

Table S1. Microarray Analysis of Rap1-WT versus Rap1-KO White Adipose Tissue, Related to Results

Analysis revealed 118 deregulated genes. For each genotype, three mice were analyzed. The table shows the list of differentially expressed genes. Ranking is by p Value.

Gene Symbol	logFC [WT vs KO]	t Value	p Value
Terf2ip	-0.93009	-4.0099	0.00606
Mapk12	-0.75110	-3.8999	0.00692
Fam63b	0.74167	3.7802	0.00801
Raly	-0.72633	-3.7551	0.00826
Hmgcs2	-0.58801	-3.7347	0.00847
Id1	-0.80697	-3.6954	0.00890
Dennd5b	-0.54040	-3.5652	0.01048
Fam53b	0.52287	3.5637	0.01050
Bhlhb9	-0.58515	-3.5016	0.01137
Dock9	-0.60167	-3.4619	0.01196
Nr4a1	-0.57139	-3.4573	0.01203
Ifit2	-0.63751	-3.4510	0.01213
Mafb	-0.97356	-3.3986	0.01298
Ifit1	-0.72589	-3.3834	0.01323
Fam217b	0.60909	3.3801	0.01329
Mal2	0.63019	3.3403	0.01399
Amot	-0.56250	-3.3339	0.01411
B230214O09Rik	-0.64306	-3.3245	0.01428
Postn	-0.77287	-3.2639	0.01546
Tstd3	0.62569	3.2576	0.01559
Sc4mol	0.61626	3.1615	0.01770
Fst	-0.79022	-3.1492	0.01799
Enpp2	-0.47443	-3.1485	0.01801

Rgmb	-0.46898	-3.1247	0.01859
Alas1	0.66434	3.0891	0.01949
Numb	-0.46980	-3.0850	0.01960
Syn2	0.47054	3.0679	0.02005
Gpr160	-0.51373	-3.0482	0.02059
Tpst1	-0.77637	-3.0417	0.02077
Simc1	-0.45830	-3.0315	0.02106
Klhl24	-0.43996	-3.0204	0.02137
Hes1	-0.40597	-3.0109	0.02165
Anks1	0.49298	3.0046	0.02183
Dcun1d5	-0.49679	-2.9971	0.02206
Lama2	-1.05910	-2.9872	0.02235
Setd5	-0.53591	-2.9547	0.02336
Enpp3	-0.59154	-2.9536	0.02339
St3gal6	-0.86604	-2.9412	0.02379
Clk2	-0.44891	-2.9166	0.02460
Memo1	0.43634	2.9061	0.02495
3110045C21Rik	0.44758	2.9005	0.02514
Psmc8	-0.77659	-2.8919	0.02544
Atp10d	-0.52159	-2.8885	0.02556
Tmem86a	-0.75045	-2.8702	0.02620
Mid1ip1	0.81477	2.8629	0.02646
Usp18	-0.68447	-2.8433	0.02718
Pydc4	-0.46191	-2.8388	0.02735
Icam2	-0.59665	-2.8143	0.02829
Cyp51	0.72924	2.8031	0.02872
P2ry14	-0.59779	-2.7990	0.02889

Bclaf1	-0.50821	-2.7938	0.02909
4930445K14Rik	-0.42289	-2.7912	0.02920
AA407331	-0.43503	-2.7763	0.02980
Pafah1b1	-0.44926	-2.7731	0.02994
Taf13	0.36342	2.7683	0.03013
Clk1	-0.64631	-2.7671	0.03018
Ahctf1	-0.47829	-2.7549	0.03070
Pdgfra	-1.07283	-2.7450	0.03112
Kpna1	0.42141	2.7422	0.03124
A030001D16Rik	0.54739	2.7364	0.03149
Myh10	-0.39114	-2.7336	0.03161
Vav3	-0.53335	-2.7231	0.03207
Efcab14	-0.46119	-2.7225	0.03210
1810010H24Rik	-0.42608	-2.7145	0.03246
Ces1f	-0.63053	-2.7039	0.03294
Acaa1b	-0.63956	-2.7003	0.03310
Kctd12	-0.75684	-2.6961	0.03329
A530020G20Rik	-0.55624	-2.6829	0.03391
Hsd17b7	0.62855	2.6712	0.03447
9130004J05Rik	-0.39400	-2.6700	0.03452
Rps6kb1	-0.51596	-2.6566	0.03517
Trav9d-3	-0.82703	-2.6555	0.03523
Sparcl1	-0.62877	-2.6526	0.03537
Prrc2c	-0.47020	-2.6522	0.03539
Mmp2	-1.22833	-2.6502	0.03549
Hs6st2	-0.79398	-2.6492	0.03553
Irf7	-0.47938	-2.6442	0.03578

