

Table S1. Genes upregulated &gt;2-fold by Smad4 loss

GeneSymbol	A_SMAD4_KO_1	A_SMAD4_KO_2	A_SMAD4_KO_3	A_SMAD4_WT_1	A_SMAD4_WT_2	A_SMAD4_WT_3	logFC	logCPM	PValue	FDR
Al747448	550.7263437	834.2114653	765.9011651	77.94865292	72.25539655	82.5158702	3.208174893	8.633895927	1.17E-69	3.41E-66
Lrg1	90.82418325	79.18527923	44.41957548	7.202718706	8.574553453	7.35401951	3.211925964	5.30657947	1.57E-41	2.28E-38
Nrp1	31.0846605	33.9192425	28.43015988	6.579406511	7.022263603	6.712899861	2.20086193	4.245445092	1.06E-38	1.12E-35
Vsig1	29.78597523	32.78860109	36.46565701	7.375860983	6.209159397	4.940392594	2.415890143	4.292880174	2.55E-37	2.46E-34
Dhrs9	23.79526572	26.08551269	33.77356152	5.298153664	4.102480316	4.600976309	2.576611425	4.025119694	6.67E-37	5.96E-34
Hif1a	309.4222405	368.2660615	394.1472524	103.5390814	94.17225085	103.484254	1.83125996	7.838275627	1.59E-35	1.32E-32
Ifit2	61.41524569	54.83610871	43.31826369	11.87756017	13.15750444	13.50122556	2.049799567	5.045465962	3.95E-34	3.06E-31
Atp12a	197.0650175	276.0380259	258.7266917	62.50436185	68.81818331	69.16549632	1.868024411	7.279845781	5.98E-33	4.34E-30
Ly6c1	25.8899194	22.24940788	25.16701384	5.956094315	5.987403704	5.619225164	2.060166616	3.921948236	7.46E-32	4.56E-29
H60c	9.802979189	12.19477528	7.9947078	0.969596749	1.515330567	1.206813458	3.020453855	2.491595201	8.78E-30	4.63E-27
F13a1	3.39333895	2.826603542	3.426303343	0.277027643	0.147837128	0.037712921	4.312602857	0.776769432	1.10E-29	5.40E-27
Pcsk6	5.739351063	4.68408587	4.160511202	0.51942683	0.443511385	0.301703365	3.504877423	1.412029846	1.12E-29	5.40E-27
Gsta3	41.30657043	48.25416047	55.39190405	14.50932278	13.30534156	14.36862274	1.78047466	4.963849632	1.10E-28	5.09E-26
Sifn5	33.47256569	26.7315935	28.59331718	8.20694391	5.026462369	5.430660561	2.24720097	4.163375431	3.35E-27	1.49E-24
181000818Rik	5.82313721	7.793349766	6.118398827	0.900339838	0.665267078	1.093674696	2.886284089	1.907989137	1.68E-26	6.71E-24
Sipi	35.44154014	32.14252028	32.26435648	11.21961952	8.389757042	8.749397571	1.814227563	4.418587475	2.02E-25	7.10E-23
Egln3	67.28027597	75.51069462	96.01807225	28.25681954	21.06679081	21.68492933	1.749124326	5.690866955	1.17E-24	3.74E-22
Trf	36.06993625	46.51781829	31.77488457	11.25424798	8.057123503	8.03285208	2.062637376	4.562692985	1.19E-24	3.74E-22
Cp	2.262225967	6.420428045	3.711828622	0.207770732	0.073918564	0.075425841	5.042065512	1.10541726	2.36E-24	7.03E-22
B3gnt5	185.0835985	289.2019224	205.6189899	60.77293908	62.90469817	72.89907545	1.790283883	7.190779907	2.59E-24	7.51E-22
Naip6	96.81489276	110.6817187	80.19181396	35.90970817	34.00253955	37.07180092	1.427020122	6.040111396	2.24E-23	5.78E-21
Abca13	7.834004736	8.560570727	6.199977478	1.315881302	0.960941335	1.546229743	2.559179826	2.144904203	4.38E-23	1.11E-20
Steap4	28.4035038	48.49644077	35.4867132	9.938366676	8.168001349	9.164239697	2.042285645	4.541826281	6.88E-23	1.66E-20
Hoxd13	40.38492281	58.83373372	26.10516833	5.194268298	6.800507911	8.070565001	2.643047657	4.598808946	1.19E-22	2.82E-20
Apobec2	4.901489594	6.904988653	5.221033666	1.142739026	0.665267078	0.565693808	2.826429501	1.70472507	3.96E-22	8.84E-20
2310079G19Rik	3.896055831	3.190023997	3.752617947	0.657940651	0.258714975	0.226277523	3.210080797	1.019608177	8.14E-22	1.72E-19
Gm11545	101.7163824	109.9548778	82.27206956	39.23403988	40.58129177	40.27739916	1.291334837	6.109259432	6.07E-21	1.17E-18
Naip7	2.723049775	3.714964655	3.059199413	0.484798374	0.258714975	0.377129206	3.060841085	0.852382543	1.34E-20	2.51E-18
Zfp750	32.88606266	36.42280564	32.01962053	10.73482115	12.49223736	12.82239299	1.49129323	4.518641006	1.88E-20	3.46E-18
Abcg1	11.01787832	10.57957326	9.340755542	2.597134149	2.845864723	2.941607804	1.882658581	2.717678366	9.99E-20	1.68E-17
Gsdmc3	200.751608	237.7577379	218.6715741	86.32873911	48.60145599	52.00611746	1.813385938	7.136523863	1.25E-19	2.05E-17
Rbm24	6.409640239	7.470309361	4.527615132	0.865711383	1.256615592	1.093674696	2.514699008	1.858997317	2.88E-19	4.52E-17
Bmp3	65.98159069	57.82423246	62.32608938	15.51354798	23.91265553	24.17398208	1.549728526	5.379899693	9.63E-19	1.36E-16
Hoxd11	4.356879639	6.016627539	2.284202229	0.311656098	0.406552103	0.414842126	3.469144403	1.216488037	1.71E-18	2.25E-16
Trim6	16.04504713	17.40380181	15.70389032	5.99072277	5.026462369	4.714115071	1.641400644	3.438577019	1.79E-18	2.33E-16
Skil	99.87308712	112.4584409	107.4798727	55.19775778	45.45991701	47.10343779	1.113658965	6.284783057	7.64E-18	9.44E-16
Stom	126.2238303	141.4109372	117.3101002	65.44778055	52.00170995	53.89176349	1.16748583	6.535276709	1.09E-17	1.30E-15
Smoc2	85.41997678	80.11402039	74.76683366	37.98741548	38.73332766	35.48785825	1.098442677	5.877427556	2.69E-17	3.03E-15
Akt3	47.75810374	50.79810365	28.75647449	13.0202992	10.64427325	13.27494804	1.784623875	4.775679936	3.35E-17	3.67E-15
Pmpa1	47.79999681	41.26841171	34.34461208	16.03297481	15.7076949	15.42458451	1.387219239	4.830667823	3.60E-17	3.83E-15
Stxbp1	32.04820119	32.74822104	21.29202792	10.25002277	7.872327092	7.504871193	1.746524998	4.22035053	4.87E-17	5.05E-15
Rps15a-ps6	3.309552803	7.995250019	6.934185337	0.623312196	0.850063489	0.942823014	2.913299726	1.793947394	7.06E-17	7.06E-15
Ltf	12.06520516	14.98099877	8.321022404	3.151189434	2.43931262	2.187349393	2.180792033	2.850338855	1.19E-16	1.15E-14
Ces2f	3.225766656	5.41092678	3.630249971	0.277027643	0.850063489	0.565693808	2.856398145	1.237139649	1.52E-16	1.46E-14

