

Table S3a.
Genes Upregulated in Adipose Tissue by MR (Normalized to Control)

Gene Symbol	Gene name	MR	p value	MRC	p value	Function
<i>Lipid Metabolism</i>						
ELOVL6	ELOVL family member 6	4.04	3.12E-05	-1.39	1.16E-02	Uses malonyl-CoA as a 2-carbon donor in the first and rate-limiting step of fatty acid elongation.
ACACA	Acetyl-CoA carboxylase alpha	3.35	3.33E-06	-1.28	1.61E-01	Carboxylation of acetyl-CoA to malonyl-CoA, the rate-limiting step in fatty acid synthesis.
GPAM	Glycerol-3-phosphate acyltransferase, mitochondrial	2.78	4.39E-05	-1.20	1.35E-01	Initial and committing step in glycerolipid biosynthesis.
SCD	Stearoyl-CoA desaturase (delta-9-desaturase)	2.66	1.76E-04	-1.22	3.02E-01	Rate-limiting step in the synthesis of unsaturated fatty acids.
ACSM5	Acyl-CoA synthetase medium-chain family member 5	2.48	1.57E-05	-1.04	4.31E-01	Unknown
LGALS12	Lectin, galactoside-binding, soluble, 12	2.22	2.01E-04	-1.02	8.42E-01	A primary regulator of the early stages of adipose tissue development.
ACAT2	Acetyl-CoA acetyltransferase 2	1.90	1.05E-03	-1.21	3.04E-01	Lipid metabolism, cytosolic acetoacetyl-CoA thiolase.
INSIG1	Insulin induced gene 1	1.87	6.68E-04	-1.08	6.58E-01	Regulates cholesterol concentrations in cells.
PNPLA3	Patatin-like phospholipase domain containing 3	1.81	1.27E-04	-1.00	9.94E-01	Mediates triacylglycerol hydrolysis in adipocytes.
CPT1B	Carnitine palmitoyltransferase 1B (muscle)	1.80	1.16E-03	1.02	8.19E-01	Rate-controlling enzyme of the long-chain fatty acid beta-oxidation pathway in mitochondria.
HSD17B12	Hydroxysteroid (17-beta) dehydrogenase 12	1.79	5.17E-05	-1.21	8.16E-02	Reduces 3-ketoacyl-CoA to 3-hydroxyacyl-CoA during the second step of fatty acid elongation.
RETN	Resistin	1.77	2.91E-02	-1.36	2.48E-01	Hormone secreted by adipocytes.
PPARGC1A	Peroxisome proliferator-activated receptor gamma, coactivator 1 alpha	1.76	1.28E-04	-1.08	5.22E-01	Regulates the genes involved in energy metabolism.
LPIN1	Lipin 1	1.73	3.65E-05	-1.12	3.92E-02	Normal adipose tissue development.
ACSL1	Acyl-CoA synthetase long-chain family member 1	1.72	3.80E-03	-1.16	4.35E-01	Converts free long-chain fatty acids into fatty acyl-CoA esters.
LIPE	Lipase, hormone-sensitive	1.71	1.48E-02	-1.12	6.21E-01	Hydrolyzes stored triglycerides to free fatty acids.
ACLY	ATP citrate lyase	1.68	1.02E-02	-1.27	2.42E-01	Formation of acetyl-CoA and oxaloacetate from citrate and CoA.
GPD1	Glycerol-3-phosphate dehydrogenase 1 (soluble)	1.65	6.64E-03	-1.15	3.66E-01	Mitochondrial glycerol 3-phosphate dehydrogenase.
DGAT2	Diacylglycerol O-acyltransferase 2	1.62	2.66E-02	-1.13	5.68E-01	Synthesis of triglycerides.

MGLL	Monoglyceride lipase	1.61	1.53E-02	-1.12	6.10E-01	Hydrolyzes intracellular triglyceride stores in adipocytes to fatty acids and glycerol.
CLYBL	Citrate lyase beta-like	1.52	1.00E-04	-1.13	8.46E-02	Unknown

Carbohydrate Metabolism

GYS2	Glycogen synthase 2 (liver)	3.00	8.42E-07	1.09	7.78E-01	Rate-limiting step in the synthesis of glycogen.
PYGL	Phosphorylase, glycogen, liver	2.33	1.73E-04	-1.12	5.00E-01	Releases glucose-1-phosphate from glycogen stores.
PDHB	Pyruvate dehydrogenase (lipoamide) beta	1.80	1.53E-05	-1.16	9.28E-02	Catalyzes the conversion of pyruvate to acetyl-CoA and CO ₂ .
GCGR	Glucagon receptor	1.79	5.00E-04	1.03	5.78E-01	Controls blood glucose levels.
PCK1	Phosphoenolpyruvate carboxykinase 1 (soluble)	1.78	4.95E-02	-1.18	5.75E-01	Formation of phosphoenolpyruvate from oxaloacetate.
IDH3A	Isocitrate dehydrogenase 3 (NAD+) alpha	1.76	1.42E-04	-1.09	4.10E-01	Decarboxylation of isocitrate to 2-oxoglutarate.
LDHA	Lactate dehydrogenase A	1.74	1.63E-03	1.11	1.60E-01	Conversion of L-lactate and NAD to pyruvate and NADH in the final step of anaerobic glycolysis.
PDK1	Pyruvate dehydrogenase kinase, isozyme 1	1.72	6.53E-05	-1.15	3.26E-02	Oxidative decarboxylation of pyruvate.
PC	Pyruvate carboxylase	1.71	1.04E-03	-1.33	2.59E-02	Carboxylation of pyruvate to oxaloacetate.
PFKM	Phosphofructokinase, muscle	1.65	4.22E-02	1.21	2.51E-01	Phosphorylation of fructose-6-phosphate to fructose-1,6-bisphosphate.
PFKFB3	6-Phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	1.61	2.23E-02	-1.23	3.08E-01	Biosynthesis and degradation of fructose 2,6-bisphosphate.
MDH1	Malate dehydrogenase 1, NAD (soluble)	1.57	9.36E-04	-1.17	1.39E-01	Oxidation of malate to oxaloacetate.
MDH2	Malate dehydrogenase 2, NAD (mitochondrial)	1.57	2.74E-04	-1.04	6.51E-01	Reversible oxidation of malate to oxaloacetate.
PFKFB1	6-Phosphofructo-2-kinase/fructose-2,6-biphosphatase 1	1.57	9.89E-03	-1.16	3.27E-01	Synthesis and degradation of fructose-2,6-biphosphate.
ACO2	Aconitase 2, mitochondrial	1.56	9.15E-04	-1.08	3.70E-01	Interconversion of citrate to isocitrate.

Amino Acid Metabolism

AADAT	Aminoadipate aminotransferase	2.87	1.40E-06	-1.01	9.35E-01	L-lysine catabolism and the transamination of kynurenine to produce kynurenine acid.
PSAT1	Phosphoserine aminotransferase 1	1.85	1.11E-03	-1.18	1.92E-01	Phosphoserine aminotransferase
ASPA	Aspartoacylase	1.67	2.67E-03	-1.18	2.66E-01	Conversion of N-acetyl_L-aspartic acid (NAA) to aspartate and acetate.
FAH	Fumarylacetoacetate hydrolase (fumarylacetoacetase)	1.65	7.01E-03	-1.10	5.20E-01	Last enzyme in the tyrosine catabolism pathway.

Nucleotide/Nucleoside Metabolism

AMPD1	Adenosine monophosphate deaminase 1	3.32	3.26E-02	1.37	5.20E-01	Deamination of AMP to IMP, plays an important role in the purine nucleotide cycle.
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Metabolism Oxidation/Reduction

CBR1	Carbonyl reductase 1	4.51	3.44E-06	-1.12	4.89E-01	NADPH-dependent oxidoreductases with wide specificity for carbonyl compounds.
CBR3	Carbonyl reductase 3	2.37	1.19E-07	-1.05	6.76E-01	Reduction of biologically and pharmacologically active carbonyl compounds to their corresponding alcohols.
CBR1	Carbonyl reductase 1	1.95	1.98E-03	-1.34	7.54E-02	NADPH-dependent oxidoreductase with wide specificity to carbonyl compounds.
MAOB	Monoamine oxidase B	1.91	3.46E-03	1.24	2.38E-01	Oxidative deamination of biogenic and xenobiotic amines.

Transport

SLC36A2	Solute carrier family 36 (proton/amino acid symporter), member 2	2.30	7.62E-04	-1.03	8.34E-01	Regulates pH-dependent, Na(+)-independent uptake of glycine, proline, and alpha(methyl)aminoisobutyric acid.
AQP7	Aquaporin 7	1.93	2.97E-03	-1.20	4.18E-01	Facilitates water, glycerol and urea transport.
SLC2A4	Solute carrier family 2 (facilitated glucose transporter), member 4	1.89	8.20E-04	-1.03	7.91E-01	Glucose transport.
SLC22A3	Solute carrier family 22 (extraneuronal monoamine transporter), member 3	1.85	5.10E-03	1.02	8.95E-01	Organic cation transporters.
SORL1	Sortilin-related receptor, L(DLR class) A repeats-containing	1.81	6.34E-05	-1.08	3.30E-01	Belongs to the families of vacuolar protein sorting 10 (VPS10) domain-containing receptor proteins, low density lipoprotein receptor (LDLR) proteins, and fibronectin type III repeats proteins.
ATP1A2	ATPase, Na+/K+ transporting, alpha 2 polypeptide	1.77	1.77E-02	-1.05	7.79E-01	Subfamily of Na+/K+ -ATPases responsible for establishing and maintaining the electrochemical gradients of Na and K ions across the plasma membrane.
KCNN3	Potassium intermediate/small conductance calcium-activated channel, subfamily N, member 3	1.60	1.25E-02	-1.03	8.16E-01	Member of the KCNN family of potassium channels, is activated before membrane hyperpolarization.