Ifit3	-0.82707	-2.6252	0.03674
Tnxb	-0.98296	-2.6224	0.03689
Dennd4a	0.46222	2.6044	0.03782
Pyhin1	-0.67904	-2.5987	0.03812
Sh2b3	-0.52124	-2.5965	0.03824
Oaf	-0.47821	-2.5929	0.03844
Nrbf2	0.43941	2.5807	0.03910
St6galnac4	-0.38926	-2.5805	0.03911
Ogt	-0.39209	-2.5605	0.04022
Dpp7	-0.36337	-2.5440	0.04116
Ilf3	-0.40414	-2.5245	0.04230
Rtp4	-0.78424	-2.5205	0.04254
Akap8l	-0.43925	-2.5196	0.04259
Ttc30a1	0.43645	2.5189	0.04263
Ednrb	-0.84907	-2.5164	0.04278
March7	-0.46942	-2.5114	0.04308
Kdm3a	-0.33842	-2.5097	0.04319
Zscan26	-0.42964	-2.5050	0.04347
Snrnp48	-0.45363	-2.5046	0.04350
Frmd4a	-0.57246	-2.5046	0.04350
Pde4b	-0.66520	-2.4961	0.04402
Grtp1	0.51350	2.4872	0.04457
Ap2b1	-0.57384	-2.4828	0.04485
Actn4	-0.39663	-2.4819	0.04491
Sox18	-0.49705	-2.4785	0.04512
Nrcam	-0.42692	-2.4772	0.04521
Gbp6	-0.37907	-2.4744	0.04538

Idi1	0.78439	2.4742	0.04540
Tmem140	-0.44286	-2.4721	0.04553
Leo1	0.52365	2.4707	0.04562
Arpc3	-0.42771	-2.4649	0.04599
1500012F01Rik	-0.37308	-2.4506	0.04693
Xaf1	-0.46399	-2.4363	0.04789
Smyd1	-0.99178	-2.4344	0.04801
Ntn4	-0.57687	-2.4324	0.04815
Megf9	0.51605	2.4280	0.04845
Tm4sf1	-0.43267	-2.4207	0.04895
Klf4	-0.92237	-2.4152	0.04933
Rbm47	0.44231	2.4149	0.04935
Sept4	-0.49214	-2.4118	0.04957
Dpm1	0.46628	2.4087	0.04979

Table S2. Gene Ontology of Differentially Expressed Genes in Wild-Type versus Knockout Rap1 White Adipose Tissue, Related to Results

The top 10 gene ontologies by adjusted p-value (FDR) are listed below.

Gene Ontology Name	# Genes in Overlap	FDR	Description
Negative Regulation of Cellular Metabolic Process	8	2.11E-05	Any process that stops, prevents or reduces the frequency, rate or extent of the chemical reactions and pathways by which individual cells transform chemical substances.
Negative Regulation of Metabolic Process	8	2.11E-05	Any process that stops, prevents or reduces the frequency, rate or extent of the chemical reactions and pathways within a cell or an organism.
Negative Regulation of Nucleic Acid Metabolism	7	5.71E-05	Any process that stops, prevents or reduces the frequency, rate or extent of the chemical reactions and pathways involving nucleobases, nucleosides, nucleotides and nucleic acids.
Regulation of Nucleic Acid Metabolism	10	6.62E-05	Any process that modulates the frequency, rate or extent of the chemical reactions and pathways involving nucleobases, nucleosides, nucleotides and nucleic acids.
Regulation of Cellular Metabolic Process	11	6.62E-05	Any process that modulates the frequency, rate or extent of the chemical reactions and pathways by which individual cells transform chemical substances.
Regulation of Metabolic Process	11	6.62E-05	Any process that modulates the frequency, rate or extent of the chemical reactions and pathways within a cell or an organism.
Negative Regulation of Cellular Process	10	6.79E-05	Any process that stops, prevents or reduces the frequency, rate or extent of cellular processes, those that are carried out at the cellular level, but are not necessarily restricted to a single cell.
Negative Regulation of Biological Process	10	9.07E-05	Any process that stops, prevents or reduces the frequency, rate or extent of a biological process.
Negative Regulation of Transcription	6	1.83E-04	Any process that stops, prevents or reduces the frequency, rate or extent of transcription.
System Development	10	6.09E-04	The process whose specific outcome is the progression of an organismal system over time, from its formation to the mature structure

Table S3. Gene Set Enrichment Analysis of Differentially Expressed Genes in Wild-Type versus Knockout Rap1 White Adipose Tissue, Related to Results

The top 10 gene sets by adjusted p-value (FDR) are listed below.

