

Supplemental Results

Mcmm2 is a very small locus at the distal end of chromosome 1 with a Bayesian credible interval of 184.65-184.89 Mb. This locus harbors only three genes; *Tlr5*, *Susd4*, and *4922505E12Rik (Ccdc185)*. There are numerous SNPs and Indels between the AKR and DBA/2 strains in this region¹, although none of these genes have a missense mutation or an aberrant translation termination codon, nor did they have a BMDM cis-eQTL in our prior studies.

Mcmm4 is located in the middle of chromosome 5 with a Bayesian credible interval of 68.02-107.43 Mb and harbors 428 genes. The top candidates for this locus are *Mepe*, *Spp1*, and *Pkd2*. *Mepe* has 27 non-synonymous SNPs between AKR and DBA/2 mice, 4 of which are predicted to be deleterious by PROVEAN. Additionally, MEPE was associated with cardiovascular risk factors in a human GWAS study.² *Spp1* and especially *Pkd2* had strong BMDM cis-eQTL LOD scores in our prior studies, and both had many PubMed hits when searched for associations with cholesterol and atherosclerosis.

Mcmm5 is located at the distal end of chromosome 6 with a Bayesian credible interval of 118.95-122.59 Mb and harbors 64 genes. *Bid* and *Atp6v1e1* stood out as top candidates because of their relatively strong BMDM cis-eQTL scores in our prior studies.

Mcmm6 is located at the proximal end of chromosome 9 with a Bayesian credible interval of 3.58-34.82 Mb and harbors 318 genes. *Casp1* is the top candidate for this locus, as it had a modest BMDM cis-eQTL LOD score in our prior studies and had many PubMed hits for our terms of interest: cholesterol, lysosome, autophagy, and atherosclerosis. *Fli1* is also a candidate due to its strong BMDM cis-eQTL score.

Mcmm7 is a very large locus located on chromosome 10 with a Bayesian credible interval of 3.15-129.61 Mb and harbors 1,462 genes. It is difficult to settle on a top candidate gene for this interval, but *Os9* seems plausible, as it had a strong BMDM cis-eQTL in prior studies and was shown to be associated with lipid storage in adipocytes.³

Mcmm8 is located at the proximal end of chromosome 11 with a Bayesian credible interval of 4.03-36.44 Mb and harbors 468 genes. *Camk2b* is the strongest candidate gene for this locus, as it had a very strong BMDM cis-eQTL. Also, SNPs near CAMK2B are associated with metabolic syndrome in a human GWAS study.⁴

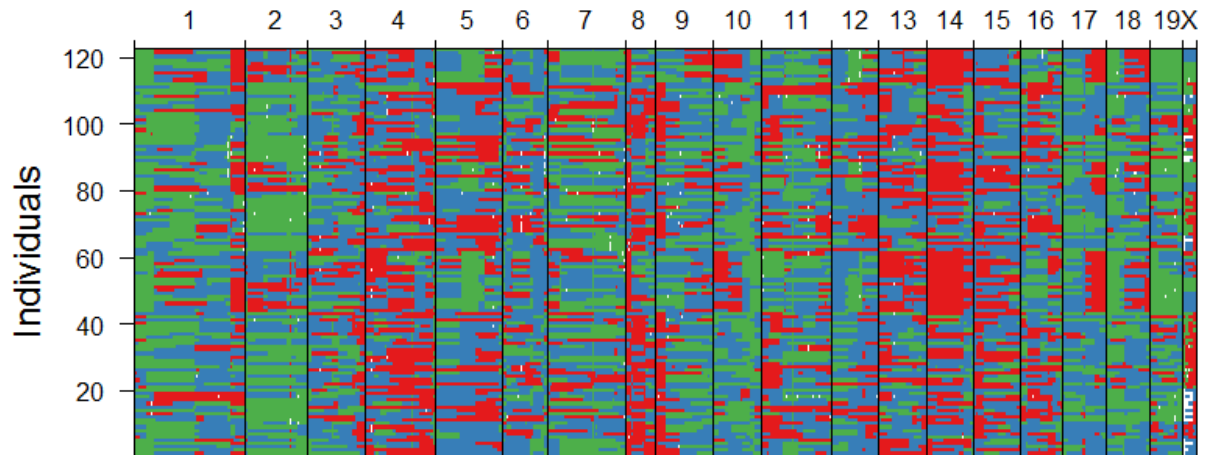
Mcmm9 is located at the distal end of chromosome 12 with a Bayesian credible interval of 79.09-95.60 Mb and harbors 220 genes. There is no clear candidate gene at this locus.

Mcmm10 is located at the distal end of chromosome 17 with a Bayesian credible interval of 68.68-89.29 Mb and harbors 191 genes. The strongest candidate is *Dync2li1* which had a very strong BMDM cis-eQTL. SNPs near DYNC2LI1 are also associated with C-reactive protein levels and total cholesterol levels in a human GWAS study.⁵

Supplemental Figure and Tables

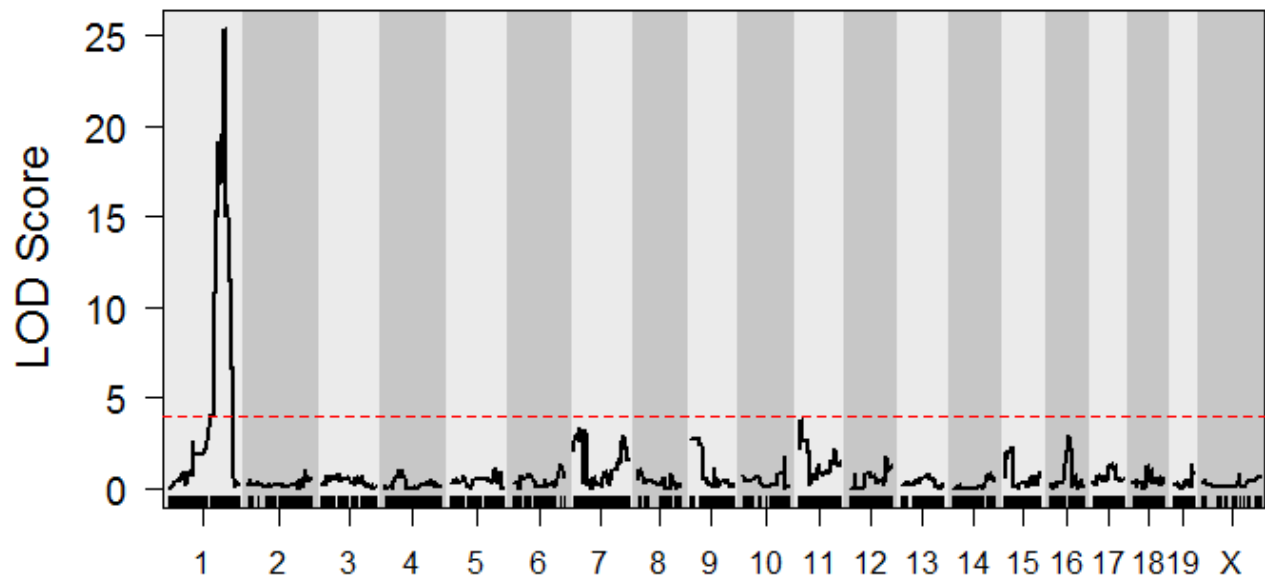
Supplemental Figure I
Supplemental Figure II
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Supplemental Figure I. Genotype map for 122 F4 AKR x DBA/2 mice. Results from the GeneSeek MegaMUGA SNP array. Red denotes an AKR allele for a specific marker, green denotes DBA/2, and blue denotes a heterozygous genotype. White denotes markers that did not satisfy our quality filtering criteria. 16,975 informative SNPs were used for QTL analyses.

