

図2-5 MuRF1 は-AA時にCK量を減少させる

実験7日目に採取した各群のマウス骨格筋を用いて、骨格筋中のCK活性を測定した。CK活性量は、筋重量あたりに換算した相対値で表した。

mean ± S.D. (n=3) * :p<0.05

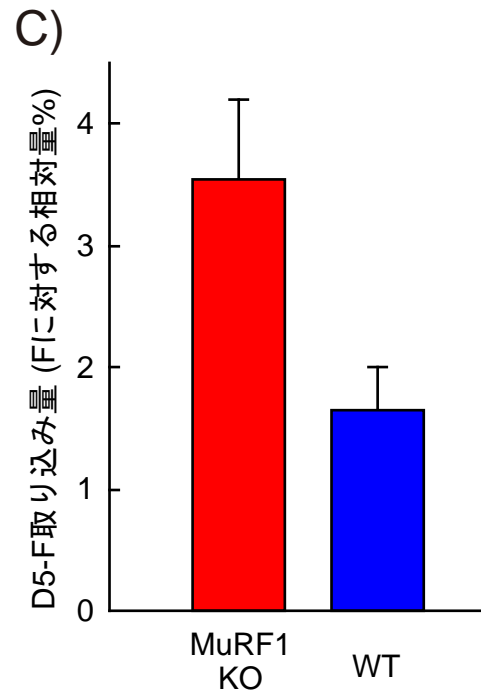
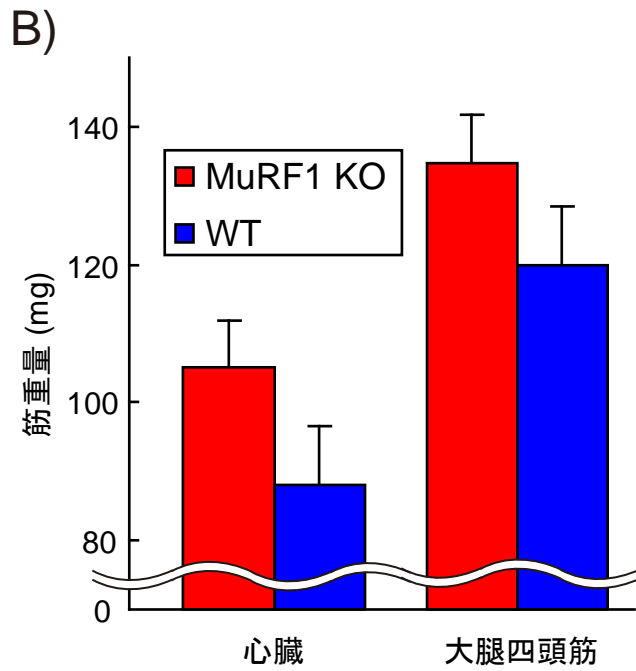
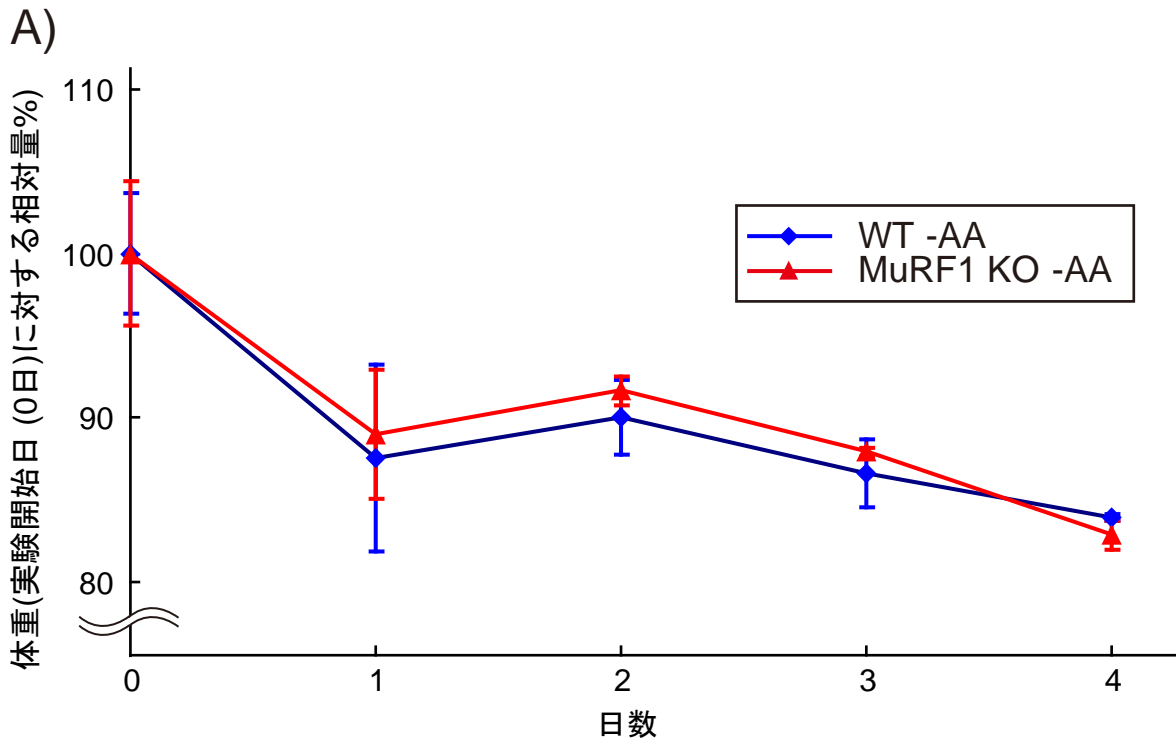


図2-6 MuRF1 は筋タンパク質合成を負に制御する

WTマウスとMuRF1 KOマウスを-AA条件下で飼育した。実験開始48時間後に、マウスの腹腔内に重水素ラベルしたフェニルアラニン (D5-F)を投与し、更に48時間(合計で実験開始から4日間)飼育した。