Pathway / Gene Set	Collection	# Genes in Overlap	FDR	Description
Interferon Signaling	Reactome	8	1.50E-06	Genes involved in Interferon Signaling
Interferon Alpha Beta Signaling	Reactome	6	2.34E-06	Genes involved in Interferon alpha/beta signaling
Cytokine Signaling in Immune System	Reactome	8	3.12E-05	Genes involved in Cytokine Signaling in Immune system
Developmental Biology	Reactome	9	3.26E-05	Genes involved in Developmental Biology
Immune System	Reactome	12	8.37E-05	Genes involved in Immune System
Axon Guidance	Reactome	6	2.54E-03	Genes involved in Axon guidance
Focal Adhesion	KEGG	5	1.02E-02	Focal adhesion
Regulation of Actin Cytoskeleton	KEGG	5	1.25E-02	Regulation of actin cytoskeleton
Leukocyte Transendothelial Migration	KEGG	4	1.42E-02	Leukocyte transendothelial migration
ATF2 Pathway	PID	3	3.15E-02	ATF-2 transcription factor network

Table S4. Microarray Analysis of Rap1-KO versus Rap1-WT Liver Tissue, Related to Results

Analysis revealed 62 deregulated genes. For each genotype, three mice were analyzed. The table shows the list of differentially expressed genes. Ranking is by p Value.

Gene Symbol	logFC[WT vs KO]	t Value	P Value	FDR
Hsd3b5	2.1322	9.4781	5.38E-19	3.326E-15
Serpina12	1.6147	7.9591	2.85E-14	8.818E-11
Mt2	-1.5532	-7.5885	3.38E-13	6.964E-10
Chka	-1.2626	-6.4922	3.13E-10	4.713E-07
Mt1	-1.2912	-6.4585	3.81E-10	4.713E-07
Serpina4-ps1	1.6926	6.3467	7.31E-10	7.531E-07
Creld2	1.1558	5.6542	3.41E-08	3.009E-05
Egfr	1.0750	5.5839	4.94E-08	3.817E-05
Rgs16	1.1849	5.5578	5.66E-08	3.888E-05
Arrdc3	1.0549	5.3940	1.32E-07	8.168E-05
Cyp2b10	-1.0241	-5.2138	3.28E-07	1.844E-04
Mup10	0.9839	5.0945	5.91E-07	3.046E-04
Id1	-0.9466	-4.7881	2.55E-06	1.214E-03
Elovl6	0.9102	4.7265	3.40E-06	1.456E-03
Lpl	-1.0131	-4.7178	3.53E-06	1.456E-03
Slc22a7	0.8989	4.6658	4.48E-06	1.733E-03
Gsta2	-0.9298	-4.6073	5.85E-06	2.009E-03
Agxt2l1	-0.8932	-4.6072	5.85E-06	2.009E-03
Mid1	-0.8355	-4.3242	2.03E-05	6.615E-03
Ero1b	0.8267	4.2660	2.61E-05	8.058E-03
Sdf2l1	0.8355	4.2212	3.15E-05	9.271E-03
Nipal1	-0.8116	-4.1981	3.47E-05	9.754E-03

Esm1	-0.8333	-4.1573	4.11E-05	1.093E-02
Egr1	-0.9205	-4.1499	4.24E-05	1.093E-02
Hspa1b	0.7957	4.1138	4.93E-05	1.218E-02
Nnmt	-0.7931	-4.0377	6.72E-05	1.599E-02
Klf10	0.7880	4.0184	7.27E-05	1.665E-02
Angptl4	0.7880	3.9536	9.43E-05	2.083E-02
Mmd2	-0.8070	-3.9149	0.000110012	2.266E-02
Slco1a1	0.7870	3.9126	0.000111014	2.266E-02
Aacs	0.7445	3.9068	0.000113619	2.266E-02
Terf2ip	-0.7365	-3.8642	0.000134346	2.595E-02
Cyp7a1	-0.8243	-3.8482	0.000143009	2.633E-02
Cyp7b1	0.7579	3.8400	0.00014767	2.633E-02
Hyou1	0.7582	3.8375	0.000149088	2.633E-02
Ugt2b37	0.7293	3.7799	0.000186316	3.151E-02
Lepr	-0.7280	-3.7768	0.000188568	3.151E-02
Elovl3	0.7495	3.7229	0.000231744	3.770E-02
Id2	-0.7677	-3.7137	0.000239925	3.803E-02
Ppargc1a	-0.7158	-3.6806	0.000271909	4.202E-02
Cyp2b13	-0.8034	-3.6077	0.000357023	5.383E-02
Vldlr	-0.6976	-3.5928	0.000377239	5.553E-02
Cyp3a16	0.7437	3.5056	0.000518949	7.461E-02
Sult5a1	0.6750	3.4823	0.000564581	7.932E-02
Vnn1	0.7384	3.4555	0.000621457	8.537E-02
Skil	-0.6697	-3.4465	0.000641739	8.624E-02
Gas2	-0.6580	-3.4109	0.000728292	9.579E-02
Sdc1	-0.6534	-3.3754	0.000825547	1.063E-01
Id3	-0.7032	-3.3691	0.000843915	1.065E-01

