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SUPPLEMENTAL MATERIALS AND METHODS

Microarray processing and data.

The manufacturer's protocols were followed for the determination of gene expression using the GeneChip Mouse Genome 430 2.0 array (Affymetrix). Hybridized arrays were scanned with a scanner (Gene Chip 3000), and image generation and feature extraction were performed using operating software (GeneChip; both from Affymetrix). All arrays passed the manufacturer's quality specifications with respect to background and percent-present call rates.

To generate the demonstrated heat map (Fig. 6 A), a list of 290 differentially expressed probe sets (Table S1) from *Socs3* h-KO and littermate control mice were identified by the following procedure. Raw microarray data were processed and analyzed with Bioconductor (1) and normalized with the Bioconductor GeneChip Robust Multi-Array Average package (2). After data normalization, genes with significant evidence for differential expression were identified using the limma package (3) in Bioconductor. p-values were calculated with a modified *t* test in conjunction with an empirical Bayes method to moderate the standard errors of the estimated log-fold changes. p-values were adjusted for multiplicity with the Bioconductor package q value (4). Before adjusting p-values for multiplicity, normalized values were nonspecifically filtered by omitting values whose interquartile range was <0.25. The final list of 290 probe sets (Table S1) was determined by further filtering for fold change > 1.5 and unadjusted $P < 0.01$ (for which we found that the false discovery rate = 0.084).

The overall average intensity for the represented genes in the control littermate arrays was calculated and used as the baseline reference (black) in the demonstrated heatmap (Fig. 6 A). The shades of red or green in each bar on the heat map correspond to an intensity score relative to baseline. Affymetrix accession numbers for probe sets that were differentially regulated in *Socs3* h-KO samples were submitted to NIH DAVID for analysis (Dennis, G., Jr., B.T. Sherman, D.A. Hosack, J. Yang, W. Gao, H.C. Lane, and R.A. Lempicki. 2003. *Genome Biol.* 4:P3). Pathways were categorized by Kyoto Encyclopedia of Genes and Genomes (KEGG) annotation. The percentage of total genes in a given enriched KEGG pathway (Fig. 6 B) was calculated by dividing the number of differentially expressed genes for each pathway identified via DAVID by the total number of genes in the pathway according to KEGG annotation.

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Table S1. Genes and identifiers