Slc7a11	11.60438135	11.06413386	15.29599707	3.497473987	1.330534156	1.772507267	2.516713207	2.89589952	3.27E-16	2.96E-14
Paqr8	53.91638554	49.95012259	65.79318205	26.31762604	20.17976804	20.89295799	1.331340721	5.305222179	3.77E-16	3.36E-14
Cxcl5	1.885188306	5.653207084	1.753940997	0.173142277	0.073918564	0.188564603	4.368864376	0.727676558	6.27E-16	5.48E-14
Areg	19.06134842	19.18052403	17.13151671	7.652888625	6.024362986	5.920928529	1.496420724	3.646830545	7.44E-16	6.40E-14
Hspa12a	20.31814063	21.15914651	11.33943249	3.566730898	5.063421651	4.110708342	2.05106542	3.451640605	1.26E-15	1.03E-13
Adcy2	10.55705451	12.55819574	13.54205607	4.155414638	3.843765341	3.99756958	1.610182766	3.025101049	1.50E-15	1.20E-13
Il1rn	90.02821486	113.4679422	132.7284652	53.53559192	45.16424275	47.06572487	1.205596579	6.32854068	2.18E-15	1.69E-13
Itga2	78.17247507	73.57245219	78.68260891	33.62423011	39.694269	38.5048919	1.043236495	5.834861363	2.63E-15	2.02E-13
Anxa8	24.25608953	24.95487127	27.49200539	10.35390814	11.19866248	9.918498109	1.284891047	4.174931551	3.07E-15	2.35E-13
Tcf4	52.61770026	59.76247489	50.53797431	25.20951547	24.65184118	25.87106351	1.105094968	5.315137957	3.51E-15	2.63E-13
C3	103.7272499	121.1805318	67.18001912	34.76696914	36.40489289	36.73238463	1.436588075	6.059398341	3.58E-15	2.67E-13
Gpr110	12.98685277	15.86935989	10.72759261	2.943418702	3.252416827	4.63868923	1.869967682	3.074719461	6.16E-15	4.52E-13
Ms4a18	22.49658045	24.02613011	18.80387906	6.267750413	8.315838478	8.636258809	1.492960567	3.885936762	6.60E-15	4.79E-13
Macc1	15.66800947	20.39192555	23.37228352	7.410489438	5.580851601	6.63747402	1.597067788	3.723175677	8.69E-15	6.23E-13
Reg3b	6802.010765	8764.651503	5046.373774	2524.414393	2367.168101	2535.628214	1.472662935	12.19025603	8.76E-15	6.24E-13
B4galt6	83.70236076	86.21140803	91.49045712	47.99503907	39.17683905	43.36985865	1.001488613	6.030452165	1.21E-14	8.33E-13
Gm13826	7.331287855	9.973872498	9.259176891	3.116560979	2.217556927	2.074210631	1.837468656	2.509635636	1.65E-14	1.09E-12
Abcc4	35.06450248	32.74822104	33.7327722	16.65628701	12.45527808	13.0109576	1.268303223	4.58368521	2.20E-14	1.43E-12
Ankdd1b	3.26765973	4.643705819	3.467092669	0.692569106	0.480470668	1.055961776	2.348376516	1.204244486	2.54E-14	1.64E-12
Ifi44	25.7223471	17.32304171	23.20912622	8.518600008	7.170100732	7.919713319	1.487505626	3.907179408	2.69E-14	1.72E-12
Lama4	5.865030284	9.287411638	2.488148856	0.554055285	0.628307796	0.716545491	3.20814185	1.71229753	2.76E-14	1.74E-12
Cald1	4.147414272	5.168646477	4.36445783	0.934968294	1.293574874	1.31995222	1.946947913	1.539985137	4.06E-14	2.49E-12
Lama3	8.378614691	7.026128804	13.01179484	2.562505694	2.180597645	2.300488154	2.009294081	2.569274057	4.86E-14	2.96E-12
Prune2	4.901489594	6.339667944	6.730238709	1.766051221	1.774045542	1.621655584	1.796817699	1.960535241	5.92E-14	3.56E-12
Podxl	8.085363177	8.560570727	3.099988739	0.8450169919	1.034859899	1.018248855	2.978016603	1.896578966	8.36E-14	4.90E-12
Cldn8	116.4208511	160.9548817	132.6060972	57.20620819	63.23733171	70.14603225	1.105235885	6.645750937	1.01E-13	5.78E-12
Zfp608	39.71463364	35.85748493	30.63278346	14.12840977	16.44688054	15.12288115	1.216550736	4.663848235	1.14E-13	6.43E-12
Hook1	335.4378392	363.905016	387.1722778	191.9108994	159.5901802	176.4964682	1.041052622	8.072129404	2.15E-13	1.18E-11
Ubn2	97.44328886	110.8432389	79.947078	49.62257647	43.46411578	46.53774398	1.045517158	6.156812602	2.32E-13	1.26E-11
Pla2g2a	105.7381174	93.72209744	62.85635061	35.84045125	36.95928212	36.69467171	1.260315596	5.954112474	2.33E-13	1.26E-11
Gm9159	2.555477481	4.401425515	3.263146041	0.865711383	0.70222636	0.565693808	2.248508706	1.071006896	4.19E-13	2.21E-11
Ereg	3.854162758	3.513064402	5.54734827	1.246624391	0.70222636	1.018248855	2.112796753	1.42421172	6.86E-13	3.51E-11
Me1	42.39579034	39.57244959	48.70245466	17.48736994	21.39942435	21.2700872	1.11940706	4.992729706	8.04E-13	4.06E-11
Rdx	10.22190992	11.95249498	11.09469654	1.454395123	3.252416827	3.545014533	2.013528219	2.794949082	8.70E-13	4.35E-11
Fam124a	35.56721936	44.74109606	35.07881994	16.41388782	17.59261829	18.17762771	1.14493104	4.805562382	8.81E-13	4.39E-11
Zbed6	67.99245822	79.71021988	52.53665126	27.0448236	31.93281975	29.98177185	1.170578751	5.591954834	9.20E-13	4.55E-11
B3galt2	19.14513457	25.19715157	23.37228352	3.566730898	6.320037243	8.711684651	1.865593586	3.848224478	1.86E-12	8.76E-11
Sppl2a	623.4946122	736.9763035	736.940744	344.6223873	332.9292134	366.7958654	1.006011014	9.032502269	2.26E-12	1.05E-10
Pgap1	53.79070632	51.68646477	78.0299797	29.57270084	20.80807584	22.96716862	1.322444972	5.420940257	2.43E-12	1.12E-10
Osmr	6.493426386	9.771972245	3.671039296	0.51942683	1.182697028	1.35766514	2.704093997	1.945993974	2.52E-12	1.16E-10
Grhl3	4.692024227	4.805226021	1.876308974	0.51942683	0.739185642	0.565693808	2.632296684	1.15757947	3.10E-12	1.41E-10
Tmem181c-ps	31.54548431	32.38480058	36.91433959	16.82942928	9.313739095	11.65329245	1.414432404	4.532263893	4.83E-12	2.10E-10
Pdgfa	48.84732365	37.06888645	29.8985756	14.23229514	16.89039193	15.65086203	1.307878188	4.761520538	5.80E-12	2.47E-10
Reg3g	3253.835015	4051.774657	2527.592134	1532.066749	899.6628454	945.0103635	1.542014656	11.10439043	6.14E-12	2.59E-10
Myo3a	3.309552803	3.068883846	3.140778064	0.969596749	0.628307796	0.905110094	1.918304932	1.033419593	6.36E-12	2.66E-10
Sulf2	156.0516986	135.9596304	134.5639849	83.55846268	58.58046216	55.36256739	1.110564416	6.701136615	7.39E-12	3.09E-10

D10Bwg1379e	32.25766656	30.325418	25.9012217	11.91218863	14.2662829	13.99149353	1.139452071	4.42471049	1.05E-11	4.28E-10
Alpk1	43.73636869	47.0023789	37.52617947	22.54312441	20.69719799	19.64843161	1.02779031	4.995471736	1.38E-11	5.52E-10
Tnip3	54.79614008	83.42518454	66.36423261	31.13098133	32.26545329	33.48907346	1.078450485	5.652052246	1.63E-11	6.44E-10
Gyk	74.15074002	119.8479902	95.16149642	38.09130085	41.50527382	49.81876807	1.160062743	6.125119582	1.67E-11	6.58E-10
Lbp	8.546186985	15.54631948	9.299966217	1.869936587	3.32635391	3.281024089	1.97878957	2.807961874	1.77E-11	6.92E-10
Csta1	1.717616012	2.261282834	2.732884809	0.58868374	0.332633539	0.452555047	2.27140043	0.481195301	1.85E-11	7.20E-10
Ghr	12.02331208	14.81947857	11.09469654	3.324331711	4.472073137	5.392947641	1.525452129	3.096068741	2.16E-11	8.26E-10
A730098P11Rik	1.801402159	2.503563137	2.773674135	0.58868374	0.443511385	0.527980888	2.169870697	0.573021925	2.90E-11	1.09E-09
Spats2l	60.15845348	56.85511124	39.72880305	18.80325124	24.94751543	23.98541748	1.210560929	5.226604715	3.06E-11	1.14E-09
C1galt1	177.2077007	216.9620119	208.5558213	78.98750658	98.2008126	113.478178	1.052277276	7.218531008	3.22E-11	1.18E-09
Prpf40a	194.0487162	261.9857683	261.5411552	120.4723961	108.6233302	125.7725901	1.015848371	7.482052267	4.12E-11	1.47E-09
Clmp	6.116388725	6.904988653	6.199977478	2.631762604	2.143638363	2.262775234	1.446123826	2.143431071	4.41E-11	1.57E-09
Clca4	1382.55521	1822.957384	1474.248592	849.3321236	665.1562004	701.8374517	1.078249878	10.16664936	4.84E-11	1.69E-09
F3	28.90622068	31.90023997	31.77488457	13.0202992	14.93154998	16.59368505	1.055906982	4.516822761	6.40E-11	2.16E-09
BC005561	13.82471424	16.79810105	13.17495214	6.544778055	5.654770165	6.260344814	1.245583745	3.380618575	6.64E-11	2.23E-09
Tmem184c	13.44767658	19.09976393	14.03152798	6.5101496	5.839566575	6.562048178	1.29990158	3.453259599	9.31E-11	3.05E-09
Slc28a3	57.98001366	69.89786759	42.54326651	26.31762604	25.87149749	25.79563767	1.127694362	5.372864645	1.13E-10	3.64E-09
Defb37	6.954250194	8.439430575	14.11310663	1.696794311	2.882824006	2.979320725	1.965464328	2.632836966	1.18E-10	3.76E-09
Per2	24.42366182	29.15439653	27.12490147	9.83448131	13.67493439	13.1995222	1.137184601	4.293138052	1.23E-10	3.90E-09
Taf4b	21.44925361	23.90498995	25.24859249	12.29310164	10.90298823	10.18248855	1.079941642	4.118721956	1.26E-10	3.99E-09
Stx19	2.890622068	2.503563137	2.896042111	0.865711383	0.813104207	0.64111965	1.827235472	0.859849868	1.44E-10	4.51E-09
Ido1	100.339109	175.2897997	46.74456704	25.76357076	25.24318969	26.43675732	2.057316635	6.058469035	1.48E-10	4.59E-09
Mfsd2a	33.38877954	26.40855309	19.90519085	11.28887643	5.469973754	4.67640215	1.892070506	4.076808915	1.68E-10	5.14E-09
Sp100	37.82944533	35.37292433	27.45121607	13.92063904	16.59471767	16.78224965	1.089692853	4.626069967	3.39E-10	9.63E-09
lnns1abp	708.5794444	815.7981623	745.4657131	453.5635078	303.5465841	325.5002174	1.0680283	9.126143874	4.29E-10	1.19E-08
Nox1	282.5268874	395.9263961	321.8277783	189.8331921	138.9669008	151.8699311	1.057212058	7.947589407	4.32E-10	1.20E-08
Ttc14	82.23610319	112.0546404	92.10229701	56.963809	36.40489289	43.06815529	1.069420497	6.139842682	4.53E-10	1.26E-08
Wfdc18	25.51288173	40.98575136	27.77753067	13.15881302	12.6031152	14.55718734	1.225465953	4.48990388	4.68E-10	1.29E-08
Ttl7	9.844872262	10.70071341	9.463123519	3.220446345	4.545991701	4.336985865	1.310889676	2.818727877	4.72E-10	1.30E-08
Mdm4	55.80157384	65.57720217	43.11431707	29.39955857	24.31920764	25.34308262	1.05660093	5.344568973	5.26E-10	1.43E-08
Kcnq1ot1	30.74951592	48.45606072	31.8156739	18.04142522	13.45317869	15.38687159	1.243239569	4.720017599	5.52E-10	1.50E-08
Egr1	20.15056833	17.1615215	20.92492399	8.795627651	9.868128327	8.711684651	1.088662033	3.838718759	5.55E-10	1.50E-08
Lgr5	22.45468737	22.04750763	13.62363472	6.5101496	7.687530682	8.372268366	1.364845355	3.752591508	5.67E-10	1.52E-08
Gsdmc2	615.9957521	752.522623	776.791915	393.8986792	207.0458985	210.815226	1.401987283	8.945084761	5.71E-10	1.53E-08
Scel	5.194741109	5.976247489	5.302612317	1.939193498	1.884923388	2.375913996	1.409383162	1.934066494	5.95E-10	1.58E-08
Ddx26b	43.4012241	55.36104937	39.60643507	22.23146831	20.4754423	25.22994386	1.026312117	5.10536285	6.26E-10	1.66E-08
Il18	105.3610797	146.9026241	151.2060297	51.73491225	66.45278926	75.50126697	1.058919581	6.637539556	7.75E-10	2.02E-08
Ccdc141	8.378614691	10.41805305	6.159188152	2.320106506	2.919783288	3.394162851	1.531818393	2.493747028	1.66E-09	4.00E-08
Col4a1	4.692024227	11.71021467	4.81314041	1.800679677	1.552289849	1.621655584	2.089134724	2.137043256	1.76E-09	4.20E-08
Trpv3	5.446099549	5.572446983	3.630249971	1.419766668	1.995801235	1.395378061	1.604229838	1.714926862	2.14E-09	4.99E-08
A630089N07Rik	15.33286488	24.51069071	17.33546334	9.315054481	6.393955807	6.901464463	1.337108652	3.737399656	2.18E-09	5.07E-08
Ces2g	26.72778086	42.52019328	30.87751941	16.65628701	14.74675357	14.33090981	1.130099642	4.605939804	2.47E-09	5.68E-08
Ttpa	3.435232023	5.37054673	4.242089853	1.419766668	0.480470668	1.433090981	1.96253708	1.470197608	2.69E-09	6.10E-08
4933407K13Rik	9.132690013	13.4869369	8.688126334	4.570956102	3.511131802	3.695866215	1.408403576	2.85211365	2.73E-09	6.17E-08
Creb3l2	12.06520516	11.95249498	9.585491495	4.328556915	4.989503087	5.242095959	1.206670673	3.011749146	2.93E-09	6.58E-08
Adrbk2	25.17773715	24.18765031	14.27626393	5.782952038	8.131042067	9.390517221	1.449797243	3.859540762	3.15E-09	6.97E-08