Cholesterol Ester/Free Cholesterol

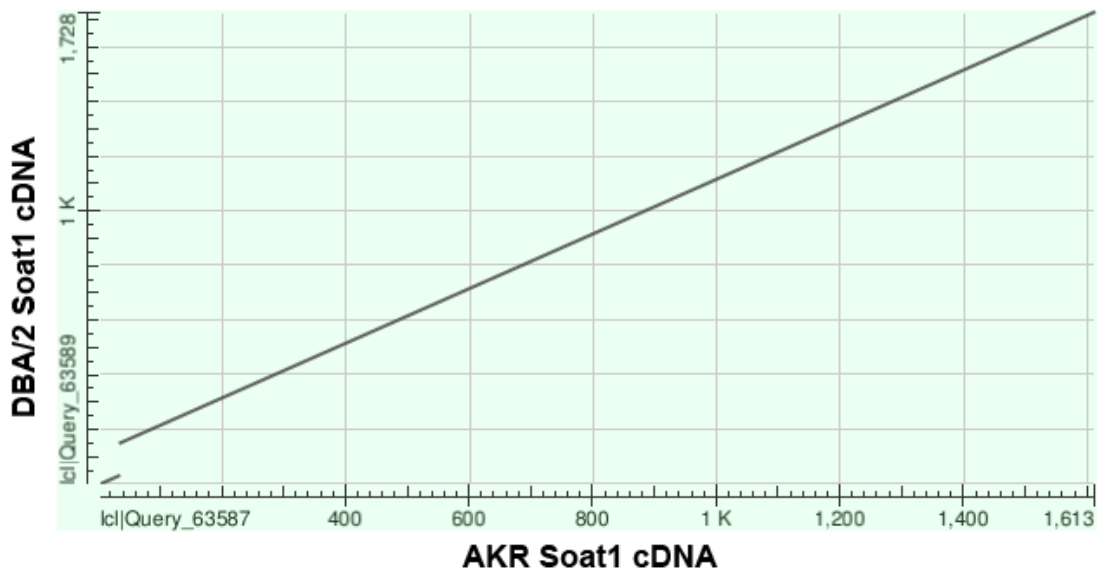


Supplemental Figure II. LOD plot for CE/FC ratio when a lower acLDL concentration was used. *Mcmm1* was the only locus to reach the genome wide significance threshold of 3.99 ($\alpha = 0.05$) determined permutation analysis. Max LOD score for *Mcmm1* = 25.4.

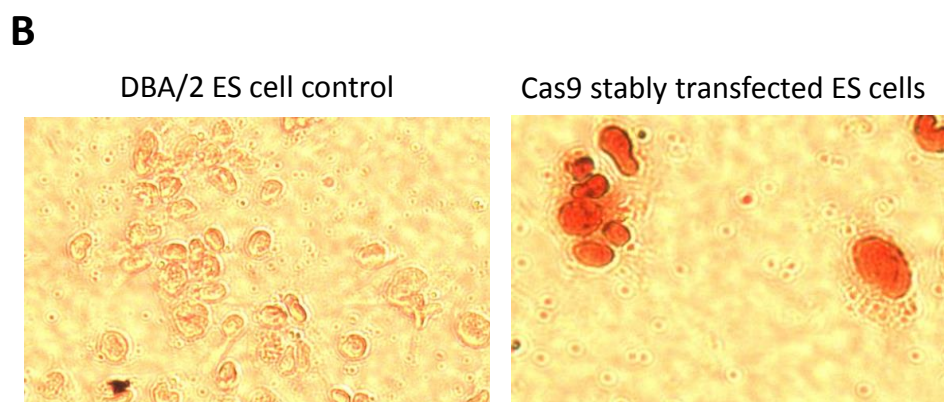
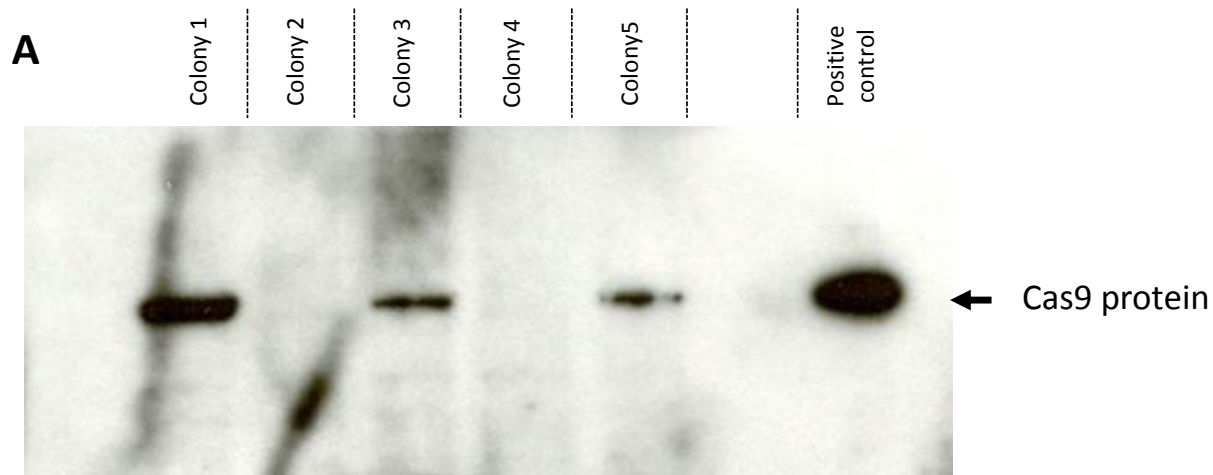
A

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GAACAATTTACCACATGTTTCATCGCACTCCTCATCCTCTTCGTCCTCAGCACGGTCGTCGTGGACTACATTGATG
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GATAT

