

## Supplemental figure 4A

Gene	Protein	G609G/G609G vs +/-			Function
		Reg.	Fold change	P-value	
Adipoq	Adiponectin	up	6.1539	0.0374	Adiponectin is a protein hormone that modulates glucose metabolism and fatty acid oxidation
Cdkn1a	p21	up	14.2264	0.032219	p21 is a cyclin-dependent kinase inhibitor (CKI) that inhibits the activity of cyclin-CDK2 or -CDK1 complexes, and thus functions as a regulator of cell cycle progression at G1 phase
Cfd	Adipsin	Up	3.7425	0,018678	Adipsin (which in human subjects corresponds to complement factor D46) is the rate-limiting enzyme in the alternative pathway of complement activation.
Dio2	Deiodinase, Iodothyronine, type II	Up	4,6751	0,003692	It activates thyroid hormone by converting the prohormone thyroxine (T4) by outer ring deiodination (ORD) to bioactive 3,3',5'-triiodothyronine (T3)
Klf15	Kruppel-like factor 15	up	11.2785	0.01178	KLF15 plays an essential role in adipogenesis in 3T3-L1 cells through its regulation of PPAR gamma expression
Klf4	Kruppel-like factor 4	up	2.584	0.037216	Klf4 is important in regulating pluripotency and adipocyte differentiation
Pparg	peroxisome proliferator activated receptor gamma	up	2.166	0.055952	PPAR gamma regulates fatty acid storage and glucose metabolism.
Ppargc1a	peroxisome proliferative activated receptor, gamma, coactivator 1 alpha	up	5.15533	0.0936	Transcription coactivator that plays a central role in the regulation of cellular energy metabolism
Ppargc1b	peroxisome proliferative activated receptor, gamma, coactivator 1 beta	up	1.8372	0.084945	Transcription coregulator that plays a role in fat oxidation, in non-oxidative glucose metabolism, and in the regulation of energy expenditure.
Sirt1	Sirtuin 1	up	2.476	0.005788	NAD-dependent protein deacetylase that links transcriptional regulation directly to intracellular energetics and participates in cell cycle, metabolism, apoptosis and autophagy
Slc2a4	Solute carrier family 2, member 4 (GLUT4)	up	2.24	0.059194	Protein that unctions as an insulin-regulated facilitative glucose transporter
Tsc22d3	TSC22 domain family, member 3	up	6.3401	0.048788	Transcriptional regulator that plays a key role in the anti-inflammatory and immunosuppressive effects of this steroid and chemokine
Lep	Leptin	down	43.0368	0.03325	Leptin plays a key role in regulating energy intake and energy expenditure, including appetite/hunger and metabolism
Sfrp5	secreted frizzled-related sequence protein 5	down	17.0063	0.19608	Sfrp5 is an anti-inflammatory adipokine that modulates metabolic dysfunction in obesity
Wnt10b	Wingless related MMTV integration site 10b	down	4,9674	0,001923	The WNT gene family consists of structurally related genes that encode secreted signaling proteins. These proteins have been implicated in oncogenesis and in several developmental processes, including regulation of cell fate and patterning during embryogenesis

Gene	Protein	LCS/LCS vs +/-			Function
		Reg.	Fold change	P-value	
E2f1	E2F transcription factor 1	up	1.795	0.221001	Transcription factor that plays a role in the control of cell cycle and action of tumor suppressor proteins
Lep	Leptin	up	6.9131	0.034099	Leptin plays a key role in regulating energy intake and energy expenditure, including appetite/hunger and metabolism
Sfrp5	secreted frizzled-related sequence protein 5	up	9.3697	0.093636	Sfrp5 is an anti-inflammatory adipokine that modulates metabolic dysfunction in obesity
Ppara	peroxisome proliferator activated receptor alpha	down	1.6533	0.063465	PPARalpha regulates fatty acid synthesis and oxidation, gluconeogenesis, ketogenesis and lipoprotein assembly
Ppargc1a	peroxisome proliferative activated receptor, gamma, coactivator 1 alpha	down	1.8268	0.040326	Transcription coactivator that plays a central role in the regulation of cellular energy metabolism