Gpx2	1199.608158	973.0784593	988.5293038	642.3232177	460.4017774	445.9552857	1.029400283	9.616588082	3.60E-09	7.82E-08
Hif3a	10.43137529	12.76009599	9.585491495	4.467070736	5.174299497	4.789540912	1.183418685	2.983533528	7.36E-09	1.48E-07
Gm4951	17.97212851	7.38954926	9.218387566	1.6275374	2.95674257	3.809004977	2.042727893	2.842387952	1.12E-08	2.16E-07
Gm684	4.817703447	5.209026527	4.976297712	2.008450408	2.106679081	2.111923552	1.267371547	1.841853094	1.15E-08	2.23E-07
Ago3	9.928658409	10.74109346	7.54602522	4.36318537	3.991602469	3.620440374	1.234480763	2.752815893	1.45E-08	2.74E-07
Sptsb	210.7640526	215.9525106	459.2878053	119.1911432	102.1554558	117.9660155	1.384659438	7.674176514	2.49E-08	4.48E-07
201001618Rik	10.97598525	13.2446566	8.157865102	5.055754477	2.143638363	2.149636472	1.787191691	2.804747211	3.12E-08	5.50E-07
Fut9	13.86660731	26.24703289	14.48021056	6.683291876	6.356996525	7.99513916	1.375917997	3.660023826	3.16E-08	5.57E-07
Robo2	34.68746482	51.00000391	29.7354183	19.35730652	16.66863624	18.29076647	1.087223816	4.824312162	3.40E-08	5.92E-07
Plekh2	6.242067945	4.805226021	8.565758357	2.701019515	2.291475492	2.300488154	1.424182042	2.177880695	3.54E-08	6.12E-07
Arrdc3	50.48115351	67.07126405	92.87729419	36.63690573	31.78498263	33.26279594	1.049097468	5.702135858	3.60E-08	6.21E-07
Mrc1	3.016301289	2.503563137	3.222356715	1.177367481	1.071819182	0.565693808	1.623631754	0.982041635	4.00E-08	6.83E-07
Grk4	7.205608634	9.327791688	6.526292082	3.739873174	2.069719799	2.866181963	1.406732992	2.41458006	4.08E-08	6.96E-07
Dsel	15.29097181	24.18765031	17.7433566	8.518600008	8.722390581	9.579081824	1.093440254	3.812451795	5.60E-08	9.24E-07
Wwc2	14.830148	15.74821973	14.68415718	6.094608136	8.057123503	8.183703763	1.019797344	3.499225987	5.73E-08	9.44E-07
Slc16a6	19.1032415	21.11876646	26.18674698	12.98567074	8.981105556	9.616794744	1.070982912	4.033551487	6.31E-08	1.03E-06
Xkr9	10.51516144	13.3254167	9.463123519	4.224671549	4.952543804	5.619225164	1.171073905	3.010270145	6.33E-08	1.03E-06
Gbp4	14.70446878	14.65795837	7.056553314	2.943418702	4.582950983	4.600976309	1.586586771	3.020958212	6.45E-08	1.04E-06
Gsap	10.97598525	12.88123614	13.01179484	5.782952038	6.09828155	6.411196496	1.011291702	3.207708146	7.04E-08	1.12E-06
Mia2	18.05591466	18.17102277	17.45783132	6.648663421	9.202861249	10.25791439	1.040913136	3.737422819	7.26E-08	1.15E-06
Pbx3	14.57878956	13.93111746	10.44206733	6.406264234	5.950444422	6.109493132	1.0758046	3.264798028	7.30E-08	1.16E-06
Gm6402	3.937948905	5.249406578	6.199977478	1.523652034	1.884923388	2.375913996	1.41287026	1.836657445	7.99E-08	1.25E-06
Nos2	91.95529624	112.8218614	53.23006979	40.58454963	40.7291289	37.37350428	1.120122029	5.973120676	9.29E-08	1.43E-06
Mir8116	3.686590464	4.199525262	3.915775249	1.973821953	1.071819182	1.433090981	1.390778003	1.46632809	1.08E-07	1.64E-06
Nckap5	4.692024227	4.320665414	2.732884809	1.246624391	1.182697028	1.697081425	1.507546188	1.426658392	1.20E-07	1.78E-06
Arntl2	2.806835922	5.289786629	3.426303343	1.489023579	1.145737746	1.282239299	1.552443421	1.390650876	1.41E-07	2.07E-06
Cfh	42.6052557	87.6247098	18.88545771	0.277027643	4.804706676	5.091244276	3.872857984	4.729788749	1.67E-07	2.40E-06
Cap2	14.74636186	19.38242429	15.54073302	9.799852855	6.726589346	7.240880749	1.061889845	3.618934986	1.94E-07	2.72E-06
Bex2	5.57177877	5.087886376	5.588137595	1.904565043	2.882824006	2.187349393	1.22002743	1.969003854	2.03E-07	2.83E-06
Slfn4	60.87063573	52.61520593	59.9603085	38.36832849	19.40362311	19.61071869	1.163556313	5.38697239	2.60E-07	3.51E-06
Bicd1	13.23821121	17.04038135	15.21441842	5.921465859	7.022263603	8.975675095	1.054471003	3.495265993	2.64E-07	3.55E-06
Lcn2	10.93409217	18.33254297	6.689449384	3.739873174	4.139439598	4.110708342	1.583743604	3.004288195	2.92E-07	3.88E-06
Nlrp10	7.205608634	9.40855179	9.055230264	4.605584557	2.95674257	3.809004977	1.172366256	2.636994079	3.12E-07	4.12E-06
Ccl20	2.848728995	7.026128804	4.038143226	1.246624391	1.367493439	1.772507267	1.664966668	1.629330995	4.11E-07	5.21E-06
Tc2n	79.2198019	111.7316	119.4311451	26.97556669	51.22556502	58.56816564	1.182572722	6.220243379	4.30E-07	5.43E-06
Ubxn10	8.671866205	8.197150272	8.606547683	4.778726834	4.102480316	3.582727454	1.028754832	2.67164558	4.53E-07	5.68E-06
Eya2	6.954250194	6.016627539	6.730238709	3.739873174	2.661068313	2.300488154	1.174161979	2.25743199	5.86E-07	7.12E-06
Ttyh1	22.03575664	21.19952656	13.13416281	9.176540659	8.981105556	9.31509138	1.036420648	3.808807961	8.34E-07	9.68E-06
Rgma	5.320420329	5.168646477	5.261822991	2.874161791	2.365394056	1.923358949	1.132156904	1.952124921	8.61E-07	9.93E-06
Rhoj	4.650131154	7.066508855	2.977620762	2.008450408	1.663167696	0.942823014	1.664716383	1.705762605	9.56E-07	1.09E-05
Tnfrsf8	7.917790883	6.05700759	5.261822991	3.566730898	1.92188267	1.772507267	1.399261823	2.156741794	1.02E-06	1.16E-05
Il18bp	36.94969079	33.11164149	18.15124985	11.04647725	14.82067213	13.76521601	1.154292635	4.41544979	1.13E-06	1.27E-05
4732471J01Rik	7.624539369	7.954869968	7.301289267	4.536327647	2.661068313	3.243311169	1.12828732	2.485892816	1.27E-06	1.40E-05
Pfkfb3	6.577212533	5.41092678	3.467092669	2.527877238	1.034859899	1.621655584	1.568859924	1.799602112	1.27E-06	1.41E-05
Gm11992	6.954250194	5.209026527	5.588137595	2.250849596	2.882824006	3.054746566	1.116473346	2.126699394	1.59E-06	1.72E-05
Lif	12.81928048	10.09501265	8.892072962	5.782952038	4.804706676	5.128957197	1.015273828	2.99366544	1.76E-06	1.87E-05