Dio1	0.6524	3.3607	0.000869201	1.075E-01
Cyp2d9	0.7033	3.3314	0.000962601	1.167E-01
Dbp	0.8196	3.3237	0.000988618	1.175E-01
Hao2	-0.7095	-3.2980	0.001080454	1.260E-01
Nucb2	0.6328	3.2849	0.001130413	1.294E-01
9030619P08Rik	0.6377	3.2741	0.001172967	1.318E-01
Got1	-0.6318	-3.2615	0.001224608	1.352E-01
Aldh1b1	-0.6276	-3.2299	0.001363727	1.479E-01
Cyp3a44	0.6247	3.1929	0.001544967	1.647E-01
Rsad2	-0.6076	-3.1800	0.0016132	1.674E-01
Ptbp1	0.6155	3.1780	0.001624262	1.674E-01
Prom1	-0.6348	-3.1272	0.001923001	1.949E-01
Fabp5	0.6093	3.1192	0.001974347	1.969E-01

Table S5. Gene Ontology of Differentially Expressed Genes in Wild-Type versus Knockout Rap1 Liver, Related to Results
The top 10 gene ontologies by adjusted p-value (FDR) are listed below.

Gene Ontology Name	# Genes in Overlap	FDR	Description
Nucleobase, Nucleoside, Nucleotide, and Nucleic Acid Metabolic Process	11	2.57E-05	The chemical reactions and pathways involving nucleobases, nucleosides, nucleotides and nucleic acids.
Regulation of Cellular Metabolic Process	9	2.57E-05	Any process that modulates the frequency, rate or extent of the chemical reactions and pathways by which individual cells transform chemical substances.
Regulation of Metabolic Process	9	2.57E-05	Any process that modulates the frequency, rate or extent of the chemical reactions and pathways within a cell or an organism.
Regulation of Nucleobase, Nucleoside, Nucleotide, and Nucleic Acid Metabolic Process	8	3.78E-05	Any process that modulates the frequency, rate or extent of the chemical reactions and pathways involving nucleobases, nucleosides, nucleotides and nucleic acids.
Negative Regulation of Transcription Factor Activity	3	7.17E-05	Any process that stops, prevents, or reduces the frequency, rate or extent of the activity of a transcription factor, any factor involved in the initiation or regulation of transcription.
Negative Regulation of DNA Binding	3	8.36E-05	Any process that stops, prevents. or reduces the frequency, rate or extent of DNA binding, selective interaction with deoxyribonucleic acid.
Negative Regulation of Binding	3	8.36E-05	Any process that stops or reduces the rate or extent of binding, the selective interaction of a molecule with one or more specific sites on another molecule.
Transcription	8	8.36E-05	The synthesis of either RNA on a template of DNA or DNA on a template of RNA.
Lipid Metabolic Process	6	8.53E-05	The chemical reactions and pathways involving lipids, compounds soluble in an organic solvent but not, or sparingly, in an aqueous solvent.
Negative Regulation of Nucleobase, Nucleoside, Nucleotide, and Nucleic Acid Metabolic Process	5	1.97E-04	Any process that stops, prevents, or reduces the frequency, rate or extent of the chemical reactions and pathways involving nucleobases, nucleosides, nucleotides and nucleic acids.

Table S6. Gene Set Enrichment Analysis of Differentially Expressed Genes in Wild-Type versus Knockout Rap1 Liver, Related to Results

The top 10 gene sets by adjusted p-value (FDR) are listed below.

Pathway / Gene Set	Collection	# Genes in Overlap	FDR	Description
Metabolism of Lipids and Lipoproteins	Reactome	9	1.22E-06	Genes involved in Metabolism of lipids and lipoproteins
PPAR Signaling Pathway	KEGG	4	2.80E-04	PPAR signaling pathway
REACTOME_ Fatty Acid Triacylglycerol and Ketone Body Metabolism	Reactome	5	2.80E-04	Genes involved in Fatty acid, triacylglycerol, and ketone body metabolism
Biological Oxidations	Reactome	4	3.30E-03	Genes involved in Biological oxidations
Circadian Clock	Reactome	3	4.69E-03	Genes involved in Circadian Clock
Transcriptional Regulation of White Adipocyte Differentiation	Reactome	3	9.82E-03	Genes involved in Transcriptional Regulation of White Adipocyte Differentiation
Synthesis of Very Long Chain Fatty Acyl-CoAs	Reactome	2	1.16E-02	Genes involved in Synthesis of very long-chain fatty acyl-CoAs
TGF-beta Signaling Pathway	KEGG	3	1.16E-02	TGF-beta signaling pathway
Endogenous Sterols	Reactome	2	1.16E-02	Genes involved in Endogenous sterols
Primary Bile Acid Biosynthesis	Reactome	2	1.16E-02	Genes involved in Integrin cell surface interactions