A) 実験開始から4日間の体重変化

B) 実験開始4日目のWTマウスとMuRF1 KOの心臓、骨格筋の重量

C) 筋タンパク質へのD5-Fの取り込み量

表2-1代表的な遺伝子の絶食時における発現量変化

MuRFs, atrogin-1

Probe Set ID	Gene	WT starved	WT control	KO starved	KO control	WT ratio	KO ratio
1438704_at	MuRF1	5171.3	1284.9	103.9	86.6	4.02	1.20
1419440_at	MuRF3	3383.5	2982.4	4026.8	3112.7	1.13	1.29
1448747_at	atrogin-1	5074.9	763.9	5789.7	995.6	6.64	5.82

calpain^{*1}

Probe Set ID	Gene	WT starved	WT control	KO starved	KO control	WT ratio	KO ratio
1426043_a_at	p94	478.6	1098.2	420.9	882.7	0.44	0.48
1433681_x_at	p94	543.4	714.0	307.6	643.5	0.76	0.48
1417229_at	μCL	116.3	216.0	108.6	157.2	0.54	0.69
1417228_at	μCL	96.2	230.0	120.5	191.9	0.42	0.63
1416257_at	mCL	243.1	325.3	300.0	286.9	0.75	1.05
1449165_at	calpain5	16.3	6.3	0.5	1.5	2.59	0.33
1418671_at	calpain5	14.4	21.5	2.0	17.0	0.67	0.12
1421952_at	calpain6	2.3	12.2	1.9	1.3	0.19	1.46
1450429_at	calpain6	29.9	42.3	24.2	70.4	0.71	0.34
1423098_at	calpain7	256.3	340.3	273.6	375.6	0.75	0.73
1423096_at	calpain7	131.6	180.8	179.2	260.7	0.73	0.69
1423097_s_at	calpain7	177.2	332.3	274.3	353.9	0.53	0.78
1452959_a_at	calpain10	10.0	23.3	6.5	23.7	0.43	0.27
1416265_at	calpain10	40.4	38.5	11.0	21.8	1.05	0.50
1449970_at	calpain12	5.5	0.7	6.1	9.5	7.86	0.64
1437960_at	calpain13	5.8	0.8	1.2	1.2	7.25	1.00
1426400_a_at	30K (CAPNS1)	1203.3	1178.5	1012.0	1114.7	1.02	0.91
1429067_at	30K-2 (CAPNS2)	3.0	3.5	0.9	1.2	0.86	0.75
1451413_at	calpastatin	311.7	314.5	196.7	365.3	0.99	0.54
1426098_a_at	calpastatin	614.4	254.5	524.8	352.8	2.41	1.49
1435972_at	calpastatin	339.6	306.7	224.1	333.1	1.11	0.67

TAT^{*2}

Probe Set ID	Gene	WT starved	WT control	KO starved	KO control	WT ratio	KO ratio
1451557_at	tyrosine aminotransferase	2.4	2.9	15.0	4.3	0.83	3.49

Proteasome関連^{*3}

Probe Set ID	Gene	WT starved	WT control	KO starved	KO control	WT ratio	KO ratio
1456059_at	proteasome 19S subunit, non-ATPase, 11	1262.6	397.5	733.4	357.3	3.18	2.05
1434356_a_at	proteasome 20S subunit, alpha type 5	2359.8	1047.3	1801.3	1225.0	2.25	1.47
1431013_at	proteasome 19S subunit, non-ATPase, 11	31.1	1.7	21.1	21.9	18.29	0.96
1429370_a_at	proteasome 19S subunit, non-ATPase, 11	2566.4	777.0	2800.5	860.1	3.30	3.26
1424681_a_at	proteasome 20S subunit, alpha type 5	1722.2	624.4	1214.9	757.8	2.76	1.60
1423568_at	proteasome 20S subunit, alpha type 7	1866.7	724.9	1682.7	983.1	2.58	1.71
1423567_a_at	proteasome 20S subunit, alpha type 7	1827.7	698.1	1372.4	949.3	2.62	1.45
1423296_at	proteasome 19S subunit, non-ATPase, 8	4143.7	1893.3	4046.1	2331.7	2.19	1.74
1418874_a_at	proteasome 19S subunit, non-ATPase, 4	3303.7	1592.2	3082.4	2252.2	2.07	1.37
1416291_at	proteasome 19S subunit, ATPase, 4	1744.7	701.2	1249.3	697.9	2.49	1.79
1416290_a_at	proteasome 19S subunit, ATPase, 4	740.7	251.8	634.3	353.6	2.94	1.79
1415695_at	Similar to proteasome subunit, alpha type 1	2092.9	853.7	1808.8	1022.0	2.45	1.77

Ub関連^{*3}

Probe Set ID	Gene	WT starved	WT control	KO starved	KO control	WT ratio	KO ratio
1425023_at	Similar to ubiquitin specific protease 3	124.5	53.3	200.0	56.1	2.34	3.57
1425022_at	Similar to ubiquitin specific protease 3	265.5	128.8	439.3	126.3	2.06	3.48

エネルギー代謝関連^{*3}

Probe Set ID	Gene	WT starved	WT control	KO starved	KO control	WT ratio	KO ratio
1415864_at	2,3-bisphosphoglycerate mutase	127.7	406.5	119.4	351.0	0.31	0.34
1415865_s_at	2,3-bisphosphoglycerate mutase	261.1	735.4	184.2	687.0	0.36	0.27
1416383_a_at	pyruvate decarboxylase	133.8	316.7	179.5	329.9	0.42	0.54
1422315_x_at	phosphorylase kinase gamma	332.1	1103.6	345.2	1070.6	0.30	0.32
1423828_at	fatty acid synthase	36.1	356.1	36.2	777.1	0.10	0.05
1425164_a_at	phosphorylase kinase, gamma-subunit	353.0	1206.0	342.9	1119.1	0.29	0.31
1448119_at	2,3-bisphosphoglycerate mutase	153.0	457.3	100.6	389.0	0.33	0.26
AFFX-PyruCarbMur/L09192_3_at	pyruvate carboxylase	115.1	238.8	142.2	211.5	0.48	0.67