2210407C18Rik	411.0129437	580.6651276	273.0029557	152.2959465	202.1303139	228.2008823	1.118155735	8.266400113	1.77E-06	1.88E-05
Bglap3	4.566345007	4.239905313	2.488148856	1.6275374	1.552289849	1.131387617	1.383699964	1.405229805	2.05E-06	2.15E-05
Myot	2.471691334	2.543943188	1.713151671	0.865711383	0.665267078	0.942823014	1.437983619	0.666504119	2.10E-06	2.20E-05
Srd5a2	7.456967075	8.479810626	6.403924105	4.36318537	2.587149749	3.281024089	1.123454732	2.453446348	2.87E-06	2.92E-05
Gsdmcl-ps	4.356879639	2.826603542	4.609193783	2.14696423	1.108778464	1.018248855	1.454518492	1.446687063	3.02E-06	3.05E-05
Ppp1r12b	5.781244137	5.572446983	3.915775249	2.320106506	2.143638363	2.526765678	1.125618201	1.909887493	3.03E-06	3.05E-05
D930048N14Rik	12.06520516	10.78147351	9.503912844	6.683291876	4.767747394	4.525550468	1.015167453	3.018276641	3.08E-06	3.09E-05
Tex12	2.387905187	2.624703289	3.099988739	1.489023579	0.739185642	0.754258411	1.431323824	0.929169768	3.14E-06	3.15E-05
Adamts3	2.346012114	3.230404048	3.874985924	1.315881302	1.108778464	1.395378061	1.304561176	1.17936579	3.15E-06	3.15E-05
Clca2	23.46012114	34.04038266	15.86704762	12.95104229	9.905087609	10.71046944	1.127470004	4.15901241	3.26E-06	3.24E-05
Rel	4.398772713	4.885986123	3.059199413	1.766051221	1.515330567	2.036497711	1.213248802	1.581450805	3.71E-06	3.61E-05
Gad2	4.147414272	5.087886376	5.098665689	2.597134149	2.143638363	2.074210631	1.069524551	1.839198795	3.80E-06	3.69E-05
Dcblid2	9.719193042	8.358670474	6.485502756	3.532102442	4.287276726	4.186134183	1.032568718	2.6179296	3.99E-06	3.84E-05
Spry4	7.456967075	6.380047995	4.201300528	2.978047157	2.328434774	2.63990444	1.179727908	2.129629984	4.52E-06	4.30E-05
Khdc1a	3.141980509	6.420428045	3.222356715	1.800679677	0.258714975	0.829684252	2.13409062	1.408876618	5.51E-06	5.11E-05
Mx2	3.39333895	2.584323238	3.385514017	1.835308132	0.739185642	0.905110094	1.416140863	1.132767694	8.34E-06	7.28E-05
Adamts15	48.21892755	37.1092665	20.59860938	13.36658375	17.85133327	17.64964682	1.116084886	4.690952019	9.62E-06	8.25E-05
Cav2	10.01244456	14.41567806	16.88678076	5.228896753	6.911385757	7.957426239	1.040555884	3.361573167	1.01E-05	8.62E-05
Tac1	23.96283802	57.01663145	44.25641818	16.79480083	19.07098958	22.81631694	1.093883773	4.939916761	1.17E-05	9.81E-05
Muc1	73.31287855	86.29216813	45.07220469	14.92486424	35.48091084	35.37471949	1.25486582	5.597969152	1.30E-05	0.00010701
Proz	3.896055831	3.916864908	3.222356715	1.731422766	1.92188267	1.659368505	1.05248234	1.474019295	1.33E-05	0.0001089
Lonrf3	20.40192677	23.5415695	16.56046616	13.92063904	7.576652835	8.409981286	1.014945784	3.918051517	1.44E-05	0.0001168
Gm3002	3.602804317	5.249406578	4.690772434	2.770276425	0.997900617	1.169100538	1.4473638	1.646852934	1.52E-05	0.00012193
lgj	26.3507432	21.44180687	25.69727507	5.159639842	11.71609243	14.63261318	1.222575612	4.131461778	1.66E-05	0.00013125
Pear1	19.85731682	15.62707958	17.21309537	12.25847318	7.170100732	5.99635437	1.049288493	3.70778993	1.76E-05	0.0001384
Arid3a	10.8921991	11.22565407	6.036820176	3.635987808	4.472073137	4.864966753	1.117922509	2.785643434	1.83E-05	0.00014266
Eaf2	4.063628125	10.377673	6.893396012	2.527877238	2.808905441	3.35644993	1.295529176	2.336444017	2.32E-05	0.00017516
Efcab5	6.91235712	4.845606072	4.446036481	2.66639106	2.734986877	2.564478598	1.022168374	2.027287414	2.32E-05	0.00017553
Zfp37	4.733917301	5.693587135	6.893396012	2.181592685	3.030661134	3.281024089	1.029742028	2.121353215	2.55E-05	0.00018973
Nccrp1	2.890622068	3.311164149	2.692095484	1.6275374	1.404452721	0.754258411	1.223626403	1.117338898	2.68E-05	0.00019786
Rab31	6.200174871	4.885986123	10.19733138	4.016900817	2.328434774	2.63990444	1.240664921	2.348026852	3.92E-05	0.00027418
Fam198b	5.404206476	9.933492447	12.52232293	5.090382932	3.252416827	3.507301613	1.231293827	2.736959918	3.98E-05	0.00027769
Krt83	2.890622068	2.624703289	2.324991554	1.592908945	0.960941335	0.829684252	1.201426074	0.946983129	4.00E-05	0.00027876
Sun3	2.513584407	3.472684352	2.161834252	0.761826017	1.626208413	0.942823014	1.290812172	0.975123886	5.57E-05	0.00036994
Gm16386	4.147414272	5.37054673	3.344724692	2.66639106	1.182697028	1.734794346	1.198011665	1.645271611	6.35E-05	0.00041478
Cacna2d1	2.974408215	3.068883846	5.139455014	1.211995936	2.032760517	1.734794346	1.168103191	1.456248381	7.27E-05	0.00046346
Trim29	2.806835922	2.503563137	4.201300528	1.939193498	1.034859899	1.055961776	1.230419443	1.209556335	7.47E-05	0.00047436
Il34	3.309552803	3.109263896	4.894719061	1.419766668	2.069719799	1.923358949	1.064342249	1.505585317	8.25E-05	0.00051543
Zc3h12c	3.560911244	3.109263896	2.528938182	1.03885366	1.478371285	1.810220187	1.089514644	1.205203227	9.46E-05	0.00057713
Gbp5	12.06520516	12.51781569	2.732884809	1.315881302	3.104579698	3.281024089	1.826170411	2.550543982	9.51E-05	0.00057905
Lrp8	20.3600337	18.00950257	16.60125548	12.77790001	4.17639888	3.771292057	1.404819245	3.661703957	9.57E-05	0.0005827
Chad	3.51901817	4.118765161	2.284202229	1.211995936	1.811004824	1.508516823	1.13050302	1.299247404	9.63E-05	0.00058573
Mir17hg	13.99228653	11.91211493	9.830227448	8.483971553	3.880724623	3.695866215	1.150706232	3.117490955	0.00010453	0.00062837
St8sia5	4.943382668	8.964371233	7.219710616	4.190043094	8.964371233	2.866181963	1.007655835	2.412727792	0.000107573	0.000643
Slc16a3	5.194741109	4.320665414	4.649983108	3.289703255	1.441412003	1.131387617	1.264710694	1.761287703	0.000109909	0.00065324
Tgtp1	47.08781456	43.16627409	14.31705325	7.02957643	14.93154998	16.74453673	1.43398142	4.578821719	0.000122431	0.00071632

D7Ertd715e	4.817703447	6.420428045	5.057876363	3.809130085	2.143638363	2.111923552	1.010146584	2.041491179	0.000162588	0.00091219
Mndal	1.759509085	3.149643947	2.284202229	1.004225204	0.960941335	1.31995222	1.130822053	0.851595532	0.0001718	0.00095432
Foxq1	13.69903502	13.1638965	6.444713431	4.120786183	6.320037243	5.543799323	1.059216564	3.045305901	0.000190023	0.00103851
Gbp2	126.056258	131.3159245	59.91951918	26.10985531	57.32384657	62.49030938	1.120707347	6.271078498	0.000204915	0.00110422
Zfp618	5.781244137	4.68408587	3.507881994	1.6275374	2.587149749	2.715330281	1.012742218	1.820104932	0.000205968	0.00110843
Camsap2	14.9977203	18.85748363	7.953918475	4.674841468	6.726589346	8.221416683	1.091764449	3.361345328	0.000220565	0.00117878
I830012O16Rik	2.094653673	1.817102277	2.406570205	1.142739026	1.071819182	0.829684252	1.04670052	0.696506496	0.000267877	0.00138694
Rims2	2.639263628	4.966746224	2.36578088	2.008450408	1.034859899	1.169100538	1.236814061	1.275838074	0.000278443	0.00143522
Ccl8	2.052760599	2.866983593	2.284202229	1.177367481	1.515330567	0.565693808	1.138883696	0.85042376	0.000381736	0.00185872
Slc16a12	6.242067945	5.572446983	3.9973539	3.913015451	1.92188267	1.885646028	1.028667725	1.99158904	0.000645314	0.00288886
Gbp7	67.82488592	74.42043325	27.08411214	14.99412115	30.6022856	33.26279594	1.102620347	5.371346215	0.000778951	0.00337895
Igf1p4	11.98141901	8.72209093	7.668393196	7.375860983	2.993701852	3.130172407	1.068090827	2.813142316	0.001007614	0.00418972
F830016B08Rik	19.31270686	24.71259097	7.097342639	3.566730898	7.724489964	9.805359347	1.277274814	3.592872419	0.001324876	0.00526143
3930402G23Rik	6.702891753	5.491686882	7.382867918	5.055754477	0.997900617	1.470803902	1.374071342	2.191059572	0.001831477	0.00691547
Reg3a	2.890622068	2.261282834	1.590783695	1.558280489	1.034859899	0.754258411	1.000016702	0.801251714	0.001854747	0.00698569
Gbp9	7.750218589	7.187649007	3.059199413	1.939193498	3.585050366	3.243311169	1.037789694	2.171441873	0.001978503	0.00736577