## Supplemental figure 4B

Gene	Protein	G609G/G609G vs +/-			Function
		Reg.	Fold change	P-value	
Acaa1a	Acetyl-Coenzyme A acyltransferase 1A	up	1.6239	0.011172	This gene encodes an enzyme operative in the beta-oxidation system of the peroxisomes
Acad10	Acyl-Coenzyme A dehydrogenase family, member 10	up	1.8474	0.028319	Acyl-CoA dehydrogenase participates in the beta-oxidation of fatty acids in mitochondria. Acyl-CoA dehydrogenase only active with R- and S-2-methyl-C15-CoA
Acadl	Acyl-Coenzyme A dehydrogenase, long-chain	up	2.2784	0.045664	This protein is one of the four enzymes that catalyze the initial step of mitochondrial beta-oxidation of straight-chain fatty acid
Acadsb	Acyl-Coenzyme A dehydrogenase, short/branched chain	up	1.8712	0.01275	Short/branched chain acyl-CoA dehydrogenase catalyzes the dehydrogenation of acyl-CoA derivatives in the metabolism of fatty acids or branch chained amino acids
Acadvl	Acyl-Coenzyme A dehydrogenase, very long chain	up	2.4436	0.041491	The protein is targeted to the inner mitochondrial membrane where it catalyzes the first step of the mitochondrial fatty acid beta-oxidation pathway. This acyl-Coenzyme A dehydrogenase is specific to long-chain and very-long-chain fatty acids
Acat1	Acetyl-Coenzyme A acetyltransferase 1	up	1.8245	0.057322	a mitochondrially localized enzyme that catalyzes the reversible formation of acetoacetyl-CoA from two molecules of acetyl-CoA
Acot3	Acyl-CoA thioesterase 3	up	3.4474	0.04137	Acyl-CoA thioesterases catalyze the hydrolysis of acyl-CoAs to the free fatty acid and coenzyme A (CoASH), providing the potential to regulate intracellular levels of acyl-CoAs, free fatty acids and CoASH
Acot6	Acyl-CoA thioesterase 6	up	1.6245	0.021967	Acyl-CoA thioesterases catalyze the hydrolysis of acyl-CoAs to the free fatty acid and coenzyme A (CoASH), providing the potential to regulate intracellular levels of acyl-CoAs, free fatty acids and CoASH
Acot8	Acyl-CoA thioesterase 8	up	1.9622	0.039177	Acyl-CoA thioesterases catalyze the hydrolysis of acyl-CoAs to the free fatty acid and coenzyme A (CoASH), providing the potential to regulate intracellular levels of acyl-CoAs, free fatty acids and CoASH
Acox1	Acyl-Coenzyme A oxidase 1, palmitoyl	up	1.7994	0.072648	This protein is the first enzyme of the fatty acid beta-oxidation pathway, which catalyzes the desaturation of acyl-CoAs to 2-trans-enoyl-CoAs
Acsm3	Acyl-CoA synthetase medium-chain family member 3	up	4.1482	0.0144	This protein has medium-chain fatty acid:CoA ligase activity with broad substrate specificity (in vitro). Acts on acids from C(4) to C(11) and on the corresponding 3-hydroxy- and 2,3- or 3,4-unsaturated acids (in vitro)
Aldh2	Aldehyde dehydrogenase 2, mitochondrial	up	1.7153	0.097939	Aldehyde dehydrogenase is the second enzyme of the major oxidative pathway of alcohol metabolism
Bdh2	3-hydroxybutyrate dehydrogenase, type 2	up	1.8207	0.02479	Dehydrogenase that mediates the formation of 2,5-dihydroxybenzoic acid (2,5-DHBA), a siderophore that shares structural similarities with bacterial enterobactin and associates with LCN2, thereby playing a key role in iron homeostasis and transport
Crat	Carnitine acetyltransferase	up	1.5508	0.212862	Key enzyme in the metabolic pathway in mitochondria, peroxisomes and endoplasmic reticulum. CRAT catalyzes the reversible transfer of acyl groups from an acyl-CoA thioester to carnitine and regulates the ratio of acylCoA/CoA in the subcellular compartments
Echs1	Enoyl Coenzyme A hydratase, short chain, 1, mitochondrial	up	2.1214	0.042878	In the second step of the mitochondrial fatty acid beta-oxidation pathway, this enzyme catalyzes the hydration of 2-trans-enoyl-coenzyme A (CoA) intermediates to L-3-hydroxyacyl-CoAs
Ehadh	Enoyl-Coenzyme A, hydratase/3-hydroxyacyl Coenzyme A dehydrogenase	up	8.5209	0.178875	The protein encoded by this gene is a bifunctional enzyme and is one of the four enzymes of the peroxisomal beta-oxidation pathway.
Gpd2	Glycerol phosphate dehydrogenase 2, mitochondrial	up	1.6403	0.261949	Localized to the inner mitochondrial membrane, it catalyzes the conversion of glycerol-3-phosphate to dihydroxyacetone phosphate, using FAD as a cofactor
Hadha	Hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), alpha subunit	up	1.5476	0.059643	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2