	Gene symbol	GenBank	LocusLink	Affymetrix	Fold change
Down-regulated in *Socs3* h-KO	Isoc1	AK010892	66307	1425050_at	−1.55
	Tmem37	BC024613	170706	1417611_at	−1.53
	Galk1	NM_016905	14635	1417177_at	−1.53
	2610110G12Rik	AK002569	73242	1429603_at	−1.54
	Mosc1	BB667876	66112	1446074_at	−1.5
	Hsd17b13	AV050442	243168	1460606_at	−1.62
	Lip1	AI596237	16889	1450872_s_at	−1.6
	Acsl1	BC006692	14081	1423883_at	−1.62
	Prr6	AK014046	73139	1428706_at	−1.56
	Rabep1	AF248489	54189	1426023_a_at	−1.54
	Cd59a	AK005507	12509	1429830_a_at	−1.56
	Atp1b1	NM_009721	11931	1418453_a_at	−1.51
	Aox1	NM_009676	11761	1419435_at	−1.59
	Gabarapl1	AF180518	57436	1416418_at	−1.53
	Creld1	NM_133930	171508	1416537_at	−1.51
	Decr2	BE952632	26378	1423495_at	−1.61
	Psen2	BC010403	19165	1425869_a_at	−1.53
	Pank1	BC023496	75735	1418715_at	−1.58
	Mtx3	AU067765	382793	1434807_s_at	−1.59
	Slc25a22	AK018760	68267	1452653_at	−1.55
	Acat1	BG070487	110446	1424182_at	−1.69
	Nuak2	AK004737	74137	1429049_at	−1.56
	Tbl1x	BF682509	21372	1434644_at	−1.57
	Npepl1	BG076209	228961	1434507_at	−1.63
	Dgat2	AK002443	67800	1422677_at	−1.57
	Prkcn	NM_029239	75292	1420567_at	−1.77
	unknown	BB822342		1441765_at	−1.74
	Fcgr2b	M14216	14130	1451941_a_at	−1.65
	Ccnd1	NM_007631	12443	1448698_at	−1.73
	Trak1	BB010301	67095	1452742_at	−1.62
	Abhd10	BB478745	213012	1427958_at	−1.7
	Fabp2	NM_007980	14079	1418438_at	−1.64
	2310016A09Rik	BC024580	69574	1451322_at	−1.64
	Elovl5	NM_134255	68801	1415840_at	−1.6
	Zfp35	NM_011755	22694	1417778_at	−1.73
	Samd10	BB526577	229011	1435756_at	−1.7
	Akr1c20	NM_054080	116852	1422061_at	−1.7
	Klf15	BC013486	66277	1448181_at	−1.65
	Igfbp2	AK011784	16008	1454159_a_at	−1.67
	Pbx1	AU042527	18514	1447096_at	−1.63
	Abcd2	NM_011994	26874	1419748_at	−1.53
	Lrp4	AF247637	228357	1426288_at	−1.63
	Oprs1	AF226605	18391	1451956_a_at	−1.55
	5730472N09Rik	BI556043	108958	1454621_s_at	−1.51
	Lrfn3	AV062156	233067	1456767_at	−1.63
	Aqp11	BF472491	66333	1429254_at	−1.51
	1300013J15Rik	NM_026183	67473	1418395_at	−1.63
	D10Ertd214e	NM_134007	52637	1416849_at	−1.59
	Znrf3	BB367706	407821	1459243_at	−1.59
	Prim2	NM_008922	19076	1418036_at	−1.5
	Parp16	BC014731	214424	1426950_at	−1.71
	Tsc22d3	AF201289	14605	1425281_a_at	−1.68
	Entpd8	AK008590	72090	1429550_at	−1.74
	Ttc23	NM_025905	67009	1448902_at	−1.68
	Bche	BB667452	12038	1436098_at	−1.69
	Slc29a1	AF305501	63959	1451782_a_at	−1.69
	5830404H04Rik	BB834407	207781	1437731_at	−1.61
	Nr1i3	AF009328	12355	1425392_a_at	−1.93
	Rdh16	NM_009040	19683	1420541_at	−1.88
	Lyzs	AW208566	17105	1423547_at	−1.93
	Lsm10	NM_138721	116748	1417515_at	−1.83
	Eva1	BC015076	14012	1416237_at	−2.03
	3110049J23Rik	NM_026085	67307	1449462_at	−1.88
	Usp46	AV300436	69727	1435325_at	−1.91
	Fcgr2b	BM224327	14130	1435476_a_at	−1.79