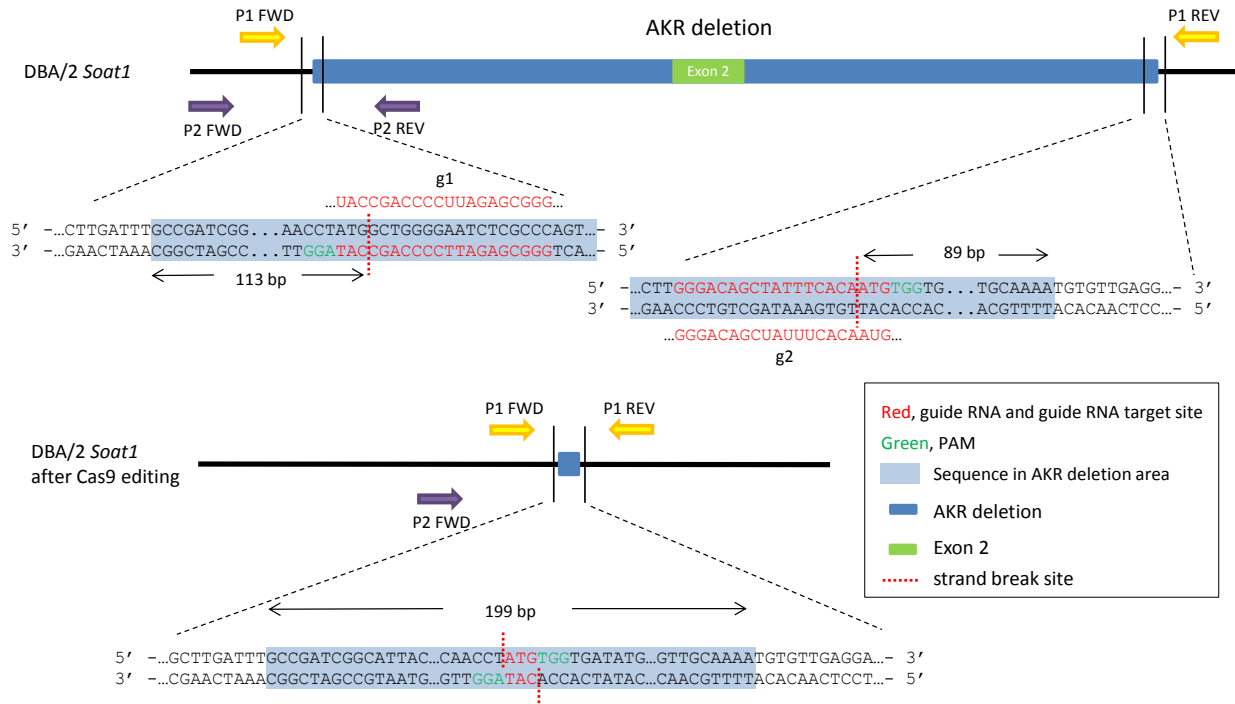
B



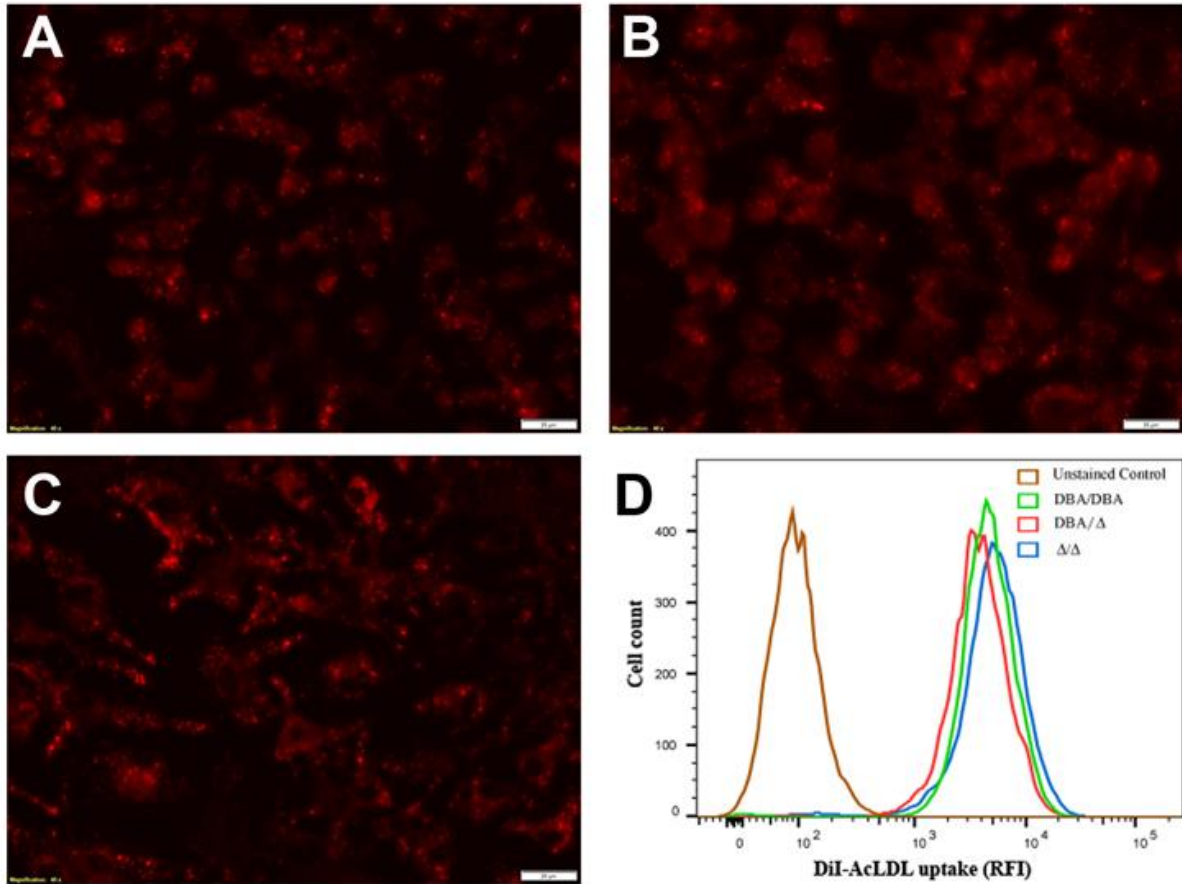
Supplemental Figure III. Alignment of AKR and DBA/2 *Soat1* cDNAs. **A.** DBA/2 *Soat1* cDNA sequenced from 3 overlapping cDNA PCR fragments. The sequence deleted in the AKR *Soat1* cDNA is underlined. **B.** AKR and DBA/2 cDNA sequence matrix alignment plot from Blast 2n analysis. The break in the line shows the 118 pb deletion in the AKR cDNA.



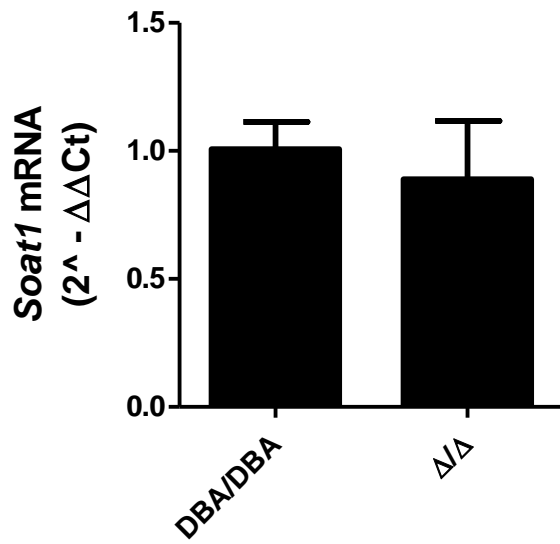
Supplemental Figure IV. DBA/2 ES cells stably transfected with Cas9. A. Western blot of Cas9 protein from 5 different transfected colonies. Positive control was Cas9 protein obtained from New England BioLabs (#M0386). Colony 1 was expanded for further study. **B.** Immunohistochemistry of Cas9 protein in Colony 1 cell line vs. control DBA/2 ES cells.



Supplemental Figure V. Cas9 editing of DBA/2 *Soat1* genomic region to delete exon 2 and flanking sequence. Top. Design of two sgRNAs flanking exon 2 to create a deletion similar but not identical to the 6818bp deletion observed in AKR *Soat1* gene. **Bottom.** Sequencing the deleted allele by PCR, which displayed a 6619bp deletion. We expected the deletion junction to contain a repeat of an ATG sequence based upon the Cas9 cut site 3bp upstream of the PAM sequence; however, the repeated ATG sequence was modified during non-homologous end joining to remove one copy of the ATG sequence.



Supplemental Figure VI. DiI AcLDL uptake by ESDMs. A-C. DiI AcLDL uptake after a 30 min incubation at 37°C observed by epifluorescence microscopy of DBA/DBA, DBA/Δ, and Δ/Δ ESDMs, respectively. Scale bar show 20 μm. All images were taken at the same settings for comparison of fluorescent intensity. **D.** Flow cytometry data showing that all three cell lines had similar levels of DiI AcLDL uptake, and <3 % of cells were negative for uptake of DiI AcLDL. Brown, unstained control cells; green, DBA/DBA cells; red, DBA/Δ cells; and blue, Δ/Δ cells. For all panels, ESDMs were analyzed 14 days after plating macrophage progenitor cells.



Supplemental Figure VII. *Soat1* mRNA qPCR. cDNA was prepared from RNA isolated from DBA/DBA and Δ/Δ ESDMs and assessed for *Soat1* mRNA levels by qPCR normalized to *Actb* mRNA levels as described in the online-only Supplemental Methods section (n=3 RNA preps assayed in triplicate \pm S.D.)