Table S7. Microarray Analysis of [Rap1-WT versus Rap1-KO] and [Rap1-WT versus Rap1-Mutant] Mouse Embryonic Fibroblasts, Related to Results

Analysis revealed 187 deregulated genes. For each genotype, three mice were analyzed. The table shows the list of differentially expressed genes. Ranking is by p Value. Differentially expressed genes that are bound by Rap1 based on the ChIP-seq data are marked as well as if the ChIP-binding site contains a TTAGGG motif. In addition, differentially expressed genes that are not fully or partially rescued by expression of Rap1 Δ TRF2 are marked.

Gene Symbol	logFC (WT vs KO)	t Value	P Value	Rap1 Bound	TTAGGG
Col3a1	3.3086	5.6872	1.374E-04		
Col5a2	2.7193	4.1305	1.648E-03	✓	
Prss35	1.5021	4.0537	1.879E-03	✓	✓
Aspn	2.0758	3.8789	2.538E-03	✓	✓
Adamts12	1.7769	3.7954	2.933E-03		
Slc7a5	1.5469	3.7563	3.140E-03		
Prss23	2.1896	3.7017	3.454E-03	✓	
Col4a2	1.4512	3.6539	3.756E-03		
Col5a1	2.3214	3.5401	4.588E-03		
Bmp4	1.7372	3.5224	4.733E-03		
Tgfb2	1.6195	3.4154	5.719E-03		
Pycr1	1.5418	3.4137	5.736E-03		
Fndc1	1.7392	3.3767	6.125E-03		
Htra1	2.3720	3.3648	6.256E-03		
Nid2	1.7873	3.3622	6.285E-03		
Col1a1	2.8724	3.3244	6.721E-03		
Pappa	1.5212	3.3046	6.963E-03		
Pck2	1.8683	3.2705	7.398E-03		
Jag1	1.1582	3.1419	9.307E-03	✓	✓
Pdgfrl	1.4010	3.1278	9.546E-03		

logFC [WT vs Mut]	Not Rescued
0.0887	
0.5272	
0.0823	
-0.3687	
-0.0822	
0.7915	
0.2723	
0.1380	
0.7517	
0.5091	
-0.0699	
0.7539	
-0.1901	
1.2930	
0.7114	
0.8146	
-0.3061	
1.2682	
-0.2725	
0.6602	

Aldh1l2	2.2664	3.1170	9.732E-03	✓	✓
Serpinb6b	1.4600	3.0912	1.019E-02	✓	
Ifit3	1.8372	3.0882	1.025E-02		
Fbn1	2.3845	3.0823	1.035E-02		
Cdkn1c	1.7914	3.0572	1.083E-02		
Gm22	1.1863	3.0456	1.106E-02		
Asns	1.8418	3.0454	1.106E-02		
H19	2.7181	3.0431	1.111E-02		
Mreg	-1.6876	-3.0421	1.113E-02	✓	✓
Gm9706	1.2664	3.0337	1.130E-02		
Nrn1	-1.3744	-2.9930	1.215E-02		
Trib3	1.4191	2.9901	1.221E-02		
Mx1	1.2787	2.9882	1.226E-02		
Ccdc80	1.6501	2.9695	1.267E-02		
Abcb1a	-1.0785	-2.9575	1.295E-02	✓	
Ctla2a	1.1572	2.9493	1.314E-02		
Cthrc1	2.5856	2.9404	1.336E-02		
Gclc	-1.7501	-2.9385	1.340E-02		
Adamts1	1.7944	2.9297	1.361E-02	✓	
Adamts5	2.0679	2.9085	1.414E-02		
Adamts4	1.1856	2.8795	1.489E-02		
Rspo3	2.0068	2.8585	1.547E-02	✓	
Pxdn	1.5100	2.8423	1.592E-02		
Wisp1	2.0515	2.8406	1.597E-02	✓	
Moxd1	1.4768	2.8311	1.625E-02		
Actg2	1.8323	2.8284	1.633E-02		
Boc	1.0348	2.8062	1.699E-02		

2.5633	✓
-0.3096	
-1.9287	
0.4874	
-0.2032	
0.2277	
1.8136	✓
1.2497	
-1.1689	
-0.0157	
0.3048	
1.4610	✓
-0.3557	
0.0464	
-0.4264	
-0.5546	
1.3169	
-0.8430	
1.0879	
-0.0281	
0.7987	
-0.2121	
0.9245	
0.3631	
-0.1166	
0.6320	
0.3645	