	SLC25A30	Solute carrier family 25, member 30	1.59	1.38E-02	-1.02	8.76E-01	Transport of solutes across the inner mitochondrial membrane.
	NHEDC2	Na+/H+ exchanger domain containing 2	1.58	7.80E-05	-1.00	9.61E-01	Sodium hydrogen antiporter.
<i>Immune Response</i>							
	MIF	Macrophage migration inhibitory factor (glycosylation-inhibiting factor)	3.43	1.70E-04	1.37	2.07E-01	Lymphokine involved in cell-mediated immunity, immunoregulation, and inflammation.
	CXCL13	Chemokine (C-X-C motif) ligand 13	2.56	1.32E-02	1.39	2.99E-01	B lymphocyte chemoattractant.
	MPO	Myeloperoxidase	1.73	1.00E-02	-1.06	7.57E-01	Produces hypohalous acids central to the microbicidal activity of neutrophils.
	CXCL14	Chemokine (C-X-C motif) ligand 14	1.60	2.33E-03	-1.15	4.12E-01	Involved in immunoregulatory and inflammatory processes, displays chemotactic activity for monocytes but not for lymphocytes.
	MMD	Monocyte to macrophage differentiation-associated	1.57	9.74E-05	-1.12	1.34E-01	Expressed by in vitro differentiated macrophages but not freshly isolated monocytes.
<i>Signal Transduction</i>							
	DUSP4	Dual specificity phosphatase 4	1.81	2.27E-04	1.09	4.02E-01	Negative regulation of mitogen-activated protein (MAP) kinase superfamily (MAPK/ERK, SAPK/JNK, p38), which are associated with cellular proliferation and differentiation.
	RGS7	Regulator of G-protein signaling 7	1.73	2.14E-03	-1.31	2.04E-02	GTPase activating protein.
	ACVR1C	Activin A receptor, type IC	1.67	1.87E-02	-1.06	7.09E-01	A type I receptor for the TGFB family of signaling molecules.
	PDE3B	Phosphodiesterase 3B, cGMP-inhibited	1.65	2.03E-03	-1.13	2.43E-01	Hydrolysis of cAMP and cGMP.
	TSHR	Thyroid stimulating hormone receptor	1.56	1.69E-02	-1.12	5.33E-01	Major controller of thyroid cell metabolism.
	SUCNR1	Succinate receptor 1	1.54	3.23E-02	-1.23	2.24E-01	G-protein-coupled receptor for succinate.
<i>Others</i>							
	MYL1	Myosin, light chain 1, alkali; skeletal, fast	4.41	4.46E-02	1.27	7.44E-01	Myosin alkali light chain expressed in fast skeletal muscle.
	CA5B	Carbonic anhydrase VB, mitochondrial	2.53	1.50E-06	-1.09	4.49E-01	Reversible hydration of carbon dioxide.
	TTPA	Tocopherol (alpha) transfer protein	2.34	1.03E-03	-1.06	6.29E-01	Binds alpha-trocopherol, a form of vitamin E.
	BCHE	Butyrylcholinesterase	2.10	1.65E-05	-1.18	1.54E-01	Responsible for suxamethonium sensitivity.

B3GALT1	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 1	2.08	5.78E-03	-1.04	7.83E-01	Type II membrane-bound glycoproteins
C10orf58	Chromosome 10 open reading frame 58	2.07	6.36E-04	-1.04	6.97E-01	Unknown
Pdha1	Pyruvate dehydrogenase (lipoamide) alpha 1	1.76	1.09E-05	-1.09	3.78E-01	Catalyzes the interconversion of pyruvate and lipoamide to S-acetyldihydrolipoamide and CO ₂ .
ABCD2	ATP-binding cassette, sub-family D (ALD), member 2	1.74	7.72E-03	-1.32	1.30E-01	Member of the superfamily of ATP-binding cassette (ABC) transporter.
CA4	Carbonic anhydrase IV	1.67	5.99E-04	-1.22	1.11E-01	Reversible hydration of carbon dioxide.

Table S3b.
Genes Downregulated in Adipose Tissue by MR (Normalized to Control)

Gene Symbol		Gene name	MR	p value	MRC	p value	Function
<i>Lipid Metabolism</i>							
FABP3		Fatty acid binding protein 3, muscle and heart	-2.96	2.84E-02	-1.27	5.29E-01	Uptake, intracellular metabolism and/or transport of long-chain fatty acids.
<i>Amino Acid Metabolism</i>							
SAT1		Spermidine/spermine N1-acetyltransferase 1	-1.70	1.47E-02	-1.15	3.72E-01	Rate-limiting enzyme in the catabolic pathway of polyamine metabolism.
Ckmt1		Creatine kinase, mitochondrial 1	-1.69	3.27E-02	-1.18	3.61E-01	Transfer of phosphate to creatine in energy transduction.
<i>Nucleotide/Nucleoside Metabolism</i>							
TOP2A		Topoisomerase (DNA) II alpha 170kDa	-1.66	1.10E-02	-1.06	7.38E-01	Controls and alters the topologic states of DNA during transcription.
<i>Metabolism Oxidation/Reduction</i>							
PRDX4		Peroxiredoxin 4	-2.07	1.08E-02	-1.03	8.30E-01	Antioxidant enzyme.
XDH		Xanthine dehydrogenase	-1.54	2.39E-02	-1.05	7.34E-01	Oxidative metabolism of purines.
<i>Transport</i>							
MUP		Major urinary protein pseudogene	-2.05	3.15E-02	-1.06	8.53E-01	Transport of small, hydrophobic molecules.
TF		Transferrin	-1.88	4.64E-05	1.24	2.55E-01	Binds to ferric iron.
SLC9A3R1		Solute carrier family 9 (sodium/hydrogen exchanger), member 3 regulator 1	-1.64	2.02E-02	-1.21	2.53E-01	Sodium/hydrogen exchanger regulatory cofactor.
KCNMB1		Potassium large conductance calcium-activated channel, subfamily M, beta member 1	-1.59	3.78E-04	1.06	5.43E-01	Large conductance, voltage and calcium-sensitive potassium channels.
SLC39A14		Solute carrier family 39 (zinc transporter), member 14	-1.56	8.38E-03	-1.08	6.30E-01	Shows structural characteristics of zinc transporters.

	SCNN1B	Sodium channel, nonvoltage-gated 1, beta	-1.55	4.89E-03	-1.12	4.59E-01	Controls fluid and electrolyte transport across epithelia.
	SCNN1G	Sodium channel, nonvoltage-gated 1, gamma	-1.55	9.87E-03	-1.01	9.47E-01	Controls fluid and electrolyte transport across epithelia.
	KCNK1	Potassium channel, subfamily K, member 1	-1.53	1.99E-02	-1.17	4.13E-01	Member of the superfamily of potassium channel proteins.
<i>Immune Response</i>							
	APOB48R	Apolipoprotein B48 receptor	-1.61	1.03E-02	1.00	9.96E-01	Binds to the apolipoprotein B48 of dietary triglyceride (TG)-rich lipoproteins.
	CCR5	Chemokine (C-C motif) receptor 5	-1.57	3.06E-02	1.05	7.54E-01	May play a role in granulocyte lineage proliferation and differentiation.
	CCL7	Chemokine (C-C motif) ligand 7	-1.53	3.67E-02	-1.08	6.60E-01	Attracts macrophages during inflammation and metastasis.
	CCR2	Chemokine (C-C motif) receptor 2	-1.50	4.17E-03	1.11	4.35E-01	Involved in monocyte infiltration in inflammatory diseases.
	LBP	Lipopolysaccharide binding protein	-3.46	5.74E-03	-1.15	7.69E-01	Involved in the acute-phase immunologic response to gram-negative bacterial infections.
<i>Signal Transduction</i>							
	RAB25	RAB25, member RAS oncogene family	-2.40	3.82E-02	-1.48	2.95E-01	Small GTPase involved in membrane trafficking.
	SFRP2	Secreted frizzled-related protein 2	-2.27	6.07E-05	-1.33	7.90E-02	Soluble modulators of Wnt signaling.
	PIK3R3	Phosphoinositide-3-kinase, regulatory subunit 3 (gamma)	-1.85	3.36E-02	-1.31	2.61E-01	Regulatory subunit of phosphatidylinositol 3-kinase.
	TNFRSF21	Tumor necrosis factor receptor superfamily, member 21	-1.76	1.48E-02	-1.02	9.33E-01	Activator of NF-kappaB and MAPK8/JNK, and inducer of cell apoptosis.
	SFRP4	Secreted frizzled-related protein 4	-1.66	9.06E-03	1.08	7.39E-01	Soluble modulators of Wnt signaling.
	DUSP18	Dual specificity phosphatase 18	-1.55	1.24E-03	-1.15	1.17E-01	Modulator of signaling pathways.
<i>Others</i>							
	CEACAM4	Carcinoembryonic antigen-related cell adhesion molecule 4	-5.70	3.28E-02	-1.72	3.46E-01	Cell-cell adhesion molecule [RGD].
	EPCAM	Epithelial cell adhesion molecule	-5.50	4.27E-02	-1.76	3.69E-01	Carcinoma-associated antigen.
	Expi	Extracellular proteinase inhibitor	-4.59	6.86E-04	-1.85	2.35E-01	May mediate the invasive and metastatic potential of mammary adenocarcinomas.

TSPAN1	Tetraspanin 1	-3.85	2.54E-02	-1.05	9.19E-01	Regulation of cell development, activation, growth and motility.
CRABP1	Cellular retinoic acid binding protein 1	-2.57	1.23E-03	1.35	1.34E-01	Vitamin A-directed differentiation in epithelial tissue.
CLDN7	Claudin 7	-2.04	9.32E-03	-1.03	9.18E-01	Component of tight junction strands, maintains cell polarity and signal transduction.
GUSB	Glucuronidase, beta	-1.97	1.38E-02	-1.38	1.18E-01	Degrades glycosaminoglycans, including heparan sulfate, dermatan sulfate, and chondroitin-4,6-sulfate.
MMP12	Matrix metalloproteinase 12 (macrophage elastase)	-1.83	4.72E-02	-1.01	9.89E-01	Degrades soluble and insoluble elastin.
OCM2	Oncomodulin 2	-1.79	3.61E-03	-1.65	7.28E-03	Similar to the oncomodulin gene.
UCP2	Uncoupling protein 2 (mitochondrial, proton carrier)	-1.77	4.81E-02	-1.24	1.55E-01	Separates oxidative phosphorylation from ATP synthesis with energy dissipated as heat.
STAP2	Signal transducing adaptor family member 2	-1.76	2.66E-02	-1.30	1.13E-01	Mediates the interactions linking proteins involved in signal transduction pathways.
ACE	Angiotensin I converting enzyme (peptidyl-dipeptidase A) 1	-1.54	4.72E-04	-1.01	9.20E-01	Conversion of angiotensin I into angiotensin II.

