0.6714	ND
		Zfp260(206)	altTxEnd	chr7:29815020-29816173	regulation of transcription, DN/	NA	-0.372	-0.2961	ND
		D8Ertd325e(817)	altTxEnd	chr8:126284166-126287517	regulation of transcription, DN/	NA	0.5705	0.6548	ND
		Raly(101)	altTxStart	chr2:154548877-154737064	mRNA processing, RNA splicir	NA	-0.4942	-0.5925	ND
		D17Wsu155e(74)	altTxStart	chr17:6036378-6037351	DNA repair, nucleotide-excisio	NA	-0.6353	-0.5002	ND
		Rpo2tc1(47)	altTxStart	chr15:11938519-11940690	regulation of transcription, DN/	NA	-0.6986	-0.3187	ND
		Cpeb3(202)	altTxStart	chr19:37239886-37272453	nucleic acid binding, nucleotid	NA	0.3057	0.3393	ND
		Rorc(166)	altTxStart	chr3:94460457-94472586	regulation of transcription, DN	NA	0.4524	0.353	ND
	Cell growth	Fntb(227)	altMutEx	chr12:77829168-77838930	negative regulation of cell proli	0.2596	-0.7021	-0.4351	ND
		Et14(335)	altTxEnd	chr2:20661452-20725855	embryonic skeletal developme	NA	0.8506	1.5471	ND
		Flt1(2387)	altTxStart	chr5:147956571-147988552	angiogenesis, cell migration, p	NA	0.601	0.5397	ND
	Others	1110028E10Rik(172)	altCassette	chr9:21102944-21104098	transport	NA	-1.5728	-0.8631	O
		Aplp2(36)	altCassette	chr9:30903050-30907271	protein binding, DNA binding, s	-0.3224	0.6653	0.3423	O
		Add1(87)	altCassette	chr5:34936977-34942149	structural molecule activity, cal	NA	0.449	0.3722	O
		A2bp1(93)	altCassette	chr16:7200837-7209405	nucleic acid binding, nucleotid	-0.5572	1.2469	0.791	O
		Picalm(24)	altCassette	chr7:90066930-90070861	phospholipid binding	NA	0.7725	0.8076	O
		Rab6ip2(84)	altCassette	chr6:119739508-119745107	retrograde transport, endosom	-0.3151	1.381	0.9231	O
		Dpp9(119)	altCassette	chr17:55823160-55823708	proteolysis	NA	-0.9597	-0.5146	S
		Ap1gbp1(36)	altCassette	chr11:83855503-83857005	endocytosis, protein transport	NA	0.8446	0.5584	S
		Rtn2(6)	alt3Prime	chr7:18449683-18451618	Unknown	NA	0.5186	0.3191	ND
		Fcgrt(12)	alt5Prime	chr7:44970213-44970465	IgG binding, receptor activity, I	NA	-0.653	-0.7053	ND
		C3(6)	alt5Prime	chr17:56889474-56889606	positive regulation of phagocyt	NA	0.871	0.9394	ND
		D11Bwg0280e(78)	altCassette	chr11:6297677-6298573	metal ion binding, zinc ion binc	NA	-1.4536	-1.4976	ND
		Ap1b1(21)	altCassette	chr11:4932611-4933702	protein transport, vesicle-medi	NA	-1.6339	-1.3892	ND
		1700113I22Rik(54)	altCassette	chr11:101235261-101237969	Unknown	NA	-0.9178	-0.7366	ND
		Ankrd11(97)	altCassette	chr8:125786230-125794772	DNA binding	NA	-0.3937	-0.5878	ND
		Picalm(150)	altCassette	chr7:90052780-90064356	receptor-mediated endocytosi	NA	0.5818	0.4571	ND
		5230400G24Rik(172)	altCassette	chr1:82606347-82608252	Unknown	NA	0.8173	0.4908	ND
		Pcm1(165)	altCassette	chr8:42792620-42808351	Unknown	NA	1.1507	1.011	ND
		AF114378(117)	altMutEx	chr14:33396645-33407701	electron transport	NA	-0.8657	-0.8283	ND
		Tacc2(231)	altMutEx	chr7:130533437-130542351	protein binding	NA	0.8347	0.6724	ND
		Fbxo14(384)	altTxEnd	chr8:124450463-124464564	Unknown	NA	-0.6817	-0.4553	ND
		Trp53inp2(131)	altTxEnd	chr2:155073419-155077453	Unknown	-0.1167	-0.4736	-0.4033	ND
		Itch(3471)	altTxEnd	chr2:154865412-154894736	ubiquitin-dependent protein ca	NA	-0.3903	-0.3894	ND
		D10Ertd641e(923)	altTxEnd	chr10:59383657-59386201	Unknown	NA	-0.359	-0.3045	ND
		Ddb1(858)	altTxEnd	chr19:10680020-10696138	ubiquitin cycle	NA	0.3571	0.3154	ND
		Fgfr1op2(2122)	altTxEnd	chr6:146549904-146555246	unknown	-0.3187	0.5665	0.3391	ND
		BC031353(576)	altTxEnd	chr9:74740370-74790881	unknown	NA	0.3101	0.3617	ND
		Zfpn1a5(208)	altTxEnd	chr7:131183254-131184917	nucleic acid binding, zinc ion b	NA	0.3506	0.3982	ND
		Dtna(396)	altTxEnd	chr18:23712639-23798834	protein binding, calcium ion bi	NA	0.6604	0.5198	ND
		Pcbp4(133)	altTxEnd	chr9:106312055-106320650	Unknown	NA	0.6659	0.5664	ND
		UBE2D2(2098)	altTxEnd	chr18:35927326-35986687	ubiquitin cycle, ubiquitin-deper	0.2025	0.5334	0.6422	ND
		Ctsc(261)	altTxEnd	chr7:88156582-88163871	proteolysis	NA	0.5792	0.6457	ND
		BC031353(576)	altTxEnd	chr9:74740370-74790881	Unknown	NA	0.824	0.7425	ND
		Fbxo14(1363)	altTxEnd	chr8:124438223-124464564	Unknown	0.224	1.3737	1.086	ND
		Et14(836)	altTxEnd	chr2:20631193-20661476	Unknown	0.7003	0.6854	1.2503	ND
		Dtna(396)	altTxEnd	chr18:23712639-23798834	protein binding, calcium ion bi	NA	1.2945	1.416	ND
		Ppm2c	altTxStart	chr4:11888865-11889380	calcium ion binding, catalytic a	NA	-2.992	-2.7218	ND
		Trappc9(84)	altTxStart	chr15:72663358-72776076	Unknown	NA	-1.3829	-1.4214	ND
		Dpp8(183)	altTxStart	chr9:64830620-64835124	proteolysis	NA	-0.6597	-1.1618	ND
		Slc25a46(86)	altTxStart	chr18:31743207-31753457	transport	NA	-0.8837	-0.8025	ND
		Gpr108(330)	altTxStart	chr17:56930639-56933456	Unknown	NA	-0.6878	-0.7725	ND
		BC033455(212)	altTxStart	chr5:130507263-130525179	Unknown	NA	-0.3623	-0.5905	ND
		Obfc2b(505)	altTxStart	chr10:127811717-127814418	nucleic acid binding	NA	-0.7689	-0.5661	ND
		Hspa4(468)	altTxStart	chr11:53114471-53143495	ATP binding, nucleotide bindin	NA	-0.508	-0.5137	ND
		Zc3h11a(132)	altTxStart	chr1:135474991-135488797	metal ion binding, nucleic acid	NA	-0.8933	-0.4947	ND
		Comt(306)	altTxStart	chr16:18321213-18339931	dopamine catabolic process, c	NA	-0.4113	-0.416	ND
		2010005J08Rik(44)	altTxStart	chr11:5617923-5641114	structural constituent of ribos	0.2386	-0.6323	-0.3898	ND
		Jtv1(134)	altTxStart	chr5:144156541-144163242	Unknown	NA	-0.3387	-0.2917	ND

		Atp5c1(645)	altTxStart	chr2:9981388-9987560	transporter activity, hydrogen i	NA	0.4535	0.3504	ND
		Uaca(175)	altTxStart	chr9:60592685-60638958	protein binding	NA	0.3118	0.3575	ND
		Ghitm(112)	altTxStart	chr14:36033858-36046946	Unknown	NA	0.4269	0.4318	ND
		Park7(306)	altTxStart	chr4:149741163-149757705	ND	NA	0.5345	0.5651	ND
		Macrod2	altTxStart	chr2:140086927-140087130	Unknown	NA	0.6658	0.6178	ND
		AK009836(130)	altTxStart	chr9:77025606-77133639	ND	NA	0.5267	0.8588	ND
		Pcif1(247)	altTxStart	chr2:164570851-164574142	Unknown	-1.2326	0.4332	-0.7449	ND
		Schip1(209)	altTxStart	chr3:68672147-68684195	ND	NA	-0.7518	0.3377	ND
MBNL1 Knockout only	Cytoskeleton and muscle contraction	Capzb(113)	altCassette	chr4:138559899-138563093	actin binding	-0.4172	0.5382	0.1574	M
		Fn1(273)	altCassette	chr1:71545845-71548582	Regulation of actin cytoskeletc	1.8877	-1.9362	NA	M
		Fn1(270)	altCassette	chr1:71535694-71538190	Regulation of actin cytoskeletc	2.3858	-2.7001	NA	M
	Metabolism	Car3(156)	altCassette	chr3:14846030-14848298	one-carbon compound metabc	-1.2418	0.6335	NA	S
		Asb11(213)	altCassette	chrX:159781316-159789847	intracellular signaling cascade	-0.4523	0.4597	NA	ND
		Anapc13(101)	altTxStart	chr9:102482716-102490039	cell cycle, cell division, mitosis	0.3988	-0.8874	NA	ND
		Pcif1(125)	altTxStart	chr11:49745377-49800487	cell division, regulation of sma	1.4352	-1.7474	NA	ND
		Jag2(20)	alt5Prime	chr12:113360513-113360985	growth factor activity, Notch bi	0.8253	-1.1562	NA	ND
	DNA transcription and mRNA processing	D3Jfr1(93)	altCassette	chr3:103169088-103170220	regulation of transcription, DN	0.5901	-0.6076	NA	F
		Hmx1(1125)	altTxEnd	chr5:35706031-35709623	DNA binding, sequence-specif	0.4574	-0.2962	NA	ND
		Drap1(157)	altTxEnd	chr19:5422868-5423340	negative regulation of transcrip	0.5155	-0.4215	NA	ND
		Smarcd3(138)	altTxStart	chr5:24108778-24132603	heart morphogenesis, muscle	0.3728	-0.4728	NA	ND
		Scaf1(274)	altTxStart	chr7:44871201-44884324	mRNA processing	0.2963	-0.5257	NA	ND
	Cell growth	Bat3(54)	altCassette	chr17:34746824-34747300	apoptosis, proton transport, re	-0.3433	0.7636	NA	S
		Chd7(57)	altTxStart	chr4:8618567-8678792	heart development, adult walki	0.5245	-0.6425	NA	ND
	Others	Usp5(69)	alt5Prime	chr6:124783637-124784174	ubiquitin cycle, ubiquitin-deper	-0.3387	0.3164	NA	ND
		Sugt1(108)	altCassette	chr14:78353939-78359010	ubiquitin cycle	0.485	-0.6578	NA	ND
		Kua(301)	altTxStart	chr2:167345861-167380985	Unknown	-0.6676	0.5861	NA	ND
		Hmox2(75)	altTxStart	chr16:4641689-4681056	heme oxidation	0.3665	-0.3058	NA	ND
		AW011752(484)	altTxStart	chr11:29073437-29088463	Unknown	0.3817	-0.4458	NA	ND
		2900010J23Rik(27)	altTxStart	chr2:32100859-32110054	Unknown	0.4098	-0.8507	NA	ND
		5730469M10Rik(126)	altTxStart	chr14:39906564-39922422	Unknown	0.4838	-0.5989	NA	ND
		Lin54(44)	altTxStart	chr5:100720577-100726119	Unknown	0.6867	-0.5946	NA	ND
HSALR only	Cytoskeleton and muscle contraction	ZAK(2084)	altTxEnd	chr2:72169281-72239106	cytoskeleton organization and	-1.1977	NA	-1.8907	ND
		Mtap1b(1642)	altTxEnd	chr13:100535844-100541815	cytoskeletal regulatory protein	0.2968	NA	0.3858	ND
	Signaling transduction	Dnm1l(67)	alt5Prime	chr16:16227872-16272088	GTP binding, GTPase activity,	-0.8641	NA	-0.8203	ND
		Uaca(6)	alt5Prime	chr9:60652494-60654218	DNA damage response, signal	0.5034	NA	0.4065	ND
		Ramp2(210)	altTxStart	chr11:101062644-101064172	G-protein coupled receptor prc	-4.3226	NA	-4.3585	ND
		Gnai3(249)	altTxStart	chr3:108246371-108273958	G-protein coupled receptor prc	-4.0354	NA	-4.0929	ND
		Gfra4(36)	altTxStart	chr2:130733112-130734497	coreceptor activity, GPI anchoi	-0.6385	NA	-0.6057	ND
		Ptp4a2	altTxStart	chr4:129341358-129351147	protein amino acid dephospho	-0.4576	NA	-0.3433	ND
	DNA transcription and mRNA processing	Eif4g3(702)	altCassette	chr4:137398695-137460151	regulation of translational initia	0.5227	NA	-0.7489	ND
		Thra(120)	altTxEnd	chr11:98573082-98584378	ligand-dependent nuclear rece	0.4766	NA	0.3451	ND
		Phf17(102)	altTxStart	chr3:41688299-41701033	regulation of transcription, DN	-2.9382	NA	-3.5931	ND
		C1d(85)	altTxStart	chr11:17157651-17163643	negative regulation of transcrip	-0.6577	NA	-0.3802	ND
		Phf17(76)	altTxStart	chr3:41688299-41701033	regulation of transcription, DN	-2.6358	NA	-2.7545	ND
	Others	Car3(93)	altCassette	chr3:14843653-14845991	one-carbon compound metabc	-1.1408	NA	-0.5745	S
		Rpn2(48)	altCassette	chr2:157013301-157017163	protein amino acid N-linked gly	-0.6277	NA	-0.7149	H
		2310030N02Rik(57)	altCassette	chr4:10989284-10997361	ND	-0.6818	NA	-0.5159	ND
		Etfa(15)	alt3Prime	chr9:55280462-55283421	electron transport	5.5072	NA	4.8036	ND
		Rere(393)	altTxEnd	chr4:149419635-149459457	chromatin remodeling, multice	-5.4728	NA	-6.3357	ND
		Gpihbp1(609)	altTxEnd	chr15:75423909-75425347	cholesterol transport, lipid tran	0.351	NA	-0.6701	ND
		AK006195(66)	altTxEnd	chr3:88381321-88382704	Unknown	0.5061	NA	0.5257	ND
		Bcas2(598)	altTxEnd	chr3:103303491-103306414	Unknown	0.5969	NA	0.7117	ND
		Dsip1(330)	altTxStart	chrX:135887433-135889221	Unknown	NA	0.2215	-0.4488	ND
		Nudt4(66)	altTxStart	chr10:94981149-94991801	diphosphoinositol-polyphospha	-2.2457	NA	-2.3912	ND
		Col4a2(4066)	altTxStart	chr8:11313467-11445049	extracellular matrix structural c	-0.6353	NA	-0.4544	ND
		AI314180(45)	altTxStart	chr4:58973121-59005937	binding	0.3147	NA	0.3017	ND
		Dazap2(156)	altTxStart	chr15:100443703-100447750	protein binding	0.3392	NA	0.3319	ND