Gene Name	Chr	Mb Position	Gene Description	Mb from LOD peak	eQTL LOD	PubMed cholesterol ^a	PubMed lysosome ^a	PubMed autophagy ^a	PubMed atherosclerosis ^a	Nonsynon snps	LOD nearest flanking marker	PROVEAN deleterious aa change
Zfp648	1	156.05	zinc finger protein 648	0.30	-	0	0	0	0	6	10.8	0
n-R5s220	1	156.16	nuclear encoded rRNA 5S 220	0.19	-	0	0	0	0	0	10.8	0
Cacna1e	1	156.24	calcium channel, voltage-dependent, R type, alpha 1E subunit	0.11	-	1	2	1	0	1	10.8	0
Gm9530	1	156.91	predicted gene 9530	0.56	-	0	0	0	0	0	10.8	0
Ier5	1	156.94	immediate early response 5	0.60	-	0	0	0	0	0	10.8	0
Mr1	1	156.98	major histocompatibility complex, class I-related	0.63	-	0	2	0	0	4	10.8	0
Stx6	1	157.01	syntaxin 6	0.66	9.1	3	4	1	0	1	10.8	0
BC034090	1	157.06	cDNA sequence BC034090	0.71	-	0	0	0	0	9	10.8	0
Xpr1	1	157.12	xenotropic and polytropic retrovirus receptor 1	0.78	-	0	0	1	1	0	10.8	0
AC116712.1	1	157.16	NA	0.82	-	0	0	0	0	0	10.8	0
Gm5532	1	157.37	predicted gene 5532	1.02	-	0	0	0	0	0	10.8	0
Acbd6	1	157.41	acyl-Coenzyme A binding domain containing 6	1.06	-	0	0	0	0	0	10.8	0
Lhx4	1	157.55	LIM homeobox protein 4	1.20	-	0	0	0	0	0	10.8	0
Qsox1	1	157.63	quiescin Q6 sulfhydryl oxidase 1	1.28	-	0	1	1	2	0	10.8	0
Cep350	1	157.69	centrosomal protein 350	1.34	-	0	0	0	0	0	10.8	0
U2	1	157.8	U2 spliceosomal RNA	1.45	-	4	2	4	4	0	10.8	0
Tor1aip1	1	157.85	torsin A interacting protein 1	1.50	2.6	0	0	0	0	0	10.8	0
Tor1aip2	1	157.88	torsin A interacting protein 2	1.54	-	0	0	0	0	0	10.8	0
Fam163a	1	157.92	family with sequence similarity 163, member A	1.58	-	0	0	0	0	0	10.8	0
Tdrd5	1	158.19	tudor domain containing 5	1.84	-	0	0	0	0	0	10.8	0
Nphs2	1	158.24	nephrosis 2 homolog, podocin (human)	1.89	-	17	3	4	2	0	10.8	0
9430070O13Rik	1	158.3	RIKEN cDNA 9430070O13 gene	1.95	-	0	0	0	0	0	10.8	0
Gm2000	1	158.3	predicted gene 2000	1.95	-	0	0	0	0	0	10.8	0
Soat1	1	158.36	sterol O-acyltransferase 1	2.01	23.2	26	1	1	3	0	10.8	0
Gm10031	1	158.45	predicted pseudogene 10031	2.11	-	0	0	0	0	0	10.8	0
Abl2	1	158.49	v-abl Abelson murine leukemia viral oncogene homolog 2 (arg, Abelson)	2.14	-	1	0	0	0	0	10.8	0
Tor3a	1	158.58	torsin family 3, member A	2.24	2.7	0	0	0	0	0	10.8	0
Fam20b	1	158.61	family with sequence similarity 20, member B	2.26	-	0	0	0	0	0	10.8	0
Gm15428	1	158.72	predicted pseudogene 15428	2.38	-	0	0	0	0	0	10.8	0
Ralgps2	1	158.73	Ral GEF with PH domain and SH3 binding motif 2	2.39	-	0	0	0	0	0	10.8	0
Angpt1	1	158.77	angiopoietin-like 1	2.42	-	1	0	0	2	0	10.8	0
1700057K13Rik	1	159.03	RIKEN cDNA 1700057K13 gene	2.68	-	0	0	0	0	3	10.8	0
Rasal2	1	159.07	RAS protein activator like 2	2.72	-	0	0	0	0	0	10.8	0
Gm6058	1	159.31	predicted gene 6058	2.97	-	0	0	0	0	0	10.8	0

^a, Number of PubMed results for gene name AND listed subject term

Yellow highlighting denotes our top candidate genes at this QTL

Supplemental Table I. All genes in Mcmm1 locus.

Differentiation day*	% Dil AcLDL positive
Unstained Control	0.87%
Day 3	1.35%
Day 5	2.44%
Day 7	41.3%
Day 9	68.7%
Day 11	87.4%
Day 13	96.9%

Supplemental Table II. Time course of DBA/2 ESDM differentiation. ES cells were differentiated into ESDMs, as described in the methods section. The percentage of Dil acLDL uptake was measured by flow cytometry over the differentiation period, and was used as a proxy for differentiation into ESDMs.

*, Number of days after plating EB derived macrophage progenitors in differentiation medium.

Supplemental Table III. Top candidate genes at *Mcmm2* -*Mcmm10*

Locus	Gene Name	Chr	Mb Position	Gene Description	Mb from LOD peak	eQTL LOD	PubMed cholesterol ⁸	PubMed lysosome ⁹	PubMed autophagy ⁹	PubMed atherosclerosis ⁹	Nonsynon snps	LOD nearest flanking marker	PROVEAN deleterious aa change
Mcmm2	4922505E12Rik ^b	1	184.68	RIKEN cDNA 4922505E12 gene	0.02	0	0	0	0	0	0	5.6	0
Mcmm2	Sus4 ^b	1	184.69	sushi domain containing 4	0.04	0	0	0	0	0	0	5.6	0
Mcmm2	Tlr5 ^b	1	184.88	toll-like receptor 5	0.23	0	4	5	8	8	0	5.6	0
Mcmm3	Stk35	2	129.63	serine/threonine kinase 35	10.65	22.7	0	0	0	0	0	4.7	0
Mcmm3	Ciao1	2	127.07	cytosolic iron-sulfur protein assembly 1 homolog (S. cerevisiae)	8.09	16.3	1	0	0	0	0	4.7	0
Mcmm3	Mertk	2	128.52	c-mer proto-oncogene tyrosine kinase	9.55	14	10	3	4	23	0	4.7	0
Mcmm3	Vps39	2	120.14	vacuolar protein sorting 39 (yeast)	1.17	12.9	0	13	5	0	0	4.7	0
Mcmm3	Adam33	2	130.88	a disintegrin and metallopeptidase domain 33	11.9	12.8	1	0	0	4	0	4.7	0
Mcmm3	Nduaf1	2	119.48	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, assembly factor 1	0.51	8.4	0	0	1	0	0	4.7	0
Mcmm3	Fahd2a	2	127.26	fumarylacetoacetate hydrolase domain containing 2A	8.29	6.9	0	0	0	0	0	4.7	0
Mcmm3	Bcl2l1	2	127.95	BCL2-like 11 (apoptosis facilitator)	8.98	6.7	4	12	38	2	0	4.7	0
Mcmm3	2010106G01Rik	2	126.72	RIKEN cDNA 2010106G01 gene	7.74	3.8	0	0	0	0	0	4.7	0
Mcmm3	Ncaph	2	126.93	non-SMC condensin I complex, subunit H	7.96	3.3	0	0	0	0	0	4.7	0
Mcmm3	Ccndbp1	2	120.83	cyclin D-type binding-protein 1	1.86	3.1	0	0	0	0	1	4.7	0
Mcmm3	Atp8b4	2	126.15	ATPase, class I, type 8B, member 4	7.17	2.8	0	0	0	0	0	4.7	0
Mcmm3	Blvra	2	126.9	biliverdin reductase A	7.92	2.5	0	0	0	0	0	4.7	0
Mcmm3	Casc5	2	118.87	cancer susceptibility candidate 5	0.1	-	0	2	0	0	18	4.7	1
Mcmm3	Epb4.2	2	120.84	erythrocyte protein band 4.2	1.87	-	0	0	0	0	1	4.7	1
Mcmm3	Fbn1	2	125.13	fibrillin 1	6.15	-	8	1	0	16	3	4.7	1
Mcmm3	Ganc	2	120.23	glucosidase, alpha; neutral C	1.26	-	0	0	0	0	10	4.7	1
Mcmm3	Nusap1	2	119.44	nucleolar and spindle associated protein 1	0.47	-	1	0	0	0	1	4.7	1
Mcmm3	Pla2g4f	2	120.13	phospholipase A2, group IVF	1.15	-	0	0	0	0	7	4.7	2
Mcmm3	Spnb5	2	119.87	spectrin beta 5	0.9	-	0	0	0	0	35	4.7	6
Mcmm3	Tmem62	2	120.8	transmembrane protein 62	1.83	-	0	0	0	0	1	4.7	1
Mcmm3	Zfyve19	2	119.03	zinc finger, FYVE domain containing 19	0.06	-	0	0	0	0	4	4.7	1
Mcmm3	Aqr	2	113.93	aquarius	5.05	-	0	1	1	0	2	4.5	1
Mcmm3	Lbp	2	158.13	lipopolysaccharide binding protein	39.16	7.2	73	4	7	37	3	4.4	1
Mcmm3	Actr5	2	158.45	ARPS actin-related protein 5 homolog (yeast)	39.48	2.5	0	0	0	0	1	4.4	0
Mcmm3	Bpi	2	158.08	bactericidal permeability increasing protein	39.11	-	15	3	5	7	4	4.4	1
Mcmm3	Snhg11	2	158.2	small nucleolar RNA host gene 11	39.23	-	0	0	0	0	3	4.4	1
Mcmm3	Smox	2	131.32	spermine oxidase	12.34	11.4	0	0	0	0	0	4.3	0
Mcmm3	Ugcc	2	155.67	ubiquinol-cytochrome c reductase complex chaperone, CBP3 homolog (yeast)	36.7	2.5	0	0	0	0	0	4	0
Mcmm3	Olfir1290	2	111.33	olfactory receptor 1290	7.64	-	0	0	0	0	2	4	1
Mcmm3	Olfir1289	2	111.32	olfactory receptor 1289	7.65	-	0	0	0	0	1	4	1
Mcmm3	Zfp341	2	154.44	zinc finger protein 341	35.47	-	0	0	0	0	2	4	1
Mcmm3	Cstf1	2	172.2	cleavage stimulation factor, 3' pre-RNA, subunit 1	53.22	3.9	0	0	0	0	0	3.7	0
Mcmm3	Lama5	2	179.91	laminin, alpha 5	60.94	-	2	1	0	0	10	3.6	1
Mcmm3	Pofut1	2	153.07	protein O-fucosyltransferase 1	34.09	6.7	0	0	0	0	0	3.4	0
Mcmm3	8430427H17Rik	2	153.23	RIKEN cDNA 8430427H17 gene	34.26	4.8	0	0	0	0	0	3.4	0
Mcmm3	Dnmt3b	2	153.48	DNA methyltransferase 3B	34.5	2.6	0	0	3	4	0	3.4	0
Mcmm3	Pdrg1	2	152.83	p53 and DNA damage regulated 1	33.86	2.5	0	0	1	1	0	3.4	0
Mcmm3	Bpifa2	2	153.83	BPI fold containing family A, member 2	34.86	-	0	0	0	0	12	3.4	2
Mcmm3	Sys1	2	164.28	SYS1 Golgi-localized integral membrane protein homolog (S. cerevisiae)	45.31	30.4	0	0	0	0	0	3.2	0
Mcmm3	Snx21	2	164.61	sorting nexin family member 21	45.64	3.1	0	0	0	0	0	3.2	0
Mcmm3	Acot8	2	164.62	acyl-CoA thioesterase 8	45.64	2.6	0	0	0	0	0	3.2	0
Mcmm3	Zfp663	2	165.18	zinc finger protein 663	46.2	-	0	0	0	0	6	3.2	2
Mcmm3	Cd93	2	148.26	CD93 antigen	29.29	6.5	2	0	0	5	1	3.1	1
Mcmm3	Cst3	2	148.7	cystatin C	29.72	2.9	45	18	2	64	0	3.1	0
Mcmm3	Napb	2	148.52	N-ethylmaleimide sensitive fusion protein attachment protein beta	29.55	2.6	2	1	1	0	0	3.1	0
Mcmm3	Cst11	2	148.58	cystatin-like 1	29.6	-	0	0	0	0	1	3.1	1
Mcmm3	Snx5	2	144.08	sorting nexin 5	25.1	8.2	0	3	0	0	0	2.7	0
Mcmm3	Dstrn	2	143.74	destrin	24.77	6.1	0	0	1	0	0	2.7	0
Mcmm3	Csrp2bp	2	144.19	cysteine and glycine-rich protein 2 binding protein	25.22	3.3	0	0	0	0	0	2.7	0
Mcmm3	Sec23b	2	144.38	SEC23B (S. cerevisiae)	25.41	2.4	0	0	0	0	0	2.7	0
Mcmm3	Kif16b	2	142.44	kinesin family member 16B	23.47	-	1	2	0	0	6	2.7	1
Mcmm3	MacroD2	2	140.22	MACRO domain containing 2	21.25	-	0	0	0	0	5	2.7	3
Mcmm3	Cd44	2	102.65	CD44 antigen	16.32	-	69	78	46	79	3	2.3	1
Mcmm3	Chst1	2	92.44	carbohydrate (keratan sulfate Gal-6) sulfotransferase 1	26.53	15.5	0	0	0	0	0	2.1	0
Mcmm3	Slc35c1	2	92.29	solute carrier family 35, member C1	26.68	13.2	0	0	0	0	0	2.1	0
Mcmm3	Kbtbd4	2	90.74	kelch repeat and BTB (POZ) domain containing 4	28.23	12.9	0	0	0	0	1	2.1	0
Mcmm3	Sfp1	2	90.92	SFFV proviral integration 1	28.05	5.6	0	0	0	0	1	2.1	0
Mcmm3	Lrp4	2	91.3	low density lipoprotein receptor-related protein 4	27.68	5.4	6	1	1	3	0	2.1	0
Mcmm3	Acp2	2	91.04	acid phosphatase 2, lysosomal	27.93	5.2	1	8	1	0	0	2.1	0