*1 calpain5、calpain6、calpain12、calpain13はWTとMuRF1 KO間で差があるが、GOCSソフトウェアの判定ではいずれも発現が認められなかった

*2 tyrosine aminotransferaseのMuRF1 KOマウスの発現量は、GCOSソフトウェアでは変化していないと判定された

*3 Proteasome、Ub、エネルギー代謝関連については、「発現量が2倍以上変動しているもの」「GOCSソフトウェアの判定でstarved群でcontrol群に対し増加、もしくは減少と判断され、かつ、いずれかの群で発現しているとされたもの」の2つを満たすもののみ記載した。

表2-2絶食時にMuRF1依存的に発現制御を受ける候補遺伝子

MuRF1依存的に発現量が5倍以上に変化した遺伝子

Probe Set ID	Gene Title	Gene Symbol	Biological Process	Molecular Function	WT starved	WT control	KO starved	KO control	WT ratio	KO ratio
1443668_x_at	expressed sequence C79407	C79407	?	DNA binding	18.8	0.2	8.8	11	94.0	0.8
1421010_at	myelin-associated oligodendrocytic basic protein	Mobp	?	structural constituent of myelin sheath	24.3	0.3	4	0.5	81.0	8.0
1420680_at	cathepsin 8	Cts8	proteolysis	cysteine-type endopeptidase activity peptidase activity cysteine-type peptidase activity	19.8	0.3	0.3	1.2	66.0	0.3
1446027_at	BG069132	BG069132	?	?	26	0.4	3.2	0.5	65.0	6.4
1434616_at	1434616_at	Slc38a10	transport, ion transport sodium ion transport amino acid transport	sodium ion binding	31.2	0.5	1	3.2	62.4	0.3
1423650_at	ring finger protein 26	Rnf26	?	protein binding, zinc ion binding metal ion binding	38	0.7	8.9	12.6	54.3	0.7
1454468_at	RIKEN cDNA 5430434N17 gene	S430434N17Rik	?	?	16	0.3	1.4	1	53.3	1.4
1442634_at	BE991239	BE991239	?	?	26.1	0.5	4.3	11.6	52.2	0.4
1449228_at	SH3-domain GRB2-like 2	Sh3gl2	endocytosis	protein binding, lipid binding	31.1	0.6	8.8	8.7	51.8	1.0
1458745_at	DNA segment, Chr 18, ERATO Doi 201, expressed	D18Ertu201e	?	?	10.1	0.2	2.3	4.6	50.5	0.5
1429105_at	discs, large (Drosophila) homolog-associated protein 1	Dlgap1	cell-cell signaling synaptic transmission	kinase activity	24.9	0.5	0.3	1.6	49.8	0.2
1444656_at	cDNA sequence BC030499	BC030499	protein amino acid phosphorylation	nucleotide binding, protein kinase activity protein serine/threonine kinase activity ATP binding, kinase activity transferase activity	29.2	0.6	8.2	5.6	48.7	1.5
1430072_at	RIKEN cDNA 1700057K13 gene	1700057K13Rik	?	?	23.9	0.5	10.4	2.3	47.8	4.5
1458979_at	BB332816	BB332816	?	?	18.9	0.4	6	2.8	47.3	2.1
1446493_at	CDC14 cell division cycle 14 homolog A (S. cerevisiae)	Cdc14a	protein amino acid dephosphorylation cell cycle dephosphorylation cell division	phosphoprotein phosphatase activity protein tyrosine phosphatase activity protein tyrosine/serine/threonine phosphatase activity hydrolase activity, phosphatase activity	25.9	0.6	8.8	20.9	43.2	0.4
1431174_at	BG297411	BG297411	?	?	23.6	0.6	3.6	9.1	39.3	0.4
1443488_at	BB260131	BB260131	?	?	19.5	0.5	6.8	9.6	39.0	0.7
1441304_at	predicted gene, EG432681 predicted gene, EG625917 predicted gene, EG626367 predicted gene, EG626903 predicted gene, EG667682 predicted gene, EG668409 predicted gene, EG668536 predicted gene, EG668850 predicted gene, EG668880 predicted gene, ENSMUSG00000059999 predicted gene, ENSMUSG00000066956 predicted gene, ENSMUSG00000066956 similar to ribosomal protein L31 hypothetical protein LOC675768 ribosomal protein L31	EG432681, EG625917, EG626367, EG626903, EG667682, EG668409, EG668536, EG668850, ENSMUSG00000059999, ENSMUSG00000066956, LOC638399, LOC673582, LOC675768, Rpl31	translation	structural constituent of ribosome	11	0.3	0.6	1.6	36.7	0.4
1454150_at	RIKEN cDNA 4930453O03 gene	4930453O03Rik	?	?	28.2	0.8	1.8	10.7	35.3	0.2