Extra validation in AltCassette exons beyond sepscore cutoff>0.3

Grouping	Gene name	Splicing Mode	FVB_MBNL1-HSALR sepscore	FVB MBNL1-wt sepscore	FVB HSALR wt-sepscore	Validation
Both HSALR and MBNL1KO	BC047531(116)/Eif4g3	altCassette	NA	NA	-0.7489	S
	Vldlr(84)	altCassette	NA	NA	1.1598	O
MBNL1KO only	Ndrg2(42)	altCassette	NA	1.6857	NA	M
	Dmwd(75)	altCassette	NA	-0.2427	NA	O
	Xpa(192)	altCassette	NA	NA	NA	O
	Pacsin2(123)	altCassette	NA	0.5125	NA	F
	Exoc7(93)	altCassette	NA	0.3172	NA	F
	Cacna2d1(21)	altCassette	NA	-0.3829	NA	F
	Akr1a4(90)	altCassette	NA	0.5531	NA	S
	Sdfr2(59)	altCassette	NA	NA	NA	S
	2610015J01Rik(74)/RBr	altCassette	NA	-0.8454	NA	S
HSALR only	Itga7(113)	altCassette	NA	NA	0.4716	O
	BC054358(93)/Sec31a	altCassette	NA	NA	0.6124	F
	Ubtf(111)	altCassette	NA	NA	-0.3241	F
	Zmynd11(96)	altCassette	NA	NA	-0.494	F
	G7018701 RC a at(57)	altCassette	-0.6818	NA	-0.5159	F
	Tmc6 (145)	altCassette	NA	NA	NA	F
	Usf2(201)	altCassette	NA	NA	-0.4924	S
	Nfix(148)	altCassette	NA	NA	-0.4902	S
	Hdac2	altCassette	NA	NA	-0.4223	S
	Strn3(111)	altCassette	NA	NA	0.5763	S
	AK129064(225)/Arhgef7	altCassette	NA	NA	-0.848	S
	AK031374(108)/Huwe1	altCassette	NA	NA	-0.3961	S
	AK078881 (45)	altCassette	NA	NA	NA	S
	Fxr1h(92)	altCassette	NA	NA	NA	S
	BC047531/Eif4g3 (1953	altCassette	NA	NA	NA	S
	G6868353@J910214/Cc	altCassette	NA	NA	NA	S
	Taf12 (252)	altCassette	NA	NA	NA	S
	Fkbp6 (120)	altCassette	NA	NA	NA	S
	1110006G06Rik/FAM98(	altCassette	NA	NA	NA	S
Data from Heart	Ppp1r12a(171)	altCassette	NA	NA	NA	O

Validation Table Summary for AltCassette exons.

Validated/Called->	KO + HSA +	KO + HSA -	KO - HSA +
Total	45	17	23
tested	27	15	21
KO - HSA -	0	4	5
KO + HSA +	23	2	1
KO + HSA -	0	4	0
KO - HSA +	0	0	1
1band	4	5	14
TP (no 1 band) (with 1 band)	100%(23/23) 85.2%(23/27)	40% (4/10) 27%(4/15)	14%(1/7) 5%(1/21)
Not tested	18	2	2

Supplementary Table 1. Grouping of aberrant exons in quadriceps skeletal muscle of two mouse models in the FVB background. Microarray data (*MBNL* $^{\Delta E3/\Delta E3}$ vs HSA$^{\mathrm{LR}}$, *MBNL1*$^{\Delta E3/\Delta E3}$ vs wt and *HSA*^{LR} vs wt) are analyzed by separation score analysis. Altered splicing events identified from splicing microarrays were divided into three groups by using separation score above 0.3: Overlapping group (*MBNL1*$^{\Delta E3/\Delta E3}$ vs wt $\geq$ 0.3 and *HSA*^{LR} vs wt $\geq$ 0.3); *MBNL1*$^{\Delta E3/\Delta E3}$ only group (*MBNL1*$^{\Delta E3/\Delta E3}$ vs wt $\geq$ 0.3; *HSA*^{LR} vs wt $\leq$ 0.3; *MBNL1*$^{\Delta E3/\Delta E3}$ vs *HSA*^{LR} $\geq$ 0.3); *HSA*^{LR} only group (*MBNL1*$^{\Delta E3/\Delta E3}$ vs wt $\leq$ 0.3; *HSA*^{LR} vs wt $\geq$ 0.3; *MBNL1*$^{\Delta E3/\Delta E3}$ vs *HSA*^{LR} $\geq$ 0.3). Those events are further grouped in this table by function acquired from Aceview. Chromosome coordinates in UCSC genome browser for mouse (mm8, 2006) are shown, and validation results are labeled with O (overlapping), M (*MBNL1*$^{\Delta E3/\Delta E3}$ only), H (*HSA*^{LR} only), F (false positive), S (single band in RT-PCR) and ND (Not determined).

Gene Name	Real Name	Splicing mode	Data Source	Repressed/activated	150bp upstream intron+40bp exon	40bp exon+150bp downstream intron
Cacna2d1	Cacna2d1	altCassette	H	-	[illegible]	[illegible]
Ubtf	Ubtf	altCassette	SM/H	-	[illegible]	[illegible]
AK035230	Ppp1r12a	altCassette	SM/H	-	[illegible]	[illegible]
Dmwd	Dmwd	altCassette	SM	-	[illegible]	[illegible]
Mllt3	Mllt3	altCassette	SM	-	[illegible]	[illegible]
Fgfr1	Fgfr1	altCassette	SM/H	-	[illegible]	[illegible]
Rnpc2	Rnpc2	altCassette	SM	-	[illegible]	[illegible]
BC047205	BC047205	altCassette	SM	-	[illegible]	[illegible]
Atf2	Atf2	altCassette	H	-	[illegible]	[illegible]
Fip1l1	Fip1l1	altCassette	SM	-	[illegible]	[illegible]
AK012697	Rsrc2	altCassette	SM	-	[illegible]	[illegible]
Sars1	Sars1	altCassette	SM	-	[illegible]	[illegible]
Tpd52l2	Tpd52l2	altCassette	SM	-	[illegible]	[illegible]
Gtf2i	Gtf2i	altCassette	H	-	[illegible]	[illegible]
Zfyve21	Zfyve21	altCassette	H	-	[illegible]	[illegible]
Hdac7a	Hdac7a	altCassette	SM	-	[illegible]	[illegible]
Ttc3	Ttc3	altCassette	SM	-	[illegible]	[illegible]
F3	F3	altCassette	H	-	[illegible]	[illegible]
Anks1	Anks1	altCassette	H	-	[illegible]	[illegible]
Opn1mw	Opn1mw	altCassette	SM	-	[illegible]	[illegible]
Stk2	Stk2	altCassette	SM	-	[illegible]	[illegible]
BC019977	Rprc1	altCassette	SM/H	-	[illegible]	[illegible]
AF150755	Macf1	altCassette	SM	-	[illegible]	[illegible]
Cryzl1	Cryzl1	altCassette	SM	-	[illegible]	[illegible]
AK011541	Ranbp3	altCassette	SM	-	[illegible]	[illegible]
Anapc10	Anapc10	altCassette	SM	-	[illegible]	[illegible]
Pdlim7	Pdlim7	altCassette	SM/H	-	[illegible]	[illegible]
Nfix	Nfix	altCassette	SM/H	-	[illegible]	[illegible]
Smyd1	Smyd1	altCassette	SM/H	-	[illegible]	[illegible]
Csda	Csda	altCassette	SM/H	-	[illegible]	[illegible]
Mtdh	Mtdh	altCassette	SM/H	-	[illegible]	[illegible]
Gnas	Gnas	altCassette	SM	-	[illegible]	[illegible]
Mbnl1	Mbnl1	altCassette	SM/H	-	[illegible]	[illegible]
Camk2g	Camk2g	altCassette	SM/H	-	[illegible]	[illegible]
Opa1	Opa1	altCassette	SM	-	[illegible]	[illegible]
Camk2g	Camk2g	altCassette	SM	-	[illegible]	[illegible]
1110028E10Rik	Slc44a2	altCassette	SM/H	-	[illegible]	[illegible]
BC060652	D11bwg0280e	altCassette	SM	-	[illegible]	[illegible]
AK032084	ANKRD11	altCassette	SM/H	-	[illegible]	[illegible]
1700113I22Rik	AARSD1	altCassette	SM	-	[illegible]	[illegible]
Akt2	Akt2	altCassette	SM	-	[illegible]	[illegible]
Mlf1	Mlf1	altCassette	SM	-	[illegible]	[illegible]
Jag2	Jag2	altCassette	SM	-	[illegible]	[illegible]
Ap1b1	Ap1b1	altCassette	SM	-	[illegible]	[illegible]
zasp_cypher	zasp	altCassette	16717059	-	[illegible]	[illegible]
m-titin	m-titin	altCassette	16717059	-	[illegible]	[illegible]
Mbnl2	Mbnl2	altCassette	16717059	-	[illegible]	[illegible]
TNNT3	TNNT3	altCassette	17702765; 18286170	-	[illegible]	[illegible]
CLCN1	CLCN1	altCassette	14671308	-	[illegible]	[illegible]
mouse-TNT	cTNT	altCassette	15257297	-	[illegible]	[illegible]
Fn1	Fn1	altCassette	SM/H	-	[illegible]	[illegible]
Fn1	Fn1	altCassette	SM/H	-	[illegible]	[illegible]
Sugt1	Sugt1	altCassette	SM	-	[illegible]	[illegible]
AK129064	Arhgef7	altCassette	H	-	[illegible]	[illegible]
Add3	Add3	altCassette	SM/H	+	[illegible]	[illegible]
Tmem63b	Tmem63b	altCassette	SM/H	+	[illegible]	[illegible]
Xpa	Xpa	altCassette	SM	+	[illegible]	[illegible]
Itga7	Itga7	altCassette	SM	+	[illegible]	[illegible]
AF459099	Stau2	altCassette	SM	+	[illegible]	[illegible]
Rpn1	Rpn1	altCassette	SM	+	[illegible]	[illegible]
Sorbs1	Sorbs1	altCassette	H	+	[illegible]	[illegible]
Vldlr	Vldlr	altCassette	SM	+	[illegible]	[illegible]
Yif1	Yif1	altCassette	SM	+	[illegible]	[illegible]
Tlk1	Tlk1	altCassette	SM/H	+	[illegible]	[illegible]
Nkiras1	Nkiras1	altCassette	SM	+	[illegible]	[illegible]
Ctbp1	Ctbp1	altCassette	SM	+	[illegible]	[illegible]
Eapp	Eapp	altCassette	SM	+	[illegible]	[illegible]
Luc7l2	Luc7l2	altCassette	H	+	[illegible]	[illegible]
Mrpl10	Mrpl10	altCassette	SM	+	[illegible]	[illegible]
Dscr5	Dscr5	altCassette	SM	+	[illegible]	[illegible]
Bnipl	Bnipl	altCassette	SM	+	[illegible]	[illegible]
Col4a3bp	Col4a3bp	altCassette	SM	+	[illegible]	[illegible]
Senp6	Senp6	altCassette	SM	+	[illegible]	[illegible]
Tcea1	Tcea1	altCassette	SM	+	[illegible]	[illegible]
Scp2	Scp2	altCassette	H	+	[illegible]	[illegible]
Gfpt1	Gfpt1	altCassette	SM	+	[illegible]	[illegible]
Abi1	Abi1	altCassette	SM/H	+	[illegible]	[illegible]
Bgn	Bgn	altCassette	SM	+	[illegible]	[illegible]
Srrm1	Srrm1	altCassette	SM/H	+	[illegible]	[illegible]
Mllt1	Mllt1	altCassette	SM	+	[illegible]	[illegible]
Postn	Postn	altCassette	SM	+	[illegible]	[illegible]
Zdhhc16	Zdhhc16	altCassette	SM	+	[illegible]	[illegible]
Hrb	Hrb	altCassette	SM	+	[illegible]	[illegible]
Picalm	Picalm	altCassette	SM/H	+	[illegible]	[illegible]
5730461K03Rik	ECD	altCassette	SM	+	[illegible]	[illegible]
Pcm1	Pcm1	altCassette	SM	+	[illegible]	[illegible]
Myo5a	Myo5a	altCassette	SM	+	[illegible]	[illegible]
Gba	Gba	altCassette	SM	+	[illegible]	[illegible]
Picalm	Picalm	altCassette	SM/H	+	[illegible]	[illegible]
Ppp2r5c	Ppp2r5c	altCassette	SM/H	+	[illegible]	[illegible]
Aplp2	Aplp2	altCassette	SM/H	+	[illegible]	[illegible]
Hnrpa2b1	Hnrpa2b1	altCassette	SM/H	+	[illegible]	[illegible]
Erc1	Erc1	altCassette	SM	+	[illegible]	[illegible]
Add1	Add1	altCassette	SM/H	+	[illegible]	[illegible]
Anxa6	Anxa6	altCassette	SM	+	[illegible]	[illegible]
Tlk2	Tlk2	altCassette	SM/H	+	[illegible]	[illegible]
Spag9	Spag9	altCassette	SM/H	+	[illegible]	[illegible]
Sorbs1	Sorbs1	altCassette	SM/H	+	[illegible]	[illegible]
Vldlr	Vldlr	altCassette	SM	+	[illegible]	[illegible]
A2bp1	A2bp1	altCassette	SM/H	+	[illegible]	[illegible]
2810004N20Rik	2810004N20Rik	altCassette	SM	+	[illegible]	[illegible]
Ndel1	Ndel1	altCassette	SM	+	[illegible]	[illegible]
Ncoa2	Ncoa2	altCassette	SM	+	[illegible]	[illegible]
Mgrn1	Mgrn1	altCassette	SM/H	+	[illegible]	[illegible]
Mtmr3	Mtmr3	altCassette	SM	+	[illegible]	[illegible]
Mff	Mff	altCassette	SM	+	[illegible]	[illegible]
Nrap	Nrap	altCassette	16717059	+	[illegible]	[illegible]
Gfpt1	Gfpt1	altCassette	SM	+	[illegible]	[illegible]
serca1	serca1	altCassette	16717059; 17728322	+	[illegible]	[illegible]
INSR	INSR	altCassette	16946708;15257297	+	[illegible]	[illegible]
Ndrg2	Ndrg2	altCassette	SM/H	+	[illegible]	[illegible]
Capzb	Capzb	altCassette	SM	+	[illegible]	[illegible]
Ppp2r2d	Ppp2r2d	altCassette	SM	+	[illegible]	[illegible]
Asb11	Asb11	altCassette	SM	+	[illegible]	[illegible]
Oxnad1	Oxnad1	altCassette	SM	+	[illegible]	[illegible]