Il8	2.0111	2.7981	1.724E-02		
Crispld2	0.9466	2.7979	1.724E-02	✓	
Arhgap6	-1.0991	-2.7959	1.731E-02		
Ifi27l2a	1.6952	2.7956	1.732E-02		
Ifi44	1.6090	2.7855	1.763E-02		
P4ha1	1.6848	2.7840	1.768E-02	✓	
Pgm5	0.9257	2.7724	1.805E-02		
Tor3a	1.3108	2.7681	1.819E-02		
Cxcl2	1.9902	2.7629	1.836E-02		
Aldh18a1	2.1502	2.7571	1.855E-02		
Col4a5	1.2952	2.7461	1.892E-02		
Diras2	1.3334	2.7459	1.893E-02		
Slc1a6	1.5757	2.7415	1.908E-02		
Mfap5	1.4628	2.7275	1.956E-02	✓	
Npr3	1.1612	2.6960	2.070E-02	✓	
Matn2	1.7116	2.6902	2.092E-02	✓	
Crabp2	2.0081	2.6880	2.100E-02		
Spock3	1.3992	2.6769	2.142E-02		
Piezo2	0.9128	2.6602	2.207E-02		
Sertad4	1.6463	2.6601	2.208E-02	✓	
Col11a1	2.2862	2.6517	2.241E-02		
Col1a2	2.6931	2.6455	2.266E-02	✓	
Arsj	1.5750	2.6424	2.278E-02	✓	
Kcnma1	1.0406	2.6393	2.291E-02		
Sparc	1.5498	2.6379	2.297E-02	✓	
Kdelr3	1.8465	2.6373	2.299E-02	✓	
Lrrc17	1.8698	2.6248	2.351E-02		

-0.3073	
0.3180	
-0.2637	
-0.4010	
-0.7443	
1.8964	✓
-0.0903	
0.0150	✓
2.5010	
1.6404	
-0.2425	
0.8146	
0.2699	
1.1999	
1.1175	✓
1.2571	
1.1900	
0.0893	
-0.1406	
0.6821	
0.1036	
0.5597	
0.1177	
0.0128	
0.4328	
1.5295	
0.0179	

Mei4	1.2568	2.6137	2.399E-02		
Nedd9	1.1532	2.6085	2.421E-02	✓	
Lbh	1.2679	2.5996	2.460E-02	✓	
Postn	3.2059	2.5954	2.478E-02		
Slc7a3	1.0788	2.5942	2.484E-02		
Hmcn1	1.1458	2.5912	2.497E-02		
Slc7a2	-1.4652	-2.5884	2.510E-02		
P4ha2	2.2520	2.5760	2.566E-02		
Myo7a	1.0028	2.5733	2.578E-02		
Scd2	1.7926	2.5722	2.583E-02		
Ncoa7	1.2422	2.5701	2.593E-02		
Id2	-1.2548	-2.5667	2.609E-02		✓
Cyr61	2.0647	2.5654	2.615E-02	✓	
Col6a2	1.8228	2.5615	2.633E-02	✓	
Fzd2	1.6931	2.5559	2.659E-02		
Gbp7	0.9942	2.5532	2.673E-02		
Dusp6	-1.0308	-2.5473	2.701E-02		
Col4a1	1.0083	2.5444	2.715E-02		
Ly6a	1.4986	2.5403	2.734E-02	✓	
Plat	1.8975	2.5183	2.844E-02		
Gulp1	1.9521	2.5139	2.866E-02	✓	
Chac1	0.8576	2.5052	2.911E-02	✓	✓
Olfml2b	1.4561	2.5001	2.938E-02		
Psph	1.0863	2.4978	2.950E-02		
Col6a3	1.4045	2.4897	2.993E-02		
Col5a3	1.0566	2.4875	3.004E-02		
Igf2	2.4621	2.4850	3.018E-02		

0.6916	
0.6429	
1.2800	✓
-1.2868	
0.4923	
-0.3088	
-1.0415	
2.4276	✓
0.4880	
1.4322	
0.7906	
-0.4003	✓
1.5036	
0.4588	
0.4879	
-0.9990	
-0.3356	
-0.1342	
0.3889	
1.5563	
1.1076	
1.0017	✓
-0.3137	
1.2024	✓
0.8723	
0.3182	
-0.5922	