Mcmm3	Ambra1	2	91.57	autophagy/beclin 1 regulator 1	27.4	3.2	0	11	90	0	0	2.1	0
Mcmm3	Olf1241	2	89.32	olfactory receptor 1241	29.65	-	0	0	0	0	1	2.1	1
Mcmm3	Olf52	2	86.02	olfactory receptor 52	32.95	-	0	0	0	0	1	2.1	1
Mcmm4	Slain2	5	73.31	SLAIN motif family, member 2	32.14	3.8	0	0	0	0	0	5.7	0
Mcmm4	Sgcb	5	74.02	sarcoglycan, beta (dystrophin-associated glycoprotein)	31.42	3.1	0	0	0	0	0	5.7	0
Mcmm4	Srd5a3	5	76.57	steroid 5 alpha-reductase 3	28.87	9.7	0	0	0	0	1	5.7	0
Mcmm4	Cep135	5	77.02	centrosomal protein 135	28.42	5.3	0	0	0	0	0	5.7	0
Mcmm4	Epha5	5	84.49	Eph receptor A5	20.95	-	0	0	0	0	2	5.7	1
Mcmm4	Cenpc1	5	86.44	centromere protein C1	19	-	0	0	0	0	2	5.7	1
Mcmm4	Tmprss11g	5	86.91	transmembrane protease, serine 11g	18.53	-	0	0	0	0	1	5.7	1
Mcmm4	Npffr2	5	89.96	neuropeptide FF receptor 2	15.48	-	0	0	0	0	3	5.7	1
Mcmm4	Cox18	5	90.64	COX18 cytochrome c oxidase assembly homolog (S. cerevisiae)	14.8	6.6	0	0	0	0	3	5.7	1
Mcmm4	Ankrd17	5	90.66	ankyrin repeat domain 17	14.78	6.3	0	0	0	0	1	5.7	0
Mcmm4	Arhgap24	5	102.91	Rho GTPase activating protein 24	2.53	4.7	0	0	1	0	0	5.7	0
Mcmm4	Ibsp	5	104.73	integrin binding sialoprotein	0.71	-	1	0	2	2	6	5.7	2
Mcmm4	Mepe	5	104.75	matrix extracellular phosphoglycoprotein with ASARM motif (bone)	0.69	-	0	0	0	1	27	5.7	4
Mcmm4	Spp1	5	104.86	secreted phosphoprotein 1	0.58	6.9	29	7	6	82	0	5.7	0
Mcmm4	Pkd2	5	104.89	polycystic kidney disease 2	0.55	19.5	26	10	8	14	5	5.7	0
Mcmm4	Lrrc8c	5	105.95	leucine rich repeat containing 8 family, member C	0.51	5.7	0	0	0	0	0	5.7	0
Mcmm4	Lrrc8d	5	106.13	leucine rich repeat containing 8D	0.69	4	0	0	0	0	0	5.7	0
Mcmm5	Apobec1	6	122.53	apolipoprotein B mRNA editing enzyme, catalytic polypeptide 1	2.4	7.9	44	3	1	31	0	4.1	0
Mcmm5	A2m	6	121.59	alpha-2-macroglobulin	1.46	-	6	0	0	4	9	4.1	2
Mcmm5	Mug2	6	121.96	murinoglobulin 2	1.83	-	0	0	0	0	1	4.1	1
Mcmm5	Bid	6	120.84	BH3 interacting domain death agonist	0.71	6.4	168	73	74	59	0	3.5	0
Mcmm5	Atp6v1e1	6	120.75	ATPase, H+ transporting, lysosomal V1 subunit E1	0.61	8.4	0	3	1	0	0	3.5	0
Mcmm6	Fli1	9	32.23	Friend leukemia integration 1	0.53	15.7	3	2	0	4	0	5.3	0
Mcmm6	Casp1	9	5.3	caspase 1	26.4	5.1	104	104	139	121	0	4.6	0
Mcmm6	Bbs9	9	22.28	Bardet-Biedl syndrome 9 (human)	9.42	2.7	0	0	0	0	0	4.4	0
Mcmm6	Casp1	9	5.3	caspase 1	26.4	5.1	104	104	139	121	0	4.6	0
Mcmm6	Bbs9	9	22.28	Bardet-Biedl syndrome 9 (human)	9.42	2.7	0	0	0	0	0	4.4	0
Mcmm7	Obfc2b	10	127.84	oligonucleotide/oligosaccharide-binding fold containing 2B	0.31	4.9	0	0	0	0	0	4.6	0
Mcmm7	Cdk2	10	128.13	cyclin-dependent kinase 2	0.61	2.8	22	4	36	56	0	4.6	0
Mcmm7	Atp5b	10	127.52	ATP synthase, H+ transporting mitochondrial F1 complex, beta subunit	0	2.6	7	1	3	5	0	4.6	0
Mcmm7	Olf822	10	129.51	olfactory receptor 822	1.99	-	0	0	0	0	1	4.6	1
Mcmm7	Tbk1	10	120.98	TANK-binding kinase 1	6.54	7.3	5	8	64	8	0	4.5	0
Mcmm7	Tmem5	10	121.52	transmembrane protein 5	6.01	3.3	0	0	0	0	0	4.5	0
Mcmm7	Os9	10	126.53	amplified in osteosarcoma	0.99	7.4	0	2	1	0	2	4.2	0
Mcmm7	Mars	10	126.73	methionine-tRNA synthetase	0.79	5.9	53	0	2	33	1	4.2	0
Mcmm7	Ndufa4l2	10	126.95	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 4-like 2	0.57	3.2	0	0	2	0	0	4.2	0
Mcmm7	Mett11	10	126.48	methyltransferase like 1	1.05	2.6	0	0	0	0	1	4.2	0
Mcmm7	Cdk4	10	126.5	cyclin-dependent kinase 4	1.02	2.6	14	6	33	44	0	4.2	0
Mcmm7	Nab2	10	127.1	Ngfi-A binding protein 2	0.43	2.5	0	0	0	3	0	4.2	0
Mcmm7	Reps1	10	17.78	RalBP1 associated Eps domain containing protein	109.75	4.4	0	0	0	0	1	3	0
Mcmm7	Mum1	10	79.69	melanoma associated antigen (mutated) 1	47.83	3.3	0	0	0	0	0	3	0
Mcmm7	Hcn2	10	79.18	hyperpolarization-activated, cyclic nucleotide-gated K+ 2	48.34	-	4	1	1	1	1	3	1
Mcmm7	Sf3b5	10	12.73	splicing factor 3b, subunit 5	114.8	19.2	0	0	0	0	0	2.9	0
Mcmm7	Aig1	10	13.37	androgen-induced 1	114.16	3.1	0	1	0	0	3	2.9	0
Mcmm7	Phactr2	10	12.93	phosphatase and actin regulator 2	114.59	-	0	0	0	0	5	2.9	1
Mcmm7	Utrn	10	12.1	utrophin	115.42	-	0	0	0	1	1	2.9	1
Mcmm7	Apa3	10	80.73	amyloid beta (A4) precursor protein-binding, family A, member 3	46.79	2.5	0	1	0	0	0	2.8	0
Mcmm7	Hmg20b	10	80.81	high mobility group 20 B	46.72	2.5	0	0	0	0	0	2.8	0
Mcmm7	Gm6713	10	85.17	predicted gene 6713	42.35	-	0	0	0	0	0	2.8	2
Mcmm7	Fam26e	10	33.81	family with sequence similarity 26, member E	93.71	3.8	0	0	0	0	0	2.7	0
Mcmm7	Ifngr1	10	19.31	interferon gamma receptor 1	108.21	2.7	1	0	1	3	1	2.7	0
Mcmm7	Stx7	10	23.87	syntaxin 7	103.65	3.5	0	3	1	0	0	2.6	0
Mcmm7	Il22ra2	10	19.34	interleukin 22 receptor, alpha 2	108.18	-	0	0	0	0	2	2.6	1
Mcmm7	Taar1	10	23.64	trace amine-associated receptor 1	103.88	-	0	0	0	0	1	2.6	1
Mcmm7	Slc25a3	10	90.58	solute carrier family 25 (mitochondrial carrier, phosphate carrier), member 3	36.94	12.6	0	0	0	0	0	1.9	0
Mcmm7	Gnptab	10	87.84	N-acetylglucosamine-1-phosphate transferase, alpha and beta subunits	39.68	14.3	2	33	0	0	4	1.8	0
Mcmm7	Chpt1	10	87.92	choline phosphotransferase 1	39.61	9.6	1	0	0	0	0	1.8	0
Mcmm7	Stab2	10	86.3	stabilin 2	41.22	5.8	0	2	0	3	15	1.8	1
Mcmm7	Utp20	10	88.21	UTP20, small subunit (SSU) processome component, homolog (yeast)	39.31	-	0	0	0	0	3	1.8	1
Mcmm7	Fgd6	10	93.5	FYVE, RhoGEF and PH domain containing 6	34.03	20	1	0	0	0	0	1.7	0
Mcmm7	Vezt	10	93.4	vezatin, adherens junctions transmembrane protein	34.12	10.5	0	0	0	0	0	1.7	0
Mcmm7	Hal	10	92.95	histidine ammonia lyase	34.57	9.2	23	0	2	7	0	1.7	0