Table S2. Genes downregulated &gt;2-fold by Smad4 loss in mouse colon

GeneSymbol	A_SMAD4_KO_1	A_SMAD4_KO_2	A_SMAD4_KO_3	A_SMAD4_WT_1	A_SMAD4_WT_2	A_SMAD4_WT_3	logFC	logCPM	PValue	FDR
Id3	3.141980509	3.916864908	2.855252786	107.2443261	133.0903749	117.287183	-5.16997234	5.941028174	1.02E-187	1.19E-183
Mal	6.996143267	10.74109346	5.792084223	222.1415409	177.0349614	187.5840669	-4.63883313	6.671062742	2.34E-106	1.36E-102
Sult1a1	53.79070632	65.41568197	76.92866792	543.1473217	699.2696178	738.4189847	-3.33600951	8.503800243	2.08E-71	8.07E-68
Id1	45.95670158	53.7862274	47.92745748	205.5545108	237.7960212	224.3164515	-2.1765279	7.087866225	7.42E-54	1.72E-50
Selenbp1	95.55810055	87.14014919	120.0021957	531.5814176	567.8054513	535.7120366	-2.43335592	8.335939708	1.95E-52	3.76E-49
Sct	0.963540689	1.049881316	1.468415718	22.4738675	16.89039193	14.33090981	-3.94097607	3.278096684	4.72E-49	7.83E-46
Mptx1	14.70446878	38.23990792	19.78282287	838.1125041	462.7302122	477.8981294	-4.61175083	8.270439027	7.17E-41	9.25E-38
Pdzd7	0.12567922	0.080760101	0.081578651	4.467070736	3.843765341	4.261560024	-5.38355921	1.187947811	8.48E-41	9.85E-38
Cox7c	28.36161073	22.37054803	28.38937056	81.16909927	92.06557177	86.32487517	-1.71386052	5.822265489	7.05E-33	4.81E-30
Cyp4b1	0.083786147	0.080760101	0.36710393	3.462845532	5.469973754	5.35523472	-4.706193	1.378061874	2.88E-32	1.86E-29
Tst	66.4424145	52.77672613	73.13526064	206.3163368	253.3928382	220.9600016	-1.82313385	7.186289455	7.14E-31	4.14E-28
Cspg4	0.083786147	0.242280304	0.163157302	3.532102442	3.215457545	3.167885327	-4.29448231	0.896177821	3.77E-30	2.09E-27
Zg16	571.4215219	470.6294897	581.1663099	1617.772176	2387.680503	2360.300847	-1.97146365	10.3789802	3.63E-27	1.56E-24
Enpep	1.759509085	1.655582075	2.855252786	27.77202117	14.19236434	16.40512045	-3.21588766	3.452062132	5.31E-27	2.20E-24
Smad4	47.84188989	59.19715418	46.09193783	132.4538416	147.7632099	152.3224862	-1.49783013	6.610896244	1.79E-26	6.94E-24
Mpst	76.20350062	60.61045595	92.55097959	320.0708125	268.9896553	241.9283854	-1.8571804	7.466579424	6.70E-26	2.51E-23
Ces1d	3.183873583	2.988123744	6.607870733	45.32864801	28.9391179	29.94405893	-3.02606877	4.297908881	7.28E-26	2.64E-23
Prss23	2.471691334	2.180522732	2.610516833	10.45779351	17.81437398	17.76278559	-2.66125529	3.172870144	3.81E-25	1.30E-22
Uqcr11	75.44942529	59.47981453	78.11155836	214.8695653	220.609955	187.998909	-1.54922667	7.124689009	4.29E-25	1.42E-22
Arhgef19	12.1489913	10.01425255	11.25785384	36.53302036	37.84630489	32.39539877	-1.67571402	4.554610868	1.83E-24	5.60E-22
Acaa1a	27.94268	24.59145082	30.26567953	68.91062608	84.89547104	74.33216643	-1.4620253	5.699053692	3.96E-24	1.12E-21
Ugt8a	0	0.121140152	0.040789326	1.869936587	1.884923388	1.923358949	-4.99566799	0.118780038	5.57E-24	1.54E-21
Nts	2.220332893	1.574821973	1.672362346	11.84293172	8.463675606	9.692220585	-2.45500526	2.597496685	7.95E-24	2.15E-21
Bcat2	32.509025	28.30641547	30.99988739	72.99678381	81.4582578	76.48180291	-1.33061545	5.75263948	1.39E-23	3.66E-21
Cdkn1a	76.32917984	73.24941179	75.7865668	191.1490734	184.9072885	171.0280948	-1.27949576	7.009755476	5.51E-23	1.36E-20
Kcnf1	3.644697391	3.149643947	3.956564575	13.15881302	13.60101582	15.16059407	-1.961747	3.155299746	1.80E-22	4.18E-20
Ndufb8	94.76213216	75.99525523	103.8496228	238.3130295	286.6561921	252.8651324	-1.50206014	7.455629265	3.54E-22	8.06E-20
Mettl7a1	52.91095177	58.10689281	69.05632809	161.7148863	144.8064674	148.3249166	-1.33668995	6.727232997	4.63E-22	1.02E-19
Dio1	15.54233025	17.32304171	14.60257853	39.23403988	50.48637938	53.06207924	-1.58813517	4.992533782	6.01E-22	1.29E-19
Slc27a4	53.83259939	40.94537131	53.27085912	123.6582139	127.5834419	116.8346279	-1.31398666	6.428721113	1.07E-21	2.21E-19
Slc25a34	14.24364497	11.75059472	12.80784821	34.45531304	48.3797003	39.90026996	-1.66101924	4.757646971	1.48E-21	3.01E-19
Phgr1	51.40280113	42.52019328	58.32873548	129.1641383	151.6808938	119.5122453	-1.39479461	6.527159622	3.83E-21	7.67E-19
Lpo	30.12111981	35.73634478	38.30117666	78.88362122	122.5939388	112.2336516	-1.59026201	6.124575173	4.01E-21	7.89E-19
Ndufa13	76.32917984	52.65558598	66.64975789	192.3610693	201.871599	160.8833191	-1.50469442	6.968765304	1.28E-20	2.44E-18
Sepw1	32.63470422	26.12589274	36.22092105	77.74088219	89.18274776	80.1399562	-1.37908602	5.836254309	2.32E-20	4.21E-18
Rplp2	194.8027916	156.6745963	192.8927203	486.9799671	491.8171672	423.9309401	-1.36558649	8.342724211	6.80E-20	1.22E-17
Fam189a2	10.76651988	10.98337376	13.62363472	37.98741548	34.07645812	31.11315947	-1.54409604	4.537631599	7.31E-20	1.29E-17
Etfb	79.59683957	70.18052794	96.09965091	216.4971027	218.4293573	196.5220291	-1.36070378	7.193279466	7.83E-20	1.36E-17
Hsd17b14	0.502716881	0.888361113	0.571050557	3.462845532	5.026462369	5.242095959	-2.79339362	1.452140148	9.75E-20	1.67E-17
Aqp1	41.18089121	33.11164149	52.41428328	103.8507375	148.0588842	137.3881696	-1.61921265	6.428434069	1.15E-19	1.91E-17
Id2	6.91235712	9.489311891	7.015763988	22.68163823	25.46494538	28.13383874	-1.70233892	4.065697588	1.44E-19	2.32E-17
Trappc6a	23.58580036	21.72446722	21.04729196	52.98153664	57.95215437	50.27132311	-1.28050619	5.249835632	2.32E-19	3.68E-17
Phospho1	4.48255886	3.3515442	5.873662874	17.2795992	19.73625665	16.36740753	-1.9605107	3.500412197	3.93E-19	6.08E-17
Smad6	6.032602578	5.087886376	7.423657243	20.67318783	21.17766866	18.8941732	-1.71125073	3.738419136	4.60E-19	7.03E-17

Ndufa7	50.60683273	50.5154433	57.67610627	107.7983814	131.0945737	116.6460633	-1.16264843	6.423605264	5.16E-19	7.79E-17
Usp2	13.11253199	15.10213892	12.80784821	32.62000491	39.76818756	40.95623173	-1.46547916	4.69218242	5.50E-19	8.18E-17
Adra2a	11.93952593	6.218527792	14.76573584	55.68255615	46.23606194	46.72630858	-2.17454902	4.92656499	5.85E-19	8.60E-17
Cox17	22.87361811	19.38242429	23.94333408	58.86837404	51.59515784	53.28835676	-1.30667885	5.264962655	6.22E-19	9.03E-17
Tff3	159.1936791	124.7743564	119.3903558	318.5817889	393.0619654	349.3347832	-1.39525958	7.931810677	8.22E-19	1.18E-16
Ndufs7	60.451705	50.31354305	59.26688997	130.6531619	139.7430457	114.3832881	-1.17827341	6.532798355	1.02E-18	1.43E-16
Isoc2a	13.11253199	11.10451391	14.0723173	40.13437971	35.37003299	31.9051308	-1.48816236	4.609715379	1.09E-18	1.51E-16
Hmgcs2	337.5324928	395.5225956	732.4539182	2003.186883	2307.959331	2214.238705	-2.15464245	10.37934013	1.13E-18	1.54E-16
Slc51a	18.13970081	12.96199624	26.30911496	64.61669762	72.03364086	67.27985029	-1.82845537	5.449395045	1.38E-18	1.87E-16
Gpt	24.17230338	18.45368312	31.44856997	69.49930982	77.39273677	70.03289349	-1.5500098	5.603804395	1.55E-18	2.07E-16
Kazald1	0.251358441	0.201900253	0.36710393	2.043078864	2.771946159	2.602191519	-3.15259483	0.569955195	2.60E-18	3.35E-16
Prap1	13.40578351	9.085511385	13.70521337	43.59722525	34.15037668	35.78956162	-1.64939852	4.649181324	3.29E-18	4.19E-16
Tgfb1	3.770376611	3.674584605	2.36578088	11.66978944	12.67703377	13.0109576	-1.92760933	2.998246824	4.43E-18	5.59E-16
Ndufa2	42.94040029	40.4608107	52.21033666	99.93772205	103.1163971	97.5633255	-1.14835947	6.186366521	7.25E-18	9.05E-16
Atg4d	52.57580719	40.703091	45.52088727	100.4225204	113.3541183	98.20444515	-1.1685119	6.233611774	8.19E-18	1.00E-15
Cd320	8.211042397	6.904988653	8.606547683	20.74244474	23.72785912	23.30658491	-1.51397556	3.942407557	9.39E-18	1.14E-15
Rps19	175.657657	172.8266166	228.1346976	445.6682199	514.6210443	487.2509337	-1.32787245	8.398679717	1.29E-17	1.53E-15
Cpm	5.446099549	5.733967185	5.751294897	17.21034229	53.25832554	55.62655783	-2.89536157	4.583432264	1.51E-17	1.77E-15
Retsat	37.45240767	37.71496726	41.72748	74.90134885	99.8639803	97.33704798	-1.21863769	6.02125921	1.52E-17	1.77E-15
Ethe1	238.2878018	190.9572593	250.7727732	571.923568	566.0314057	519.3069162	-1.28516203	8.606121392	1.93E-17	2.21E-15
Acaa2	81.4401348	79.30641938	104.7877772	192.4995831	273.0551763	259.1631901	-1.44840663	7.367777073	1.94E-17	2.21E-15
Nudt14	12.81928048	10.70071341	12.88942686	29.81510003	35.22219586	31.03773363	-1.39959348	4.472748942	3.21E-17	3.56E-15
Naprt1	31.00087436	26.36817304	25.81964305	60.80756754	69.63128752	60.68008919	-1.20000785	5.518459383	3.22E-17	3.56E-15
Acaa1b	0.586503028	0.444180557	1.223679765	5.090382932	3.954643187	4.864966753	-2.61754398	1.495968815	3.46E-17	3.76E-15
Sgk1	28.73864839	18.93824373	22.02623578	55.89032688	108.3276559	109.0657663	-1.97091396	5.840305879	3.60E-17	3.83E-15
Tstd1	47.79999681	44.37767561	66.89449384	132.5230985	132.7207821	124.9806188	-1.2945393	6.518469293	3.75E-17	3.96E-15
Pbld1	0.670289175	0.524940658	0.571050557	2.73564797	4.435113855	4.148421262	-2.6696055	1.199038447	4.09E-17	4.28E-15
Crip1	122.2020953	112.5795811	161.4033611	343.4450198	337.73392	315.1291642	-1.33039111	7.859291512	5.18E-17	5.32E-15
St3gal5	2.387905187	1.049881316	3.671039296	29.71121466	15.48593921	15.65086203	-3.09581869	3.52322063	6.40E-17	6.51E-15
Azgp1	0.586503028	0.484560607	0.81578651	2.978047157	3.954643187	4.186134183	-2.548338	1.190794375	6.50E-17	6.56E-15
Ndufb2	21.70061205	26.16627279	31.40778064	59.28391551	72.18147799	67.88325702	-1.32990138	5.541031466	7.80E-17	7.73E-15
Rpl36	144.1121727	99.13302422	133.0139905	302.1679011	364.7881146	308.6425419	-1.37456722	7.816570572	7.86E-17	7.73E-15
D10Jhu81e	30.41437133	31.53681952	32.10119918	62.95453177	70.14871747	66.03532391	-1.08200312	5.614163026	9.46E-17	9.23E-15
Ndufs6	72.55880323	58.18765291	72.19710616	144.3660302	144.0672817	145.5718734	-1.0966534	6.731672932	1.69E-16	1.61E-14
Gm11127	0.377037661	0.68646086	0.407893255	2.943418702	3.104579698	2.828469042	-2.57760077	0.879987484	1.72E-16	1.62E-14
Rab17	8.378614691	8.600950778	10.68680328	22.64700978	28.5325658	25.72021183	-1.47396013	4.13350167	1.97E-16	1.85E-14
Adck3	11.31112983	11.02375381	14.43942123	28.672361	37.73542705	35.29929365	-1.46695527	4.53626261	2.04E-16	1.89E-14
Ovol1	21.1560021	17.76722226	16.60125548	45.53641874	44.2402607	42.12533227	-1.24839838	4.970857915	2.10E-16	1.93E-14
Mt2	56.63943531	42.64133343	31.93804188	110.9149424	120.7459747	123.0572598	-1.43473433	6.341905709	3.10E-16	2.83E-14
Pmm1	14.57878956	10.94299371	15.01047179	32.51611954	39.73122828	35.97812622	-1.41668928	4.638995247	3.33E-16	3.00E-14
Tbx3	11.64627442	12.23515533	12.97100551	29.50344393	28.38472867	30.28347521	-1.25809166	4.389447998	4.27E-16	3.79E-14
Surf1	42.85661415	41.75297232	43.72615695	79.22990577	91.32638613	89.1156313	-1.01658491	6.017498241	6.13E-16	5.39E-14
Ctsf	1.047326836	1.130641417	1.060522463	4.016900817	4.656869547	4.827253832	-2.05345667	1.538916539	7.29E-16	6.31E-14
Aldh16a1	51.36090806	37.43230691	43.76694627	97.68687245	109.6212308	89.83217679	-1.16459676	6.164638538	9.22E-16	7.87E-14
Fam195a	13.36389043	10.41805305	13.33810944	40.65380654	33.63294673	28.66181963	-1.47187835	4.553250326	1.01E-15	8.58E-14
Acer1	11.98141901	9.247031587	25.20780317	73.75860983	74.58383132	68.29809914	-2.22158872	5.459333441	1.03E-15	8.65E-14

