Mthfd2	1.6072	2.4847	3.019E-02		
Agtr2	1.1509	2.4771	3.061E-02		
Tubb2b	2.0461	2.4715	3.091E-02		
Reck	1.0034	2.4710	3.094E-02		
Cela1	-1.3810	-2.4698	3.100E-02		
Fibin	1.2758	2.4655	3.124E-02		
Igsf3	1.3724	2.4640	3.133E-02	✓	
Cxcl3	1.7015	2.4607	3.151E-02		
Ifi47	1.2052	2.4587	3.162E-02		
Pdlim2	1.3829	2.4481	3.223E-02	✓	✓
Itm2a	1.4033	2.4282	3.338E-02		
Pdgfd	1.8230	2.4226	3.372E-02		
Perp	-1.8998	-2.4194	3.391E-02		
Abi3bp	1.1379	2.4117	3.438E-02		
Glipr2	1.2576	2.4113	3.440E-02	✓	
Kcnj15	1.3368	2.4031	3.491E-02		
Adamts2	1.1752	2.3986	3.519E-02		
Lpp	1.2824	2.3976	3.525E-02		
Agrn	1.2321	2.3956	3.537E-02		
Lama4	1.5795	2.3934	3.552E-02		
Cxcl10	1.9461	2.3920	3.560E-02		
Col8a1	1.2692	2.3906	3.569E-02		
Nupr1	1.6348	2.3877	3.588E-02		
Tnc	2.0613	2.3819	3.625E-02		
Pkia	1.2808	2.3796	3.639E-02		
Wls	1.6031	2.3751	3.668E-02		
Fkbp7	1.3835	2.3732	3.681E-02		

1.9112	✓
-0.2552	
1.1009	
0.5838	
-1.2274	
-0.1742	
0.6867	
0.3301	
-1.3054	
0.4722	
1.0620	
0.9702	
-1.6443	
-1.0743	
1.1670	✓
-0.1447	
-0.1219	
1.0388	
0.4604	
0.9943	
1.0949	✓
1.2072	✓
1.6798	✓
2.2004	
0.4269	
0.5261	
0.2661	

Fam101b	1.2022	2.3730	3.682E-02		
Ttc39c	-1.0269	-2.3661	3.727E-02		
Plekha4	1.1088	2.3657	3.730E-02		
Adamts6	0.9736	2.3557	3.797E-02	✓	
Tmtc1	0.8054	2.3553	3.799E-02		
Vegfc	0.9649	2.3515	3.825E-02		
Ncam1	1.8308	2.3489	3.843E-02		
Prkcdbp	1.3863	2.3482	3.847E-02		
Kdm5b	0.8792	2.3468	3.857E-02		
Serpinb9	1.3580	2.3455	3.866E-02		
Tmeff1	1.4450	2.3420	3.890E-02	✓	
Sspn	1.4423	2.3375	3.921E-02		
lsg20	1.3752	2.3369	3.925E-02		
Specc1	1.4630	2.3367	3.926E-02	✓	
Slc35d1	-1.2964	-2.3325	3.956E-02		
Sema3e	1.5191	2.3299	3.974E-02		
Ephb2	1.0987	2.3283	3.985E-02		
Ogn	2.4014	2.3242	4.014E-02		
Glul	-1.2858	-2.3175	4.062E-02		
Dnmt3a	0.8292	2.3153	4.078E-02	✓	
Itgb1	1.0287	2.3121	4.101E-02	✓	
Selm	1.6085	2.3066	4.141E-02	✓	✓
Sorcs2	1.0537	2.3022	4.173E-02	✓	
Igfbp6	1.0916	2.2996	4.192E-02		
Cercam	1.0091	2.2947	4.228E-02		
Cyb5r1	1.4119	2.2943	4.231E-02		
Bmp2	-1.3995	-2.2900	4.264E-02		

0.1224	
0.1290	
-0.0650	
0.4117	
-0.1263	
0.3741	
1.5725	
0.9920	
0.3094	
-0.7770	
0.3584	
0.4889	
1.7070	✓
0.8466	
-1.3101	✓
0.7842	
0.8166	
-1.1457	
-0.9354	
0.0345	
0.7020	
0.6023	
0.1693	
0.8895	
0.5367	
1.3166	✓
-0.5828	

Xaf1	1.3675	2.2859	4.294E-02		
Tmem45a	1.9016	2.2839	4.309E-02		
Tmem243	-1.6149	-2.2754	4.374E-02		
Nov	1.9837	2.2697	4.419E-02		
Bcat1	1.5627	2.2669	4.441E-02		
Tgfr2	1.0093	2.2650	4.455E-02	✓	
Tfpi	0.9785	2.2646	4.459E-02		
Ddah2	1.2925	2.2644	4.460E-02		
Ppic	1.6199	2.2594	4.500E-02		
Fut11	0.7798	2.2498	4.576E-02	✓	
Fads3	1.3502	2.2436	4.626E-02		
Zfp521	1.5204	2.2426	4.635E-02	✓	
Maged2	1.2527	2.2405	4.652E-02		
Sephs2	-1.6081	-2.2306	4.733E-02		
Vcl	1.3216	2.2303	4.735E-02	✓	✓
Herc6	0.9077	2.2299	4.739E-02		
Fkbp9	1.1539	2.2285	4.751E-02		
Speg	1.7534	2.2278	4.756E-02		
Cdon	1.4480	2.2273	4.760E-02		
Adm	1.8641	2.2270	4.763E-02		
Pfkfb3	1.3271	2.2242	4.786E-02		
Oasl2	1.5240	2.2233	4.794E-02		
Pfkl	1.1498	2.2217	4.807E-02		
Arhgap28	0.9962	2.2215	4.809E-02	✓	
Fam214a	-1.0763	-2.2176	4.842E-02		
Sulf1	1.9567	2.2133	4.879E-02		
Prkd1	1.7641	2.2131	4.880E-02		