Supplementary Table 2. Motif searching list with sequences of Mbnl1-regulated exons identified from splicing microarrays in mouse skeletal muscle, heart and in the literature. +/– indicates the Mbnl1-repressed exons whose inclusion increases on loss of Mbnl1 (–), and Mbnl1-activated exons whose skipping increases on loss of Mbnl1 (+). The upstream intron sequences (150-40) includes 150bp upstream intron and 40bp exon near 3’ss, and the downstream intron (40-150) includes 150bp downstream intron and 40bp exon near 5’ss. Median conservation score for the indicated sequence is from the UCSC genome browser.

Expression changes grouped by cutoff (q<0.05; FC>1.5)

Grouping	Function Category	Gene Name	Coordinates in 2006 mouse Genome browser	Function	HSALR-wt-q value	HSALR-wt-d value	HSALR-wt-fold change	Log2FC(HSALR-wt)	MBNL1-wt-q value	MBNL1-wt-d value	MBNL1-wt-fold change	Log2FC(MBNL1-wt)	HSALR-MBNL1-q-value	HSALR-MBNL1-d-value	HSALR-MBNL1-fold change	Validation
Both HSALR and MBNL1KO	Ion channels and ion transport	Cacng1	chr11:107519307-107532566	calcium ion transport	0	8.73	2.25	1.169925	0	7.49	1.7	0.76553475	0.025	4.56	1.32	ND
		Atp1b4	chrX:34560880-34581339	ion transport, potassium ion transport	0	7.61	1.96	0.97085365	0.036	3.44	2.19	1.13093087	0.46	-0.648	-1.11	ND
		Tnnc1	chr14:30037320-30040720	Calcium signaling pathway	0.034	-2.73	-1.82	-0.8639385	0	-8.48	-4.78	-2.2570106	0.253	2.12	2.61	O
	Cytoskeleton and muscle contraction	Myoz2	chr3:122998229-123026971	structural molecule activity in actin cytoskeleton	0.009	-4.38	-1.56	-0.641546	0.036	3.44	1.52	0.60407132	0.015	-5.31	-2.37	ND
		Nrap	chr19:56373293-56443285	actin cytoskeleton organization and biogenesis	0.003	6.42	1.54	0.62293035	0.02	4.13	1.56	0.64154603	0.527	-0.112	-1	ND
		Rock2	chr12:16920669-17003586	actin cytoskeleton organization and biogenesis	0.005	-5.47	-1.63	-0.704872	0.011	-4.12	-1.62	-0.6959938	0.527	-0.0653	-1	ND
		Myl2	chr5:122361595-122367471	cardiac myofibril assembly	0.016	-3.57	-1.53	-0.6135317	0	-10.4	-2.32	-1.2141248	0.225	2.21	1.51	ND
		Pdlim7	chr13:55505430-55523056	actin cytoskeleton organization and biogenesis	0	-16	-2.67	-1.4168397	0	-14.8	-2.89	-1.5310695	0.373	1.77	1.12	O
		Tnni1	chr1:137616243-137627374	actin binding, structural constituent of cytoskeleton	0.045	-2.33	-1.63	-0.704872	0.006	-6.43	-3.16	-1.6599246	0.308	1.95	1.94	ND
		Pdlim3	chr8:47384287-47418363	actin filament organization	0	9.94	1.96	0.97085365	0.049	3.09	1.74	0.79908731	0.563	0.953	1.12	ND
	Metabolism	Khk	chr5:31198194-31207826	carbohydrate metabolic process	0.007	-4.94	-1.56	-0.641546	0.02	-3.4	-1.53	-0.6135317	NA	NA	NA	ND
		Gpd2	chr2:57053682-57182985	gluconeogenesis	0.009	-4.19	-1.51	-0.5945485	0.006	-5.74	-1.55	-0.6322682	0.605	0.228	1.02	ND
		Irs1	chr1:82,097,506-82,185,189	insulin secretion, protein kinase B signaling cascade, signal transduction	0.034	-2.7	-1.58	-0.6599246	0.049	-2.57	-1.55	-0.6322682	0.51	-0.366	-1.01	ND
		Ace	chr11:105784057-105805349	metabolic process, proteolysis	0.016	-3.6	-2.03	-1.0214797	0.049	-2.58	-1.55	-0.6322682	0.113	-2.4	-1.3	ND
		Gpd1	chr15:99545626-99553039	gluconeogenesis	0.008	-4.53	-1.63	-0.704872	0.023	-3.36	-1.58	-0.6599246	0.527	-0.259	-1.02	ND
		Lpin1	chr12:16562115-16636593	lipid metabolic process	0.007	-5.17	-1.56	-0.641546	0.006	-5.92	-1.64	-0.7136958	0.598	0.654	1.03	ND
		Acot7	chr4:151021933-151115647	fatty acid catabolic process	0.004	-6.67	-1.86	-0.8953026	0.006	-6.67	-1.87	-0.9030383	NA	NA	NA	ND
		Zfp106	chr2:120198270-120255272	insulin receptor signaling pathway	0.006	4.71	1.72	0.78240856	0.005	5.91	2.07	1.04963077	0.225	-1.69	-1.2	ND
		Fbp2	chr13:62846507-62867993	metabolic process, gluconeogenesis	0	15.8	5.5	2.45943162	0.006	5.27	2.43	1.28095631	0	8.38	2.26	ND
		Igfbp5	chr1:72791271-72808072	insulin-like growth factor binding	0	-7.49	-3.16	-1.6599246	0.006	-6.12	-2.66	-1.4114262	0.373	-1.01	-1.18	O
		Pfkfb3	chr2:11389287-11471694	fructose 2,6-bisphosphate metabolic process	0.014	-3.7	-2.71	-1.4382929	0.027	-3.11	-2.19	-1.1309309	0.339	-1.09	-1.23	ND
		Mod1	chr9:86378093-86492941	malate metabolic process	0.016	-3.58	-1.88	-0.9107327	0.009	-4.39	-2.29	-1.1953476	0.373	1.7	1.21	ND
	Signaling pathway	Il1r2	chr1:40029313-40069769	cell surface receptor linked signal transduction	0.018	-3.39	-1.66	-0.7311832	0.043	-2.74	-1.5	-0.5849625	0.339	-1.15	-1.08	ND
		Htra1	chr7:130727382-130776801	negative regulation of BMP signaling pathway, negative regulation of TGF beta receptor signaling pathway	0	-7.12	-1.88	-0.9107327	0.006	-5.32	-1.51	-0.5945485	0.156	-2.01	-1.24	ND
		Tsku	chr7:98226059-98236480	protein binding, transferase activity	0.009	-4.32	-1.81	-0.8559897	0.049	-2.58	-1.54	-0.6229304	NA	NA	NA	ND
		Slc8a3	chr12:82118293-82252028	transport, cell communication	0.009	4.27	1.56	0.64154603	0.011	4.59	1.56	0.64154603	0.605	0.0251	1	ND
		Snx3	chr10:42190445-42223782	cell communication, protein transport, intracellular signaling cascade	0.008	-4.54	-1.53	-0.6135317	0.006	-4.68	-1.58	-0.6599246	0.585	0.735	1.03	ND
		Tnfrsf19	chr14:59918145-60000579	receptor activity	0.014	3.93	2	1	0.023	3.91	1.62	0.69599381	0.532	1.25	1.2	ND
		Calm1	chr12:100600590-100610856	cell cycle, G-protein coupled receptor protein signaling pathway	0	-9.17	-1.62	-0.6959938	0	-10.2	-1.71	-0.7739963	0.581	0.773	1.05	ND
		Sort1	chr3:108412187-108489565	endocytosis	0	-7.8	-1.95	-0.9634741	0.006	-5.63	-1.71	-0.7739963	0.373	-1.04	-1.13	ND
		Atrnl1	chr19:57664294-58186588	G-protein coupled receptor protein signaling pathway	0.008	4.57	2.77	1.46988598	0.023	3.87	1.73	0.79077204	0.156	2.54	1.59	ND
		Asb5	chr8:56049027-56086533	intracellular signaling cascade	0.009	-4.37	-1.62	-0.6959938	0.006	-5.59	-1.87	-0.9030383	0.178	2.45	1.15	ND
		Csnk1d	chr11:120775370-120807423	Wnt receptor signaling pathway	0.007	-5.15	-1.76	-0.8155754	0.006	-5.86	-1.98	-0.9855004	0.527	1.29	1.08	ND
		Dok5	chr2:170423144-170570973	MAPKKK cascade	0	8.58	1.85	0.88752527	0.023	3.94	2.05	1.03562391	0.434	-0.749	-1.1	ND
		Centb5	chr4:154735674-154751050	regulation of GTPase activity	0.016	-3.59	-1.98	-0.9855004	0.009	-4.54	-2.32	-1.2141248	0.568	0.903	1.17	ND
		Gdf8	chr1:53006207-53012624	transforming growth factor beta receptor signaling pathway	0	-8.27	-1.84	-0.8797058	0	-9.44	-2.38	-1.2509616	0.373	1.71	1.28	ND
		Zfp289	chr2:91065829-91077769	regulation of GTPase activity	0.01	-4.13	-2.69	-1.4276062	0.006	-5.21	-2.96	-1.5655972	NA	NA	NA	ND
		Tbc1d1	chr5:64439345-64630621	regulation of Rab GTPase activity	0	7.34	4.09	2.03210084	0	7.99	3.21	1.6825733	0.339	1.82	1.27	ND
		Gadd45b	chr10:80333219-80335333	activation of MAPKK activity	0.006	4.8	2.52	1.33342373	0.005	5.71	2.53	1.33913738	0.527	-0.0269	-1	ND
		Plcd4	chr1:74476095-74499184	intracellular signaling cascade	0.004	-6.44	-1.61	-0.6870607	0.006	-5.19	-1.53	-0.6135317	0.46	-0.646	-1.04	ND
	DNA transcription and mRNA processing	Nfil3	chr13:52979641-52993471	regulation of transcription	0.024	-3.04	-1.64	-0.7136958	0.049	-2.53	-1.5	-0.5849625	0.434	-0.77	-1.09	ND
		Hlx1	chr1:186427930-186433396	regulation of transcription	0.021	3.53	1.52	0.60407132	0.005	5.99	1.57	0.65076456	0.51	-0.326	-1.03	ND
		Sra1	chr18:36793220-36796267	positive regulation of transcription from RNA polymerase II promoter, apoptosis	0.018	-3.41	-1.85	-0.8875253	0.027	-3.1	-1.73	-0.790772	0.373	-1.07	-1.07	ND
		Irf5	chr6:29476742-29487329	regulation of transcription	0	6.91	1.79	0.83995959	0.049	3.05	1.83	0.87184365	0.488	-0.528	-1.08	ND
		Smad3	chr9:63444772-63556000	negative regulation of transcription	0	-7.46	-1.71	-0.7739963	0	-7.71	-1.96	-0.9708537	0.253	2.13	1.14	ND
		Rxrg	chr1:169435058-169476298	regulation of transcription	0.014	-3.71	-1.87	-0.9030383	0.015	-3.83	-1.98	-0.9855004	0.59	0.717	1.05	ND
		Cugbp2	chr2:6456970-6802268	mRNA splice site selection, mRNA processing	0.01	-4.07	-1.55	-0.6322682	0.009	-4.23	-1.57	-0.6507646	0.605	0.374	1.01	ND
		Sox18	chr2:181599242-181601046	DNA binding, transcription factor activity	0.005	-5.41	-1.61	-0.6870607	0.006	-4.82	-1.59	-0.6690268	0.527	-0.126	-1.01	ND
		Klf5	chr14:98181833-98196541	DNA binding, protein binding, transcription factor activity	0.009	4.46	1.84	0.87970577	0.003	6.23	2.03	1.02147973	0.403	-0.907	-1.1	ND
		Runx1	chr16:92492962-92586187	DNA binding, protein binding, transcription factor activity	0	8.4	2.28	1.18903382	0.005	6.02	2.28	1.18903382	0.527	-0.00534	-1	ND
	Cell cycle and development	Anapc13	chr9:102482197-102490054	cell cycle, cell division, mitosis, ubiquitin cycle	0.028	-2.85	-1.55	-0.6322682	0.02	-3.54	-1.5	-0.5849625	0.585	0.758	1.08	ND
		Grem2	chr1:176670459-176758494	cytokine activity	0.004	-6.14	-2.66	-1.4114262	0.02	-3.5	-1.55	-0.6322682	NA	NA	NA	ND
		Pacs2	chr12:113462315-113522209	apoptosis	0.005	-5.9	-1.53	-0.6135317	0.006	-6.53	-1.63	-0.704872	0.253	2.1	1.06	ND
		Cntfr	chr4:41846166-41885710	positive regulation of cell proliferation	0.004	-6.13	-1.7	-0.7655347	0	-10.2	-1.72	-0.7824086	0.605	0.0866	1.01	ND
		Lta4h	chr10:92883194-92914695	leukotriene biosynthetic process, proteolysis	0.014	-3.73	-1.67	-0.7398481	0.006	-5.12	-1.77	-0.8237494	NA	NA	NA	ND
		Cdkn1a	chr17:28818664-28828386	cell cycle arrest, negative regulation of apoptosis	0.009	4.3	1.53	0.61353165	0.016	4.3	1.8	0.84799691	0.206	-1.79	-1.17	ND
		Nfatc2	chr2:168167616-168292860	cytokine production	0	9.84	1.92	0.94110631	0	15.4	1.9	0.92599942	0.605	0.189	1	ND
		Calm3	chr7:16073900-16082554	cell cycle, G-protein coupled receptor protein signaling pathway	0	-10.5	-1.63	-0.704872	0	-7.56	-1.64	-0.7136958	0.605	0.091	1	ND
		Trp63	chr16:25679630-25807429	anti-apoptosis	0	8.7	2.04	1.02856915	0	7.88	1.91	0.93357264	0.545	1.11	1.06	ND
		Casp12	chr9:5345501-5373032	induction of apoptosis	0	-7.18	-2.59	-1.3729521	0	-9.56	-2.61	-1.3840498	NA	NA	NA	O
		Fhl1	chrX:53078570-53140129	involvement in muscle development or hypertrophy	0	15.5	2.73	1.44890095	0	7.35	3.3	1.72246602	0.206	-1.8	-1.21	O
		Chm	chrX:109157535-109302459	blood vessel development	0.009	-4.38	-1.57	-0.6507646	0.009	-4.48	-1.51	-0.5945485	0.51	-0.334	-1.02	ND
		Cyr61	chr3:145584361-145587367	patterning of blood vessels, regulation of cell growth	0.006	4.94	1.61	0.68706069	0.027	3.75	1.52	0.60407132	0.604	0.611	1.06	ND
	Cell adhesion	Vegfa	chr17:45480574-45495331	angiogenesis	0.011	-3.89	-1.5	-0.5849625	0.011	-4.19	-1.57	-0.6507646	0.598	0.668	1.04	ND
		Lims1	chr10:57718903-57820045	cell-cell adhesion, cell-matrix adhesion	0	7.08	1.92	0.94110631	0.003	7.06	1.64	0.71369581	0.434	1.54	1.14	ND
		Cntnap2	chr6:44989694-47230955	cell adhesion	0	11.2	2.45	1.29278175	0.006	5.55	1.69	0.75702325	0.025	4.55	1.44	ND
		Ctnna3	chr10:62825454-64398299	cell-cell adhesion	0	13	2.8	1.48542683	0	7.84	1.97	0.97819563	0.007	6.37	1.51	ND
		Fermt3	chr19:7066021-7086475	cell adhesion	0.007	-5.2	-1.97	-0.9781956	0.011	-3.95	-1.67	-0.7398481	NA	NA	NA	ND
	Others	Cox8b	chr7:140750262-140751743	electron transport	0.004	-6.25	-1.52	-0.6040713	0.011	-4.08	-1.52	-0.6040713	0.527	-0.0302	-1	ND
		Cd82	chr2:93219950-93263333	Unknown	0.008	-4.65	-1.93	-0.9486008	0.023	-3.32	-1.54	-0.6229304	0.044	-3.55	-1.27	ND
		Btaf1	chr19:36991222-37079201	ATP-dependent helicase activity	0.018	-3.41	-1.56	-0.641546	0.031	-2.94	-1.56	-0.641546	NA	NA	NA	ND
		Arl6ip5	chr6:97176254-97198777	glutamate transport	0.004	5.67	1.52	0.60407132	0.043	3.22	1.58	0.65992456	0.51	-0.35	-1.04	ND
		Smtnl1	chr2:84612015-84623491	Unknown	0	8.67	1.75	0.80735492	0.003	6.85	1.59	0.66902677	0.308	1.9	1.09	ND
		Mb	chr15:76842742-76877923	enucleate erythrocyte differentiation	0	11.8	1.62	0.69599381	0	18.6	1.63	0.70487196	0.527	-0.185	-1	ND
		Rap2ip	chr11:102209765-102218643	Unknown	0.024	-2.95	-1.67	-0.7398481	0.02	-3.5	-1.67	-0.7398481	NA	NA	NA	ND
		Pi16	chr17:29045893-29055914	endopeptidase inhibitor activity	0.004	-6.62	-2.81	-1.4905701	0.006	-5.06	-1.68	-0.7484612	0.046	-3.39	-1.67	ND
		Laptm4b	chr15:34182614-34228884	transport	0.034	-2.72	-1.65	-0.722466	0.023	-3.25	-1.69	-0.7570232	0.605	0.551	1.09	ND
		Pdrg1	chr2:152700331-152706824	protein folding	0	-8.37	-1.61	-0.6870607	0	-8.09	-1.72	-0.7824086	0.532	1.26	1.07	ND
		Cd74	chr18:60929217-60938020	antigen processing and presentation	0.039	-2.61	-1.58	-0.6599246	0.016	-3.61	-1.74	-0.7990873	0.605	0.533	1.08	ND
		Ppfia4	chr1:136114816-136129096	Unknown	0.045	-2.46	-1.64	-0.7136958	0.015	-3.87	-1.76	-0.8155754	0.605	0.326	1.07	ND
		Ccndbp1	chr2:120699848-120708353	protein binding	0.004	5.38	2.07	1.04963077	0.016	4.3	1.92	0.94110631	0.605	0.556	1.08	ND
		Slc47a1	chr11:61159596-61194530	multidrug transport	0.003	5.87	1.68	0.74846123	0	7.48	1.94	0.95605665	0.178	-1.84	-1.15	ND
		Acvr2a	chr2:48636165-48724172	anterior/posterior pattern formation	0.005	-5.37	-2.48	-1.3103401	0.006	-4.62	-2.09	-1.0635029	0.123	-2.22	-1.18	O
		Pkdcc	chr17:83123627-83133389	protein amino acid phosphorylation	0	-9.31	-1.64	-0.7136958	0	-13.2	-2.12	-1.0840643	0.013	5.54	1.3	ND
		Klhdc6	chr6:88579499-88603577	methyltransferase activity	0	-8.32	-1.54	-0.6229304	0	-11.7	-2.18	-1.1243281	0	7.68	1.41	ND
		Amotl1	chr9:14292363-14393887	identical protein binding, component of tight junctions	0	-17.8	-2.09	-1.0635029	0	-16.1	-2.19	-1.1309309	0.585	0.737	1.04	O
		Ucp2	chr7:100367445-100376102	mitochondrial transport	0	8.04	1.67	0.7398481	0	14.2	2.44	1.28688115	0.012	-7.27	-1.45	ND
		Phlda3	chr1:137582543-137585545	Unknown	0	11.2	3.98	1.99276843	0	7.36	3.18	1.66902677	0.156	2.49	1.25	ND
		Cilp	chr9:65063185-65078611	Unknown	0	9.01	5.24	2.38956681	0.005	5.82	3.22	1.68706069	0.031	4.05	1.64	ND
		Plekho1	chr3:96074246-96081244	Unknown	0	15.5	3.34	1.7398481	0	7.81	3.39	1.76128527	0.527	-0.162	-1.01	O
		Smox	chr2:131183079-131216613	polyamine oxidase activity, oxidoreductase activity, FAD binding	0.008	-4.59	-5.04	-2.3334237	0.011	-3.93	-3.4	-1.7655347	0.178	-1.88	-1.46	O
		Prepl	chr17:84971811-84998531	proteolysis	0	13.2	2.98	1.57531233	0	13.1	3.55	1.82781902	0.09	-2.6	-1.19	O
		Hspb7	chr4:140692854-140697386	response to stress, protein folding	0	17.1	3.08	1.62293035	0.02	4.14	3.96	1.98550043	0.308	-1.22	-1.28	ND
		Msrb3	chr10:120184163-120301912	protein repair	0	-8.08	-1.56	-0.641546	0	-9.12	-1.61	-0.6870607	0.545	1.13	1.03	ND
		Pla2g7	chr17:43031204-43075242	inflammatory response	0.011	-3.85	-2.22	-1.1505597	0.031	-3.01	-1.74	-0.7990873	0.113	-2.42	-1.29	ND