Mcmm7	Elk3	10	92.71	ELK3, member of ETS oncogene family	34.81	3.7	0	0	1	0	0	1.7	0
Mcmm7	Zfc3h1	10	114.82	zinc finger, C3H1-type containing	12.7	3	1	0	0	0	0	0.8	0
Mcmm7	Tph2	10	114.52	tryptophan hydroxylase 2	13.01	-	3	0	0	0	1	0.8	1
Mcmm7	Mdm1	10	117.58	transformed mouse 3T3 cell double minute 1	9.95	3	0	1	0	0	1	0.4	0
Mcmm7	Slc35e3	10	117.17	solute carrier family 35, member E3	10.35	2.8	0	0	0	0	0	0.4	0
Mcmm7	Nup107	10	117.19	nucleoporin 107	10.34	2.4	0	0	0	0	0	0.4	0
Mcmm7	Otogl	10	107.2	otogelin-like	20.32	-	0	0	0	0	3	0.2	1
Mcmm8	4930415F15Rik	11	11.36	RIKEN cDNA 4930415F15 gene	4.09	-	0	0	0	0	1	6	1
Mcmm8	Myo1g	11	6.41	myosin IG	0.87	-	0	1	1	0	2	6	1
Mcmm8	Npc1l1	11	6.11	NPC1-like 1	1.16	-	395	4	2	61	2	6	1
Mcmm8	Pkd1l1	11	8.73	polycystic kidney disease 1 like 1	1.45	-	0	0	0	1	1	6	1
Mcmm8	Camk2b	11	5.87	calcium/calmodulin-dependent protein kinase II, beta	1.4	24.8	1	0	0	0	0	6	0
Mcmm8	Ccm2	11	6.45	cerebral cavernous malformation 2 homolog (human)	0.83	9.5	0	0	3	0	0	6	0
Mcmm8	Ascc2	11	4.54	activating signal cointegrator 1 complex subunit 2	2.74	5.5	0	0	0	0	0	6	0
Mcmm8	Nipsnap1	11	4.77	4-nitrophenylphosphatase domain and non-neuronal SNAP25-like protein homolog 1	2.5	3.9	0	0	1	1	0	6	0
Mcmm8	Figln1	11	11.69	figletin-like 1	4.41	3.5	0	0	0	0	1	6	0
Mcmm8	Aebp1	11	5.76	AE binding protein 1	1.51	2.8	6	0	0	5	0	6	0
Mcmm8	Osm	11	4.14	oncostatin M	3.14	2.4	27	11	3	24	0	6	0
Mcmm8	Il9r	11	32.09	interleukin 9 receptor	24.81	-	0	0	0	1	10	4.6	1
Mcmm8	Spred2	11	19.82	sprouty-related, EVH1 domain containing 2	12.55	10.8	0	1	1	1	0	4.2	0
Mcmm8	Vrk2	11	26.37	vaccinia related kinase 2	19.1	8.9	0	0	1	0	3	4.2	0
Mcmm8	Etaa1	11	17.84	Ewing's tumor-associated antigen 1	10.57	7.3	0	0	0	0	2	4.2	0
Mcmm8	Psmc4	11	30.67	proteasome (prosome, macropain) activator subunit 4	23.4	5.8	0	0	1	0	0	4.2	0
Mcmm8	Ehbp1	11	21.91	EH domain binding protein 1	14.63	3.5	2	0	1	0	1	4.2	0
Mcmm8	Egfr	11	16.65	epidermal growth factor receptor	9.38	2.6	755	298	234	508	0	4.2	0
Mcmm8	Peli1	11	20.99	pellino 1	13.72	2.6	0	0	0	0	0	4.2	0
Mcmm8	Ugp2	11	21.22	UDP-glucose pyrophosphorylase 2	13.95	2.5	0	0	0	0	0	4.2	0
Mcmm8	Comm1	11	22.73	COMM domain containing 1	15.46	2.5	5	1	0	0	0	4.2	0
Mcmm9	Gtf2a1	12	92.79	general transcription factor II A, 1	2.81	-	1	0	0	0	1	5.7	1
Mcmm9	Mpp5	12	79.85	membrane protein, palmitoylated 5 (MAGUK p55 subfamily member 5)	15.75	2.8	0	0	0	0	1	4.9	0
Mcmm9	Slc10a1	12	82.05	solute carrier family 10 (sodium/bile acid cotransporter family), member 1	13.55	-	12	0	0	0	1	4.9	1
Mcmm10	Dync2li1	17	85.03	dynein cytoplasmic 2 light intermediate chain 1	3.53	22.8	0	0	0	0	1	5.3	0
Mcmm10	Lrpprc	17	85.1	leucine-rich PPR-motif containing	3.46	7.3	1	3	10	1	5	5.3	0
Mcmm10	Pigf	17	87.4	phosphatidylinositol glycan anchor biosynthesis, class F	1.16	2.7	3	0	0	6	1	5.3	0
Mcmm10	Ttc7	17	87.68	tetratricopeptide repeat domain 7	0.88	2.6	0	0	0	0	0	5.3	0
Mcmm10	Msh6	17	88.37	mutS homolog 6 (E. coli)	0.19	-	1	0	2	0	2	5.3	1
Mcmm10	Fez2	17	78.77	fasciculation and elongation protein zeta 2 (zygin II)	9.79	3.7	0	1	1	0	0	4.9	0
Mcmm10	Heatr5b	17	79.15	HEAT repeat containing 5B	9.41	-	0	0	0	0	2	4.9	1
Mcmm10	Vit	17	78.91	vitron	9.65	-	102	19	9	36	11	4.9	1
Mcmm10	Mta3	17	84.11	metastasis associated 3	4.45	4.3	1	0	0	1	2	4.8	0
Mcmm10	Thada	17	84.59	thyroid adenoma associated	3.97	-	4	0	0	0	14	4.8	1
Mcmm10	Pleckhh2	17	84.91	pleckstrin homology domain containing, family H (with MyTH4 domain) member 2	3.65	-	0	0	1	0	11	4.8	2
Mcmm10	Pkdcc	17	83.61	protein kinase domain containing, cytoplasmic	4.95	10.8	0	0	0	0	2	4.5	0
Mcmm10	Hnrpll	17	80.43	heterogeneous nuclear ribonucleoprotein L-like	8.13	6.6	0	0	0	0	1	4	0
Mcmm10	Galm	17	80.53	galactose mutarotase	8.03	4.9	1	0	0	0	2	4	0
Mcmm10	Srsf7	17	80.6	serine/arginine-rich splicing factor 7	7.96	3.1	0	0	0	0	0	4	0
Mcmm10	Fam179a	17	72.02	family with sequence similarity 179, member A	16.54	-	0	0	0	0	5	3.7	1
Mcmm10	Myom1	17	71.37	myomesin 1	17.19	-	0	0	0	0	5	3.7	1