1430681_at	crystallin, lambda 1	Cry1l	fatty acid metabolic process metabolic process oxidation reduction	catalytic activity, binding oxidoreductase activity L-gulonate 3-dehydrogenase activity	21	0.6	7.4	7.5	35.0	1.0
1425313_at	calcium response factor	Carf	regulation of transcription, DNA-dependent	transcription factor activity protein binding	20.9	0.6	8.4	1.6	34.8	5.3
1426498_at	jumonji, AT rich interactive domain 1C (Rbp2 like)	Jarid1c	transcription regulation of transcription, DNA-dependent chromatin modification oxidation reduction	DNA binding, iron ion binding protein binding, zinc ion binding oxidoreductase activity oxidoreductase activity, acting on single donors with incorporation of molecular oxygen, incorporation of two atoms of oxygen, metal ion binding	27.3	0.8	7.7	20.3	34.1	0.4
1448058_s_at	budding uninhibited by benzimidazoles 3 homolog (S. cerevisiae)	Bub3	mitotic sister chromatid segregation chromosome segregation	protein binding	30.5	0.9	1.9	1.4	33.9	1.4
1442922_at	checkpoint with forkhead and ring finger domains	Chfr	protein polyubiquitination mitotic cell cycle ubiquitin-dependent protein catabolic process cell cycle mitosis cell division	ubiquitin-protein ligase activity protein binding zinc ion binding ligase activity metal ion binding	30.4	0.9	0.4	4.9	33.8	0.1
1455414_at	tetratricopeptide repeat domain 16	Ttc16	?	binding	23.3	0.7	4.5	1.6	33.3	2.8
1431341_at	BF143676	BF143676	?	?	54.3	1.7	20.4	10.9	31.9	1.9
1449539_at	membrane-spanning 4-domains, subfamily A, member 6D	Ms4a6d	signal transduction	receptor activity	12.7	0.4	1.8	2	31.8	0.9
1427303_at	ectonucleotide pyrophosphatase/phosphodiesterase 3	Enpp3	metabolic process	nucleic acid binding, catalytic activity endonuclease activity phosphodiesterase I activity nucleotide diphosphatase activity hydrolase activity, metal ion binding	25.2	0.8	5.4	7.4	31.5	0.7
1447914_x_at	RIKEN cDNA 2600010E01 gene	2600010E01Rik	?	?	16.5	0.6	5.4	0.4	27.5	13.5
1458053_at	abl-interactor 2	Abi2	learning or memory, dendrite development, cell migration peptidyl-tyrosine phosphorylation camera-type eye development	protein binding	10.2	0.4	6.2	3.5	25.5	1.8
1436598_at	inducible T-cell co-stimulator	Icos	protein binding	integral to plasma membrane external side of plasma membrane membrane, integral to membrane	25.1	1	1.4	6.3	25.1	0.2
1423469_at	RIKEN cDNA 1700129C05 gene	1700129C05Rik	?	?	31.9	1.3	1.6	8.7	24.5	0.2
1440930_a_at	scratch homolog 2, zinc finger protein (Drosophila)	Srct2	transcription, regulation of transcription, DNA-dependent	nucleic acid binding, DNA binding zinc ion binding, metal ion binding	49.6	2.1	2	0.8	23.6	2.5
1441783_at	RIKEN cDNA 2410022M11 gene	2410022M11Rik	?	?	32.5	1.4	8.7	6.4	23.2	1.4
1447557_at	RAB interacting factor	Rabif	transport small GTPase mediated signal transduction, protein transport	guanyl-nucleotide exchange factor activity zinc ion binding, metal ion binding	25.2	1.1	1.9	2.2	22.9	0.9
1422083_at	toll-like receptor 9	Tlr9	inflammatory response immune response signal transduction response to virus positive regulation of interferon-gamma biosynthetic process innate immune response positive regulation of interferon-alpha biosynthetic process positive regulation of interferon-beta biosynthetic process	receptor activity transmembrane receptor activity protein binding, siRNA binding	20.2	0.9	10.2	23.4	22.4	0.4
1431649_at	RIKEN cDNA 1700108M19 gene	1700108M19Rik	?	?	11	0.5	0.8	1.2	22.0	0.7
1441892_x_at	BB341238	BB341238	?	?	21.2	1	1.4	1.5	21.2	0.9