		Fam162a	chr16:35886533-35918803	Unknown	0.005	-5.52	-1.51	-0.5945485	0.006	-4.96	-1.57	-0.6507646	0.605	0.31	1.03	ND
		Setd8	chr5:124700547-124722925	chromatin modification	0.007	-5.03	-1.65	-0.722466	0.006	-5.48	-1.81	-0.8559897	0.532	1.24	1.09	ND
		1700001O2	chr2:30617345-30625573	Unknown	0.016	-3.56	-1.6	-0.6780719	0.011	-3.94	-1.74	-0.7990873	0.605	0.435	1.05	ND
HSALR only	cytoskeleton and muscle contraction	Myh2	chr11:66987414-67013707	actin binding	0.016	-3.54	-1.51	-0.5945485	0.049	2.97	1.43	0.51601515	0.012	-5.65	-2.18	ND
		Mtap1b	chr13:100524597-100616713	cytoskeletal regulatory protein binding	0	6.97	1.97	0.97819563	0.214	1.39	1.15	0.20163386	0.013	5.55	1.69	ND
		Epb41l2	chr10:25088272-25212651	cortical actin cytoskeleton organization and biogenesis	0	10.3	1.55	0.63226822	0.115	-1.77	-1.12	-0.1634987	0	9.58	1.71	ND
	Metabolism	Grb10	chr11:11830510-11937358	insulin-like growth factor receptor signaling pathway	0	-8.68	-1.77	-0.8237494	0.133	-1.69	-1.13	-0.1763228	0	-8.39	-1.72	ND
		Kdr	chr5:76214972-76260125	growth factor binding, ATP binding, kinase activity	0.039	-2.54	-1.68	-0.7484612	0.517	-0.0172	-1	0	0.035	-3.84	-1.67	ND
		Sparc	chr11:55237923-55263289	transmembrane receptor protein tyrosine kinase signaling pathway	0.011	-3.92	-2.05	-1.0356239	0.405	0.731	1.1	0.13750352	0	-8.82	-2.26	H
		Efna3	chr3:89400878-89408806	GPI anchor binding	0.024	3.38	1.55	0.63226822	NA	NA	NA	NA	0.046	3.68	1.86	ND
		Rgs5	chr1:171492175-171530201	G-protein coupled receptor protein signaling pathway, negative regulation of signal transduction	0.004	-6.68	-1.57	-0.6507646	0.184	-1.35	-1.09	-0.1243281	0.016	-4.98	-1.43	H
	DNA transcription	Ankrd33	chr15:100943788-100948056	regulation of transcription	0.014	3.92	1.85	0.88752527	0.405	0.648	1.1	0.13750352	0.046	3.62	1.68	ND
		Sox17	chr1:4481008-4486494	regulation of transcription, DNA-dependent	0.006	5.02	1.76	0.81557543	NA	NA	NA	NA	0.015	4.79	1.91	ND
	Cell cycle and development	Ccna1	chr3:55133403-55142984	cell cycle, cell differentiation, cell division	0	9.35	1.9	0.92599942	0.08	-2.04	-1.27	-0.3448285	0	10.3	2.43	ND
		Phf17	chr3:41652353-41713406	apoptosis, regulation of transcription	0.028	3.28	2.22	1.15055968	0.016	-3.62	-1.26	-0.3334237	0.04	3.9	3.11	ND
		Eng	chr2:32468603-32504124	heart development, regulation of transforming growth factor beta receptor signaling pathway, cell adhesion	0	-7	-1.6	-0.6780719	0.242	-1.15	-1.06	-0.0840643	0.012	-6.37	-1.51	ND
		Tgfb3	chr12:86945846-86967637	embryonic development	0.004	5.22	1.74	0.79908731	0.242	1.3	1.09	0.12432814	0.022	4.77	1.58	ND
		Thbs1	chr2:117803362-117818573	inflammatory response, negative regulation of angiogenesis, cell adhesion	0.005	-5.38	-1.51	-0.5945485	0.332	0.932	1.06	0.08406426	0.012	-6.77	-1.61	ND
		Lox	chr18:52641435-52655072	blood vessel development, collagen fibril organization	0.016	-3.48	-2.22	-1.1505597	0.155	1.66	1.26	0.33342373	0.012	-5.7	-2.81	ND
	cell adhesion	Fbln5	chr12:102147614-102220141	cell adhesion	0.005	-5.52	-1.67	-0.7398481	0.524	0.136	1	0	0	-7.56	-1.68	H
		Nid1	chr13:13229816-13304386	cell-matrix adhesion, glomerular basement membrane development, cell adhesion	0.016	-3.56	-1.55	-0.6322682	0.527	0.103	1.01	0.01435529	0.04	-3.66	-1.57	ND
		Thbs2	chr17:14403750-14430687	ECM-receptor interaction, Focal adhesion, TGF-beta signaling pathway	0.011	-3.89	-1.84	-0.8797058	0.508	0.225	1.02	0.02856915	0.022	-4.59	-1.87	ND
		Col15a1	chr4:47229292-47334265	structural molecule activity, extracellular matrix structural constituent conferring tensile strength	0.005	-5.53	-1.75	-0.8073549	0.359	0.853	1.1	0.13750352	0.028	-4.18	-1.93	ND
		Fbn1	chr2:124992035-125197879	extracellular matrix structural constituent	0.018	-3.39	-1.53	-0.6135317	0.096	2.2	1.29	0.36737107	0.028	-4.2	-1.98	H
		Col1a2	chr6:4455696-4491543	extracellular matrix structural constituent	0.021	-3.17	-2.12	-1.0840643	0.458	0.49	1.1	0.13750352	0.028	-4.21	-2.33	H
		Col1a1	chr11:94752359-94767937	extracellular matrix structural constituent	0.018	-3.43	-2.63	-1.3950628	0.441	0.529	1.1	0.13750352	0	-7.75	-2.91	ND
		Eln	chr5:134987222-135031881	extracellular matrix structural constituent	0.007	-4.76	-1.56	-0.641546	0.155	1.73	1.19	0.25096157	0.022	-4.75	-1.87	H
		Tnc	chr4:63446148-63507087	fibronectin binding, protein binding, receptor binding	0.024	-2.97	-1.53	-0.6135317	0.08	2.3	1.29	0.36737107	0.012	-5.83	-1.98	ND
	Others	Serpinb6a	chr13:33925391-34010149	Unknown	0	12.9	1.79	0.83995959	0.096	2.19	1.18	0.23878686	0.007	6.21	1.51	ND
		Ccdc80	chr16:45012875-45047256	Unknown	0.021	-3.14	-1.55	-0.6322682	0.508	-0.088	-1.01	-0.0143553	0.015	-5.45	-1.53	ND
		Syne1	chr10:4795848-5008032	Connects nuclei to the cytoskeleton by interacting with the nuclear envelope and with F-actin in the cytoplasm	0.006	4.69	1.71	0.77399633	0.306	1.06	1.08	0.11103131	0.04	3.86	1.57	ND
		Samsn1	chr16:75741473-75791946	phosphotyrosine binding	0.003	6.23	1.53	0.61353165	0.275	-1.01	-1.16	-0.2141248	0.025	4.53	1.79	ND
		C1qc	chr4:136161877-136164990	complement activation, complement activation	0.034	-2.7	-1.52	-0.6040713	0.115	2.03	1.24	0.31034012	0.012	-5.99	-1.9	ND
		Fmod	chr1:135853925-135865298	protein binding, transferase activity	0.014	-3.78	-2.06	-1.0426443	0.332	-0.825	-1.07	-0.0976108	0.044	-3.54	-1.91	ND
		Tnmd	chrX:129197357-129211925	Unknown	0.01	-4.13	-1.79	-0.8399596	0.275	1.2	1.12	0.16349873	0.012	-5.91	-2.02	ND
		Kera	chr10:97036896-97043375	protein binding, transferase activity	0.007	-4.91	-2.89	-1.5310695	0.405	-0.537	-1.07	-0.0976108	0.028	-4.24	-2.68	H
		Tm4sf1	chr3:57374992-57389848	Unknown	0.011	4.06	3.33	1.73552218	0.359	0.857	1.06	0.08406426	0.031	4.17	3.49	ND
		Nfkbiz	chr16:55736328-55763805	inflammatory response, regulation of transcription	0	12.9	5.22	2.38404981	0.066	2.72	1.35	0.43295941	0	11.2	3.14	ND
		Gjb6	chr14:56077413-56087687	protein binding, gap junction channel activity	0.004	5.25	1.55	0.63226822	0.242	-1.12	-1.11	-0.1505597	0.013	5.41	1.58	ND
		Atg16l1	chr1:89587241-89623593	autophagy, protein transport	0	7.29	3.85	1.94485845	NA	NA	NA	NA	0	7.29	3.95	ND
		Psmb9	chr17:33792386-33797618	ubiquitin-dependent protein catabolic process	0	9.51	3.98	1.99276843	NA	NA	NA	NA	0	9.82	4.54	ND
MBNL1 only	Metabolism	Pla2g12a	chr3:129870652-129887833	lipid catabolic process, phospholipid metabolic process, lipid catabolism	0.011	3.97	1.33	0.41142625	0.005	5.87	2.13	1.09085343	0.031	-3.95	-1.6	ND
	cell cycle and development	Thbs4	chr13:93852338-93895511	cell adhesion	0.063	-2.03	-1.47	-0.5558162	0.023	3.8	1.55	0.63226822	0.025	-4.4	-2.28	ND
		Nbl1	chr4:138354367-138364968	cell cycle, negative regulation of progression through cell cycle	0.238	-0.857	-1.08	-0.1110313	0.027	3.72	2.24	1.16349873	0.04	-3.75	-2.32	ND
	Others	BC011467	chr11:72267832-72306115	Unknown	0.193	1.9	1.2	0.26303441	0.011	-4.16	-1.5	-0.5849625	0.007	6.62	1.8	ND
		Bgn	chrX:69736363-69748649	protein binding, transferase activity	0.17	-1.21	-1.18	-0.2387869	0.009	5.21	1.79	0.83995959	0.012	-6.35	-2.09	ND
		H19	chr7:142385072-142385908	Unknown	0.332	-0.453	-1.05	-0.0703893	0.003	6.75	1.98	0.98550043	0	-10.1	-2.09	ND
		Egln3	chr12:55100607-55125474	Unknown	0.332	-0.256	-1.03	-0.0426443	0.036	-2.85	-1.61	-0.6870607	0	7.25	1.56	ND