0.0698	
2.3809	✓
-0.9490	
-0.0889	
1.5836	✓
0.5834	
0.7818	
0.9085	
1.0214	
0.6015	
1.3011	✓
0.0181	
0.7351	
-1.3606	
0.8131	
-0.6473	
0.6583	
1.4236	
0.3428	
2.7680	
1.5937	
-0.8735	
1.1194	✓
0.7080	
-1.1301	✓
0.8702	
0.8893	

App	1.2677	2.2128	4.883E-02		
Trim30a	1.1404	2.2069	4.933E-02		
Fam114a1	0.9465	2.2064	4.938E-02		
Edil3	1.4905	2.2018	4.978E-02	✓	
Lamc1	1.0830	2.2007	4.988E-02	✓	

0.2572	
-0.1960	
0.3421	
1.1540	
0.5112	

Table S8. Gene Ontology of Differentially Expressed Genes in Wild-Type versus Knockout Rap1 MEFs, Related to Results

The top 10 gene ontologies by adjusted p-value (FDR) are listed below.

Gene Ontology Name	# Genes in Overlap	FDR	Description
Organ Development	22	9.16E-14	Development of a tissue or tissues that work together to perform a specific function or functions. Development pertains to the process whose specific outcome is the progression of a structure over time, from its formation to the mature structure.
Anatomical Structure Development	27	9.16E-14	The biological process whose specific outcome is the progression of an anatomical structure from an initial condition to its mature state.
Multicellular Organismal Development	25	8.15E-12	The biological process whose specific outcome is the progression of an organism over time from an initial condition (e.g. a zygote or a young adult) to a later condition (e.g. a multicellular animal or an aged adult).
System Development	23	8.15E-12	The process whose specific outcome is the progression of an organismal system over time, from its formation to the mature structure.
Skeletal Development	9	1.76E-08	The process whose specific outcome is the progression of the skeleton over time, from its formation to the mature structure.
Amino Acid and Derivative Metabolic Process	8	3.62E-07	The chemical reactions and pathways involving amino acids, organic acids containing one or more amino substituents, and compounds derived from amino acids.
Amino Acid Metabolic Process	7	1.31E-06	The chemical reactions and pathways involving amino acids, organic acids containing one or more amino substituents.
Negative Regulation of Biological Process	15	1.69E-06	Any process that stops, prevents, or reduces the frequency, rate or extent of a biological process. Biological processes are regulated by many means; examples include the control of gene expression, protein modification or interaction with a protein or substrate molecule.
Nitrogen Compound Biosynthetic Process	5	2.46E-06	The chemical reactions and pathways resulting in the formation of organic and inorganic nitrogenous compounds.
Tissue Development	8	2.46E-06	The process whose specific outcome is the progression of a tissue over time, from its formation to the mature structure.

Table S9. Gene Set Enrichment Analysis of Differentially Expressed Genes in Wild-Type versus Knockout Rap1 MEFs, Related to Results

The top 10 gene sets by adjusted p-value (FDR) are listed below.

Pathway / Gene Set	Collection	# Genes in Overlap	FDR	Description
Focal Adhesion	KEGG	18	2.20E-14	Focal adhesion
Extracellular Matrix Organization	Reactome	14	2.41E-14	Genes involved in Extracellular matrix organization
ECM Receptor Interaction	KEGG	15	2.52E-14	ECM-receptor interaction
Collagen Formation	Reactome	14	3.55E-14	Genes involved in Collagen formation
NCAM1 Interactions	Reactome	11	4.11E-14	Genes involved in NCAM1 interactions
NCAM Signaling for Neurite Out Growth	Reactome	11	5.98E-14	Genes involved in NCAM signaling for neurite out-growth
Signaling by PDGF	Reactome	13	6.83E-14	Genes involved in Signaling by PDGF
Axon Guidance	Reactome	14	4.07E-11	Genes involved in Axon guidance
Developmental Biology	Reactome	16	9.70E-11	Genes involved in Developmental Biology
Integrin Cell Surface Interactions	Reactome	9	1.01E-09	Genes involved in Integrin cell surface interactions