Oaz1	1.424364497	3.109263896	3.589460645	5.021126021	5.211258779	6.712899861	-1.05728086	2.09815926	0.000331306	0.001658388
Gnb1l	1.633829865	1.615202024	2.324991554	4.8826122	3.400253955	2.866181963	-1.00031635	1.532648394	0.000350543	0.001737446
Tubb2b	0.670289175	0.969121214	1.101311789	2.389363417	1.589249131	1.885646028	-1.09375594	0.615607394	0.00039449	0.001913598
Adhfe1	1.08921991	1.534441923	1.101311789	1.6275374	3.437213237	3.130172407	-1.13042888	1.056212913	0.000431811	0.00206444
Pxdc1	1.298685277	0.524940658	1.142101114	4.36318537	1.73708626	1.772507267	-1.40939196	0.939722901	0.000503155	0.00233345
Alox5	1.424364497	0.767220961	1.223679765	3.220446345	2.143638363	1.923358949	-1.09538485	0.914454651	0.000513707	0.002371018
Hck	2.848728995	2.220902783	3.9973539	8.65711383	5.580851601	4.186134183	-1.02340183	2.231424751	0.000645759	0.002889732
C430002E04Rik	0.921647616	1.413301771	0.856575836	2.66639106	1.774045542	2.074210631	-1.02674834	0.779188505	0.000744933	0.003266275
Vwa5b2	1.927081379	1.009501265	0.774997185	2.285478051	2.845864723	2.489052757	-1.03761496	0.98704434	0.000902542	0.003833409
Fgf12	0.921647616	2.099762631	2.243412903	2.770276425	4.250317444	3.695866215	-1.01990724	1.465324624	0.000910332	0.003862257
Mogat2	4.356879639	3.311164149	12.11442968	17.31422766	14.70979428	13.16180928	-1.19108066	3.452699979	0.000979469	0.004088792
Alpi	6.954250194	4.966746224	19.8236122	28.63773255	22.98867348	21.23237428	-1.19825268	4.134086246	0.001202259	0.004849138
Pdzd4	1.005433763	1.33254167	1.509205044	4.328556915	1.884923388	2.074210631	-1.10679703	1.091305341	0.001312123	0.005226878
Vsig2	7.959683957	6.824228551	9.422334193	36.94856182	10.93994751	9.956211029	-1.25692511	3.788697773	0.00134488	0.005326295
Ang4	6.870464047	10.66033336	16.47888751	68.97988299	13.41621941	15.23601991	-1.52117577	4.466345249	0.002107264	0.007760509
Dbp	4.356879639	4.239905313	11.17627519	6.059979681	23.02563276	20.96838383	-1.33881522	3.553518179	0.00221157	0.00806785



**Table S3. IPA-identified Inflammatory Genes Upregulated by *Smad4* Loss in Mouse Colon**

Molecule Name	Entrez Gene ID for Human	Entrez Gene ID for Mouse		
ABCC4	10257	239273		
ADAMTS3	9508	330119		
ADAMTS15	170689	235130		
AREG	374	11839		
BGLAP	632	12097 12096 12095		
C3	718	12266		
C1GALT1	56913	94192		
C4A/C4B	720 721	625018 12268		
CACNA2D1	781	12293		
Ccl8		20307		
CCL20	6364	20297		
CFH	3075	12628		
CMA1	1215	17228		
COL4A1	1282	12826		
CXCL6	6372	20311		
EGLN3	112399	112407		
EGR1	1958	13653		
EREG	2069	13874		
F3	2152	14066		
F13A1	2162	74145		
GABBR1	2550	54393		
GAD2	2572	14417		
GBP2	2634	14469		
GBP5	115362	229898		
GBP6	163351	634650 17472 626578 236573 100702		
GHR	2690	14600		
GJA1	2697	14609		
GPX2	2877	14776		
GSDMC	56169	83492 270328 74548 331063		
H60b/H60c		667281 670558		
HIF1A	3091	15251		
IDO1	3620	15930		
IFI16	3428	100504287 545384 226691 236312 15951 102639543 100033459 15950 226695 381308 100040462 623121		
IFI44	10561	99899		
IFIT2	3433	15958		
IGFBP4	3487	16010		
Igha		238447		
IGKC	3514	16071		
IL18	3606	16173		
IL34	146433	76527		

IL18BP	10068	16068		
IL1RN	3557	16181		
ITGA2	3673	16398		
IVNS1ABP	10625	117198		
KRT15	3866	16665		
LBP	3929	16803		
LCN2	3934	16819		
LIF	3976	16878		
LTF	4057	17002		
Ly6a (includes others)		57248 546644 110454 17071 17067 100041546 546643		
MIR17HG	407975	75957		
MRC1	4360	17533		
MUC2	4583	17831		
Mx1/Mx2		17858 17857		
Naip1 (includes others)		17952 17951 17940		
NFATC2	4773	18019		
NLRP10	338322	244202		
NOS2	4843	18126		
NRP1	8829	18186		
OSMR	9180	18414		
PDE11A	50940	241489		
PEAR1	375033	73182		
PF4	5196	56744		
PRUNE2	158471	353211		
RAB31	11031	106572		
REG3A	5068	18489		
REL	5966	19696		
SIGLEC1	6614	20612		
SLC7A11	23657	26570		
SLFN5	162394	327978		
SLFN12L	100506736	20558 20557		
SLPI	6590	20568		
SPATS2L	26010	67198		
SPRY4	81848	24066		
SRD5A2	6716	94224		
STEAP4	79689	117167		
TAC1	6863	21333		
TCF4	6925	21413		
TF	7018	22041		
TICAM2	353376	225471		
TNFRSF8	943	21941		
TNFSF13B	10673	24099		

TRIM6	117854	94088		
TRPV3	162514	246788		

**Table S4. IPA-identified Master Regulators of Genes Upregulated by *Smad4* Loss in Mouse Colon**

Master Regulator	Molecule Type	Depth	Predicted Activation State	Notes	Activation z-score	p-value of overlap	Network bias-corrected p-value	Causal network	Target-connected regulators
IL27RA	transmembrane	3	Activated	biased	2.785	8.94E-17	1.00E-04	29 (6)	4
JAK2	kinase	3			1.768	9.69E-17	1.00E-04	32 (5)	4
JAK2	kinase	2	Activated	biased	2.043	3.24E-16	1.00E-04	29 (4)	3
PRKAA1	kinase	3		biased	-1	7.55E-16	1.00E-04	36 (10)	7
PIAS3	transcription	3		biased	1.677	2.51E-15	1.00E-04	43 (6)	5
STAT1	transcription	2			0.928	4.83E-15	1.00E-04	29 (3)	3
AR	ligand-dependent	3	Activated	biased	3.101	2.38E-14	1.40E-03	65 (18)	14
FGFR3	kinase	3			0.392	4.76E-14	1.00E-04	26 (5)	3
GRB2	kinase	3		biased	1.671	1.00E-13	2.00E-04	29 (8)	5
IL6	cytokine	3			1.155	1.04E-13	2.00E-04	48 (7)	5
STAT3	transcription	2			0.2	1.15E-13	1.00E-04	25 (2)	2
CEBPA	transcription	2	Activated		2.043	1.19E-13	1.00E-04	29 (2)	2
PIAS3	transcription	2			0.928	4.36E-13	1.00E-04	29 (3)	2
PTPN11	phosphatase	2	Inhibited	biased	-3.3	4.82E-13	1.00E-04	18 (3)	2
IL6	cytokine	2			0.408	5.17E-13	1.00E-04	24 (4)	3
CAV1	transmembrane	3			-1.511	5.30E-13	7.00E-04	53 (9)	7
PPM1D	phosphatase	3	Inhibited		-3.266	5.36E-13	1.60E-03	54 (13)	10
AFAP1L2	other	3			0.18	1.06E-12	1.00E-04	31 (7)	4
TIMP3	other	3		biased	-0.626	1.16E-12	1.00E-04	23 (5)	2
STAT1	transcription	1	Activated	biased	3.153	1.36E-12	1.00E-04	17 (1)	1
PTPN1	phosphatase	2			-0.209	2.15E-12	1.00E-04	23 (4)	3
Calcineurin protein	complex	3	Activated	biased	2.832	2.30E-12	1.00E-03	45 (6)	4
APP	other	3	Activated		3.111	3.52E-12	2.60E-03	50 (8)	7
PTPRB	phosphatase	3			-0.186	3.54E-12	1.00E-04	29 (5)	2
PTPRO	phosphatase	3			-0.186	3.54E-12	1.00E-04	29 (5)	2
PRKAA1	kinase	2			1.091	4.24E-12	1.00E-04	21 (3)	2