Atp1b1	AV152334	11931	1439036_a_at	−1.75
Acsl1	BI413218	14081	1450643_s_at	−1.77
Pnkd	NM_019999	56695	1418746_at	−1.76
2610020O08Rik	BB168118	67050	1435662_at	−1.86
Rogdi	BC006914	66049	1451421_a_at	−1.83
Ypel3	BI660196	66090	1426624_a_at	−1.92
Acsl1	BI413218	14081	1422526_at	−1.89
Abcb4	NM_008830	18670	1449818_at	−1.79
Vnn3	NM_011979	26464	1420723_at	−1.82
0610039N19Rik	BB775176	67442	1424716_at	−1.92
Vnn1	NM_011704	22361	1418486_at	−1.87
Comtd1	AK007659	69156	1428635_at	−1.68
Ppil1	AK004331	68816	1428892_at	−1.64
Smarca2	BM230202	67155	1452333_at	−1.62
Dnase2b	NM_019957	56629	1450237_at	−1.7
Tnrc6a	BI080625	233833	1434898_at	−1.82
Bcdo2	NM_133217	170752	1421221_at	−1.94
9830124H08Rik	AV272797	219105	1442007_at	−1.95
Stard3nl	AK018331	76205	1430274_a_at	−1.89
Cyp2c38	AF047725	13097	1452501_at	−1.99
Acsl1	BI413218	14081	1460316_at	−1.97
Mtnr1a	NM_008639	17773	1450352_at	−1.88
Aox3	NM_023617	71724	1418858_at	−1.99
Dusp19	NM_024438	68082	1418038_s_at	−1.9
Fbxo21	BC021871	231670	1451543_at	−2.09
Srd5a1	AV003635	78925	1454649_at	−2.02
Bbox1	AI874739	170442	1459030_at	−2.13
Ank3	BB628935	11735	1452124_at	−2.12
C730027J19Rik	BB667617	272428	1437662_at	−2.16
Dpys	AW490997	64705	1436291_a_at	−2.03
Cbr1	NM_007620	12408	1460196_at	−2.04
Vnn1	AV360029	22361	1447845_s_at	−2.01
Socs3	NM_007707	12702	1416576_at	−2.1
G0s2	NM_008059	14373	1448700_at	−2.2
Dapk2	BC022165	13143	1451453_at	−2.26
unknown	BB213500		1440264_at	−2.18
Cyp3a25	AF204959	56388	1424973_at	−2.17
Cyp4a10	BC010747	13117	1424853_s_at	−2.1
Pdk1	BB553369	228026	1435836_at	−2.11
1810021J13Rik	NM_025464	66279	1417174_at	−1.89
2310007H09Rik	AK009207	76429	1452889_at	−1.81
0610042E07Rik	NM_026158	67441	1418537_at	−2.28
Rarres1	BB035017	109222	1438055_at	−2.01
Ahnak	BC028439	66395	1428057_a_at	−2.38
Hpgd	AV026552	15446	1419905_s_at	−2.19
Daf1	NM_010016	13136	1460242_at	−2.36
Cd52	NM_013706	23833	1460218_at	−2.29
Ssh1	BB053082	231637	1455854_a_at	−2.26
Dpys	AK004899	64705	1425688_a_at	−2.52
Klkb1	BC026555	16621	1449034_at	−2.44
Nqo2	AV380561	18105	1455590_at	−2.63
9130022K13Rik	AK018646	75761	1429272_a_at	−2.57
Tbx3	BB728182	21386	1437479_x_at	−2.58
Klb	NM_031180	83379	1449568_at	−3.19
Sdro	BB143568	70061	1456074_at	−3
Abcg5	NM_031884	27409	1419393_at	−2.83
Slc2a2	NM_031197	20526	1449067_at	−2.72
Car14	NM_011797	23831	1450725_s_at	−2.72
Fmo1	BC011229	14261	1417429_at	−2.72
Src	BG868120	20779	1450918_s_at	−2.68
Zfp707	BC026404	69020	1427093_at	−2.54
Ddah1	AW556888	69219	1454995_at	−3.03
Eps8l2	NM_133191	98845	1417843_s_at	−2.74
Socs3	BB241535	12702	1455899_x_at	−4.59
Socs3	BB831725	12702	1456212_x_at	−3.42
9030618K22Rik	AK018558	71527	1431916_at	−6.59
Hsd3b3	M77015	15494	1427377_x_at	−4.4
Keg1	NM_029550	64697	1416833_at	−5.36