^a, Number of PubMed results for gene name AND listed subject term

^b, While these genes did not meet our eQTL or PROVEAN criteria, these are the only 3 genes in this interval

Yellow highlighting denotes our top candidate genes at each QTL

Supplemental Table IV. All amino acid variants determined to be "deleterious" by PROVEAN for Mcmm QTLs compared to reference allele

QTL Locus	Gene	Chr	Mb Position	dbSNP	Protein Accession	Reference allele	AKR/J allele	DBA/2J allele	AA Variant	PROVEAN Score
Mcmm3	Zfp663	2	165.18	rs28245427	NP_001005425.1	A	G	- ^a	H444Q	-6.03
Mcmm3	Pla2g4f	2	120.13	rs27459550	NP_001019316.1	C	A	-	D507Y	-6.02
Mcmm3	Aqr	2	113.97	rs28271968	NP_033832.2	G	A	-	P346S	-5.09
Mcmm3	Macro2	2	140.25	rs50246652	NP_082663.1	G	-	T	V66F	-5.00
Mcmm3	Spnb5	2	119.90	rs223277097	XP_006500600.1	T	C	-	E1184G	-4.92
Mcmm3	Fbn1	2	125.21	rs27452005	NP_032019.2	C	-	T	D492N	-4.66
Mcmm3	Olfr1241	2	89.32	rs232833676	NP_666666.1	T	C	-	T237A	-4.59
Mcmm3	Zfyve19	2	119.04	rs33333368	NP_001158299.1	C	T	-	P164L	-4.41
Mcmm3	Olfr1289	2	111.32	rs27464429	NP_666516.1	T	G	-	L9R	-4.28
Mcmm3	Zfp341	2	154.46	rs13476853	NP_955008.2	A	-	G	D439G	-4.22
Mcmm3	Spnb5	2	119.90	rs27441671	XP_006500600.1	G	T	-	A1059D	-4.18
Mcmm3	Macro2	2	140.25	rs27219685	NP_082663.1	A	-	G	Q55R	-4.00
Mcmm3	Macro2	2	140.25	rs48383988	NP_082663.1	G	-	T	L63F	-4.00
Mcmm3	Lbp	2	158.15	rs27303831	NP_032515.2	T	C	-	Y284H	-3.96
Mcmm3	Cd44	2	102.67	rs29864230	NP_001034239.1	G	-	A	H361Y	-3.53
Mcmm3	Spnb5	2	119.89	rs46195182	XP_006500600.1	T	A	-	Q1584L	-3.48
Mcmm3	Spnb5	2	119.91	rs250549899	XP_006500600.1	C	A	-	Q409H	-3.33
Mcmm3	Spnb5	2	119.87	rs27457713	XP_006500600.1	C	T	-	E3148K	-3.31
Mcmm3	Pla2g4f	2	120.13	rs27459553	NP_001019316.1	G	A	-	A526V	-3.25
Mcmm3	Lama5	2	179.93	rs29578434	NP_001074640.1	C	-	T	D1058N	-3.23
Mcmm3	Epb4.2	2	120.85	rs27422960	NP_038541.1	A	-	T	C398S	-3.11
Mcmm3	Bpi	2	158.09	rs48239330	NP_808518.1	G	-	A	D149N	-3.00
Mcmm3	Cst11	2	148.58	rs28210804	NP_808323.1	C	-	T	T99M	-2.90
Mcmm3	Olfr52	2	86.02	rs28028940	NP_666794.1	C	-	A	D299Y	-2.88
Mcmm3	Nusap1	2	119.45	rs33363555	NP_001036117.1	C	-	T	T85M	-2.83
Mcmm3	Kif16b	2	142.54	rs27203630	NP_001074602.1	T	-	C	D929G	-2.80
Mcmm3	Casc5	2	118.90	rs27471478	NP_083893.2	A	T	-	K967N	-2.80
Mcmm3	Zfp663	2	165.18	rs253362248	NP_001005425.1	C	G	-	G446A	-2.75
Mcmm3	Olfr1290	2	111.33	rs27464412	NP_001265716.1	G	C	-	L17V	-2.74
Mcmm3	Spnb5	2	119.91	rs27441617	XP_006500600.1	T	C	-	H91R	-2.72
Mcmm3	Cd93	2	148.27	rs29880912	NP_034870.1	T	-	G	N264H	-2.71
Mcmm3	Ganc	2	120.25	rs27443939	NP_766260.2	C	T	-	T90I	-2.63
Mcmm3	Bpifa2	2	153.84	rs27347441	NP_032979.1	A	-	G	S212G	-2.57
Mcmm3	Bpifa2	2	153.84	rs242278248	NP_032979.1	C	-	A	P178H	-2.53
Mcmm3	Tmem62	2	120.82	rs27423047	NP_780494.1	T	-	C	V393A	-2.50
Mcmm4	lbsp	5	104.74	rs49148059	NP_032344.2	G	-	T	G197V	-5.96
Mcmm4	Mepe	5	104.77	rs49877953	NP_444402.2	G	-	A	G271S	-5.26
Mcmm4	Mepe	5	104.77	rs46782475	NP_444402.2	C	-	T	S313L	-4.84
Mcmm4	Epha5	5	84.54	rs33093662	NP_031963.2	G	-	A	R532C	-4.09
Mcmm4	lbsp	5	104.74	rs52386424	NP_032344.2	G	-	A	G143E	-3.50
Mcmm4	Npffr2	5	90.00	rs33223269	NP_573455.2	T	-	C	I89T	-3.37
Mcmm4	Mepe	5	104.77	rs51820957	NP_444402.2	C	-	A	S267R	-3.19
Mcmm4	Tmprss11g	5	86.92	rs31680434	NP_796136.2	T	-	C	T238A	-3.16
Mcmm4	Mepe	5	104.77	rs47716354	NP_444402.2	T	-	C	L371P	-3.04
Mcmm4	Cenpc1	5	86.47	rs31660491	NP_031709.2	T	-	G	K418T	-3.01
Mcmm4	Cox18	5	90.65	rs31692127	NP_001028482.2	A	-	G	Y252H	-2.58
Mcmm5	Mug2	6	122.03	rs30427541	NP_032672.2	C	-	A	H1064Q	-7.31
Mcmm5	A2m	6	121.61	rs30949689	NP_783327.2	C	-	A	T898K	-5.88
Mcmm5	A2m	6	121.62	rs50350755	NP_783327.2	A	C	-	E1173A	-4.70
Mcmm7	Tph2	10	114.52	rs33849125	NP_775567.2	G	-	C	P447R	-7.75
Mcmm7	Taar1	10	23.64	rs33645709	NP_444435.1	C	-	A	P77T	-7.55
Mcmm7	Stab2	10	86.40	rs48050828	NP_619614.1	C	-	T	G864D	-6.29
Mcmm7	Hcn2	10	79.19	rs247436022	NP_032252.1	C	T	-	R261C	-5.54
Mcmm7	Utrn	10	12.41	rs249408076	NP_035812.3	G	A	-	P1283L	-5.14
Mcmm7	Otogl	10	107.21	rs30631797	NP_001171038.1	T	-	C	N2170S	-4.57
Mcmm7	Gm6713	10	85.17	rs107765457	XP_006514427.1	A	-	T	I178K	-4.34