Table S3c.
Genes Upregulated in Liver by MR (Normalized to Control)

Gene Symbol	Gene name	MR	p value	MRC	p value	Function
<i>Lipid Metabolism</i>						
VLDLR	Very low density lipoprotein receptor	5.79	2.00E-09	1.14	3.63E-01	VLDL-triglyceride metabolism.
ACSM3	Acyl-CoA synthetase medium-chain family member 3	3.29	5.63E-06	1.84	9.03E-04	Unknown
ACSM2A	Acyl-CoA synthetase medium-chain family member 2A	2.14	3.70E-03	1.07	6.54E-01	Unknown
CD36	CD36 molecule (thrombospondin receptor)	1.78	6.12E-04	1.02	8.94E-01	Binds long chain fatty acids. May function in the transport and/or as a regulator of fatty acid transport.
ME1	Malic enzyme 1, NADP(+)-dependent, cytosolic	1.70	5.64E-03	-2.44	4.45E-04	Generates NADPH for fatty acid biosynthesis, links the glycolytic and citric acid cycles.
PPARGC1A	Peroxisome proliferator-activated receptor gamma, coactivator 1 alpha	1.67	1.64E-03	-1.12	4.29E-01	Regulates the genes involved in energy metabolism.
ACOT2	Acyl-CoA thioesterase 2	1.66	1.49E-05	-1.10	2.42E-01	Hydrolyzes CoA esters.
HADHB	Hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase (trifunctional protein), beta subunit	1.62	4.70E-04	1.03	7.36E-01	Mitochondrial trifunctional protein, catalyzes the last three steps of mitochondrial beta-oxidation of long chain fatty acids.
AGPAT9	1-Acylglycerol-3-phosphate O-acyltransferase 9	1.59	1.41E-04	1.01	9.18E-01	Converts glycerol-3-phosphate (G3P) to lysophosphatidic acid (LPA).
<i>Carbohydrate Metabolism</i>						
ACO2	Aconitase 2, mitochondrial	1.57	3.23E-07	1.06	1.71E-01	Interconversion of citrate to isocitrate.
FUCA2	Fucosidase, alpha-L- 2, plasma	1.52	3.31E-04	1.24	1.35E-02	Cytoplasm-specific alpha-L fucosidase.
PCK2	Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	1.51	6.11E-06	1.05	4.04E-01	Mitochondrial phosphoenolpyruvate carboxykinase. Catalyzes the conversion of oxaloacetate to phosphoenolpyruvate
<i>Mitochondrial Electron Transport Chain</i>						
NDUFAF4	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, assembly factor 4	1.83	5.13E-04	1.24	2.05E-01	Catalyzes the transfer of electrons from NADH to ubiquinone (coenzyme Q).

Amino Acid Metabolism

MTHFD2	Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	4.54	1.24E-06	2.08	1.10E-02	Converts 5,10 methylene THF to 5,10 methenyl THF.
ASNS	Asparagine synthetase (glutamine-hydrolyzing)	3.69	4.47E-07	1.32	1.54E-01	Involved in the synthesis of asparagines.
PSAT1	Phosphoserine aminotransferase 1	2.63	1.25E-05	1.42	1.05E-01	Likely a phosphoserine aminotransferase
ODC1	Ornithine decarboxylase 1	2.21	1.49E-06	1.52	1.03E-02	Rate-limiting enzyme of the polyamine biosynthesis. Catalyzes ornithine to putrescine.
PHGDH	Phosphoglycerate dehydrogenase	1.76	1.17E-05	-1.01	8.73E-01	Catalyzes the transition of 3-phosphoglycerate into 3-phosphohydroxypyruvate, which is the first and rate-limiting step in the phosphorylated pathway of serine biosynthesis, using NAD+/NADH as a cofactor.
SCPEP1	Serine carboxypeptidase 1	1.73	2.27E-03	1.51	1.44E-02	May act as a serine carboxypeptidase.
GSR	Glutathione reductase	1.70	4.44E-04	1.25	2.48E-02	Catalyzes the conversion of glutathione and NADP+ to glutathione disulfide.
GSS	Glutathione synthetase	1.69	3.72E-04	1.13	1.92E-01	ATP-dependent conversion of gamma-L-glutamyl-L-cysteine to glutathione.
GLDC	Glycine dehydrogenase (decarboxylating)	1.63	3.07E-03	1.12	4.27E-01	Degradation of glycine.
TAT	tyrosine aminotransferase	1.62	3.92E-02	-1.07	7.17E-01	conversion of L-tyrosine into p-hydroxyphenylpyruvate.
SRM	Spermidine synthase	1.58	1.66E-03	-1.01	9.31E-01	Final step of spermidine biosynthesis. Conversion of putrescine to spermidine using decarboxylated S-adenosylmethionine as the cofactor.
GPX2	Glutathione peroxidase 2 (gastrointestinal)	1.56	5.77E-06	1.06	6.97E-01	Member of the glutathione peroxidase family and encodes a selenium-dependent glutathione peroxidase that is one of two isoenzymes responsible for the majority of the glutathione-dependent hydrogen peroxide-reducing activity.

Stress Response

GADD45G	Growth arrest and DNA-damage-inducible, gamma	2.26	2.18E-02	1.53	3.04E-01	Member of a group of genes whose transcript levels are increased following stressful growth arrest. Responds to environmental stresses by mediating activation of the p38/JNK pathway via MTK1/MEKK4 kinase.
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GADD45A	Growth arrest and DNA-damage-inducible, alpha	1.81	3.55E-04	1.17	3.07E-01	Member of a group of genes whose transcript levels are increased following stressful growth arrest conditions and treatment with DNA-damaging agents. Responds to environmental stresses by mediating activation of the p38/JNK pathway via MTK1/MEKK4 kinase. DNA damage-induced transcription of this gene is mediated by both p53-dependent and -independent mechanisms.
ATF4	Activating transcription factor 4 (tax-responsive enhancer element B67)	1.67	1.04E-04	1.15	2.79E-01	Characterized as the cAMP-response element binding protein 2 (CREB-2).
<i>Nucleotide/Nucleoside Metabolism</i>						
CTPS	CTP synthase	2.10	1.25E-05	1.56	7.83E-03	Conversion of UTP to CTP, which is important in the biosynthesis of phospholipids and nucleic acids.
IMPDH2	IMP (inosine 5'-monophosphate) dehydrogenase 2	1.73	2.75E-06	1.05	4.62E-01	Rate-limiting enzyme in the de novo guanine nucleotide biosynthesis.
Dut	Deoxyuridine triphosphatase	1.67	3.50E-02	1.42	1.35E-01	Precursor of thymidine nucleotides. May inhibit peroxisome proliferator-activated receptor (PPAR) activity.
UMPS	Uridine monophosphate synthetase	1.62	2.81E-07	1.28	1.81E-03	Catalyzes the final two steps of the de novo pyrimidine biosynthetic pathway.
PPAT	Phosphoribosyl pyrophosphate amidotransferase	1.57	7.97E-04	1.36	1.63E-02	Catalyzes the first step of de novo purine nucleotide biosynthesis.
<i>Metabolism Oxidation/Reduction</i>						
GSTA3	Gutathione S-transferase alpha 3	90.50	7.46E-13	-1.33	1.43E-01	Catalyzes the double bond isomerization of precursors for progesterone and testosterone during the biosynthesis of steroid hormones.
AKR7A3	Aldo-keto reductase family 7, member A3 (aflatoxin aldehyde reductase)	6.01	1.73E-05	2.00	7.88E-03	Involved in the detoxification of aldehydes and ketones.
Aldh1a7	Aldehyde dehydrogenase family 1, subfamily A7	3.02	1.42E-04	-1.01	8.53E-01	Unknown
ALDH1A1	Aldehyde dehydrogenase 1 family, member A1	2.52	4.06E-04	1.47	5.95E-02	Second enzyme of the major oxidative pathway of alcohol metabolism. Has a high affinity for aldehydes.
CYP17A1	Cytochrome P450, family 17, subfamily A, polypeptide 1	1.81	1.09E-03	1.53	9.68E-04	Key enzyme in the steroidogenic pathway.

Transport

CYP4A11	Cytochrome P450, family 4, subfamily A, polypeptide 11	1.73	2.81E-03	-1.25	1.30E-01	Hydroxylates medium-chain fatty acids such as laurate and myristate.
UGT2B4	UDP glucuronosyltransferase 2 family, polypeptide B4	1.66	7.50E-04	1.65	4.05E-04	Catalyzes the transfer of glucuronate from UDP-glucuronate to beta-D-glucuronoside. May play a role in drug metabolism.
Sult2a6	Sulfotransferase family 2A, dehydroepiandrosterone (DHEA)-preferring, member 2	1.61	6.57E-03	1.97	3.05E-04	Expression reduced during the androgen-sensitive state of young adulthood and increased during the androgen-insensitive phases of puberty and senescence.
CYP2J2	Cytochrome P450, family 2, subfamily J, polypeptide 2	1.54	4.09E-03	1.22	9.61E-02	Predominant enzyme responsible for epoxidation of endogenous arachidonic acid.
UGDH	UDP-glucose 6-dehydrogenase	1.53	6.92E-05	1.13	3.40E-02	Converts UDP-glucose to UDP-glucuronate and thereby participates in the biosynthesis of glycosaminoglycans.
EPHX2	Epoxide hydrolase 2, cytoplasmic	1.52	5.01E-03	1.01	9.02E-01	Binds to specific epoxides and converts them to the corresponding dihydrodiols.
SLC7A11	Solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	3.19	5.83E-06	1.05	6.27E-01	Member of a heteromeric Na(+)-independent anionic amino acid transport system highly specific for cystine and glutamate.
SLC3A2	Solute carrier family 3 (activators of dibasic and neutral amino acid transport), member 2	2.98	1.98E-06	1.63	3.17E-03	Associates with integrins and mediates integrin-dependent signaling related to normal cell growth and tumorigenesis.
ADCY10	Adenylate cyclase 10 (soluble)	2.43	5.18E-07	-1.07	3.07E-01	G protein thought to function as a general bicarbonate sensor.
ABCB1	ATP-binding cassette, sub-family B (MDR/TAP), member 1	1.89	2.60E-04	1.15	3.94E-01	Member of the superfamily of ATP-binding cassette (ABC) transporters. A member of the MDR/TAP subfamily involved in multidrug resistance.
SLC7A5	Solute carrier family 7 (cationic amino acid transporter, y+ system), member 5	1.73	1.11E-04	1.11	1.20E-01	Integral membrane protein involved in liver development, carcinogenesis, and cell activation.
SLC26A8	Solute carrier family 26, member 8	1.66	3.09E-04	1.02	8.25E-01	One member of a family of sulfate/anion transporter genes.
SLC38A2	Solute carrier family 38, member 2	1.61	5.63E-03	1.30	3.74E-02	Alanine-preferring transporter.