Addional validation beyond cutoff (q<0.05; Fold change>1.5)

Grouping	Gene Name	Coordinates in 2006 mouse Genome browser	Function	HSALR-wt-q-value	HSALR-wt-d-value	HSALR-wt-fold change	Log2FC(HSALR-wt)	MBNL1-wt-q-value	MBNL1-wt-d-value	MBNL1-wt-fold change	Log2FC(MBNL1-wt)	HSALR-MBNL1-q-value	HSALR-MBNL1-d-value	HSALR-MBNL1-fold change	Validation
Both	Kcnab1	chr3:65197312-65466147	potassium channel regulator activity	NA	NA	NA	NA	0.006	-6.29	-10.6	-3.4059924	NA	NA	NA	O
MBNL1KO and HSALR	Sln	chr9:53648387-53651986	regulation of calcium ion transport	0.034	3.07	2.53	1.33913738	NA	NA	NA	NA	0.403	1.63	1.42	O
	Atf3	chr1:192870913-192883948	gluconeogenesis, regulation of transcription	0	9.15	3.06	1.61353165	0.115	2.04	3.79	1.92219785	0.46	-0.531	-1.23	O
	Igf1	chr10:87289828-87361590	insulin-like growth factor receptor binding	0.021	-3.16	-2.91	-1.5410192	0.066	-2.27	-1.89	-0.9183862	0.06	-3.19	-1.54	O
HSALR only	Actc1	chr2:113738729-113744252	structural constituent of muscle	0.021	-3.25	-11.44	-3.5160151	0.359	-0.76	-1.37	-0.4541759	0.072	-2.86	-8.32	H
	Ogn	chr13:49620007-49636437	growth factor activity, protein binding, transferase activity	0.007	-5.03	-2.68	-1.422233	0.036	-2.78	-1.43	-0.5160151	0.028	-4.31	-1.87	H
	Cav1	chr6:17256369-17291323	Focal adhension	0.005	-5.73	-1.38	-0.4646683	0.524	0.117	1	0	0.028	-4.27	-1.39	H
	Col6a1	chr10:76152507-76169760	Cell Communication, ECM-receptor interaction, Focal adhesion	0.045	-2.35	-1.4	-0.4854268	0.184	1.51	1.2	0.26303441	0.016	-4.77	-1.68	H
	Cdh5	chr8:106990827-107033630	Cell adhesion molecules (CAMs)	0.007	-5.04	-1.21	-0.275007	0.08	2.28	1.1	0.13750352	0.016	-5.02	-1.34	H
	Col4a1	chr8:11198402-11312702	Cell Communication, ECM-receptor interaction, Focal adhesion	0.024	-3.01	-1.45	-0.5360529	0.055	2.81	1.39	0.47508488	0.012	-6.3	-1.91	H
	Thrsp	chr7:97288150-97292702	Unknown	0.016	-3.55	-2.23	-1.1570437	0.441	-0.358	-1.1	-0.1375035	0.156	-2.01	-2.02	H
	Fads1	chr19:10250017-10263919	cell-cell signaling	0.016	-3.46	-1.34	-0.422233	0.486	0.326	1.02	0.02856915	0.012	-6.76	-1.4	H
MBNL1 only	Csrp3	chr7:48698418-48716033	cellular calcium ion homeostasis, cell differentiation, multicellular organismal development, striated muscle development	0.373	0.946	1.26	0.33342373	0.043	3.26	3.56	1.83187724	0.06	-3.08	-2.82	: opposite direction (see Fig 5)

Supplementary Table 3. Grouping of expression changes in quadriceps skeletal muscle of two mouse models in the FVB background. Fold change was determined by using microarray analysis. Altered mRNA levels identified from microarrays were divided into three groups using cutoffs (fold change ≥ 1.5): Overlapping group (*MBNL1*$^{ΔE3/ΔE3}$ vs wt ≥ 1.5 and *HSA*^{LR} vs wt ≥ 1.5); *MBNL1*$^{ΔE3/ΔE3}$ only group (*MBNL1*$^{ΔE3/ΔE3}$ vs wt ≥ 1.5; *HSA*^{LR} vs wt ≤ 1.5); *HSA*^{LR} only group (*MBNL1*$^{ΔE3/ΔE3}$ vs wt ≤ 1.5; *HSA*^{LR} vs wt ≥ 1.5). The events were further grouped by function acquired from Aceview. Chromosome coordinates are shown, and validation results acquired by quantitative RT-PCR are labeled with T (True) and ND (Not determined).