Mcmm7	Olf822	10	129.51	rs216067757	NP_666882.1	C	T	-	S249L	-4.32
Mcmm7	Gm6713	10	85.17	rs237987689	XP_006514427.1	C	-	T	D185N	-4.24
Mcmm7	Il22ra2	10	19.34	rs46108038	NP_839989.2	C	T	-	P30L	-3.95
Mcmm7	Utp20	10	88.24	rs50984008	NP_780367.2	G	A	-	P1225S	-3.10
Mcmm7	Phactr2	10	12.98	rs33593279	NP_001028429.1	G	-	T	S217Y	-2.56
Mcmm8	Myo1g	11	6.41	rs6153562	NP_848534.2	T	C	-	H467R	-4.62
Mcmm8	Il9r	11	32.09	rs48507356	NP_001127930.1	G	-	A	S68L	-4.37
Mcmm8	Npc1l1	11	6.13	rs26899815	NP_997125.2	C	A	-	G226C	-3.13
Mcmm8	Pkd1l1	11	8.85	rs29405661	XP_011242102.1	A	-	G	F602L	-2.97
Mcmm8	4930415F15Rik	11	11.41	rs213396354	NP_082945.1	G	T	-	R116I	-2.65
Mcmm9	Gtf2a1	12	92.80	rs29163189	NP_113568.2	A	-	G	Y367H	-3.30
Mcmm9	Slc10a1	12	82.06	rs245884573	NP_001171032.1	T	A	-	I279F	-3.29
Mcmm10	Heatr5b	17	79.19	rs49687971	NP_001074648.1	T	C	-	D1294G	-6.10
Mcmm10	Msh6	17	88.38	rs261524856	NP_034960.1	C	T	-	R384C	-5.22
Mcmm10	Thada	17	84.84	rs29751673	NP_898842.2	G	-	A	S675L	-3.63
Mcmm10	Plekhh2	17	84.97	rs29751293	NP_808274.2	C	-	T	S681L	-3.01
Mcmm10	Myom1	17	71.45	rs47080265	NP_001077403.1	T	-	A	D1100E	-2.96
Mcmm10	Fam179a	17	72.07	rs33161731	NP_796061.2	G	-	A	V783M	-2.78
Mcmm10	Vit	17	79.00	rs45906836	NP_001183957.1	A	G	-	S253G	-2.70
Mcmm10	Plekhh2	17	84.96	rs108355503	NP_808274.2	A	-	T	Q167H	-2.50

^a, denotes identical to the reference allele

Supplemental Table V. *Mcm* QTL genes cross-referenced against the human GWAS catalog for atherosclerosis relevant traits

Locus	Gene	Chr	PMID	Disease Trait
Mcmm1	Cacna1e	1	23870195	Coronary artery calcification
Mcmm1	Cacna1e	1	27098658	Presence of antiphospholipid antibodies
Mcmm3	Cst3	2	24952865	Plasma cystatin c levels in acute coronary syndrome
Mcmm3	Cst3	2	24952865	Plasma cystatin c levels in acute coronary syndrome
Mcmm3	Dstn	2	23509613	Presence of antiphospholipid antibodies
Mcmm3	Lrp4	2	24097068	HDL cholesterol
Mcmm3	Lrp4	2	20686565	HDL cholesterol
Mcmm3	Lrp4	2	28334899	HDL cholesterol levels
Mcmm3	Macrocl2	2	27098658	Presence of antiphospholipid antibodies
Mcmm3	Macrocl2	2	23509613	Presence of antiphospholipid antibodies
Mcmm3	Macrocl2	2	27098658	Presence of antiphospholipid antibodies
Mcmm3	Snx5	2	25961943	Cholesterol, total
Mcmm3	Snx5	2	25961943	LDL cholesterol
Mcmm3	Snx5	2	24097068	LDL cholesterol
Mcmm3	Snx5	2	28334899	LDL cholesterol levels
Mcmm4	Mepe	5	21779381	Cardiovascular disease risk factors
Mcmm5	Apobec1	6	28334899	HDL cholesterol levels
Mcmm7	Stab2	10	21878436	Coronary restenosis
Mcmm7	Utp20	10	17903303	Coronary artery calcification
Mcmm8	Camk2b	11	22399527	Metabolic syndrome
Mcmm8	Ehbp1	11	24097068	LDL cholesterol
Mcmm8	Ehbp1	11	28334899	LDL cholesterol levels
Mcmm8	Npc111	11	25961943	Cholesterol, total
Mcmm8	Npc111	11	20686565	Cholesterol, total
Mcmm8	Npc111	11	24097068	Cholesterol, total
Mcmm8	Npc111	11	25961943	LDL cholesterol
Mcmm8	Npc111	11	20686565	LDL cholesterol
Mcmm8	Npc111	11	24097068	LDL cholesterol
Mcmm8	Npc111	11	28334899	LDL cholesterol levels
Mcmm8	Npc111	11	28334899	Total cholesterol levels
Mcmm8	Peli1	11	21221998	Kawasaki disease
Mcmm10	Dync2li1	17	27286809	C-reactive protein levels or total cholesterol levels (pleiotropy)

Reference List

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- (3) Yu L, Nian Z, Sang J. Osteosarcoma amplified 9 is highly expressed in mouse adipocytes and controls lipid storage. *Mol Med Rep* 2011;4:687-92.
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