	SLC25A21	Solute carrier family 25 (mitochondrial oxodicarboxylate carrier), member 21	1.56	1.32E-03	-1.05	5.76E-01	Mitochondrial carriers that transport C5-C7 oxodicarboxylates across inner mitochondrial membranes. One of the species transported by ODC is 2-oxoadipate, a common intermediate in the catabolism of lysine, tryptophan, and hydroxylysine in mammals, which is converted into acetyl-CoA.
	SLC4A4	Solute carrier family 4, sodium bicarbonate cotransporter, member 4	1.56	3.05E-06	-1.20	2.26E-01	A sodium bicarbonate cotransporter.
	SLC20A1	Solute carrier family 20 (phosphate transporter), member 1	1.55	1.19E-03	1.29	9.95E-02	Sodium-dependent phosphate symporter.
	SLC22A9	Solute carrier family 22 (organic anion transporter), member 9	1.55	8.60E-03	-1.19	3.38E-01	May play a role in anion transport across a membrane.
	AQP8	aquaporin 8	1.55	1.55E-03	1.30	8.20E-03	A water channel protein.
	SLC22A5	Solute carrier family 22 (organic cation/carnitine transporter), member 5	1.50	1.42E-02	-1.08	5.31E-01	Organic cation transporter and as a sodium-dependent high-affinity carnitine transporter.
<i>Immune Response</i>							
	CD14	CD14 molecule	1.92	8.70E-05	-1.08	6.08E-01	Preferentially expressed on monocytes/macrophages. Mediates the innate immune response to bacterial lipopolysaccharide.
<i>Protein Turnover</i>							
	FARSB	Phenylalanyl-tRNA synthetase, beta subunit	1.89	4.93E-05	1.38	3.23E-02	Attaches L-phenylalanine to the terminal adenosine of the appropriate tRNA
	Rplp0	Ribosomal protein, large, P0	1.88	9.67E-04	1.12	4.50E-01	Member of the ribosomal protein family. Has similarity to other P ribosomal proteins over the carboxyl terminal sequence.
	THG1L	tRNA-histidine guanylyltransferase 1-like (S. cerevisiae)	1.86	1.35E-04	1.59	4.91E-03	Unknown
	RRS1	RRS1 ribosome biogenesis regulator homolog (S. cerevisiae)	1.83	1.40E-04	1.19	8.27E-02	Unknown
	RPL15	Ribosomal protein L15	1.79	2.78E-04	1.42	1.24E-02	Encodes a ribosomal protein that is a component of the 60S subunit.
	Npm1	Nucleophosmin (nucleolar phosphoprotein B23, numatrin)	1.74	5.06E-06	1.16	1.50E-01	RNA-associated nucleolar phosphoprotein. Involved in ribosome assembly.

LARS	Leucyl-tRNA synthetase	1.72	4.66E-06	1.28	5.66E-03	Catalyzes the ATP-dependent ligation of L-leucine to tRNA(Leu).
RPL18A	Ribosomal protein L18a	1.69	4.94E-05	1.04	6.77E-01	A ribosomal protein that is a component of the 60S subunit.
SARS	Seryl-tRNA synthetase	1.64	2.93E-04	1.49	5.42E-03	Catalyzes the transfer of L-serine to tRNA (Ser).
MRPL50	Mitochondrial ribosomal protein L50	1.64	6.18E-04	1.46	6.50E-03	Encodes a putative 39S subunit protein and belongs to the L47P ribosomal protein family.
YARS	Tyrosyl-tRNA synthetase	1.60	2.51E-05	1.20	5.07E-02	Catalyzes the aminoacylation of tRNA by their cognate amino acid, tyrosyl-tRNA synthetase.
DTD1	D-tyrosyl-tRNA deacylase 1 homolog (S. cerevisiae)	1.59	8.64E-05	1.14	8.30E-02	Hydrolyzes D-tyrosyl-tRNA(Tyr) into D-tyrosine and free tRNA(Tyr).
RPS6	Ribosomal protein S6	1.56	7.66E-03	1.06	7.48E-01	Belongs to the S6E family of ribosomal proteins. Is the major substrate of protein kinases in the ribosome.
Mars	Methionine-tRNA synthetase	1.56	1.06E-05	1.17	1.40E-02	Catalyzes the aminoacylation of tRNA by their cognate amino acid, methionyl-tRNA synthetase.
EIF2S1	Eukaryotic translation initiation factor 2, subunit 1 alpha, 35kDa	1.51	3.25E-05	1.24	1.15E-02	Catalyzes the first regulated step of protein synthesis initiation.

Signal Transduction

FGF21	Fibroblast growth factor 21	8.50	1.97E-06	1.72	1.03E-01	Member of the fibroblast growth factor (FGF) family.
SERPINA7	Serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 7	8.48	3.33E-07	1.49	1.58E-01	Encodes the major thyroid hormone transport protein.
IGFBP1	Insulin-like growth factor binding protein 1	6.39	6.96E-07	1.02	8.79E-01	Binds both insulin-like growth factors (IGFs) I and II, prolonging the half-life of the IGFs and alters their interaction with cell surface receptors.
TRIB3	Tribbles homolog 3 (Drosophila)	3.23	3.70E-08	-1.00	9.17E-01	A putative protein kinase that is induced by the transcription factor NF-kappaB.
PPP1R9A	Protein phosphatase 1, regulatory (inhibitor) subunit 9A	1.73	5.23E-07	-1.08	2.38E-01	Regulatory subunit of protein phosphatase I.
RGS5	Regulator of G-protein signaling 5	1.65	9.99E-04	1.42	1.37E-02	Regulator of G protein signaling (RGS) proteins.
IGFBP2	Insulin-like growth factor binding protein 2, 36kDa	1.56	9.65E-06	-1.10	1.32E-01	Binds to Igf-I and Igf-II.
PRKCDBP	Protein kinase C, delta binding protein	1.55	1.12E-04	1.02	8.11E-01	A binding protein of the protein kinase C, delta (PRKCD). Strongly induced by serum starvation. Protein down-regulated in various cancer cell lines, suggesting the possible tumor suppressor function of this protein.

	PPP1R14B	Protein phosphatase 1, regulatory (inhibitor) subunit 14B	1.55	3.02E-02	1.38	8.61E-02	Inhibitor for protein type-1 phosphatase (PP1) and myosin light-chain phosphatase (MLCP). Substrate of protein kinase C (PKC).
<i>Cell Proliferation or Apoptosis</i>							
	MYC	V-myc myelocytomatosis viral oncogene homolog (avian)	1.81	7.33E-04	1.19	1.63E-01	A multifunctional, nuclear phosphoprotein that plays a role in cell cycle progression, apoptosis and cellular transformation.
	FASTKD2	FAST kinase domains 2	1.65	2.63E-05	1.25	2.29E-02	May play a role in mitochondrial apoptosis.
	TNFSF10	Tumor necrosis factor (ligand) superfamily, member 10	1.61	3.94E-02	1.53	1.00E-01	Induces apoptosis in transformed and tumor cells, but does not appear to kill normal cells. Binding of this protein to its receptors triggers the activation of MAPK8/JNK, caspase 8, and caspase 3.
	Gas5	Growth arrest specific 5	1.56	1.75E-04	1.11	1.76E-01	Transcript expressed during growth arrest phase of the cell cycle. May encode a small nucleolar RNA.
	CDKL3	Cyclin-dependent kinase-like 3	1.54	3.65E-04	1.06	5.71E-01	A member of the cyclin-dependent protein kinase (CDK) family. Important regulator of cell cycle progression.
	EGR1	Early growth response 1	1.51	4.96E-04	1.21	2.54E-01	Nuclear protein. Functions as a transcriptional regulator. May be a cancer suppressor gene.
<i>Others</i>							
	CRYL1	Crystallin, lambda 1	2.24	1.25E-03	1.58	1.84E-02	Catalyzes the dehydrogenation of L-gulonate into dehydro-L-gulonate in the uronate cycle.
	DDAH1	Dimethylarginine dimethylaminohydrolase 1	2.22	4.56E-06	1.33	3.95E-02	Plays a role in nitric oxide generation by regulating cellular concentrations of methylarginines, which in turn inhibit nitric oxide synthase activity.
	CASP4	Caspase 4, apoptosis-related cysteine peptidase	1.97	3.50E-06	1.20	1.62E-01	Member of the cysteine-aspartic acid protease (caspase) family. Plays a central role in the execution-phase of cell apoptosis.
	LGALS2	Lectin, galactoside-binding, soluble, 2	1.97	1.93E-05	1.24	2.60E-01	Can bind to lymphotoxin-alpha.
	MYBBP1A	MYB binding protein (P160) 1a	1.77	1.17E-06	1.22	1.39E-01	Transcriptional activator that displays a circadian rhythm of expression in hepatocytes.
	CA2	Carbonic anhydrase II	1.70	5.56E-03	1.68	2.78E-02	Catalyzes reversible hydration of carbon dioxide.
	HSPA9	Heat shock 70kDa protein 9 (mortalin)	1.59	2.91E-06	-1.00	9.21E-01	Plays a role in cell proliferation, stress response and maintenance of the mitochondria.

LRPPRC	Leucine-rich PPR-motif containing	1.57	8.29E-06	1.09	4.25E-02	Plays a role in regulating the interaction of the cytoskeleton with a variety of cellular processes.
EPCAM	Epithelial cell adhesion molecule	1.50	5.10E-03	1.06	5.67E-01	Homotypic calcium-independent cell adhesion molecule.