Gene Name	GO annotated genes	Enriched Go Term Group	position	Function in Aceview	HSA_wt_D	HSA_wt_Q	Mbnl1_wt_D	Mbnl1_wt_Q	HSA_Mbnl1_D	HSA_Mbnl1_Q
9130005N14Rik(FAM114A1)			chr5:65,343,078-65,452,468	unknown	-3.20000	0.02100	0.64500	0.42500	-3.52000	0.04400
AA536717(FAM149B1)			chr14:21,158,544-21,211,561	unknown	-2.82000	0.02800	0.05290	0.53000	-4.46000	0.02500
Acp2	ACP2		chr2:91003768-91012981	lysosome organization and biogenesis, skeletal development	-3.29000	0.01800	-0.36300	0.44100	-3.57000	0.04400
Acsl5	ACSL5		chr19:55305311-55349877	play a key role in lipid biosynthesis and fatty acid degradation	-4.34000	0.00900	0.34900	0.48600	-4.78000	0.01600
Actn4	ACTN4		chr7:28602015-28671040	actin filament bundle formation	-7.06000	0.00000	1.05000	0.30600	-4.43000	0.02500
Aes	AES		chr10:81,020,266-81,030,878	negative regulation of transcription, regulation of growth	-3.30000	0.01800	-0.72500	0.35900	-3.50000	0.04400
AI837181			chr19:5425156-5427312	Unknown	-6.90000	0.00400	-1.57000	0.15500	-5.52000	0.01500
Als2cr2			chr1:58918116-58939664	activation of protein kinase activity	-3.36000	0.01800	-0.30100	0.45800	-3.63000	0.04000
Ap1m1	AP1M1		chr8:75169120-75186368	intracellular protein transport	-3.16000	0.02100	-0.65400	0.38300	-4.92000	0.01600
Arhgdib	ARHGDIB		chr6:136887904-136905913	actin cytoskeleton organization and biogenesis	-4.53000	0.00800	-0.27500	0.47300	-3.69000	0.04000
C1qa	C1QA		chr4:136167991-136170920	tumor necrosis factor receptor binding	-2.56000	0.03900	-0.29400	0.45800	-3.88000	0.03500
C1qc	C1QC		chr4:136161877-136164990	complement activation	-2.70000	0.03400	2.03000	0.11500	-5.99000	0.01200
Calcrl	CALCRL		chr2:84131467-84177826	G-protein signaling	-4.10000	0.01000	-1.02000	0.27500	-3.45000	0.04600
Cav1	CAV1	Vasculature	chr6:17256369-17291323	Focal adhension	-5.73000	0.00500	0.11700	0.52400	-4.27000	0.02800
Ccdc80	CCDC80	ECM/adhesion	chr16:45012875-45047256	unknown	-3.14000	0.02100	-0.08800	0.50800	-5.45000	0.01500
Cd47	CD47	ECM/adhesion	chr16:49775279-49831844	integrin-mediated signaling pathway, cell adhesion	-2.69000	0.03400	1.02000	0.30600	-3.84000	0.03500
Cdh5	CDH5	ECM/adhesion, Vasculature	chr8:106990827-107033630	cell adhesion, blood vessel maturation	-5.04000	0.00700	2.28000	0.08000	-5.02000	0.01600
Cdk4	CDK4		chr10:126466563-126470344	cyclin-dependent protein kinase activity	-2.97000	0.02400	1.46000	0.21400	-3.78000	0.03500
Ckmt2	CKMT2		chr13:92327625-92351124	muscle contraction, generation of precursor metabolites and energy	-4.05000	0.01000	-1.89000	0.09600	-3.46000	0.04600
Col12a1	COL12A1	ECM/adhesion	chr9:79384675-79504362	extracellular matrix structural constituent conferring tensile strength	-4.24000	0.00900	-0.27400	0.47300	-3.95000	0.03100
Col15a1	COL15A1	ECM/adhesion	chr4:47229292-47334265	extracellular matrix structural constituent	-5.53000	0.00500	0.85300	0.35900	-4.18000	0.02800
Col1a1	COL1A1	ECM/adhesion, Vasculature	chr11:94752359-94767937	extracellular matrix structural constituent	-3.43000	0.01800	0.52900	0.44100	-7.75000	0.00000
Col1a2	COL1A2	ECM/adhesion	chr6:4455696-4491543	extracellular matrix structural constituent	-3.17000	0.02100	0.49000	0.45800	-4.21000	0.02800
Col4a1	COL4A1	ECM/adhesion	chr8:11198402-11312702	extracellular matrix structural constituent	-3.01000	0.02400	2.81000	0.05500	-6.30000	0.01200
Col6a1	COL6A1	ECM/adhesion	chr10:76152507-76169760	extracellular matrix structural constituent	-2.35000	0.04500	1.51000	0.18400	-4.77000	0.01600
Cpxm2	CPXM2	ECM/adhesion	chr7:131871050-131993082	cell adhesion, proteolysis	-5.57000	0.00500	0.31100	0.48600	-5.20000	0.01600
Ctsb	CTSB		chr14:63,735,427-63,770,624	proteolysis	-5.54000	0.00500	0.06350	0.53000	-6.08000	0.01200
Ctsd	CTSD		chr7:142185306-142197260	proteolysis	-5.50000	0.00500	-1.19000	0.24200	-3.87000	0.03500
Ctsl	CTSL		chr13:64377944-64385196	proteolysis	-5.68000	0.00500	0.66400	0.40500	-5.05000	0.01600
Degs1	DEGS1		chr1:184112446-184119434	fatty acid desaturation, lipid metabolic process	-3.25000	0.02100	1.75000	0.15500	-4.45000	0.02500
Ehd1	EHD1		chr19:6276905-6300096	endocytosis, endosome transport	-3.83000	0.01100	-0.67700	0.35900	-5.04000	0.01600
Eln	ELN	ECM/adhesion	chr5:134987222-135031881	extracellular matrix constituent conferring elasticity	-4.76000	0.00700	1.73000	0.15500	-4.75000	0.02200
Eng	ENG	ECM/adhesion, Vasculature	chr2:32468603-32504124	regulation of TGF beta receptor signaling pathway, angiogenesis, cell adhesion	-7.00000	0.00000	-1.15000	0.24200	-6.37000	0.01200
Fads1	FADS1		chr19:10250017-10263919	oxidoreductase activity	-3.46000	0.01600	0.32600	0.48600	-6.76000	0.01200
Fbln5	FBLN5	ECM/adhesion	chr12:102147614-102220141	cell-matrix adhesion	-5.52000	0.00500	0.13600	0.52400	-7.56000	0.00000
Fbn1	FBN1	ECM/adhesion	chr2:124992035-125197879	extracellular matrix structural constituent	-3.39000	0.01800	2.20000	0.09600	-4.20000	0.02800
Fmod	FMOD	ECM/adhesion	chr1:135853925-135865298	transforming growth factor beta receptor complex assembly	-3.78000	0.01400	-0.82500	0.33200	-3.54000	0.04400
Fstl1	FSTL1	ECM/adhesion	chr16:37696293-37755753	calcium ion binding, heparin binding	-2.45000	0.04500	2.93000	0.05500	-4.88000	0.01600
Fzd4	FZD4		chr7:89279585-89285277	Wnt receptor activity	-2.48000	0.03900	0.61400	0.42500	-3.42000	0.04600
G3bp2	G3BP2		chr5:93127345-93212766	cytoplasmic sequestering of NF-kappaB, Ras protein signal transduction	-2.91000	0.02800	0.80900	0.38300	-4.06000	0.02900
Gnai2	GNAI2		chr9:107472238-107493443	GTPase activity	-3.23000	0.02100	2.40000	0.08000	-6.49000	0.01200
Gng12	GNG12		chr6:66826033-66950872	signal transduction	-3.19000	0.02100	1.26000	0.24200	-3.82000	0.03500
Grb10	GRB10		chr11:11830510-11937358	cell-cell signaling, insulin receptor signaling pathway	-8.68000	0.00000	-1.69000	0.13300	-8.39000	0.00000
Gtpbp1	GTPBP1		chr15:79518150-79548733	GTP binding, GTPase activity	-5.07000	0.00700	0.17100	0.51700	-4.74000	0.02200
Ifi30	IFI30		chr8:73691761-73695899	phosphatidylinositol 3-kinase activity	-3.18000	0.02100	-0.71600	0.35900	-7.08000	0.01200
Ifngr1	IFNGR1		chr10:19281373-19299641	signal transduction	-5.38000	0.00500	-1.71000	0.13300	-3.98000	0.03100
Inca1			chr11:70504555-70516350	regulation of transcription	-2.35000	0.04500	1.02000	0.30600	-4.74000	0.02200
Islr	ISLR		chr9:57954409-57957279	cell adhesion	-2.54000	0.03900	1.88000	0.13300	-3.35000	0.04600
Kdr	KDR	Vasculature	chr5:76214972-76260125	angiogenesis	-2.54000	0.03900	-0.01720	0.51700	-3.84000	0.03500
Kera	KERA	ECM/adhesion	chr10:97036896-97043375	response to stimulus, visual perception	-4.91000	0.00700	-0.53700	0.40500	-4.24000	0.02800
Lgals9	LGALS9		chr11:78779351-78801067	intracellular signaling cascade	-4.36000	0.00900	2.46000	0.08000	-6.24000	0.01200
Lipe	LIPE		chr7:25088286-25105061	acylglycerol lipase activity	-3.20000	0.02100	-1.47000	0.15500	-3.36000	0.04600
Lox	LOX	ECM/adhesion, Vasculature	chr18:52641435-52655072	copper ion binding, protein-lysine 6-oxidase activity	-3.48000	0.01600	1.66000	0.15500	-5.70000	0.01200
Magi3	MAGI3		chr3:104144325-104349088	apoptosis, intracellular signaling cascade	-4.49000	0.00900	-1.33000	0.18400	-3.96000	0.03100
Map4k4	MAP4K4		chr1:39845775-39970628	ATP binding, protein serine/threonine kinase activity	-2.45000	0.04500	2.12000	0.09600	-3.83000	0.03500
Mmp2	MMP2	ECM/adhesion, Vasculature	chr8:95716455-95742547	proteolysis, blood vessel maturation, collagen catabolic process	-2.48000	0.03900	2.92000	0.05500	-4.57000	0.02200
Msn	MSN		chrX:92298763-92371271	structural constituent of cytoskeleton	-3.21000	0.02100	0.51900	0.44100	-3.37000	0.04600
Mylk	MYLK		chr16:34656280-34843781	myosin light chain kinase activity, signal transducer activity	-4.35000	0.00900	0.27000	0.49800	-6.11000	0.01200
Nid1	NID1	ECM/adhesion	chr13:13229816-13304386	extracellular matrix structural constituent	-3.56000	0.01600	0.10300	0.52700	-3.66000	0.04000
Nr2f2	NR2F2	Vasculature	chr7:70225462-70240259	lipid metabolic process	-3.44000	0.01800	-1.35000	0.18400	-3.49000	0.04400
Nrp1	NRP1	ECM/adhesion, Vasculature	chr8:131245329-131389437	vascular endothelial growth factor receptor activity	-3.44000	0.01800	-0.64800	0.38300	-6.05000	0.01200
Oxct1	OXCT1		chr15:3976494-4105341	metabolic process	-4.33000	0.00900	-2.26000	0.06600	-4.97000	0.01600
Parva	PARVA	ECM/adhesion	chr7:112218886-112382868	cell adhesion	-3.21000	0.02100	-0.68600	0.35900	-3.91000	0.03500
Pdlim1	PDLIM1		chr19:40275550-40324844	response to oxidative stress, regulation of transcription	-2.36000	0.04500	1.25000	0.24200	-3.45000	0.04600
Pecam1	PECAM1	ECM/adhesion	chr11:106470307-106531371	Cell adhesion molecules (CAMs)	-3.20000	0.02100	1.55000	0.18400	-5.93000	0.01200
Plod1	PLOD1	ECM/adhesion	chr4:146753861-146780504	electron transport	-3.92000	0.01100	-0.37800	0.44100	-4.57000	0.02200
Pmp22	PMP22		chr11:62945330-62975741	negative regulation of cell proliferation	-2.91000	0.02800	1.61000	0.18400	-3.62000	0.04400
Postn	POSTN	ECM/adhesion	chr3:54449053-54478960	cell adhesion	-3.71000	0.01400	2.01000	0.11500	-6.12000	0.01200
Prkcsh	PRKCSH		chr9:21753436-21764623	protein kinase cascade	-2.52000	0.03900	1.16000	0.27500	-3.92000	0.03500
Pygl	PYGL		chr12:71109416-71149590	glycogen phosphorylase activity	-4.69000	0.00700	-0.93800	0.30600	-4.24000	0.02800
Rab3il1	RAB3IL1		chr19:10082123-10105396	protein binding, Rab guanyl-nucleotide exchange factor activity	-2.79000	0.02800	0.02500	0.53000	-3.85000	0.03500
Rangap1	RANGAP1		chr15:81531508-81572551	Ran GTPase activator activity	-2.73000	0.03400	-1.50000	0.15500	-3.49000	0.04400
Rgl1	RGL1		chr1:154279748-154387329	regulation of small GTPase mediated signal transduction	-2.53000	0.03900	1.24000	0.24200	-3.50000	0.04400
Rgs5	RGS5		chr1:171492175-171530201	GTPase activator activity	-6.68000	0.00400	-1.35000	0.18400	-4.98000	0.01600
Rxrb	RXRB		chr17:33642305-33648847	regulation of transcription	-4.21000	0.00900	0.13100	0.52400	-3.35000	0.04600
Scotin			chr9:108896032-108915172	positive regulation of I-kappaB kinase/NF-kappaB cascade	-3.00000	0.02400	1.23000	0.24200	-4.16000	0.02900
Sept8	SEPT8		chr11:53363222-53387521	cell cycle	-5.37000	0.00500	1.03000	0.30600	-9.76000	0.00000
Serpinf1	SERPINF1	Vasculature	chr11:75226225-75238818	negative regulation of angiogenesis	-3.81000	0.01100	0.90900	0.35900	-5.49000	0.01500
Sh3kbp1	SH3KBP1		chrX:154971741-155318272	cell-cell signaling	-3.46000	0.01600	-0.02510	0.51700	-4.08000	0.02900
Slc25a39	SLC25A39		chr11:102218162-102224015	transport	-5.09000	0.00700	-0.13300	0.49800	-4.27000	0.02800
Slc3a2	SLC3A2		chr19:8773926-8790296	amino acid transport, calcium ion transport, cell growth	-2.53000	0.03900	-0.55500	0.40500	-3.40000	0.04600
Smoc2	SMOC2	ECM/adhesion	chr17:14016131-14141361	calcium ion binding	-6.16000	0.00400	-0.26900	0.47300	-4.00000	0.03100
Smpd1	SMPD1		chr7:105428235-105432203	signal transduction	-4.78000	0.00700	0.75200	0.38300	-4.36000	0.02500
Sparc	SPARC	ECM/adhesion	chr11:55237923-55263289	calcium ion binding, collagen binding, copper ion binding	-3.92000	0.01100	0.73100	0.40500	-8.82000	0.00000
Spna2	SPNA2		chr2:29787568-29853457	barbed-end actin filament capping	-5.99000	0.00500	-0.91000	0.30600	-3.60000	0.04400
Thbs1	THBS1	ECM/adhesion, Vasculature	chr2:117803362-117818573	cell adhesion, negative regulation of angiogenesis	-5.38000	0.00500	0.93200	0.33200	-6.77000	0.01200
Thbs2	THBS2	ECM/adhesion	chr17:14403750-14430687	ECM-receptor interaction, Focal adhesion, TGF-beta signaling pathway	-3.89000	0.01100	0.22500	0.50800	-4.59000	0.02200
Tmem62	TMEM62		chr2:120668502-120699277	apoptosis, endocytosis	-3.43000	0.01800	-1.25000	0.21400	-4.63000	0.02200
Tnc	TNC	ECM/adhesion	chr4:63446148-63507087	cell adhesion	-2.97000	0.02400	2.30000	0.08000	-5.83000	0.01200
Tnfaip2	TNFAIP2	Vasculature	chr12:111892769-111902825	angiogenesis	-4.40000	0.00900	-2.02000	0.08000	-5.28000	0.01500
Tnmd	TNMD		chrX:129197357-129211925	unknown	-4.13000	0.01000	1.20000	0.27500	-5.91000	0.01200
Wdr40a			chr4:41479974-41503493	unknown	-2.71000	0.03400	1.09000	0.30600	-3.44000	0.04600
Zmym1	ZMYM1		chr4:126549397-126563436	protein dimerization activity, zinc ion binding	-2.76000	0.03400	-0.83500	0.33200	-4.93000	0.01600

Supplementary Table 4. List of 93 transcripts (class II genes) that are significantly down-regulated in *HSA*^{LR} mice, but not in *MBNL1*$^{\Delta E3/\Delta E3}$ mice. This class of genes was obtained as described in the text.