Hmgcl	3-hydroxy-3-methylglutaryl-Coenzyme A lyase	up	2.3867	0.010183	It is a mitochondrial enzyme that catalyzes the final step of leucine degradation and plays a key role in ketone body formation
Hmgcs2	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	up	1.7381	0.079947	It is a mitochondrial enzyme that catalyzes the first reaction of ketogenesis, a metabolic pathway that provides lipid-derived energy for various organs during times of carbohydrate deprivation, such as fasting
Mut	Methylmalonyl-Coenzyme A mutase	up	1.6958	0.038346	This enzyme is involved in the degradation of several amino acids, odd-chain fatty acids and cholesterol via propionyl-CoA to the tricarboxylic acid cycle
Eci2	Enoyl-Coenzyme A delta isomerase 2	up	1.6604	0.004512	The protein encoded is a key mitochondrial enzyme involved in beta-oxidation of unsaturated fatty acids
Ppa1	Pyrophosphatase (inorganic) 1	up	2.5324	0.041807	The pyrophosphatases catalyze the hydrolysis of pyrophosphate to inorganic phosphate, which is important for the phosphate metabolism of cells
Prkaa2	Protein kinase, AMP-activated, alpha 2 catalytic subunit	up	2.2061	0.019624	The protein encoded by this gene is a catalytic subunit of the AMP-activated protein kinase (AMPK). AMPK is an important energy-sensing enzyme that monitors cellular energy status
Prkab1	Protein kinase, AMP-activated, beta 1 non-catalytic subunit	up	1.554	0.143722	The protein encoded by this gene is a regulatory subunit of the AMP-activated protein kinase (AMPK). AMPK is an important energy-sensing enzyme that monitors cellular energy status
Prkab2	Protein kinase, AMP-activated, beta 2 non-catalytic subunit	up	3.4762	0.037142	The protein encoded by this gene is a regulatory subunit of the AMP-activated protein kinase (AMPK). AMPK is an important energy-sensing enzyme that monitors cellular energy status
Prkacb	Protein kinase, cAMP dependent, catalytic, beta	up	1.5006	0.04372	The protein encoded by this gene is a member of the Ser/Thr protein kinase family and is a catalytic subunit of cAMP-dependent protein kinase
Prkag1	Protein kinase, AMP-activated, gamma 1 non-catalytic subunit	up	2.4743	0.00011	The protein encoded by this gene is a regulatory subunit of the AMP-activated protein kinase (AMPK). AMPK is an important energy-sensing enzyme that monitors cellular energy status
Slc27a1	Solute carrier family 27 (fatty acid transporter), member 1	up	3.5913	0.022578	Involved in translocation of long-chain fatty acids (LFCA) across the plasma membrane. Plays a pivotal role in regulating available LFCA substrates from exogenous sources in tissues undergoing high levels of beta-oxidation or triglyceride synthesis
Acad11	Acyl-Coenzyme A dehydrogenase family, member 11	down	1.5562	0.226555	Acyl-CoA dehydrogenase participates in the beta-oxidation of fatty acids in mitochondria. Its exhibits maximal activity towards saturated C22-CoA
Acsbg1	Acyl-CoA synthetase bubblegum family member 1	down	3.0951	0.062566	Mediates activation of long-chain fatty acids for both synthesis of cellular lipids, and degradation via beta-oxidation. Able to activate long-chain fatty acids and very long-chain fatty acids
Acs16	Acyl-CoA synthetase long-chain family member 6	down	4.4862	0.269089	This enzyme catalyzes the formation of acyl-CoA from fatty acids, ATP, and CoA, using magnesium as a cofactor and plays a major role in fatty acid metabolism in the brain
Bdh1	3-hydroxybutyrate dehydrogenase, type 1	down	2.151	0.255326	This enzyme catalyzes the interconversion of acetoacetate and (R)-3-hydroxybutyrate, the two major ketone bodies produced during fatty acid catabolism
Cpt1a	Carnitine palmitoyltransferase 1a, liver	down	1.5654	0.098422	CPT1 is the key enzyme in the carnitine-dependent transport across the mitochondrial inner membrane and its deficiency results in a decreased rate of fatty acid beta-oxidation
Fabp1	Fatty acid binding protein 1, liver	down	3.2009	0.274616	FABPs bind long-chain fatty acids and other hydrophobic ligands. FABPs roles include fatty acid uptake, transport, and metabolism
Fabp5	Fatty acid binding protein 5, epidermal	down	4.0014	0.054228	FABPs bind long-chain fatty acids and other hydrophobic ligands. FABPs roles include fatty acid uptake, transport, and metabolism
Slc27a6	Solute carrier family 27 (fatty acid transporter), member 6	down	2.2736	0.260342	This gene encodes a member of the fatty acid transport protein family (FATP). FATPs are involved in the uptake of long-chain fatty acids and have unique expression patterns