Table S3d.
Genes Downregulated in Liver by MR (Normalized to Control)

Gene Symbol	Gene name	MR	p value	MRC	p value	Function
<i>Lipid Metabolism</i>						
SCD	Stearoyl-CoA desaturase (delta-9-desaturase)	-13.78	4.78E-06	-1.43	1.11E-02	Rate-limiting step in the synthesis of unsaturated fatty acids.
PNPLA3	Patatin-like phospholipase domain containing 3	-5.13	5.77E-04	-4.31	1.27E-03	triacylglycerol hydrolysis.
THRSP	Thyroid hormone responsive	-2.31	4.08E-04	-1.29	1.33E-01	Controls lipid metabolism
ACACB	Acetyl-CoA carboxylase beta	-2.19	1.99E-07	-1.82	5.46E-06	Carboxylation of acetyl-CoA to malonyl-CoA, the rate-limiting step in fatty acid synthesis and inhibition of carnitine-palmitoyl-CoA transferase I
ACLY	ATP citrate lyase	-2.07	1.04E-03	-1.65	1.52E-02	Formation of acetyl-CoA and oxaloacetate from citrate and CoA.
CROT	Carnitine O-octanoyltransferase	-1.93	2.76E-03	-2.57	4.60E-04	Converts 4,8-dimethylnonanoyl-CoA to its corresponding carnitine ester. Necessary for transport of medium- and long-chain acyl-CoA molecules out of the peroxisome to the cytosol and mitochondria.
INSIG1	Insulin induced gene 1	-1.93	1.03E-02	-1.83	1.33E-03	Regulates cholesterol concentrations in cells
LIPC	lipase, hepatic	-1.85	1.69E-07	-1.08	4.20E-02	triglyceride hydrolase and ligand/bridging factor for receptor-mediated lipoprotein uptake.
ELOVL5	ELOVL family member 5, elongation of long chain fatty acids	-1.55	2.98E-05	-1.17	6.78E-03	Elongation of long-chain polyunsaturated fatty acids.
<i>Carbohydrate Metabolism</i>						
GCK	Glucokinase (hexokinase 4)	-1.81	8.91E-04	-1.23	2.36E-01	Phosphorylates glucose to produce glucose-6-phosphate, the first step in most glucose metabolism pathways.
PKLR	Pyruvate kinase, liver and RBC	-1.62	1.89E-03	1.02	8.49E-01	Transphosphorylation of phohsphoenolpyruvate into pyruvate and ATP, which is the rate-limiting step of glycolysis.

Amino Acid Metabolism

OAT	Ornithine aminotransferase	-3.68	1.65E-05	-1.59	1.32E-02	Converts arginine and ornithine into glutamate and GABA.
MCEE	Methylmalonyl CoA epimerase	-1.53	7.02E-06	1.21	7.16E-04	Catalyzes the interconversion of D- and L-methylmalonyl-CoA during the degradation of branched chain amino acids.

Protein Turnover

PSMB8	Proteasome (prosome, macropain) subunit, beta type, 8 (large multifunctional peptidase 7)	-1.70	1.41E-05	1.23	1.11E-02	Member of the proteasome B-type family, 20S core beta subunit located in the class II region of the MHC (major histocompatibility complex).
ISG15	ISG15 ubiquitin-like modifier	-1.70	2.57E-02	1.71	3.65E-02	Ubiquitin-like protein that becomes conjugated to many cellular proteins upon activation by interferon-alpha and -beta.

Nucleotide/Nucleoside Metabolism

ENPP3	Ectonucleotide pyrophosphatase/phosphodiesterase 3	-1.95	1.22E-04	-1.08	3.88E-01	Hydrolysis of extracellular nucleotides.
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Metabolism Oxidation/Reduction

CYP3A4	Cytochrome P450, family 3, subfamily A, polypeptide 4	-4.05	9.78E-05	-1.09	2.82E-01	Involved in the metabolism of drugs.
NOX4	NADPH oxidase 4	-2.84	1.95E-03	1.67	3.18E-03	Catalyzes the reduction of molecular oxygen to various reactive oxygen species (ROS).
CYP4A22	Cytochrome P450, family 4, subfamily A, polypeptide 22	-2.07	8.44E-06	1.15	3.57E-01	Drug metabolism and synthesis of cholesterol, steroids and other lipids.
CYP2C9	Cytochrome P450, family 2, subfamily C, polypeptide 9	-1.86	4.30E-04	1.02	6.25E-01	Drug metabolism and synthesis of cholesterol, steroids and other lipids.
ADH1C	Alcohol dehydrogenase 1C (class I), gamma polypeptide	-1.70	1.57E-03	1.09	2.09E-01	Metabolizes alcohols, hydroxysteroids, and lipid peroxidation products.
GSTM2	Glutathione S-transferase mu 2 (muscle)	-1.69	8.36E-05	1.07	4.39E-01	Detoxification of electrophilic compounds including carcinogens, therapeutic drugs, environmental toxins and products of oxidative stress, by conjugation with glutathione.
AKR1C3	Aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II)	-1.58	5.85E-04	-1.10	2.79E-01	Conversion of aldehydes and ketones to their corresponding alcohols.

Transport

SLC6A6	Solute carrier family 6 (neurotransmitter transporter, taurine), member 6	-3.79	7.64E-08	-1.06	8.43E-01	Sodium and chloride dependent taurine transporter.
SLC34A2	Solute carrier family 34 (sodium phosphate), member 2	-2.83	5.83E-05	1.63	7.37E-02	pH-sensitive sodium-dependent phosphate transporter.
MUP	Major urinary protein pseudogene	-2.16	4.83E-02	1.03	8.54E-01	Transport of small, hydrophobic molecules.
SLC39A4	Solute carrier family 39 (zinc transporter), member 4	-1.82	3.33E-05	-1.09	4.31E-01	Zinc uptake.
SLC22A8	Solute carrier family 22 (organic anion transporter), member 8	-1.79	1.27E-04	1.10	2.80E-01	Sodium-independent transport and excretion of organic anions.
KCNN2	Potassium intermediate/small conductance calcium-activated channel, subfamily N, member 2	-1.73	1.51E-06	-1.04	4.92E-01	Forms a voltage-independent calcium-activated channel with three other calmodulin-binding subunits.
SLC29A1	Solute carrier family 29 (nucleoside transporters), member 1	-1.72	1.82E-06	-1.05	2.59E-01	Mitochondrial membrane glycoprotein. Mediates the cellular uptake of nucleosides from the surrounding medium.
TMEM37	Transmembrane protein 37	-1.65	4.89E-04	1.18	1.12E-01	Auxiliary subunit of calcium channels that control the entry of extracellular calcium into the cytoplasm.
Mk1	Mk1 protein	-1.63	1.55E-03	-1.01	9.28E-01	Potassium channel.
P2RX7	Purinergic receptor P2X, ligand-gated ion channel, 7	-1.63	2.25E-05	1.42	3.10E-02	Ligand-gated ion channel and is responsible for ATP-dependent lysis of macrophages.
SLC9A7	Solute carrier family 9 (sodium/hydrogen exchanger), member 7	-1.63	3.68E-04	-1.13	3.52E-01	Influx of sodium or potassium in exchange for hydrogen.
SLC16A10	Solute carrier family 16, member 10 (aromatic amino acid transporter)	-1.60	8.16E-04	-1.43	2.39E-02	Na(+)-independent transport of aromatic amino acids across the plasma membrane.

Immune Response

UBD	Ubiquitin D	-2.73	3.00E-03	1.68	1.64E-01	Diubiquitin protein that may function in antigen processing and presentation.
SCRN1	Uecernin 1	-2.58	4.46E-05	1.00	9.93E-01	Regulation of exocytosis in mast cells.
OAS1	2',5'-Oligoadenylate synthetase 1, 40/46kDa	-1.97	5.86E-03	1.36	6.91E-02	Innate immune response to viral infection.
CXCL12	Chemokine (C-X-C motif) ligand 12	-1.95	2.71E-05	1.28	6.67E-03	Activates lymphocytes and have been implicated in the metastasis of some cancers such as breast cancer.
CXCL9	Chemokine (C-X-C motif) ligand 9	-1.92	3.65E-04	1.50	6.23E-02	Thought to be involved in T cell trafficking. Member of the chemokine family of cytokines.

Signal Transduction

TSC22D1	TSC22 domain family, member 1	-2.96	3.56E-05	1.27	1.73E-01	Transcription factor and belongs to the large family of early response genes.
RGS16	Regulator of G-protein signaling 16	-2.51	8.45E-03	-2.05	3.66E-02	Inhibits signal transduction by increasing the GTPase activity of G protein alpha subunits.
IGFALS	Insulin-like growth factor binding protein, acid labile subunit	-2.18	2.40E-03	1.42	4.36E-02	Increase IGFs' half-life and their vascular localization.
MME	Membrane metallo-endopeptidase	-2.11	8.01E-06	-1.89	3.46E-05	Inactivates several peptide hormones including glucagon, enkephalins, substance P, neurotensin, oxytocin, and bradykinin.
PPP1R3B	Protein phosphatase 1, regulatory (inhibitor) subunit 3B	-2.03	8.35E-03	1.11	6.11E-01	Suppresses the rate at which PP1 dephosphorylates (i.e., inactivates) glycogen phosphorylase and enhances the rate at which it activates glycogen synthase.
PIK3R1	Phosphoinositide-3-kinase, regulatory subunit 1 (alpha)	-1.71	2.74E-03	1.03	7.91E-01	Phosphorylates the inositol ring of phosphatidylinositol. Plays an important role in the metabolic actions of insulin.
FGF1	Fibroblast growth factor 1 (acidic)	-1.66	7.63E-04	1.28	2.02E-01	Thought to be involved in organogenesis.
AVPR1A	arginine vasopressin receptor 1A	-1.65	6.65E-04	-1.08	5.56E-01	Receptor for arginine vasopressin, stimulates a phosphatidylinositol-calcium second messenger system.
IL1RN	Interleukin 1 receptor antagonist	-1.61	1.33E-02	1.28	1.79E-01	Inhibits the activities of interleukin 1, alpha (IL1A) and interleukin 1, beta (IL1B).