inputGenes	GO ID	Total genes with GO term	# Genes Changed	P-Value	FDR	GO Term
Smox -1	19318	119	9	0.0001	0.0112	hexose metabolic process
Igfbp5 -1	43292	67	7	0.0001	0.0114	contractile fiber
Igf1 -1	6094	29	5	0.0001	0.0133	gluconeogenesis
Pi16 -1	1649	34	5	0.0002	0.0158	osteoblast differentiation
Pfkfb3 -1	50789	2746	62	0.0001	0.016	regulation of biological process
Zfp289 -1	46364	35	5	0.0002	0.0162	monosaccharide biosynthetic process
Pdlim7 -1	6006	100	8	0.0002	0.0173	glucose metabolic process
Grem2 -1	19319	33	5	0.0001	0.019	hexose biosynthetic process
Casp12 -1	48009	12	4	0	0.02	insulin-like growth factor receptor signaling pathway
Acvr2a -1	30016	64	7	0.0001	0.02	myofibril
Pla2g7 -1	7167	237	13	0.0001	0.02	enzyme linked receptor protein signaling pathway
Amotl1 -1	5996	124	9	0.0001	0.02	monosaccharide metabolic process
Ace -1	7154	1475	39	0.0002	0.02	cell communication
Centb5 -1	1558	92	7	0.0006	0.0341	regulation of cell growth
Fermt3 -1	30334	92	7	0.0006	0.0341	regulation of cell migration
Sort1 -1	7517	183	10	0.0006	0.035	muscle development
Cd82 -1	14909	11	3	0.0006	0.0354	smooth muscle cell migration
Mod1 -1	46165	40	5	0.0004	0.0358	alcohol biosynthetic process
Htra1 -1	51094	288	13	0.0005	0.0358	positive regulation of developmental process
Rxrg -1	34103	45	5	0.0007	0.0358	regulation of tissue remodeling
Acot7 -1	7166	573	20	0.0005	0.036	cell surface receptor linked signal transduction
Sra1 -1	45667	21	4	0.0003	0.0364	regulation of osteoblast differentiation
Gdf8 -1	44449	61	6	0.0004	0.0368	contractile fiber part
Tnnc1 -1	19838	58	6	0.0003	0.0371	growth factor binding
Tsku -1	10675	24	4	0.0005	0.0372	regulation of cellular carbohydrate metabolic process
Csnk1d -1	46850	42	5	0.0005	0.0375	regulation of bone remodeling
Smad3 -1	7165	1287	35	0.0004	0.0379	signal transduction
Cntfr -1	14910	10	3	0.0004	0.0381	regulation of smooth muscle cell migration
Lta4h -1	6090	37	5	0.0003	0.039	pyruvate metabolic process
Rap2ip -1	34637	85	7	0.0004	0.0396	cellular carbohydrate biosynthetic process
Il1r2 -1	43567	4	3	0	0.04	regulation of insulin-like growth factor receptor signaling pathway
Laptm4b -1	19563	2	2	0.0002	0.0411	glycerol catabolic process
Setd8 -1	46168	2	2	0.0002	0.0411	glycerol-3-phosphate catabolic process
Nfil3 -1	4367	2	2	0.0002	0.0411	glycerol-3-phosphate dehydrogenase (NAD+) activity
Ppfia4 -1	4368	2	2	0.0002	0.0411	glycerol-3-phosphate dehydrogenase activity
Pkdcc -1	9331	2	2	0.0002	0.0411	glycerol-3-phosphate dehydrogenase complex
Rock2 -1	3700	389	15	0.001	0.044	transcription factor activity
Tnni1 -1	6071	13	3	0.001	0.0448	glycerol metabolic process
Gpd1 -1	10463	13	3	0.001	0.0448	mesenchymal cell proliferation
Calm3 -1	10464	13	3	0.001	0.0448	regulation of mesenchymal cell proliferation
Calm1 -1	30335	48	5	0.0009	0.045	positive regulation of cell migration
Asb5 -1	8284	162	9	0.001	0.0451	positive regulation of cell proliferation
Plcd4 -1	16051	98	7	0.0008	0.046	carbohydrate biosynthetic process
Sox18 -1	65007	2938	62	0.0008	0.0467	biological regulation
Pdrg1 -1	42221	711	22	0.0013	0.0473	response to chemical stimulus
1700001O22Rik -1	46849	53	5	0.0014	0.0473	bone remodeling
Irs1 -1	51272	53	5	0.0014	0.0473	positive regulation of cell motion
Cd74 -1	6109	27	4	0.0008	0.0478	regulation of carbohydrate metabolic process
Chm -1	5520	12	3	0.0008	0.048	insulin-like growth factor binding
Myoz2 -1	14812	12	3	0.0008	0.048	muscle cell migration
Khk -1	45766	12	3	0.0008	0.048	positive regulation of angiogenesis
Lpin1 -1	2053	12	3	0.0008	0.048	positive regulation of mesenchymal cell proliferation
Btaf1 -1	40012	105	7	0.0013	0.0482	regulation of locomotion
Msrb3 -1	14706	137	8	0.0013	0.0486	striated muscle development
Cugbp2 -1	10906	14	3	0.0012	0.0491	regulation of glucose metabolic process
Anapc13 -1						
Klhdc6 -1						
Myl2 -1						
Snx3 -1						
Pacs2 -1						
Cox8b -1						
Gpd2 -1						
Fam162a -1						
Vegfa -1						
Kcnab1 -1						
Hlx1 1						
Arl6ip5 1						
Cdkn1a 1						
Nrap 1						
Slc8a3 1						
Cyr61 1						
Mb 1						
Ucp2 1						
Slc47a1 1						
Zfp106 1						
Smtnl1 1						
Irf5 1						
Klf5 1						
Dok5 1						
Nfatc2 1						
Lims1 1						
Atp1b4 1						
Pdlim3 1						
Tnfrsf19 1						
Trp63 1						
Ccndbp1 1						
Cacng1 1						
Runx1 1						
Cntnap2 1						
Gadd45b 1						
Sln 1						
Fhl1 1						
Atrnl1 1						
Ctnna3 1						
Prepl 1						
Atf3 1						
Hspb7 1						
Plekho1 1						
Phlda3 1						
Tbc1d1 1						
Cilp 1						
Fbp2 1						

Supplementary Table 5. GO analysis for Class I genes. Genes in Class I are listed, and their expression changes presumably arise as an indirect consequence of the loss of Mbnl1 splicing factor function.

Input Genes	GO ID	Total Genes w	# Changed Ge	P-Value	FDR	Term	Group
ACP2	5578	110	18	0	0	proteinaceous extracellular matrix	ECM/adhesion
ACSL5	31012	112	18	0	0	extracellular matrix	ECM/adhesion
ACTN4	44421	212	21	0	0	extracellular region part	ECM/adhesion
AES	5576	409	28	0	0	extracellular region	ECM/adhesion
AP1M1	44420	40	11	0	0	extracellular matrix part	ECM/adhesion
ARHGDIB	22610	231	19	0	0	biological adhesion	ECM/adhesion
C1QA	7155	231	19	0	0	cell adhesion	ECM/adhesion
C1QC	5604	29	7	0	0	basement membrane	ECM/adhesion
CALCRL	1568	122	12	0	0	blood vessel development	Vasculature
CAV1	1944	125	12	0	0	vasculature development	Vasculature
CCDC80	48407	7	4	0	0	platelet-derived growth factor binding	Vasculature
CD47	5201	16	5	0	0	extracellular matrix structural constituent	ECM/adhesion
CDH5	30198	44	7	0	0	extracellular matrix organization	ECM/adhesion
CDK4	43062	67	8	0	0	extracellular structure organization	ECM/adhesion
CKMT2	10810	19	5	0	0	regulation of cell-substrate adhesion	ECM/adhesion
COL12A1	19838	33	6	0	0	growth factor binding	
COL15A1	8201	36	6	0	0.0006	heparin binding	ECM/adhesion
COL1A1	10926	322	16	0	0.0006	anatomical structure formation	
COL1A2	5509	287	15	0	0.0005	calcium ion binding	
COL4A1	5581	12	4	0	0.0005	collagen	ECM/adhesion
COL6A1	5515	2168	52	0	0.0005	protein binding	
CPXM2	50840	14	4	0	0.0009	extracellular matrix binding	ECM/adhesion
CTSB	10811	14	4	0	0.0009	positive regulation of cell-substrate adhesion	ECM/adhesion
CTSD	5539	46	6	0.0001	0.0008	glycosaminoglycan binding	ECM/adhesion
CTSL	30247	47	6	0.0001	0.0016	polysaccharide binding	ECM/adhesion
DEGS1	1871	48	6	0.0001	0.0015	pattern binding	
EHD1	48646	132	9	0.0002	0.003	anatomical structure formation involved in morphogenesis	
ELN	48514	104	8	0.0002	0.0029	blood vessel morphogenesis	Vasculature
ENG	1955	2	2	0.0002	0.01	blood vessel maturation	Vasculature
FADS1	60346	2	2	0.0002	0.01	bone trabecula formation	
FBLN5	5584	2	2	0.0002	0.01	collagen type I	ECM/adhesion
FBN1	1957	2	2	0.0002	0.01	intramembranous ossification	
FMOD	30155	38	5	0.0002	0.0103	regulation of cell adhesion	
FSTL1	45785	21	4	0.0002	0.0106	positive regulation of cell adhesion	ECM/adhesion
FZD4	5198	140	9	0.0002	0.0103	structural molecule activity	
G3BP2	31589	42	5	0.0004	0.0131	cell-substrate adhesion	ECM/adhesion
GNAI2	30246	91	7	0.0004	0.0127	carbohydrate binding	
GNG12	1525	74	6	0.0008	0.0318	angiogenesis	Vasculature
GRB10	5764	76	6	0.001	0.0335	lysosome	
GTPBP1	323	76	6	0.001	0.0335	lytic vacuole	
IFI30							
IFNGR1							
ISLR							
KDR							
KERA							
LGALS9							
LIPE							
LOX							
MAGI3							
MAP4K4							
MMP2							
MSN							
MYLK							
NID1							
NR2F2							
NRP1							
OXCT1							
PARVA							
PDLIM1							
PECAM1							
PLOD1							
PMP22							
POSTN							
PRKCSH							
PYGL							
RAB3IL1							
RANGAP1							
RGL1							
RGS5							
RXRB							
SEPT8							
SERPINF1							
SH3KBP1							
SLC25A39							
SLC3A2							
SMOC2							
SMPD1							
SPARC							
SPNA2							
THBS1							
THBS2							
TMEM62							
TNC							
TNFAIP2							
TNMD							
ZMYM1							

Supplementary Table 6. GO analysis for Class II genes. Genes in class II are listed, and their expression changes are significant down-regulated in *HSA*^{LR} mice, but not in *MBNL1*$^{\Delta E3/\Delta E3}$ mice.

GO annotated ge	Enriched Go Term Group	Protein Name	Human Disease or (mouse knock out phenotype)	Function in ECM, cell adhesion and vasculature
CAV1	Vasculature	caveolin, caveolae protein 1		Participates in focal adhesion
CCDC80	ECM/adhesion	coiled-coil domain containing 80		modulation of adipogenesis (PMID: 19141617)
CD47	ECM/adhesion	CD47 antigen (Rh-related antigen, integrin-associated signal transducer)		Receptor for thrombospondin 1 and associated with integrin, regulating nitric oxide signaling
CDH5	ECM/adhesion, Vasculature	cadherin 5		Transmembrane protein, mediates calcium-dependent cell–cell adhesion
COL12A1	ECM/adhesion	procollagen, type XII, alpha 1		Acts as crossbridge between fibrils and resists shear forces
COL15A1	ECM/adhesion	procollagen, type XV	Col15a1-deficient mice have skeletal myopathy and cardiovascular defects	Adhesion function in skeletal and cardiac muscle
COL1A1	ECM/adhesion, Vasculature	procollagen, type I, alpha 1	osteogenesis imperfecta Type I; Ehlers-Danlos syndrom (EDS)	Abundant, ECM organization
COL1A2	ECM/adhesion	procollagen, type I, alpha 2	osteogenesis imperfecta Type I	Abundant, ECM organization
COL4A1	ECM/adhesion	procollagen, type IV, alpha 1	Familial Porencephaly; Alport syndrome	ECM organization
COL6A1	ECM/adhesion	procollagen, type VI, alpha 1	Ullrich congenital muscular dystrophy; Bethlem myopathy	Anchors the muscle basement to the ECM
CPXM2	ECM/adhesion	carboxypeptidase X 2 (M14 family)		participates in cell adhesion and proteolysis
ELN	ECM/adhesion	elastin	Supravalvular Aortic Stenosis; Williams-Beuren Syndrome	ECM organization
ENG	ECM/adhesion, Vasculature	endoglin(TGF-ß type III receptor)	Hereditary Hemorrhagic Telangiectasia of Rendu, Osler, and Weber	Both the extracellular and intracellular domains of endoglin interact with TßR-II and ALK-5 and its cytoplasmic domain, which is phosphorylated by ALK-5 and TßR-II
FBLN5	ECM/adhesion	fibulin 5	Autosomal Recessive Cutis Laxa, Type I; age-related muscular degeneration	Elastin fiber formation
FBN1	ECM/adhesion	Fibrilin-1	Marfan Syndrome	Elastin fiber assembly and formation
FMOD	ECM/adhesion	fibromodulin	Ehlers-Danlos Syndrome, Type I	inhibits type I collagen fibrillogenesis
FSTL1	ECM/adhesion	follistatin-like 1		secreted myokine that promotes endothelial cell function and stimulates revascularization in response to ischemic insult by activating Akt-eNOS signaling.
KDR	Vasculature	kinase insert domain protein receptor/fetal liver kinase-1 (KDR/Flk-1)		Inhibits angiogenesis
KERA	ECM/adhesion	keratocan	Cornea Plana 2	keratan sulfate proteoglycan of the extracellular matrix. Based on studies in the mouse, keratocan expression is more limited to the cornea in the adult organism.
LOX	ECM/adhesion, Vasculature	lysyl oxidase	Lox knockout mice have cardiovascular dysfunction	Formation and repair of the extracellular matrix (ECM) by oxidizing lysine residues in elastin and collagen
MMP2	ECM/adhesion, Vasculature	matrix metallopeptidase 2		Degradation of the extracellular matrix components and tissue remodeling
NID1	ECM/adhesion	nidogen 1		serves as link between collagen IV and laminin.
NR2F2	Vasculature	nuclear receptor subfamily 2, group F, member 2		blood vessel morphogenesis
NRP1	ECM/adhesion, Vasculature	Neuropilin-1		Participates in angiogenesis
PARVA	ECM/adhesion	parvin, alpha		Participates in focal adhesion
PECAM1	ECM/adhesion	platelet/endothelial cell adhesion molecule 1		participates in butanoate metabolism and synthesis and degradation of ketone bodies
PLOD1	ECM/adhesion	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 1	Ehlers-Danlos syndrome type VIA, Nevo Syndrome	lysyl hydroxylase that controls cross-links
POSTN	ECM/adhesion	periostin, osteoblast specific factor	Postn knockout mice have cardiac valve disease	Regulation of collagen fiber diameter and crosslinking
SERPINF1	Vasculature	serine (or cysteine) peptidase inhibitor, clade F, member 1		Cell proliferation and negative regulation of angiogenesis
SMOC2	ECM/adhesion	SPARC related modular calcium binding 2		Regulator of cell–matrix interactions and integrin activation
SPARC	ECM/adhesion	secreted acidic cysteine rich glycoprotein		Regulator of cell–matrix interactions
THBS1	ECM/adhesion, Vasculature	thrombospondin 1		Agonist for CD47, wound healing
THBS2	ECM/adhesion	thrombospondin 2		Potent endogenous inhibitor of tumor growth and angiogenesis
TNC	ECM/adhesion	tenascin C	tenascin C-deficient mice have weak muscles	Regulation of muscle strength
TNFAIP2	Vasculature	tumor necrosis factor, alpha-induced protein 2		Participates in angiogenesis

Supplementary Table 7. List of 40 extracellular matrix transcripts. This is the set of class II genes labeled as functioning in extracellular space. Their positions in ECM and involvement in diseases are listed. See also Fig 6.