表2-2絶食時にMuRF1依存的に発現制御を受ける候補遺伝子(続)

1446289_at	AW556170	AW556170	?	?	37	1.9	10	9.2	19.5	1.1
1443956_at	zinc finger protein 397	Zfp397	transcription regulation of transcription, DNA-dependent	nucleic acid binding transcription factor activity zinc ion binding, metal ion binding	18.4	1	7.3	9	18.4	0.8
1431013_at	predicted gene, OTTMUSG00000015538 proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	OTTMUSG00000015538 Psm11	?	protein binding	31.1	1.7	21.1	21.9	18.3	1.0
1432969_at	RIKEN cDNA 4933423K11 gene	4933423K11Rik	?	?	19.6	1.1	1	0.9	17.8	1.1
1433087_at	RIKEN cDNA 5330430C04 gene	5330430C04Rik	?	?	26.6	1.5	1	6.9	17.7	0.1
1453425_at	coiled-coil domain containing 83	Ccdc83	?	?	31.8	1.8	8.1	1.8	17.7	4.5
1417798_at	RIKEN cDNA 1810019J16 gene	1810019J16Rik	?	?	44.9	2.6	3.4	2.5	17.3	1.4
1446343_at	BG068486	BG068486	?	?	11.8	0.7	3.8	1.5	16.9	2.5
1437906_x_at	thioredoxin-like 1	Txn1l	transport cell redox homeostasis	?	37.4	2.3	14.7	21.2	16.3	0.7
1449752_at	SplA/ryanodine receptor domain and SOCS box containing 1	Spsb1	intracellular signaling cascade	receptor activity	24.3	1.5	12.2	6.2	16.2	2.0
1458494_at	AW457185	AW457185	?	?	18.2	1.2	5.2	1.2	15.2	4.3
1454830_at	fibrillin 2	Fbn2	blood coagulation embryonic limb morphogenesis limb morphogenesis	transmembrane receptor activity extracellular matrix structural constituent binding, calcium ion binding	18.1	1.2	5.6	2.9	15.1	1.9
1452417_x_at	RIKEN cDNA 2010205A11 gene predicted gene, EG628498 predicted gene, ENSMUSG00000076577 immunoglobulin kappa chain, constant region immunoglobulin kappa chain variable 28 (V28) similar to Chain L, Structural Basis Of Antigen Mimicry In A Clinically Relevant Melanoma Antigen System	2010205A11Rik EG628498 ENSMUSG00000076577 Igk-C Igk-V28 LOC100047628	?	antigen binding	263.1	19.2	72.3	73.5	13.7	1.0
1457650_x_at	autophagy-related 4A (yeast)	Atg4a	autophagosome formation proteolysis protein targeting to membrane protein targeting to vacuole transport, autophagy protein transport	cysteine-type endopeptidase activity protein binding microtubule binding peptidase activity cysteine-type peptidase activity hydrolase activity	27.5	2.1	3	9	13.1	0.3
1454081_at	AK016846	AK016846	?	?	16.7	1.3	1	6.1	12.8	0.2
1425882_at	growth differentiation factor 2	Gdf2	growth	cytokine activity, growth factor activity	30.3	2.4	4.6	4.4	12.6	1.0
1455923_at	potassium channel tetramerisation domain containing 8	Kctd8	potassium ion transport	voltage-gated potassium channel activity, protein binding	10	0.8	2.5	4.7	12.5	0.5
1428720_s_at	RIKEN cDNA 2010309G21 gene immunoglobulin lambda chain, constant region 2 immunoglobulin lambda chain, constant region 3	2010309G21Rik Igl-C2 Igl-C3	?	antigen binding	36.8	3	8.5	4.8	12.3	1.8
1434638_at	BM938299	BM938299	?	?	26.4	2.3	2.3	14.9	11.5	0.2
1427602_at	diabetic embryopathy 1	Dep1	?	?	29	2.6	13.8	14.3	11.2	1.0
1432175_at	RIKEN cDNA 5430434I15 gene	5430434I15Rik	?	?	8.6	0.8	1.8	1	10.8	1.8
1439169_at	BB471557	BB471557	?	?	16.1	1.5	11.4	5.9	10.7	1.9
1437258_at	predicted gene, 100043005 small proline-rich protein 2A	100043005 Spr2a	regulation of cell shape epidermis development keratinocyte differentiation keratinization response to estradiol stimulus	structural molecule activity structural constituent of cytoskeleton	14.6	1.4	5.2	5	10.4	1.0
1420602_a_at	extraembryonic, spermatogenesis, homeobox 1	Esx1	blood vessel development placenta development regulation of transcription, DNA-dependent regulation of transcription	DNA binding transcription factor activity sequence-specific DNA binding	24.7	2.4	4.5	1.2	10.3	3.8
1437894_at	prospero-related homeobox 1	Prox1	cell fate determination lymph vessel development transcription regulation of transcription, DNA-dependent, multicellular organismal development, negative regulation of cell proliferation, endothelial cell differentiation, regulation of transcription	DNA binding transcription regulator activity	21.6	2.1	4	2.3	10.3	1.7
1439737_x_at	Mediator of RNA polymerase II transcription, subunit 6 homolog (yeast)	Med6	transcription, regulation of transcription, DNA-dependent regulation of transcription positive regulation of transcription from RNA polymerase II promoter	transcription coactivator activity protein binding transcription regulator activity	28.1	2.8	8.9	0.9	10.0	9.9
1442302_at	N-methylpurine-DNA glycosylase	Mpg	DNA repair base-excision repair response to DNA damage stimulus	DNA binding, catalytic activity alkylase DNA N-glycosylase activity hydrolase activity	16	1.6	15.8	13.2	10.0	1.2
1449302_at	ATP-binding cassette, sub-family A (ABC1), member 2	Abca2	regulation of transcription from RNA polymerase II promoter transport, cholesterol metabolic process, regulation of intracellular cholesterol transport, cholesterol homeostasis, response to steroid hormone stimulus	nucleotide binding ATP binding ATPase activity nucleoside-triphosphatase activity	55.6	5.7	9.7	17.3	9.8	0.6
1444419_at	hypothetical protein LOC100048394 prolylcarboxypeptidase (angiotensinase C)	LOC100048394 Prpc	proteolysis	carboxypeptidase activity peptidase activity, serine-type peptidase activity hydrolase activity	11.7	1.2	8.4	13.2	9.8	0.6
1427660_x_at	predicted gene, EG628498 predicted gene, ENSMUSG00000076577 immunoglobulin kappa chain, constant region immunoglobulin kappa chain variable 28 (V28) similar to Chain L, Structural Basis Of Antigen Mimicry In A Clinically Relevant Melanoma Antigen System	EG628498 ENSMUSG00000076577 Igk-C Igk-V28 LOC100047628	?	antigen binding	373.8	39.5	86.1	136.9	9.5	0.6
1422083_at	toll-like receptor 9	Tlr9	inflammatory response immune response signal transduction response to virus positive regulation of interferon-gamma biosynthetic process immune response positive regulation of interferon-alpha biosynthetic process positive regulation of interferon-beta biosynthetic process	receptor activity transmembrane receptor activity protein binding, siRNA binding	20.2	0.9	10.2	23.4	22.4	0.4
1431649_at	RIKEN cDNA 1700108M19 gene	1700108M19Rik	?	?	11	0.5	0.8	1.2	22.0	0.7
1441892_x_at	BB341238	BB341238	?	?	21.2	1	1.4	1.5	21.2	0.9
1446289_at	AW556170	AW556170	?	?	37	1.9	10	9.2	19.5	1.1
1443956_at	zinc finger protein 397	Zfp397	transcription	nucleic acid binding	18.4	1	7.3	9	18.4	0.8
1431013_at	predicted gene, OTTMUSG00000015538 proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	OTTMUSG00000015538 Psm11	?	protein binding	31.1	1.7	21.1	21.9	18.3	1.0
1432969_at	RIKEN cDNA 4933423K11 gene	4933423K11Rik	?	?	19.6	1.1	1	0.9	17.8	1.1
1433087_at	RIKEN cDNA 5330430C04 gene	5330430C04Rik	?	?	26.6	1.5	1	6.9	17.7	0.1

表2-2絶食時にMuRF1依存的に発現制御を受ける候補遺伝子(続)