LRP1	transmembran	3		biased	-1.091	4.24E-12	1.00E-04	21 (5)	2
PIN1	enzyme	3	Activated	biased	2.335	4.42E-12	2.00E-04	31 (6)	5
PTPRE	phosphatase	3		biased	1.915	4.49E-12	6.00E-04	33 (10)	6
TGFB2	kinase	3		biased	1.569	5.36E-12	2.00E-04	26 (9)	6
TGFB1	growth facto	2		biased	1.8	7.38E-12	2.00E-04	25 (4)	3
HAVCR2	other	3		biased	0.816	8.30E-12	1.00E-04	24 (9)	6
RPS6KA3	kinase	3	Activated		2.252	9.47E-12	9.00E-03	57 (15)	11
FCGR2A	transmembran	3		biased	-1.732	1.10E-11	2.00E-04	27 (7)	4
STAT3	transcription	1		biased	0.894	1.15E-11	1.00E-04	20 (1)	1
TLR9	transmembran	3	Activated	biased	3.507	8.86E-11	3.50E-03	43 (10)	7
PIAS1	transcription	3	Activated	biased	3.536	9.12E-11	1.00E-03	32 (6)	5
Hsp27	group	3	Activated	biased	2.828	1.39E-10	1.49E-02	50 (9)	6
SQSTM1	transcription	3	Activated	biased	3.656	1.81E-10	2.30E-03	33 (6)	5
AR	ligand-depen	2	Activated	biased	3.157	7.26E-10	1.60E-03	29 (3)	3
BTRC	enzyme	3			1.234	1.05E-09	7.80E-03	42 (9)	7
PPP1R13L	transcription	3	Inhibited	biased	-2.535	1.31E-08	9.10E-03	35 (3)	3
TGM2	enzyme	3	Activated	biased	2.874	1.38E-08	1.00E-02	35 (5)	3
NCOR2	transcription	3			1.257	1.70E-08	1.40E-02	31 (6)	6
ITCH	enzyme	3	Inhibited	biased	-3	1.74E-08	1.95E-02	36 (4)	3
BCL10	transcription	3	Activated	biased	2.874	1.80E-08	1.19E-02	35 (5)	3
Ikb	group	3	Inhibited	biased	-2.874	2.40E-08	1.51E-02	35 (5)	3
PPP2CB	phosphatase	3			0	2.41E-08	1.70E-02	36 (7)	4
APP	other	2	Activated	biased	3.212	2.96E-08	1.67E-02	35 (4)	3
RELA	transcription	2	Activated	biased	2.744	3.37E-08	1.32E-02	34 (2)	2
RNF31	enzyme	3		biased	-1.3	5.75E-08	2.18E-02	29 (8)	6
Gamma tubulin	group	3	Activated		2	6.61E-08	3.76E-02	36 (5)	4
Hsp27	group	2	Activated	biased	3.441	7.08E-08	2.50E-03	19 (3)	2
CHEK1	kinase	2			-0.343	8.35E-08	2.14E-02	34 (4)	3
NCOA3	transcription	2	Activated	biased	2.041	1.01E-07	1.14E-02	24 (3)	3
ARNT	transcription	2			-0.218	1.32E-07	5.40E-03	21 (3)	2

ESR1	ligand-depen	2			0.408	1.57E-07	1.07E-02	24 (3)	3
BTRC	enzyme	2			1.807	2.13E-07	2.20E-03	15 (5)	4
NCOR2	transcription	2			0	2.33E-07	3.40E-03	18 (3)	3
XIAP	enzyme	3		biased	-1.091	2.41E-07	1.51E-02	21 (8)	5
SMAD7	transcription	3			0.688	2.60E-07	1.52E-02	19 (11)	7
ESR1	ligand-depen	1			0.243	2.65E-07	3.00E-03	17 (1)	1
CAV1	transmembra	2	Inhibited	biased	-2.335	3.67E-07	3.40E-02	31 (3)	2
EGR1	transcription	3	Activated	biased	3.207	6.48E-07	3.10E-03	14 (4)	3
IL1B	cytokine	2	Activated	biased	3.771	6.55E-07	1.51E-02	18 (5)	4
TLR9	transmembra	2	Activated	biased	2.496	6.64E-07	2.50E-03	13 (4)	3
Ppp1cc	phosphatase	3	Inhibited	biased	-3.153	7.57E-07	1.55E-02	17 (9)	5
ITCH	enzyme	2		biased	-1.732	2.55E-06	7.20E-03	12 (3)	2
MUC1	other	2	Activated	biased	3.207	2.87E-06	1.43E-02	14 (3)	2
IKBKG	kinase	2	Activated	biased	3.742	4.07E-06	1.12E-02	14 (5)	4
PTPN12	phosphatase	2		biased	-1.265	5.88E-06	4.10E-03	10 (4)	3
TRAF3	enzyme	3	Inhibited	biased	-3.638	6.37E-06	3.56E-02	17 (5)	2
MAP3K8	kinase	3	Activated	biased	3	8.53E-06	3.91E-02	16 (10)	6
NFKBIA	transcription	2	Activated	biased	2.111	9.65E-06	6.90E-03	11 (3)	3
HOXA10	transcription	1	Inhibited	biased	-2.121	1.50E-05	3.60E-03	8 (1)	1
BCL2	transporter	3	Inhibited	biased	-3.207	1.51E-05	3.52E-02	14 (6)	3
ADAM17	peptidase	3			-0.775	1.59E-05	3.97E-02	15 (7)	5
ECSIT	transcription	2	Activated	biased	2.714	1.61E-05	1.39E-02	11 (3)	3
CSNK2A2	kinase	2		biased	1.667	1.61E-05	5.00E-03	9 (3)	2
MMP9	peptidase	2	Inhibited	biased	-2.53	3.08E-05	1.35E-02	10 (3)	2
Ikb	group	2	Inhibited	biased	-2.53	3.24E-05	1.35E-02	10 (3)	2
Calcineurin prote	complex	2	Activated	biased	2.53	3.24E-05	1.35E-02	10 (3)	2
PPP1R13L	transcription	2		biased	-1.667	3.77E-05	9.80E-03	9 (2)	2
SIAH2	transcription	2	Activated	biased	2.887	5.36E-05	2.95E-02	12 (2)	2
HEXIM1	transcription	3	Inhibited	biased	-2.887	6.23E-05	3.34E-02	12 (3)	2
ZBTB16	transcription	1		biased	-0.816	7.98E-05	5.50E-03	6 (1)	1

P38 MAPK	group	2	Activated	biased	2.53	8.33E-05	4.27E-02	10 (3)	2
RELA	transcription	1	Activated	biased	2.121	9.82E-05	1.48E-02	8 (1)	1
CEBPE	transcription	1	Activated	biased	2	1.15E-04	3.80E-03	4 (1)	1
NFAT5	transcription	1		biased	1.732	2.46E-04	3.20E-03	3 (1)	1
BCL2L13	other	2		biased	0.577	2.46E-04	1.90E-03	3 (3)	2
ITGB1	transmembran	3		biased	0.378	2.57E-04	3.49E-02	7 (5)	2
EGR1	transcription	1	Activated	biased	2.449	3.84E-04	1.90E-02	6 (1)	1
KAT6A	enzyme	1	Activated	biased	2	5.15E-04	8.20E-03	4 (1)	1
NEUROG1	transcription	1			-1.342	6.92E-04	1.25E-02	5 (1)	1
NFATC2	transcription	1	Activated	biased	2.449	7.58E-04	4.62E-02	6 (1)	1
Gm21596/Hmgb1	transcription	2		biased	0.577	8.00E-04	6.30E-03	3 (2)	2
IRF1	transcription	1		biased	1.342	9.98E-04	2.17E-02	5 (1)	1
MKL2	transcription	1	Inhibited	biased	-2	1.46E-03	3.22E-02	4 (1)	1
PRDM1	transcription	1	Inhibited	biased	-2.236	2.13E-03	4.27E-02	5 (1)	1
FOXA1	transcription	1			-1.342	3.11E-03	4.81E-02	5 (1)	1
DMRT1	transcription	1		biased	1.414	3.67E-03	8.20E-03	2 (1)	1
HOXC8	transcription	1			1.732	4.22E-03	3.38E-02	3 (1)	1
HIC1	transcription	1			-1	4.50E-03	3.68E-02	4 (1)	1
MYOG	transcription	1		biased	1.414	4.68E-03	3.09E-02	2 (1)	1
AEBP1	peptidase	1		biased	0	4.68E-03	2.70E-02	2 (1)	1
CERS2	transcription	1		biased	-1.414	4.68E-03	1.92E-02	2 (1)	1
SOX4	transcription	1		biased	1.342	6.27E-03	4.84E-02	5 (1)	1
Meis1	transcription	1		biased	1	1.17E-02	2.81E-02	1 (1)	1
HOXD8	transcription	1		biased	-1	1.17E-02	2.68E-02	1 (1)	1
HOXD1	transcription	1		biased	-1	1.17E-02	2.68E-02	1 (1)	1
HOXD9	transcription	1		biased	-1	1.17E-02	2.68E-02	1 (1)	1
Gm21596/Hmgb1	transcription	1		biased	1.414	1.30E-02	4.70E-02	2 (1)	1
EAF2	transcription	1			-1	2.33E-02	4.73E-02	1 (1)	1
HOXD3	transcription	1			-1	2.33E-02	2.68E-02	1 (1)	1
SMAD6	transcription	1		biased	-1	3.48E-02	2.94E-02	1 (1)	1

**Table S5. IPA-identified Master Regulators of Genes Downregulated by *Smad4* Loss in Mouse Colon**

Master Regulator	Molecule Type	Depth	Predicted Activation State	Notes	Activation z-score	p-value of overlap	Network bias-corrected p-value	Causal network	Target-connected regulators
RICTOR	other	1	Activated	biased	5.578	2.63E-18	1.00E-04	35 (1)	1
ACOX1	enzyme	2			1.622	1.29E-14	1.00E-04	38 (2)	2
PPARA	ligand-dependen	2	Inhibited		-2.335	7.12E-12	1.00E-04	53 (7)	7
ADCYAP1R1	G-protein cou	3	Inhibited	biased	-3.579	2.17E-11	4.00E-04	85 (31)	30
PPARA	ligand-dependen	1	Inhibited	biased	-2.268	6.59E-11	1.00E-04	28 (1)	1
BTK	kinase	3		biased	-1.821	2.27E-10	1.89E-02	133 (67)	60
MYC	transcription	3			1.499	3.09E-10	1.11E-02	114 (41)	36
SREBF2	transcription	3			0.442	8.43E-10	1.90E-03	82 (41)	41
PRKCA	kinase	3			-0.189	2.08E-09	1.12E-02	112 (61)	56
UBE2N	enzyme	3			1.437	2.17E-09	3.80E-02	124 (56)	53
ADCY1	enzyme	3	Inhibited	biased	-3.395	6.98E-09	2.00E-04	42 (10)	8
HDAC3	transcription	3	Activated		2.593	8.27E-09	4.90E-03	72 (31)	31
CSF1R	kinase	3			1.584	1.46E-08	4.33E-02	102 (50)	49
FLCN	other	3	Activated	biased	4.52	2.09E-08	7.90E-03	67 (12)	12
NRIP1	transcription	1	Activated	biased	3	4.67E-08	1.00E-04	9 (1)	1
CXCL3	cytokine	3		biased	-1.455	4.70E-08	1.41E-02	68 (25)	23
GP6	transmembran	3	Activated		2.717	5.01E-08	2.60E-02	78 (38)	33
N-cor	group	3			1.179	8.93E-08	2.51E-02	72 (30)	30
PPARGC1A	transcription	2	Inhibited	biased	-2.041	1.36E-07	5.00E-04	24 (4)	4
LRAT	enzyme	3			-1.25	1.50E-07	2.08E-02	64 (31)	31
APC	enzyme	1	Activated	biased	2.828	1.53E-07	1.00E-04	8 (1)	1
FLCN	other	2	Activated	biased	3.578	1.56E-07	4.00E-04	20 (4)	4
ITGA1	other	3			0.894	5.82E-07	4.39E-02	80 (44)	40
SERCA	group	3			-1.912	5.82E-07	4.56E-02	70 (37)	35
NCOA2	transcription	2			-0.539	5.94E-07	1.30E-03	31 (5)	4
LANCL2	other	3			-0.843	6.00E-07	4.93E-02	69 (30)	29