NB: These are the only 7mers or smaller with false discovery rates (FDR) < 0.1

List source	Position	7mer motif counts	p-value	FDR	notes
Down Reg Class II genes	3'UTR	CTCTCTC	1.9116E-07	0.003132	PTB/nPTB
		GGTGCTA	3.6166E-06	0.059254	MBNL
Down Reg Class II genes	5'UTR	TGCCTGC	2.6371E-08	0.000432	MBNL
		CCTGCCT	7.0103E-07	0.011486	MBNL
		TGTGCCT	2.3799E-06	0.038992	MBNL
ECM subgroup of Class II	3'UTR	GGTGCTA	7.518E-09	0.000123	MBNL
		GATCCAA	5.6486E-07	0.009255	unknown
		GACTATC	2.1134E-06	0.034626	unknown
ECM subgroup of Class II	5'UTR	CCTGCCT	2.2042E-10	3.61E-06	MBNL
		TCCCACC	1.8608E-07	0.003049	unknown
		GCACCCG	7.1793E-07	0.011763	unknown

Supplementary Table 8. Motif elements in class II genes at 3’UTR as well as 5’UTR by using Improbizer and 7mer counts. yGCy elements are underlined.

Gene Name	Alternative splicing	Purpose	Primers	primers5'-3'
Mouse Nfix	altCassette(123)	RT-PCR	L-primer	TCGACGACAGTGAGATGGAG
			R-primer	CAAACTCCTTCAGCGAGTCC
Mouse Gnas	altCassette (45)	RT-PCR	L-primer	GAGGATCCTGCATGTTAATGG
			R-primer	ATGGCCTCCTTCAGGTTGTT
Mouse camk2g	altCassette(33)	RT-PCR	L-primer	CTGCCAAAAGCCTATTGAAC
			R-primer	GCTGGGCTTACGAGACTGTT
Mouse smyd1	altCassette(39)	RT-PCR	L-primer	CTGCAACGGTTTCACTCTCA
			R-primer	CCTCGCCTTCTGAGATCTTG
Mouse anxa6	AlterCassette(18)	RT-PCR	L-primer	GAAATCGAGAGGAAGGAGGAG
			R-Primer	GGATAGCTACGGGTGCACAG
Mouse Ppp2r5c	AlterCassette(117)	RT-PCR	L-primer	GCGAGAAGAAGCATGGGTTA
			R-Primer	GACGATCCTTCTTCAGCTCCT
Mouse Picalm	AlterCassette(24)	RT-PCR	L-primer	TTGGAGTCAACCAGGTGAAA
			R-Primer	TCATGCCCGTTGGTGTAGTA
Mouse Pdlim7	AlterCassette(119)	RT-PCR	L-primer	CCTGTTCAGAGCAAACCACA
			R-Primer	CTTCGGTATCCTCCATCAGC
Mouse Fn1	AlterCassette(270)	RT-PCR	L-primer	GGTTCAAACTGCAGTGACCA
			R-Primer	ACTGGGCAGTAAAGCTGGTG
Mouse Fn1	AlterCassette(273)	RT-PCR	L-primer	TGCCCCTATCTCTGATACCG
			R-Primer	CGATATTGGTGAATCGCAGA
Mouse 2610103J23I	AlterCassette(99)	RT-PCR	L-primer	ATGCAAATGGGAAAGACTGG
			R-Primer	ACTCCTCTGCTGGTGCATTC
Mouse BC060506 (S	AlterCassette(39)	RT-PCR	L-primer	TGGGTTTCTCTTTCGTGAGG
			R-Primer	TGTGCCATTGAACAGTAGGG
Mouse Capzb	AlterCassette(113)	RT-PCR	L-primer	TGGAAAACAAAATCCGAAGC
			R-Primer	CCTCCACCAGGTCGTTCTTA
Mouse AK035230 (F	AlterCassette(171)	RT-PCR	L-primer	AAGCACCACATCAACACCAA
			R-Primer	CGTCCCTAACAGGAGTGAGGT
Mouse OPA1	AlterCassette(111)	RT-PCR	L-primer	AAACAGCATTTCGAGCAACA
			R-Primer	GCAGAAGTTCTTCTTGAAGTTGG
Mouse Mbnl1	AltExon (54)	RT-PCR	L-primer	TGACTGTCGGTTTGCTCATC
			R-Primer	GCATGTTGGCTAGAGCCTGT
Mouse Csda	AltExon (207)	RT-PCR	L-primer	GCCCAGATGGAGTTCCTGTA
			R-Primer	TTCATCTCCCCAATCTCACC
Mouse Camk2g	AltExon (63)	RT-PCR	L-primer	ACCATGCTTGTCTCCAGGAA
			R-Primer	GACACCGCCATCTGACTTCT
mouse Hnrpa2b1	AltExon (36)	RT-PCR	L-primer	CGGAGGTCTTTCTCATCTCG
			R-Primer	AGCTTTCCCCATTGCTCATA
mouse A2bp1	AltExon (93)	RT-PCR	L-primer	TTTAATGAGCGAGGCTCCAA
			R-Primer	CATTGGTGTAGGGGTTGACA
mouse add1	AltExon(87)	RT-PCR	L-primer	ATTAAGACGGCAGGACCTCA
			R-Primer	ATGGGGCTGGTATTCCTTCT
Mouse Ndrg2	AltExon(42)	RT-PCR	L-primer	AGGACAAACACCCGAGACTG
			R-Primer	GGGGGTGCCATACACAGTAA
Mouse Itga7	altExon(113)	RT-PCR	L-primer	CTGGTACTGCTGCTGTGGAA
			R-Primer	CCTTGAACTGCTGTCGGTCT
Mouse 1110028E10I	altExon(172)	RT-PCR	L-primer	GGCTTCTTCAGCGTCTATGG
			R-Primer	TGAACCGTCATTTCTCTCCA
Mouse Tlk2(96)	altExon(96)	RT-PCR	L-primer	AAGGCACTCCTAGGGGACAT
			R-Primer	GCTCTTCTGAGGCCTCCTTT
Mouse AK122487/S	AlterCassette(30)	RT-PCR	L-primer	CCAAGACTTCCCTCCAACAA
			R-primer	GAGTTCTGCTGGGGTTGGTA
Mouse AF340029/R	altExon(84)	RT-PCR	L-primer	AGGTGTACAGGAGCCACTCAA
			R-Primer	GGGACTCTTTCAGCACCTCA
Mouse Vldlr	altExon(84)	RT-PCR	L-primer	TCCCAATGGGTACAATCTCG
			R-Primer	TTTGGGGGAACACTGACTTC
Mouse Rpn2	altExon(48)	RT-PCR	L-primer	CCCTCAAGTACCTGGCTGTC
			R-Primer	CATGAACTGTCCCCACTCCT
Mouse Mef2D	altMutEx	RT-PCR	Forward(EcoN1)	GTACAACGAGCCACACGAGA
			Reverse(EcoN1)	CATGGAGCTCTGATTGGACA
Mouse Aplp2	altExon(36)	RT-PCR	L-primer	TCAGAGAACCCTGTGGATGTC
			R-Primer	AATCAGTCCCCCGTCTTGTT
Mouse Dmwd	altExon(75)	RT-PCR	L-primer	TATCATCACTGCCTGCCAAG
			R-Primer	GGGAGGGTTATGGCTAGGAG
Mouse Xpa	altExon(192)	RT-PCR	L-primer	CAGGAAGCTCTGGAAGATGC
			R-Primer	TGTTGGTGAGTGGTTGTCTCTC
Human Nfix	AltCassette(123)	RT-PCR	L-primer	AGCCCTGTTGATGACGTGTT
			R-primer	AGTGCAGGGCTGATGCTGT
Human Gnas	AltCassette(45)	RT-PCR	L-primer	GCACCATTGTGAAGCAGATG
			R-primer	TCAATCGCCTCTTTCAGGTT
Human Spag9	AltExon (39)	RT-PCR	L-primer	TCTCCATCCCATTGACAGAA
			R-Primer	CTGGGACTGCCACAAAGAAT
Human 2610103J23	AltExon (99)	RT-PCR	L-primer	TGCCTGGAGTCAAGACACTG
			R-Primer	GGAATTGGTTCCTGGGACTT
Human ppp2r5c	AltExon (117)	RT-PCR	L-primer	GGGAAGAAGCATGGGTTAAA
			R-Primer	CTTCCAAGGCTTTCTTGGTG
Human Smyld	AltCassette(39)	RT-PCR	L-primer	GTAGGCATCTTCCCCAACCT
			R-primer	CTGCTTCTTCAGCTGCCTCT
Prepl	Constitutive exon	qRTPCR	L-primer	CTGAGGACCTGCAGAGGAAG
			R-primer	TTAGGCTCGGCTGAGAAAAG
Casp12	Constitutive exon	qRTPCR	L-primer	AAAGGGATAGCCACTGCTGA

			R-primer	GAGGGAACCAGTCTTGCCTA
Plekho1	Constitutive exon	qRTPCR	L-primer	GCCGTGAGTCCTGAAGAGAA
			R-primer	GGGAGTGTTGGATTTTTGCT
Atf3	Constitutive exon	qRTPCR	L-primer	CTCTGCGCTGGAGTCAGTTA
			R-primer	GCAGGCACTCTGTCTTCTCC
Igfbp5	Constitutive exon	qRTPCR	L-primer	CCTGCACCTGAGATGAGACA
			R-Primer	GAATCCTTTGCGGTCACAGT
Fhl1	Constitutive exon	qRTPCR	L-primer	GTGTCCAAGGATGGCAAGAT
			R-Primer	GTGCCCTTGTACTCCACGTT
Pdlim7	Constitutive exon	qRTPCR	L-primer	GACTTCAATGTGCCCCTCTC
			R-Primer	CTTGTTCTGGGCTTCGATGT
Amotl1	Constitutive exon	qRTPCR	L-primer	TATTCTGGGAGGCATGAAGC
			R-Primer	TTCCGTGGAAGAAAAGTTGG
Acvr2a	Constitutive exon	qRTPCR	L-primer	GTTGCTGTGAGGGCAATATG
			R-Primer	TAGGGTGGCTTCGGTGTAAC
Smox	Constitutive exon	qRTPCR	L-primer	TTCACGGATGTCACTGTGCT
			R-Primer	GCCATTGGCTTCTGCTAGTT
Igf1	Constitutive exon	qRTPCR	L-primer	TGGATGCTCTTCAGTTCGTG
			R-Primer	GGAAGCAACACTCATCCACA
Actc1	Constitutive exon	qRTPCR	L-primer	TCGGGACCTCACTGACTACC
			R-Primer	AGGGCGACGTAACACAGTTT
Kera	Constitutive exon	qRTPCR	L-primer	TCTTTTTGTTATCCCCCATCA
			R-Primer	AGTTTGGGGTTGCCATTACA
Sln	Constitutive exon	qRTPCR	L-primer	TGGAGGTGGAGAGACTGAGG
			R-Primer	TTTGGGCAGCCTACAAGAAC
Ogn	Constitutive exon	qRTPCR	L-primer	TCCAGTTCTTCCTCCAAAGC
			R-Primer	GGAGGCACAGATTCCAGGT
Thrsp	Constitutive exon	qRTPCR	L-primer	GACAGGGCAGGTTCTGTAGG
			R-Primer	CACTCAGAGGGAGACGGAAG
Kcnab1	Constitutive exon	qRTPCR	L-primer	ATGGGTGACATTTGGAGGTC
			R-Primer	CCAGCAGCATAGACCTCAGC
Csrp3	Constitutive exon	qRTPCR	L-primer	TCGGTATACGCTGCTGAGAA
			R-primer	TTGCAGTAGAGCTCCCCATC
Tnnc1	Constitutive exon	qRTPCR	L-primer	CTGCAGGAGATGATTGACGA
			R-primer	CGACAGCTCCTCCTCAGACT
Cav1	Constitutive exon	qRTPCR	L-primer	GGGAACAGGGCAACATCTAC
			R-primer	GACCAGGTCAATCTCCTTGG
Col1a2	Constitutive exon	qRTPCR	L-primer	GGTCCAGCTGGCTCTCCT
			R-primer	GCCAGGAAGTCCAGGAGTC
Fads1	Constitutive exon	qRTPCR	L-primer	AGCTTTGAACCCACCAAGAA
			R-Primer	CAGGAAGAAGAGGTGGTTGG
Fbln5	Constitutive exon	qRTPCR	L-primer	CAGGCTACGTCCTGTTGGAT
			R-Primer	TGAAGCCCCCTTGTAGATTG
Col6a1	Constitutive exon	qRTPCR	L-primer	AAGCGCTTCATTGACAACCT
			R-Primer	CCTCGGATGATCTCCACCT
Col4a1	Constitutive exon	qRTPCR	L-primer	CCCAGGGACCAAAATTCTTT
			R-Primer	GGGCATGGTGCTGAACTTAC
Eln	Constitutive exon	qRTPCR	L-primer	TGGACCTGGAGGACTTGG
			R-Primer	CATACTGGGCAGCCTTAGCA
Fbn1	Constitutive exon	qRTPCR	L-primer	CAAGTGAACGGGGGAAATAA
			R-Primer	AGGCTCTGCCGATGTTGTAG
Sparc	Constitutive exon	qRTPCR	L-primer	ACGAGAGAGATGAGGGCAAC
			R-Primer	CCAGTGGACAGGGAAGATGT
Cdh5	Constitutive exon	qRTPCR	L-primer	GCGAGTACAGGGACACCTTC
			R-Primer	ATCGGATAGTGGGGTCTGTG
Rgs5	Constitutive exon	qRTPCR	L-primer	GAGGAGGTCCTGCAGTGG
			R-Primer	CTCAAGGTTTTCCTCACTGAAT
Nfix	exon(123bp)	Cloning	L-primer	aaaagggcccTAATACGACTCACTATAGGGTGTTACCAGGGGCCTCATTTTCCTCTC
			R-Primer	aaaaagatctATTCTAGGAACCGAGTGGGCAGCCTGG
Vldlr	Exon (84bp)	Cloning	L-primer	aaaagggcccTAATACGACTCACTATAGGGCGTTTCCTAATTTCCGGATTCTTTG
			R-Primer	aaaaagatctTCAAGAGAAATCCAGGATGTGCAG

Supplementary Table 9. Primers for RT-PCR and qRT-PCR and cloning.