1453425_at	coiled-coil domain containing 83	Ccdc83	?	?	31.8	1.8	8.1	1.8	17.7	4.5
1417798_at	RIKEN cDNA 1810019J16 gene	1810019J16Rik	?	?	44.9	2.6	3.4	2.5	17.3	1.4
1446343_at	BG068486	BG068486	?	?	11.8	0.7	3.8	1.5	16.9	2.5
1437906_x_at	thioredoxin-like 1	Txn1l	transport cell redox homeostasis	?	37.4	2.3	14.7	21.2	16.3	0.7
1449752_at	Sp1A/cyanodine receptor domain and SOCS box containing 1	Spsb1	intracellular signaling cascade	receptor activity	24.3	1.5	12.2	6.2	16.2	2.0
1458494_at	AW457185	AW457185	?	?	18.2	1.2	5.2	1.2	15.2	4.3
1454830_at	fibrillin 2	Fbn2	blood coagulation embryonic limb morphogenesis limb morphogenesis	transmembrane receptor activity extracellular matrix structural constituent binding, calcium ion binding	18.1	1.2	5.6	2.9	15.1	1.9
1452417_x_at	RIKEN cDNA 2010205A11 gene predicted gene, EG628498 predicted gene, ENSMUSG00000076577 immunoglobulin kappa chain, constant region immunoglobulin kappa chain variable 28 (V28) similar to Chain L, Structural Basis Of Antigen Mimicry In A Clinically Relevant Melanoma Antigen System	2010205A11Rik EG628498 ENSMUSG00000076577 Igk-C Igk-V28 LOC100047628	?	antigen binding	263.1	19.2	72.3	73.5	13.7	1.0
1457650_x_at	autophagy-related 4A (yeast)	Atg4a	autophagosome formation proteolysis protein targeting to membrane protein targeting to vacuole transport, autophagy protein transport	cysteine-type endopeptidase activity protein binding microtubule binding peptidase activity cysteine-type peptidase activity hydrolase activity	27.5	2.1	3	9	13.1	0.3
1454081_at	AK016846	AK016846	?	?	16.7	1.3	1	6.1	12.8	0.2
1425882_at	growth differentiation factor 2	Gdf2	growth	cytokine activity, growth factor activity	30.3	2.4	4.6	4.4	12.6	1.0
1455923_at	potassium channel tetramerisation domain containing 8	Kctd8	potassium ion transport	voltage-gated potassium channel activity, protein binding	10	0.8	2.5	4.7	12.5	0.5
1428720_s_at	RIKEN cDNA 2010309G21 gene immunoglobulin lambda chain, constant region 2 immunoglobulin lambda chain, constant region 3	2010309G21Rik Igl-C2 Igl-C3	?	antigen binding	36.8	3	8.5	4.8	12.3	1.8
1434638_at	BM938299	BM938299	?	?	26.4	2.3	2.3	14.9	11.5	0.2
1427602_at	diabetic embryopathy 1	Dep1	?	?	29	2.6	13.8	14.3	11.2	1.0
1432175_at	RIKEN cDNA 5430434I15 gene	5430434I15Rik	?	?	8.6	0.8	1.8	1	10.8	1.8
1439169_at	BB471557	BB471557	?	?	16.1	1.5	11.4	5.9	10.7	1.9
1437258_at	predicted gene, 100043005 small proline-rich protein 2A	100043005 Sprr2a	regulation of cell shape epidermis development keratinocyte differentiation keratinization response to estradiol stimulus	structural molecule activity protein binding structural constituent of cytoskeleton	14.6	1.4	5.2	5	10.4	1.0
1420602_a_at	extraembryonic, spermatogenesis, homeobox 1	Esx1	blood vessel development placenta development regulation of transcription, DNA-dependent regulation of transcription	DNA binding transcription factor activity sequence-specific DNA binding	24.7	2.4	4.5	1.2	10.3	3.8
1437894_at	prospero-related homeobox 1	Prox1	cell fate determination lymph vessel development transcription regulation of transcription, DNA-dependent, multicellular organismal development, negative regulation of cell proliferation, endothelial cell differentiation, regulation of transcription	DNA binding transcription regulator activity	21.6	2.1	4	2.3	10.3	1.7
1439737_x_at	Mediator of RNA polymerase II transcription, subunit 6 homolog (yeast)	Med6	transcription, regulation of transcription, DNA-dependent regulation of transcription positive regulation of transcription from RNA polymerase II promoter	transcription coactivator activity protein binding transcription regulator activity	28.1	2.8	8.9	0.9	10.0	9.9
1442302_at	N-methylpurine-DNA glycosylase	Mpg	DNA repair base-excision repair response to DNA damage stimulus	DNA binding, catalytic activity alkylbase DNA N-glycosylase activity hydrolase activity	16	1.6	15.8	13.2	10.0	1.2
1449302_at	ATP-binding cassette, sub-family A (ABC1), member 2	Abca2	regulation of transcription from RNA polymerase II promoter transport, cholesterol metabolic process, regulation of intracellular cholesterol transport, cholesterol homeostasis, response to steroid hormone stimulus	nucleotide binding ATP binding ATPase activity nucleoside-triphosphatase activity	55.6	5.7	9.7	17.3	9.8	0.6
1444419_at	hypothetical protein LOC100048394 prolylcarboxypeptidase (angiotensinase C)	LOC100048394 Prep	proteolysis	carboxypeptidase activity peptidase activity, serine-type peptidase activity hydrolase activity	11.7	1.2	8.4	13.2	9.8	0.6
1427660_x_at	predicted gene, EG628498 predicted gene, ENSMUSG00000076577 immunoglobulin kappa chain, constant region immunoglobulin kappa chain variable 28 (V28) similar to Chain L, Structural Basis Of Antigen Mimicry In A Clinically Relevant Melanoma Antigen System	EG628498 ENSMUSG00000076577 Igk-C Igk-V28 LOC100047628	?	antigen binding	373.8	39.5	86.1	136.9	9.5	0.6
1451688_s_at	calcium activated nucleotidase 1	Cant1	ribonucleoside diphosphate catabolic process positive regulation of I-kappaB kinase/NF- kappaB cascade	guanosine-diphosphatase activity signal transducer activity calcium ion binding, pyrophosphatase activity hydrolase activity nucleoside-diphosphatase activity uridine-diphosphatase activity metal ion binding	68.4	12.1	52.2	20.7	5.7	2.5
1424481_s_at	armadillo repeat containing, X-linked 5	Armcx5	?	receptor activity, binding	52.4	9.3	20.8	10.5	5.6	2.0

表2-2絶食時にMuRF1依存的に発現制御を受ける候補遺伝子(続)