Up-regulated in *Socs3* h-KO	Slc13a5	BI134706	237831	1435936_at	9.42
	Pap	NM_011036	18489	1448290_at	7.2
	Bmper	AK014221	73230	1429273_at	5.06
	Soat1	BC025091	20652	1426818_at	5.27
	Snx10	BB256262	71982	1459764_x_at	4.05
	Rgs5	BF585144	19737	1420941_at	4.1
	3110050K21Rik	BM249225	67302	1459488_at	4.6
	Ugt2b5	AI118428	22238	1423397_at	5.01
	Xlr4b	NM_021365	27083	1449347_a_at	3.22
	unknown	BG070581		1442625_at	4.25
	Cpne8	AK004559	66871	1431146_a_at	3.91
	Slc13a5	BE979238	237831	1459729_at	5.74
	Ppm1l	BB035578	242083	1435787_at	3.44
	Stno	BM239721	216161	1439349_at	3.59
	Spp1	NM_009263	20750	1449254_at	3.48
	Ppm1l	BB308836	242083	1438012_at	3.54
	T2bp	BB277065	211550	1426501_a_at	3.65
	B4galt1	BM248947	14595	1458616_at	4.19
	B3galt1	AK018190	26877	1460509_at	2.63
	Il17r	AK010040	16172	1420905_at	2.46
	unknown	BG067230		1445008_at	2.46
	9630050E16Rik	BB112393	320168	1443257_at	2.68
	Txndc10	BF162157	67988	1430995_at	2.43
	A2m	BB185854	232345	1434719_at	2.6
	Syt12	NM_134164	171180	1422878_at	2.68
	Steap4	AY029778	117167	1425829_a_at	2.99
	Stno	BF148215	216161	1443721_x_at	3.04
	unknown	BI466416		1447891_at	3.31
	Ccnl1	BM250672	56706	1423622_a_at	2.49
	Lrrc16	BC012229	68732	1451804_a_at	2.51
	Pim3	BB206220	223775	1437100_x_at	1.77
	Ablim1	BG065289	226251	1454708_at	1.97
	Trat1	BB622792	77647	1427532_at	2.16
	Myh9	C80049	17886	1420170_at	2.17
	Pgs1	AK016901	74451	1454045_a_at	2.05
	2310050N11Rik	BB549831	66967	1459133_at	1.99
	unknown	BG064527		1440351_at	2
	Dscr1l1	NM_030598	53901	1421425_a_at	2.51
	Fndc3b	BB470469	72007	1441230_at	2.07
	Plk3	BM947855	12795	1434496_at	2.24
	Gas6	NM_019521	14456	1417399_at	2.12
	Bfar	BF464033	67118	1440533_at	2.37
	Nfat5	BB488160	54446	1439805_at	2.27
	5330438I03Rik	BB324138	381325	1436894_at	2.5
	Tle3	NM_009389	21887	1419655_at	2.13
	Tacc2	BC004057	57752	1425745_a_at	2.2
	Tmem23	BE629162	208449	1426575_at	2.32
	Tmem23	AW985925	208449	1436499_at	2.11
	Osmr	AB015978	18414	1418674_at	2.17
	Cxcl1	NM_008176	14825	1419209_at	2.26
	S100a11	BC021916	20195	1460351_at	2.02
	Cxcl1	BB554288	14825	1457644_s_at	2.07
	Akap12	NM_031185	83397	1419706_a_at	2.11
	3110050K21Rik	AI427801	67302	1447581_at	1.99
	Zbp1	AK008179	58203	1429947_a_at	2.07
	Raph1	AV307311	77300	1434303_at	2
	Psmb8	NM_010724	16913	1422962_a_at	1.95
	Raph1	AV307311	77300	1434302_at	1.98
	9630019E01Rik	BB456107	319967	1459344_at	1.93
	Zfp292	NM_013889	30046	1419574_at	2.05
	Pfkfb3	NM_133232	170768	1416432_at	2.22
	Steap4	NM_054098	117167	1460197_a_at	2.31
	Btg3	NM_009770	12228	1449007_at	2.28
	Acvr1b	BQ043509	11479	1433725_at	2.14
	Pcm1	BG076129	18536	1436908_at	2.29
	Pld1	BM228590	18805	1437113_s_at	1.95
	D15Ertd682e	NM_028003	71919	1448555_at	1.96
	Pld1	BM228590	18805	1437112_at	1.89