Gene	Protein	LCS/LCS vs +/-			Function
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Prkag3	Protein kinase, AMP-activated, gamma 3 non-catalytic subunit	up	3.4426	0.080789	The protein encoded by this gene is a regulatory subunit of the AMP-activated protein kinase (AMPK). AMPK is an important energy-sensing enzyme that monitors cellular energy status
Actb	Actin, beta	up	1.7977	0.013061	Actin is a ubiquitous globular protein that is one of the most highly-conserved proteins known
Acot3	Acyl-CoA thioesterase 3	down	5.1024	0.048218	Acyl-CoA thioesterases catalyze the hydrolysis of acyl-CoAs to the free fatty acid and coenzyme A (CoASH), providing the potential to regulate intracellular levels of acyl-CoAs, free fatty acids and CoASH
Acot12	Acyl-CoA thioesterase 12	down	4.5689	0.163558	Hydrolyzes acetyl-CoA to acetate and CoA
Acox2	Acyl-Coenzyme A oxidase 2, branched chain	down	1.7122	0.137832	The product of this gene belongs to the acyl-CoA oxidase family. It encodes the branched-chain acyl-CoA oxidase which is involved in the degradation of long branched fatty acids and bile acid intermediates in peroxisomes
Acsbg1	Acyl-CoA synthetase bubblegum family member 1	down	3.9427	0.166871	Mediates activation of long-chain fatty acids for both synthesis of cellular lipids, and degradation via beta-oxidation. Able to activate long-chain fatty acids and very long-chain fatty acids
Acsm3	Acyl-CoA synthetase medium-chain family member 3	down	2.0297	0.051595	This protein has medium-chain fatty acid:CoA ligase activity with broad substrate specificity. Acts on acids from C(4) to C(11) and on the corresponding 3-hydroxy- and 2,3- or 3,4-unsaturated acids
Bdh2	3-hydroxybutyrate dehydrogenase, type 2	down	1.588	0.067937	Dehydrogenase that mediates the formation of 2,5-dihydroxybenzoic acid (2,5-DHBA), a siderophore that shares structural similarities with bacterial enterobactin and associates with LCN2, thereby playing a key role in iron homeostasis and transport
Crot	Carnitine O-octanoyltransferase	down	1.8182	0.296008	This gene encodes a member of the carnitine/choline acetyltransferase family. The encoded protein converts 4,8-dimethylnonanoyl-CoA to its corresponding carnitine ester. The protein plays a role in lipid metabolism and fatty acid beta-oxidation
Slc27a2	Solute carrier family 27 (fatty acid transporter), member 2	down	8.2354	0.217738	The protein encoded by this gene is an isoform of long-chain fatty-acid-coenzyme A ligase family. This enzyme convert free long-chain fatty acids into fatty acyl-CoA esters, and thereby play a key role in lipid biosynthesis and fatty acid degradation

#### **Supplemental figure 4:**

**A-** The Mouse Adipogenesis RT<sup>2</sup> Profiler™ PCR Array profiles the expression of 84 key genes involved in the differentiation and maintenance of mature adipocytes.

**B-** The Mouse Fatty Acid Metabolism RT<sup>2</sup> Profiler™ PCR Array profiles the expression of 84 key genes involved in the regulation and enzymatic pathways of fatty acid metabolism. Up-regulated genes appear in red, and down-regulated genes appear in green.

RNA samples were extracted from the adipose tissues of 4-month-old male *Lmna*<sup>G609G/G609G</sup> and *Lmna*<sup>LCS/LCS</sup> mice. (Five mice of each genotype were analyzed independently).