1440085_at	ectodysplasin A2 isoform receptor	Eda2r	multicellular organismal development programmed cell death cell differentiation positive regulation of JNK cascade positive regulation of NF-kappaB transcription factor activity	receptor activity protein binding	303.4	54	108	62.8	5.6	1.7
1441289_at	BM933567	BM933567	?	?	42.7	7.7	12.6	1.7	5.5	7.4
1439644_at	BE943682	BE943682	?	?	33	6.1	12.4	10.3	5.4	1.2
1432236_a_at	suppressor of variegation 3-9 homolog 1 (Drosophila)	Suv39h1	DNA packaging chromatin assembly or disassembly chromatin silencing, transcription regulation of transcription, DNA-dependent, cell cycle, chromatin modification, cell differentiation histone H3-K9 methylation	chromatin binding protein binding methyltransferase activity zinc ion binding protein methyltransferase activity transferase activity histone-lysine N-methyltransferase activity	37.8	7	9.9	15.3	5.4	0.6
1436455_at	aspartate-beta-hydroxylase	Asph	peptidyl-amino acid modification oxidation reduction	peptide-aspartate beta-dioxygenase activity, binding, iron ion binding, oxidoreductase activity oxidoreductase activity, acting on single donors with incorporation of molecular oxygen, incorporation of two atoms of oxygen	27.6	5.3	20.9	5.8	5.2	3.6
1430235_at	RIKEN cDNA 4933424G06 gene	4933424G06Rik	?	?	37.8	7.3	23	7.7	5.2	3.0
1440999_at	zinc finger protein 697	Zfp697	transcription, regulation of transcription, DNA-dependent	nucleic acid binding, DNA binding zinc ion binding, metal ion binding	30.4	5.9	13	4	5.2	3.3
1417121_at	gamma-aminobutyric acid (GABA-A) receptor, subunit alpha 6	Gabra6	transport, ion transport chloride transport gamma-aminobutyric acid signaling pathway	receptor activity, GABA-A receptor activity, ion channel activity extracellular ligand-gated ion channel activity, chloride channel activity neurotransmitter receptor activity chloride ion binding	21.6	4.2	0.7	2.9	5.1	0.2
1435994_at	potassium voltage-gated channel, subfamily H (cag- related), member 1	Kcnh1	two-component signal transduction system (phosphorelay) regulation of transcription, DNA-dependent, transport, ion transport potassium ion transport, signal transduction	two-component sensor activity signal transducer activity ion channel activity voltage-gated ion channel activity voltage-gated potassium channel activity potassium channel activity calmodulin binding, potassium ion binding	29.8	5.8	1.2	8.2	5.1	0.1
1428927_at	SHQ1 homolog (S. cerevisiae)	Sbq1	?	?	31.6	6.2	24.5	17.8	5.1	1.4
1423193_at	paraspeckle protein 1	Pspc1	transcription regulation of transcription, DNA-dependent	nucleotide binding, nucleic acid binding RNA binding, protein binding	28.5	5.6	8.8	4.9	5.1	1.8
1420992_at	ankyrin repeat domain 1 (cardiac muscle)	Ankd1	regulation of transcription from RNA polymerase II promoter	transcription corepressor activity protein binding	574.2	113.9	378	256.2	5.0	1.5
1425100_a_at	phosphodiesterase 6G, cGMP-specific, rod, gamma	Pde6g	activation of MAPK activity visual perception positive regulation of epidermal growth factor receptor signaling pathway positive regulation of G-protein coupled receptor protein signaling pathway, response to stimulus	3',5'-cyclic-nucleotide phosphodiesterase activity protein binding hydrolyase activity cGMP binding	42.5	8.5	15.4	2.3	5.0	6.7

MuRF1依存的に発現量が1/5以下になった遺伝子

Probe Set ID	Gene Title	Gene Symbol	Biological Process	Molecular Function	WT starved	WT control	KO starved	KO control	WT ratio	KO ratio
1453552_at	RIKEN cDNA 2310014F07 gene	2310014F07Rik	?	?	2.4	226.6	128	194.4	0.01	0.66
1459253_at	Arrestin domain containing 3	Artdc3	?	?	3.9	114.4	66.1	24.1	0.03	2.74
1442157_at	BB314361	BB314361	?	?	1.4	36.7	12	18.2	0.04	0.66
1455346_at	mannan-binding lectin serine peptidase 1	Masp1	proteolysis, immune response complement activation, classical pathway, innate immune response	catalytic activity, serine-type endopeptidase activity calcium ion binding, sugar binding peptidase activity, hydrolase activity	2.3	53.3	21	37.8	0.04	0.56
1436964_at	DNA segment, Chr 7, ERATO Doi 715, expressed	D7End715e	?	?	1.5	30.3	18.2	27.6	0.05	0.66
1443114_at	RIKEN cDNA A730059M13 gene	A730059M13Rik	?	?	0.8	12.7	8.9	8.4	0.06	1.06
1453468_at	RIKEN cDNA 4930430F08 gene	4930430F08Rik	?	?	2.2	28.4	27.1	23.6	0.08	1.15
1423100_at	FBJ osteosarcoma oncogene	Fos	regulation of transcription, DNA-dependent nervous system development response to drug	DNA binding, double-stranded DNA binding transcription factor activity sequence-specific DNA binding protein heterodimerization activity protein dimerization activity	39.1	452.9	92.7	92.2	0.09	1.01
1448619_at	7-dehydrocholesterol reductase	Dhcr7	blood vessel development steroid biosynthetic process cholesterol biosynthetic process lipid biosynthetic process post-embryonic development sterol biosynthetic process cell differentiation, lung development multicellular organism growth regulation of cell proliferation oxidation reduction	protein binding oxidoreductase activity 7-dehydrocholesterol reductase activity	5.7	62.4	6.9	10.7	0.09	0.64
1456111_at	RIKEN cDNA D930028F11 gene	D930028F11Rik	?	?	10.4	84.2	43.8	56.1	0.12	0.78
1425425_a_at	Wnt inhibitory factor 1	Wif1	multicellular organismal development Wnt receptor signaling pathway negative regulation of Wnt receptor signaling pathway	protein tyrosine kinase activity Wnt-protein binding	3.5	27.5	8.5	15.3	0.13	0.56
1434783_at	transmembrane protein 106C	Tmem106c	?	?	6.9	53.4	21.9	30.7	0.13	0.71
1442956_at	BG075869	BG075869	?	?	1.7	12.3	9.8	13.2	0.14	0.74
1431469_a_at	CXXC finger 5	Cxxc5	?	?	28.5	186.6	44	70.5	0.15	0.62
1441375_at	AU043080	AU043080	?	?	14.3	93.1	64.7	50.2	0.15	1.29
1435672_at	hypothetical protein 3830612M24	3830612M24	?	?	15.7	101.9	25.3	103.8	0.15	0.24
1447263_at	BM730703	BM730703	?	?	6.4	39.4	29.2	29.6	0.16	0.99
1424454_at	transmembrane protein 87A	Tmem87a	?	?	28.6	166.8	230.9	180.7	0.17	1.28
1418311_at	fructosamine 3 kinase	Fa3k	fructosamine metabolic process	kinase activity, transferase activity fructosamine-3-kinase activity	24.7	138.9	58.3	114.9	0.18	0.51
1446475_at	BM207891	BM207891	?	?	53.4	299	109.1	124.6	0.18	0.88
1416357_a_at	melanoma cell adhesion molecule	Mcam	cell adhesion heterophilic cell adhesion	protein binding	10.3	55.6	27.3	33.3	0.19	0.82
1450660_at	6-pyruvoyl-tetrahydropterin synthase	Pts	tetrahydropterin biosynthetic process	6-pyruvoyltetrahydropterin synthase activity, protein binding, zinc ion binding, lyase activity, identical protein binding, metal ion binding	28.6	145	94.9	140.8	0.20	0.67