Efna1	D38146	13636	1448510_at	1.75
Efna1	D38146	13636	1416895_at	1.85
Nup37	BC011102	69736	1423969_at	1.89
Hip1r	AA590970	29816	1425551_at	1.77
Cpne8	AW548480	66871	1430521_s_at	1.78
Trim3	AF220019	55992	1451663_a_at	1.81
Junb	NM_008416	16477	1415899_at	1.84
Pdgfc	NM_019971	54635	1419123_a_at	1.96
Pcm1	NM_023662	18536	1418524_at	1.99
Csnk2a1	BB283759	12995	1419035_s_at	1.76
Fndc3b	BG067509	72007	1457470_at	1.82
Stx6	BB492711	58244	1460004_x_at	1.84
3110050K21Rik	AW536655	67302	1434894_at	1.84
Atrx	BB425841	22589	1438750_at	1.85
Tbc1d10a	NM_134023	103724	1448587_at	1.89
Fabp5	BC002008	16592	1416021_a_at	1.71
Fabp5	BC002008	16592	1416022_at	1.81
Vangl1	BC024687	229658	1427234_at	1.79
5730453I16Rik	AK017661	269061	1453356_at	1.82
Iqce	AV271088	74239	1434622_at	1.7
Lass6	BQ176664	241447	1434418_at	1.89
Litaf	AV360881	56722	1416303_at	1.71
Marcksl1	AV215438	17357	1435627_x_at	1.84
Tgm1	BC026422	21816	1451416_a_at	1.85
AW112037	BG071867	98667	1435327_at	1.6
Smad1	NM_008539	17125	1448208_at	1.6
Mcm4	BC013094	17217	1416214_at	1.66
Lpgat1	BE987427	226856	1424350_s_at	1.79
Fbxl12	NM_013911	30843	1448420_a_at	1.72
Il1r1	NM_008362	16177	1448950_at	1.77
Igf2bp3	BG797580	140488	1436145_at	1.67
Ptpn2	NM_008977	19255	1417140_a_at	1.74
Slc39a14	BB769796	213053	1438490_at	1.71
Slc39a14	BB399837	213053	1427035_at	1.76
Rlf	BF020283	109263	1427171_at	1.77
Gnl2	BI666155	230737	1437565_a_at	1.8
Plec1	AW123286	18810	1419835_s_at	1.74
Xpr1	BG066856	19775	1437958_at	1.77
Apex1	AV263745	11792	1456079_x_at	1.79
Apex1	AV100480	11792	1437715_x_at	1.81
Gm489	BB817942	244049	1457707_at	1.86
Utp20	BC005522	70683	1452252_at	1.63
Plec1	BM210485	18810	1434610_at	1.7
Rnpc2	BB203348	170791	1438398_at	1.75
Adam9	NM_007404	11502	1416094_at	1.62
Mvp	BB139464	78388	1456586_x_at	1.67
Ehd4	NM_133838	98878	1449852_a_at	1.5
Fndc3b	BG064539	72007	1433833_at	1.51
Jund1	NM_010592	16478	1449117_at	1.51
Gm944	BB039066	381126	1456271_at	1.58
Ptpn1	BC010191	19246	1417068_a_at	1.69
Litaf	AV360881	56722	1416304_at	1.54
Eya3	U61112	14050	1425989_a_at	1.56
4933426M11Rik	BF144564	217684	1454606_at	1.59
Ptpn1	BB509334	19246	1438670_at	1.65
Psmb10	NM_013640	19171	1448632_at	1.6
Fath	AV088463	14107	1433857_at	1.64
Slc38a2	BM248527	67760	1426722_at	1.51
Pgm3	BG075614	109785	1435295_at	1.55
Zbtb16	BB326368	235320	1456986_at	1.57
Stom	AF093620	13830	1419097_a_at	1.67
Prg4	NM_021400	96875	1449824_at	1.68
Baz1a	BM239162	217578	1433599_at	1.68
unknown	BG069527		1459961_a_at	1.6
Snx10	AK010399	71982	1431055_a_at	1.6
Psme4	BG067940	103554	1440511_at	1.62
Fndc3b	AK005500	72007	1452783_at	1.65
Blzf1	AK006544	66352	1418973_at	1.58
Mllt4	BQ267038	17356	1436303_at	1.52

Morc3	AI452146	338467	1420091_s_at	1.53
Nfxl1	NM_133921	100978	1417145_at	1.6
Tdg	NM_011561	21665	1448462_at	1.52
Ptpn2	AV167543	19255	1438562_a_at	1.55
Slc41a2	BC026874	338365	1452445_at	1.51
Derl1	BB417749	67819	1437723_s_at	1.52
Gm944	BB053232	381126	1436827_at	1.61
Slc39a14	BC021530	213053	1425649_at	1.61
Krt1-18	NM_010664	16668	1448169_at	1.51
Slc9a3r1	BB805362	26941	1438115_a_at	1.57
Tbl2	AV274155	27368	1434224_at	1.52
Smad1	BB257769	17125	1459843_s_at	1.59
Lpgat1	BE987427	226856	1424349_a_at	1.62
Noc4l	BC024616	100608	1423827_s_at	1.66
Sptlc2	BC003227	20773	1460243_at	1.58
E430034L04Rik	NM_011816	23881	1421323_a_at	1.61
Fbxo39	BB645745	327959	1443698_at	1.59
Smarcc1	BI558117	20588	1423416_at	1.54
Abca1	BB144704	11303	1421840_at	1.58
Flot1	NM_008027	14251	1448559_at	1.61

Genes and identifiers are listed in their order of appearance (from left to right) in the heatmap in Fig. 6 A. For simpler interpretation, "fold change" for down-regulated genes is expressed as (−1/fold change).