Others

Dhrs7	Dehydrogenase/reductase (SDR family) member 7	-18.78	1.88E-07	1.27	6.86E-02	Unknown
PLA2G16	Phospholipase A2, group XVI	-2.27	2.29E-06	-1.16	7.94E-02	Gene whose expression is suppressed by HRAS
HYAL1	Hyaluronoglucosaminidase 1	-1.92	4.59E-05	-1.02	8.45E-01	Degrades hyaluronan
HYAL3	Hyaluronoglucosaminidase 3	-1.81	3.42E-04	-1.19	1.27E-01	Unknown
LYST	Lysosomal trafficking regulator	-1.78	1.22E-06	1.06	4.65E-01	Regulates intracellular protein trafficking to and from the lysosome.
F11R	F11 receptor	-1.64	1.69E-03	-1.25	1.29E-02	Regulator of tight junction assembly in epithelia.
PGCP	Plasma glutamate carboxypeptidase	-1.61	1.29E-05	1.04	7.07E-01	Plays a role in liver regeneration.
CA8	carbonic anhydrase VIII	-1.54	1.25E-05	1.33	8.42E-04	Lacks carbonic anhydrase activity (i.e., the reversible hydration of carbon dioxide).

CA5B	Carbonic anhydrase VB, mitochondrial	-1.53	3.49E-04	1.62	1.22E-05	reversible hydration of carbon dioxide in the mitochondria.
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Table S3e.
Genes Upregulated in Muscle by MR (Normalized to Control)

Gene Symbol	Gene name	MR	p value	MRC	p value	Function
<i>Lipid Metabolism</i>						
ELOVL6	ELOVL family member 6, elongation of long chain fatty acids	2.04	4.97E-02	1.07	5.56E-01	UseS malonyl-CoA as a 2-carbon donor in the first and rate-limiting step of fatty acid elongation.
LPL	Lipoprotein lipase	1.75	1.78E-02	1.23	6.27E-02	Functions as a triglyceride hydrolase and ligand/bridging factor for receptor-mediated lipoprotein uptake.
CD36	CD36 molecule (thrombospondin receptor)	1.71	2.87E-02	1.23	2.63E-01	Binds long chain fatty acids and may function in the transport and/or as a regulator of fatty acid transport.
LIPE	Lipase, hormone-sensitive	1.68	5.99E-03	1.10	2.41E-01	Converts cholesteryl esters to free cholesterol for steroid hormone production, hydrolyzes stored triglycerides to free fatty acids.
ACAA2	Acetyl-CoA acyltransferase 2	1.55	1.02E-02	1.28	5.79E-02	Last step of the mitochondrial fatty acid beta-oxidation spiral.
GPAM	Glycerol-3-phosphate acyltransferase, mitochondrial	1.54	2.00E-02	1.15	1.81E-01	Initial and committing step in glycerolipid biosynthesis.
ACSF2	Acyl-CoA synthetase family member 2	1.52	4.42E-03	1.06	1.94E-01	Unknown
<i>Carbohydrate Metabolism</i>						
LDHB	Lactate dehydrogenase B	2.58	3.36E-02	1.88	6.12E-02	Reversible conversion of lactate and pyruvate.
NDUFV3	NADH dehydrogenase (ubiquinone) flavoprotein 3	1.97	6.06E-03	1.37	2.59E-02	Rotenone-sensitive oxidation of NADH and the reduction of ubiquinone.
PDK4	Pyruvate dehydrogenase kinase, isozyme 4	1.84	1.42E-02	1.25	3.07E-01	Mitochondrial protein that inhibits the pyruvate dehydrogenase complex.
<i>Myofibrillar Proteins</i>						
TNNC1	Troponin C type 1 (slow)	5.32	2.90E-02	2.78	1.07E-01	Slow-twitch muscle inhibitory troponin subunit, blocks actin-myosin interactions and thereby mediating striated muscle relaxation.

	TNNI1	Troponin I type 1 (skeletal, slow)	5.22	1.19E-02	2.37	2.76E-02	Associates with tropomyosin. Regulates the calcium sensitivity of the myofibril contractile apparatus of striated muscles. Troponin I (TnI) blocks actin-myosin interactions and thereby mediates striated muscle relaxation.
	MYH10	Myosin, heavy chain 10, non-muscle	1.92	3.94E-02	1.32	1.17E-01	Produces motor activity with actin filaments.
<i>Calcium-Binding Protein</i>							
	S100A9	S100 calcium binding protein A9	2.24	1.97E-02	1.12	5.20E-01	Regulation of cellular processes such as cell cycle progression and differentiation.
	S100A8	S100 calcium binding protein A8	2.03	7.08E-03	1.10	4.84E-01	Regulation of cellular processes such as cell cycle progression and differentiation.
<i>Muscle Development</i>							
	MYOZ2	Myozenin 2	3.84	2.07E-02	1.98	9.39E-02	Unknown
	CSRP3	Cysteine and glycine-rich protein 3 (cardiac LIM protein)	3.21	1.65E-02	2.54	1.45E-02	Involved in regulatory processes important for development and cellular differentiation.
	MYOM3	Myomesin family, member 3	2.18	1.78E-02	1.19	7.90E-02	Unknown
<i>Transport</i>							
	ATP2A2	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	3.42	1.71E-02	1.53	1.12E-01	Calcium transport.
	AQP7	Aquaporin 7	3.23	3.43E-03	1.31	6.68E-02	Facilitates water, glycerol and urea transport.
	KCNJ2	Potassium inwardly-rectifying channel, subfamily J, member 2	1.60	4.34E-03	-1.03	8.64E-01	Inward-rectifier type potassium channel. Probably participates in establishing action potential waveform and excitability of muscle tissues.
<i>Protein Turnover</i>							
	UBE2I	Ubiquitin-conjugating enzyme E2I (UBC9 homolog, yeast)	1.69	1.84E-02	1.53	4.72E-02	Member of the E2 ubiquitin-conjugating enzyme family.
<i>Extracellular Matrix</i>							
	LEPREL1	Leprecan-like 1	1.62	2.53E-02	1.21	9.83E-02	Belongs to a family of collagen prolyl hydroxylases required for proper collagen biosynthesis, folding, and assembly.

Other

PADI2	Peptidyl arginine deiminase, type II	1.58	6.66E-03	1.43	7.99E-02	Post-translational deimination of proteins by converting arginine residues into citrullines in the presence of calcium ions.
ANGPTL4	Angiopoietin-like 4	1.50	4.18E-02	1.09	6.58E-01	Target of peroxisome proliferation activators. Serum hormone directly involved in regulating glucose homeostasis, lipid metabolism, and insulin sensitivity.

Table S3f.
Genes Downregulated in Muscle by MR (Normalized to Control)

Gene Symbol	Gene name		MR	p value	MRC	p value	Function
<i>Lipid Metabolism</i>	FABP1	Fatty acid binding protein 1, liver	-2.87	3.11E-03	-1.65	1.01E-01	Binds long-chain fatty acids and other hydrophobic ligands.
	APOH	Apolipoprotein H (beta-2-glycoprotein I)	-1.74	1.23E-02	-1.29	2.24E-01	Lipoprotein metabolism, coagulation, and the production of antiphospholipid autoantibodies.
	ACSL3	Acyl-CoA synthetase long-chain family member 3	-1.71	7.25E-03	-1.21	1.34E-01	Converts free long-chain fatty acids into fatty acyl-CoA esters.
<i>Protein Metabolism</i>	RPS2	Ribosomal protein S2	-1.63	4.37E-03	-1.45	7.66E-02	Ribosomal protein that is a component of the 40S subunit.
<i>Myofibrillar Proteins</i>	MYBPH	Myosin binding protein H	-1.97	1.17E-02	-1.52	6.31E-02	Myosin binding protein.
	TPX2	TPX2, microtubule-associated, homolog (Xenopus laevis)	-1.53	7.16E-03	-1.11	3.12E-01	Unknown
<i>Immune Response</i>	IRGM	Immunity-related GTPase family, M	-1.99	1.86E-04	1.08	5.92E-01	Plays a role in autophagy and control of intracellular mycobacteria.
	AMBP	Alpha-1-microglobulin/bikunin precursor	-1.87	4.54E-02	-1.31	3.95E-01	Regulation of inflammatory processes.
<i>Transport</i>	MUP	Major urinary protein pseudogene	-2.23	3.06E-02	-1.32	4.74E-01	Transport of small, hydrophobic molecules.
	TF	Transferrin	-1.87	1.18E-02	-1.54	7.73E-02	Iron transport.
	KCNAB1	Potassium voltage-gated channel, shaker-related subfamily, beta member 1	-1.53	1.04E-03	-1.30	1.21E-02	Voltage-gated, shaker-related subfamily, potassium channel.

Signal Transduction

SFRP2	Secreted frizzled-related protein 2	-2.43	1.01E-03	-1.74	2.89E-02	Soluble modulators of Wnt signaling.
GABRR1	Gamma-aminobutyric acid (GABA) receptor, rho 1	-1.94	1.70E-04	-1.17	1.62E-01	The major inhibitory neurotransmitter.
PRKAG3	Protein kinase, AMP-activated, gamma 3 non-catalytic subunit	-1.88	2.14E-02	-1.30	1.23E-01	A regulatory subunit of the AMP-activated protein kinase (AMPK).
PLCD4	Phospholipase C, delta 4	-1.87	9.34E-03	-1.44	4.28E-02	Generates two second messenger molecules, inositol 1,4,5-triphosphate (IP3) and diacylglycerol, from phosphatidylinositol 4,5-bisphosphate (PIP2).
SFRP4	Secreted frizzled-related protein 4	-1.87	6.55E-04	-1.37	5.89E-02	Modulator of the WNT signaling pathway.
HOPX	HOP homeobox	-1.77	5.92E-04	1.03	7.46E-01	May interact with serum response factor (SRF).
RALBP1	RalA binding protein 1	-1.63	7.02E-03	-1.35	1.20E-03	Binds the GTP-bound form of Ras-related GTPase RalA. Also interacts with Rho family member CDC42 via a specific Rho-GTPase activating domain.
IGFBP5	Insulin-like growth factor binding protein 5	-1.60	1.88E-03	-1.01	9.62E-01	May play a modulatory role in type I fiber-dominated muscles.

Extracellular Matrix

FN1	Fibronectin 1	-1.74	2.51E-03	-1.11	5.31E-01	Cell adhesion and migration.
FGB	Fibrinogen beta chain	-1.73	2.49E-02	-1.28	3.02E-01	Fibrinogen and fibrin regulate cell adhesion and spreading, and are mitogens for several cell types.
EFEMP1	EGF-containing fibulin-like extracellular matrix protein 1	-1.62	8.47E-03	-1.14	4.04E-01	Extracellular matrix glycoproteins, upregulated in malignant gliomas and may play a role in the aggressive nature of these tumors.
STIM2	Stromal interaction molecule 2	-1.53	1.89E-02	-1.18	2.49E-01	Regulate calcium concentrations in the cytosol and endoplasmic reticulum, and is involved in the activation of plasma membrane Orai Ca(2+) entry channels.