WT starved、WT control、KO starvedおよびKO controlの各欄は、各プローブのシグナルを示す。
WT ratio、KO ratioは、WTマウスとMuRF1 KOマウスそれぞれにおける、starved群のcontrol群に対するシグナル値の比を表す。

表2-3 血漿中のアミノ酸濃度

	cont		-AA	
	WT	KO	WT	KO
Aspartic acid	3.9 ± 1.1	3.7 ± 0.3	7.5 ± 3.7	3.9 ± 1.2
Serine	136.1 ± 7.7	109.4 ± 17.9	188.9 ± 23.6	184.5 ± 43.0
Asparagine	33.6 ± 3	26.4 ± 2.9	42.2 ± 9.0	41.5 ± 10.4
Glutamic acid	21.7 ± 5.4	18.5 ± 3.2	48.2 ± 17.3	31.4 ± 8.9
Glutamine	407.4 ± 27.1	411.3 ± 86.0	658.1 ± 6.8 ^c	638.3 ± 24.8 ^d
Proline	76.2 ± 12.6	71.5 ± 6.5	80.2 ± 7.7	71.6 ± 8.7
Glycine	281.3 ± 38.2	232.5 ± 34.6	238.0 ± 30.7	182.0 ± 39.2
Alanine	342.7 ± 8.1	284.4 ± 69.1	1142.9 ± 128.4 ^{d,g}	926.5 ± 35.5 ^{c,f}
Tyrosine	56.5 ± 0.9	54.6 ± 5.3	42.6 ± 4.9	41.1 ± 11.2
Tryptophan	65.2 ± 0.8	61.8 ± 8.4	55.6 ± 7.9	54.1 ± 8.5
Cystine	8.0 ± 4.4	6.0 ± 2.7	9.0 ± 2.1	10.9 ± 3.6
Threonine	178.0 ± 14.0	161.3 ± 1.0	121.1 ± 24.6	120.7 ± 25.8
Methionine	51.8 ± 3.4	46.6 ± 5.3	40.3 ± 10.1	36.9 ± 7.7
Phenylalanine	68.1 ± 0.3	64.1 ± 3.5	35.6 ± 3.0 ^{c,g}	33.4 ± 3.7 ^{c,g}
Histidine	68.05 ± 4.7	55.1 ± 6.6	63.3 ± 2.8	56.7 ± 3.2
Lysine	280.7 ± 13.8	253.2 ± 30.4	466.8 ± 1.4 ^{c,f}	427.5 ± 15.5 ^{c,g}
Arginine	112.5 ± 5.9	88.7 ± 12.2	104.4 ± 32.1	108.3 ± 3.1
Valine	231.9 ± 10.7	246.0 ± 51.9	106.1 ± 3.0 ^c	88.8 ± 6.1 ^{c,g}
Isoleucine	101.8 ± 0.4	92.7 ± 2.0	39.8 ± 0.2 ^{a,e}	32.3 ± 0.4 ^{a,e,h}
Leucine	160.2 ± 0.3	153.4 ± 7.9	79.9 ± 5.2 ^{c,f}	63.8 ± 6.7 ^{c,f}
非必須アミノ酸	1367.2 ± 93.6	1218.0 ± 214.6	2457.4 ± 178.6 ^{d,g}	2131.5 ± 186.3 ^{d,g}
必須アミノ酸	1252.8 ± 53.3	1161.0 ± 11.8	1057.1 ± 71.5	968.3 ± 20.9 ^{d,f}
分岐鎖アミノ酸	493.9 ± 11.4	492.1 ± 61.8	225.7 ± 2.4 ^{b,g}	184.9 ± 1.0 ^{b,g,h}
合計	2620.0 ± 146.9	2379.0 ± 202.9	3514.5 ± 250.1 ^{d,g}	3099.8 ± 207.2

(nmol/ml)

mean ± S.D. (n=2)

a, vs WT control p<0.0001

e, vs KO control p<0.001

b, vs WT control p<0.001

f, vs KO control p<0.01

c, vs WT control p<0.01

g, vs KO control p<0.05

d, vs WT control p<0.05

h, vs WT -AA p<0.01

必須アミノ酸 … Thr、Met、Phe、His、Lys、Arg、Val、Ile、Leuの合計

非必須アミノ酸 … 必須アミノ酸以外の合計

分岐鎖アミノ酸 … Val、Leu、Ileの合計