Other

ALB	Albumin	-3.62	1.02E-02	-1.49	4.41E-01	Carrier protein for steroids, fatty acids, and thyroid hormones, and plays a role in stabilizing extracellular fluid volume.
GPM6B	Glycoprotein M6B	-2.29	2.80E-04	-1.41	3.97E-02	Involved in cellular housekeeping functions, such as membrane trafficking and cell-to-cell communication.

MSTN	Myostatin	-2.28	1.50E-02	-1.39	1.61E-01	Member of the bone morphogenetic protein (BMP) family and the TGF-beta superfamily. Negatively regulates skeletal muscle growth.
HTRA1	HtrA serine peptidase 1	-1.78	8.89E-04	-1.18	3.07E-01	Proposed to regulate the availability of insulin-like growth factors (IGFs) by cleaving IGF-binding proteins.
HP	Haptoglobin	-1.63	3.82E-02	-1.26	3.31E-01	Produces haptoglobin, degrades hemoglobin while - at the same time - preventing loss of iron.

Table S3g.
Genes Upregulated Genes in Adipose Tissue by MRC (Normalized to Control)

Gene Symbol	Gene name	MR	p value	MRC	p value	Function
<i>Olfactory Receptors</i>						
LOC302192	Similar to RIKEN cDNA 1700001E04	1.20	3.62E-01	1.63	2.03E-02	Unknown
Olf1415	Olfactory receptor 1344	1.39	8.51E-02	1.57	1.26E-02	Interacts with odorant molecules.
OR52E8	Olfactory receptor, family 52, subfamily E, member 8	1.15	1.07E-01	1.54	4.11E-02	Interacts with odorant molecules.
Olr1590	Olfactory receptor 1590	1.08	5.50E-01	1.51	7.68E-03	Interacts with odorant molecules.

Table S3h.
Genes Downregulated in Adipose Tissue by MRC (Normalized to Control)

Gene Symbol		Gene name	MR	p value	MRC	p value	Function
<i>Carbohydrate Metabolism</i>							
SUCLG2		Succinate-CoA ligase, GDP-forming, beta subunit	-1.07	3.82E-01	-1.87	4.44E-02	Reversible reaction involving the formation of succinyl-CoA and succinate.
<i>Calcium Binding Protein</i>							
OCM2		Oncomodulin 2	-1.79	3.61E-03	-1.65	7.28E-03	Calcium ion-binding protein of the superfamily of calmodulin proteins.
S100A9		S100 calcium binding protein A9	-1.05	8.51E-01	-1.64	3.97E-02	May function in the inhibition of casein kinase.
<i>Olfactory Receptor</i>							
Olfr544		Olfactory receptor 39	-1.44	1.35E-01	-1.75	3.96E-02	Interacts with odorant molecules.
Olfr661		Olfactory receptor 161	-1.71	2.73E-02	-1.61	3.07E-02	Interacts with odorant molecules.
<i>Immune Response</i>							
FKBPL		FK506 binding protein like	-1.23	9.17E-02	-1.53	2.65E-02	Immunoregulation, protein folding and trafficking, and control of the cell cycle.

Table S3i.
Genes Upregulated in Liver by MRC (Normalized to Control)

Gene Symbol	Gene name	MR	p value	MRC	p value	Function
<i>Lipid Metabolism</i>						
ACSM3	Acyl-CoA synthetase medium-chain family member 3	3.29	5.63E-06	1.84	9.03E-04	Medium chain fatty acid synthesis.
Es1	Esterase 1	-1.66	1.68E-02	1.59	1.17E-03	Has carboxylesterase activity. May play a role in lipid metabolism.
<i>Carbohydrate Metabolism</i>						
AMY1A	Amylase, alpha 1A (salivary)	1.07	7.37E-01	3.63	1.75E-03	Catalyzes the first step in digestion of dietary starch and glycogen.
CRYL1	Crystallin, lambda 1	2.24	1.25E-03	1.58	1.84E-02	Dehydrogenation of L-gulonate into dehydro-L-gulonate in the uronate cycle, which functions as an alternative glucose metabolic pathway.
<i>Amino Acid Metabolism</i>						
MTHFD2	Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	4.54	1.24E-06	2.08	1.10E-02	Conversion of 5,10-methyl THF to 5,10-methylene THF.
GCLM	Glutamate-cysteine ligase, modifier subunit	1.46	8.37E-02	1.66	1.05E-02	First rate-limiting enzyme of glutathione synthesis.
CSAD	Cysteine sulfinic acid decarboxylase	1.13	1.06E-01	1.55	9.25E-05	Conversion of 3-sulfinio-L-alanine to hypotaurine in taurine biosynthesis.
ODC1	Ornithine decarboxylase 1	2.21	1.49E-06	1.52	1.03E-02	The rate-limiting enzyme of the polyamine biosynthesis pathway: converts ornithine to putrescine.
SCPEP1	Serine carboxypeptidase 1	1.73	2.27E-03	1.51	1.44E-02	Serine carboxypeptidase.
<i>Protein Turnover</i>						
ISG15	ISG15 ubiquitin-like modifier	-1.70	2.57E-02	1.71	3.65E-02	Ubiquitin-like protein.
<i>Nucleotide/Nucleoside Metabolism</i>						
CTPS	CTP synthase	2.10	1.25E-05	1.56	7.83E-03	Conversion of UTP to CTP.

Metabolism Oxidation/Reduction

Gstm3	Glutathione S-transferase mu 3	-1.23	1.18E-01	4.50	2.20E-03	Member of the glutathione S-transferase family.
AKR7A3	Aldo-keto reductase family 7, member A3 (aflatoxin aldehyde reductase)	6.01	1.73E-05	2.00	7.88E-03	Involved in the detoxification of aldehydes and ketones.
Sult2a6	Sulfotransferase family 2A, dehydroepiandrosterone (DHEA)-preferring, member 2	1.61	6.57E-03	1.97	3.05E-04	Increased during the androgen-insensitive phases of prepuberty and senescence.
NR1I3	Nuclear receptor subfamily 1, group I, member 3	1.78	2.33E-03	1.90	9.01E-05	Key regulator of xenobiotic and endobiotic metabolism.
ALDH1B1	Aldehyde dehydrogenase 1 family, member B1	1.14	2.01E-01	1.84	1.07E-03	Alcohol metabolism.
UGT2B4	UDP glucuronosyltransferase 2 family, polypeptide B4	1.66	7.50E-04	1.65	4.05E-04	Transfer of glucuronate from UDP-glucuronate to beta-D-glucuronoside.
AKR1C4	Aldo-keto reductase family 1, member C4 (chlordecone reductase; 3-alpha hydroxysteroid dehydrogenase, type I; dihydrodiol dehydrogenase 4)	-1.20	2.65E-01	1.64	1.50E-02	Conversion of aldehydes and ketones.
CYP17A1	Cytochrome P450, family 17, subfamily A, polypeptide 1	1.81	1.09E-03	1.53	9.68E-04	Drug metabolism, synthesis of cholesterol, steroids and other lipids, Key enzyme in the steroidogenic pathway that produces progestins, mineralocorticoids, glucocorticoids, androgens, and estrogens.
GSTM3	Glutathione S-transferase mu 3 (brain)	1.13	1.78E-01	1.52	1.32E-03	Detoxification of electrophilic compounds.
EPHX1	Epoxide hydrolase 1, microsomal (xenobiotic)	1.47	1.56E-03	1.52	5.62E-04	Converts epoxides from the degradation of aromatic compounds to trans-dihydrodiols which can be conjugated and excreted from the body.

Transport

SLC1A2	Solute carrier family 1 (glial high affinity glutamate transporter), member 2	-1.27	9.98E-04	3.02	3.54E-05	Clears the excitatory neurotransmitter glutamate from the extracellular space at synapses.
MUP	Major urinary protein pseudogene	-2.14	9.66E-04	1.65	4.36E-02	Transport of small, hydrophobic molecules.
KCNA3	Potassium voltage-gated channel, shaker-related subfamily, member 3	1.07	6.84E-01	1.57	4.51E-02	Voltage-gated potassium channel, shaker-related subfamily. Belongs to the delayed rectifier class, members of which allow nerve cells to efficiently repolarize following an action potential. Also plays an essential role in T-cell proliferation and activation.

Immune Response

TNFSF13	Tumor necrosis factor (ligand) superfamily, member 13	-1.45	2.02E-02	1.72	6.34E-03	Tumor necrosis factor (TNF) ligand family member. May be able to induce apoptosis through its interaction with other TNF receptor family proteins such as TNFRSF6/FAS and TNFRSF14/HVEM.
Mug1	Murinoglobulin 1	1.48	3.89E-03	1.67	8.35E-04	Plasma proteinase inhibitor involved in acute phase inflammatory response.
CXCL16	Chemokine (C-X-C motif) ligand 16	1.07	4.91E-01	1.52	4.81E-02	CXC chemokine.
CXCL13	Chemokine (C-X-C motif) ligand 13	-1.04	5.88E-01	1.52	2.55E-04	CXC chemokine that promotes the migration of B lymphocytes (compared to T cells and macrophages).

Signal Transduction

CDKN2C	Cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4)	1.31	7.70E-02	2.22	6.67E-04	Prevents the activation of the CDK kinases, thus function as a cell growth regulator that controls cell cycle G1 progression.
PDE6C	Phosphodiesterase 6C, cGMP-specific, cone, alpha prime	1.13	2.04E-01	1.63	2.26E-03	The alpha-prime subunit of cone phosphodiesterase.

Extracellular Matrix

CDH17	Cadherin 17, LI cadherin (liver-intestine)	1.08	5.91E-01	1.95	6.79E-04	Calcium-dependent, membrane-associated glycoprotein. Acts as a proton-dependent peptide transporter.
MMP12	Matrix metallopeptidase 12 (macrophage elastase)	-1.01	8.44E-01	4.40	1.73E-02	Degrades soluble and insoluble elastin.
DCN	Decorin	1.22	2.06E-01	1.89	7.72E-03	Cellular or pericellular matrix proteoglycan that plays a role in matrix assembly.

Other

Pbsn	Probasin	1.75	2.10E-01	31.14	5.54E-07	Displays androgen dependent expression in prostate epithelial cells.
NAT8	N-acetyltransferase 8 (GCN5-related, putative)	-1.01	9.61E-01	2.47	1.25E-03	Shows amino acid sequence similarity to N-acetyltransferases. May be localized in the secretory pathway.

TSPAN8	Tetraspanin 8	-1.02	9.23E-01	2.33	1.43E-03	Plays a role in the regulation of cell development, activation, growth and motility.
MYBL1	V-myb myeloblastosis viral oncogene homolog (avian)-like 1	1.01	7.46E-01	2.06	3.89E-02	Cell proliferation.
CAV1	Caveolin 1, caveolae protein, 22kDa	1.09	6.60E-01	1.92	2.91E-02	Links integrin subunits to the tyrosine kinase FYN, an initiating step in coupling integrins to the Ras-ERK pathway and promotes cell cycle progression. Is a tumor suppressor gene candidate and a negative regulator of the Ras-p42/44 mitogen-activated kinase cascade.
CDKN1A	Cyclin-dependent kinase inhibitor 1A (p21, Cip1)	-1.13	5.05E-01	1.82	3.28E-02	A potent cyclin-dependent kinase inhibitor. Inhibits the activity of cyclin-CDK2 or -CDK4 complexes.
OMD	Osteomodulin	-2.08	4.87E-05	1.73	5.80E-04	Cell binding keratan sulfate proteoglycan that might have a role in regulation of mineralization.
CA2	Carbonic anhydrase II	1.70	5.56E-03	1.68	2.78E-02	Catalyzes reversible hydration of carbon dioxide.
SLC3A2	Solute carrier family 3 (activators of dibasic and neutral amino acid transport), member 2	2.98	1.98E-06	1.63	3.17E-03	Associates with integrins and mediates integrin-dependent signaling related to normal cell growth and tumorigenesis.
CA5B	Carbonic anhydrase VB, mitochondrial	-1.53	3.49E-04	1.62	1.22E-05	Sequence similar to mitochondrial carbonic anhydrases (CAs), a large family of zinc metalloenzymes that catalyze the reversible hydration of carbon dioxide.
EMB	Embigin	-1.00	9.85E-01	1.59	3.22E-03	Transmembrane glycoprotein member of the immunoglobulin superfamily. May be involved in cell growth and development.
CA3	Carbonic anhydrase III, muscle specific	-1.18	6.03E-02	1.51	5.31E-04	A class of metalloenzymes that catalyze the reversible hydration of carbon dioxide.

Table S3j.
Genes Downregulated in Liver by MRC (Normalized to Control)

Gene Symbol	Gene name	MR	p value	MRC	p value	Function
<i>Lipid Metabolism</i>						
PNPLA3	Patatin-like phospholipase domain containing 3	-5.13	5.77E-04	-4.31	1.27E-03	Triacylglycerol hydrolysis.
CROT	Carnitine O-octanoyltransferase	-1.93	2.76E-03	-2.57	4.60E-04	Converts 4,8-dimethylnonanoyl-CoA to its corresponding carnitine ester. Necessary for transport of medium- and long- chain acyl-CoA molecules out of the peroxisome to the cytosol and mitochondria.
INSIG1	Insulin induced gene 1	-1.93	1.03E-02	-1.83	1.33E-03	Regulation of cholesterol concentrations in cells.
ACACB	Acetyl-CoA carboxylase beta	-2.19	1.99E-07	-1.82	5.46E-06	Carboxylation of acetyl-CoA to malonyl-CoA, the rate-limiting step in fatty acid synthesis. Inhibits carnitine-palmitoyl-CoA transferase I, the rate-limiting step in fatty acid uptake and oxidation by mitochondria.
FADS2	Fatty acid desaturase 2	-1.11	1.89E-02	-1.70	3.95E-06	Regulates the unsaturation of fatty acids through the introduction of double bonds between defined carbons of the fatty acyl chain.
ACLY	ATP citrate lyase	-2.07	1.04E-03	-1.65	1.52E-02	Formation of acetyl-CoA and oxaloacetate from citrate and CoA.
Elovl2	Elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 2	-1.20	3.49E-02	-1.58	3.04E-04	Synthesis of very long chain fatty acids.
FADS1	Fatty acid desaturase 1	-1.20	1.01E-02	-1.55	6.22E-06	Regulates the unsaturation of fatty acids through the introduction of double bonds between defined carbons of the fatty acyl chain.
ME1	Malic enzyme 1, NADP(+)-dependent, cytosolic	1.70	5.64E-03	-2.44	4.45E-04	Generates NADPH for fatty acid biosynthesis Links the glycolytic and citric acid cycles.
<i>Carbohydrate Metabolism</i>						
G6PD	Glucose-6-phosphate dehydrogenase	-1.14	5.55E-01	-1.93	3.99E-03	Cytosolic enzyme encoded by a housekeeping X-linked gene whose main function is to produce NADPH, a key electron donor in the defense against oxidizing agents and in reductive biosynthetic reactions.

<i>Amino Acid Metabolism</i>							
OAT	Ornithine aminotransferase	-3.68	1.65E-05	-1.59	1.32E-02	Mitochondrial enzyme ornithine aminotransferase is a key enzyme in the pathway that converts arginine and ornithine into the major excitatory and inhibitory neurotransmitters glutamate and GABA.	
BHMT	Betaine--homocysteine S-methyltransferase	1.07	1.87E-01	-1.53	5.39E-05	Encodes a cytosolic enzyme that catalyzes the conversion of betaine and homocysteine to dimethylglycine and methionine.	
<i>Immune Response</i>							
MME	Membrane metallo-endopeptidase	-2.11	8.01E-06	-1.89	3.46E-05	Encodes a common acute lymphocytic leukemia antigen that is an important cell surface marker in the diagnosis of human acute lymphocytic leukemia (ALL),. Is a neutral endopeptidase that cleaves peptides at the amino side of hydrophobic residues and inactivates several peptide hormones including glucagon, enkephalins, substance P, neurotensin, oxytocin, and bradykinin.	
<i>Signal Transduction</i>							
RGS16	Regulator of G-protein signaling 16	-2.51	8.45E-03	-2.05	3.66E-02	Regulator of G protein signaling family. Inhibits signal transduction by increasing the GTPase activity of G protein alpha subunits. May also play a role in regulating the kinetics of signaling in the phototransduction cascade.	
EPHA3	EPH receptor A3	-1.86	1.80E-05	-1.89	3.43E-06	Belongs to the ephrin receptor subfamily of the protein-tyrosine kinase family. The EPH receptor family is divided into 2 groups based on the similarity of their extracellular domain sequences and their affinities for binding ephrin-A and ephrin-B ligands. This gene encodes a protein that binds ephrin-A ligands.	

Other

COMT

Catechol-O-methyltransferase

-1.48

1.35E-03

-1.53

1.23E-04

Catalyzes the transfer of a methyl group from S-adenosylmethionine to catecholamines, including the neurotransmitters dopamine, epinephrine, and norepinephrine. O-methylation results in one of the major degradative pathways of the catecholamine transmitters.

Table S3k.
Genes Upregulated in Muscle by MRC (Normalized to Control)

Gene Symbol		Gene name	MR	p value	MRC	p value	Function
<i>Myofibrillar Components</i>							
TNNI1		Troponin I type 1 (skeletal, slow)	5.21	1.19E-02	2.37	2.76E-02	Slow twitch muscle inhibitory troponin subunit, blocks actin-myosin interactions and thereby mediates striated muscle relaxation.
<i>Calcium-Binding Protein</i>							
CASQ2		Calsequestrin 2 (cardiac muscle)	2.89	2.32E-02	1.91	5.24E-03	Stores calcium for muscle function.
<i>Transport</i>							
ATP1B1		ATPase, Na+/K+ transporting, beta 1 polypeptide	1.62	7.82E-02	1.61	4.61E-02	Establishes and maintains electrochemical gradients of Na and K ions across the muscle plasma membrane essential for osmoregulation, for sodium-coupled transport of a variety of organic and inorganic molecules, and for electrical excitability.
<i>Protein Turnover</i>							
UBE2I		Ubiquitin-conjugating enzyme E2I (UBC9 homolog, yeast)	1.69	1.84E-02	1.53	4.72E-02	Member of the E2 ubiquitin-conjugating enzyme family.
<i>Other</i>							
CSRP3		Cysteine and glycine-rich protein 3 (cardiac LIM protein)	3.21	1.65E-02	2.54	1.45E-02	Development and cellular differentiation.
FHL1		Four and a half LIM domains 1	1.99	4.63E-03	1.78	8.29E-03	Member of the four-and-a-half-LIM-only protein family involved in many cellular processes.
GEMIN7		Gem (nuclear organelle) associated protein 7	1.55	1.86E-01	1.74	3.56E-02	Required for pre-mRNA splicing in the nucleus.
HSPB7		Heat shock 27kDa protein family, member 7 (cardiovascular)	2.04	1.75E-02	1.60	5.63E-03	Heat shock protein that binds alpha-filamin.
RNASE6		Ribonuclease, RNase A family, k6	1.22	2.61E-01	1.53	3.10E-02	RNA degradation.

Table S3l.
Genes Downregulated in Muscle by MRC (Normalized to Control)

Gene Symbol		Gene name	MR	p value	MRC	p value	Function
<i>Signal Transduction</i>							
	SFRP2	Secreted frizzled-related protein 2	-2.43	1.01E-03	-1.74	2.89E-02	Soluble modulator of Wnt signaling.
	Taar7d	Trace amine-associated receptor 7C	-1.26	3.93E-01	-1.52	3.61E-02	Neurotransmitters/neuromodulators of trace amines.
<i>Other</i>							
	RASSF9	Ras association (RalGDS/AF-6) domain family (N-terminal) member 9	-1.11	6.03E-01	-1.69	2.59E-02	Associates with peptidylglycine alpha-amidating monooxygenase and is involved with the trafficking of this enzyme through secretory or endosomal pathways.
	NAT8B	N-acetyltransferase 8B (GCN5-related, putative, gene/pseudogene)	-1.31	3.38E-01	-1.67	7.93E-03	Drug resistance.
	SNRPD2	Small nuclear ribonucleoprotein D2 polypeptide 16.5kDa	-1.31	1.73E-01	-1.52	3.26E-02	Required for pre-mRNA splicing and small nuclear ribonucleoprotein biogenesis.