Fcgr3	group	3		biased	1.905	6.69E-07	3.80E-02	54 (21)	18
CFTR	ion channel	2			-0.728	9.41E-07	4.00E-04	17 (4)	4
CREB3L3	transcription	3			-0.25	1.51E-06	5.00E-02	64 (34)	34
ACOX1	enzyme	1			0	1.66E-06	3.00E-04	14 (1)	1
CFTR	ion channel	1			-1.265	1.66E-06	3.00E-04	10 (1)	1
SLC29A1	transporter	3	Inhibited	biased	-3.772	1.86E-06	3.00E-03	31 (4)	4
AHR	ligand-depen	2		biased	-0.143	2.26E-06	2.67E-02	49 (11)	11
GPR183	G-protein co	3			0.267	2.75E-06	4.33E-02	56 (27)	26
BMP10	growth facto	1		biased	-1.342	2.99E-06	1.00E-04	5 (1)	1
IL10RA	transmembra	1	Inhibited		-2.236	5.82E-06	1.20E-03	20 (1)	1
CREM	transcription	3	Activated	biased	3.772	6.29E-06	6.60E-03	31 (5)	5
INSIG2	other	3		biased	1.859	7.54E-06	1.77E-02	35 (9)	7
KCNA3	ion channel	3	Activated	biased	2.795	7.57E-06	1.36E-02	37 (10)	8
mGLUR Group	group	3	Inhibited	biased	-4.743	8.17E-06	2.12E-02	40 (13)	11
Creb	group	2	Inhibited	biased	-3.9	8.64E-06	6.60E-03	29 (3)	3
FABP1	transporter	3	Inhibited	biased	-2.683	9.09E-06	1.10E-03	20 (4)	4
ACVR2A	kinase	2	Inhibited	biased	-2.236	1.07E-05	3.00E-04	5 (4)	4
FGF21	growth facto	2	Inhibited		-3	1.33E-05	3.10E-03	25 (5)	5
INSIG1	other	3	Activated	biased	2.466	1.50E-05	4.47E-02	37 (10)	9
VTN	other	2		biased	0.209	1.58E-05	2.00E-03	23 (6)	5
CBX5	transcription	1	Activated	biased	3.317	1.77E-05	6.00E-04	11 (1)	1
HNF4A	transcription	1			0	2.49E-05	3.40E-03	16 (1)	1
ATP1A1	transporter	2		biased	-0.229	2.70E-05	3.60E-03	19 (6)	5
HEXIM1	transcription	3		biased	0.928	2.87E-05	1.43E-02	29 (17)	16
FFAR1	G-protein co	2	Inhibited	biased	-2.524	2.95E-05	3.10E-03	19 (3)	2
MAP4K4	kinase	1	Activated	biased	3.317	2.97E-05	6.00E-04	11 (1)	1
N-cor	group	2	Activated	biased	2.236	3.68E-05	4.00E-03	20 (3)	3
TGFB1	growth facto	1		biased	-1.8	3.90E-05	1.59E-02	25 (1)	1
GNAQ	enzyme	2		biased	-0.6	4.93E-05	7.50E-03	25 (7)	7
NR1I2	ligand-depen	1			-0.302	5.19E-05	3.70E-03	11 (1)	1

Pde3	group	3	Inhibited	biased	-2.668	5.80E-05	4.50E-03	17 (5)	4
FAAH	enzyme	2	Activated	biased	2.828	6.21E-05	4.60E-03	18 (3)	3
LHX1	transcription	1	Inhibited	biased	-3.162	7.55E-05	1.00E-03	10 (1)	1
SPDEF	transcription	2	Activated	biased	2.183	8.00E-05	6.30E-03	17 (2)	2
BMP15	growth facto	1	Inhibited	biased	-2	8.74E-05	7.00E-04	4 (1)	1
LOX	enzyme	2		biased	1.877	9.79E-05	2.51E-02	23 (6)	5
PPARGC1A	transcription	1	Inhibited	biased	-2.887	1.10E-04	7.40E-03	12 (1)	1
GPSM1	other	2			0.688	1.27E-04	6.50E-03	19 (4)	3
ATP2A2	transporter	2	Activated	biased	3.5	1.35E-04	7.50E-03	16 (3)	3
TCF7L2	transcription	3			0.6	1.35E-04	1.45E-02	25 (3)	2
SREBF2	transcription	2			0.728	1.41E-04	1.17E-02	17 (5)	5
Cyclin A	group	2			1.789	1.60E-04	2.69E-02	20 (4)	3
HDAC3	transcription	2	Activated		2.4	1.75E-04	1.46E-02	21 (5)	5
DMTF1	transcription	1		biased	-0.577	1.82E-04	5.00E-04	3 (1)	1
sGC	complex	2			1.147	1.85E-04	1.80E-02	19 (3)	2
Esrra	transcription	1	Inhibited	biased	-2.121	2.10E-04	7.80E-03	8 (1)	1
RPTOR	other	2			-1.89	2.11E-04	4.46E-02	28 (11)	11
PTN	growth facto	2			0.943	2.19E-04	1.60E-02	18 (5)	4
P-TEFb	complex	2		biased	-0.229	2.21E-04	1.61E-02	19 (14)	14
ITGA4	transmembr	2		biased	0.5	2.36E-04	1.01E-02	16 (5)	4
CAMK2A	kinase	2	Inhibited	biased	-2.5	2.47E-04	1.21E-02	16 (3)	2
CREB3L3	transcription	2		biased	0.728	2.49E-04	1.88E-02	17 (5)	5
HNF1A	transcription	1	Inhibited	biased	-3.464	2.79E-04	7.30E-03	12 (1)	1
IL6	cytokine	1	Inhibited	biased	-2	2.79E-04	1.24E-02	16 (1)	1
FZD9	G-protein co	2	Inhibited	biased	-2.524	3.14E-04	2.19E-02	19 (3)	2
TNRC6A	other	1		biased	1.732	3.14E-04	3.30E-03	3 (1)	1
EP300	transcription	1		biased	-0.816	3.19E-04	4.00E-03	6 (1)	1
GRB10	other	2			-1	3.28E-04	2.15E-02	16 (6)	5
EHF	transcription	2			1.5	3.41E-04	2.62E-02	16 (3)	3
MTM1	phosphatase	2	Activated	biased	3.3	3.53E-04	2.21E-02	18 (6)	6

NR1I3	ligand-depen	1	Inhibited	biased	-2.121	3.55E-04	6.60E-03	8 (1)	1
FTO	enzyme	2			-1	3.64E-04	4.60E-02	25 (12)	11
TGFBR1	kinase	2		biased	-1.279	3.70E-04	2.32E-02	22 (8)	8
PAX6	transcription	2		biased	-1.807	3.97E-04	2.30E-02	15 (2)	2
PXN	other	2		biased	-1.604	4.18E-04	1.47E-02	14 (4)	4
P-TEFb	complex	1		biased	1.414	4.52E-04	6.00E-03	2 (1)	1
PPP1R13B	phosphatase	1		biased	1.414	4.52E-04	7.50E-03	2 (1)	1
CCT5	other	1		biased	-1.414	4.52E-04	6.00E-03	2 (1)	1
H3F3A/H3F3B	other	1		biased	1.414	4.52E-04	6.00E-03	2 (1)	1
TCP1	other	1		biased	-1.414	4.52E-04	6.00E-03	2 (1)	1
LANCL2	other	2		biased	-1.698	4.70E-04	2.14E-02	17 (3)	2
PPARD	ligand-depen	1	Inhibited	biased	-2.714	4.98E-04	5.00E-03	11 (1)	1
NR1H4	ligand-depen	1	Inhibited		-2.333	5.03E-04	1.24E-02	9 (1)	1
FAM120A	other	2			0.775	5.06E-04	1.59E-02	15 (4)	3
FGFR4	kinase	2			-1.414	5.16E-04	1.92E-02	18 (4)	3
HDAC1	transcription	2		biased	1	5.21E-04	3.22E-02	16 (2)	2
ITGA9	other	2	Inhibited	biased	-2.324	5.93E-04	2.16E-02	15 (3)	2
DRD5	G-protein co	3	Activated	biased	2.84	6.66E-04	2.92E-02	15 (4)	3
KLB	enzyme	2			-1.414	6.72E-04	2.34E-02	18 (4)	3
PTGES	enzyme	2	Activated		3.357	7.18E-04	3.11E-02	15 (2)	2
p70 S6k	group	3	Activated	biased	2.84	7.18E-04	3.13E-02	15 (4)	3
CRY2	enzyme	1		biased	0.577	7.31E-04	8.20E-03	3 (1)	1
FABP5	transporter	2	Inhibited	biased	-2.065	7.53E-04	4.00E-02	19 (4)	3
DUOX2	enzyme	2		biased	1.941	7.70E-04	2.38E-02	13 (3)	3
TNIK	kinase	3		biased	-0.408	7.98E-04	3.77E-02	24 (6)	3
SMAD7	transcription	1			-1.342	8.18E-04	8.90E-03	5 (1)	1
PPARG	ligand-depen	1	Inhibited	biased	-3.207	8.48E-04	2.96E-02	14 (1)	1
ENAH	other	2		biased	0	8.82E-04	3.02E-02	14 (4)	3
AQP1	transporter	2	Inhibited	biased	-2.138	8.82E-04	2.73E-02	14 (2)	2
TOP3A	enzyme	3	Inhibited	biased	-2.138	8.82E-04	2.83E-02	14 (4)	4

TCF7L2	transcription	1		biased	-1	8.94E-04	1.53E-02	16 (1)	1
GDF9	growth facto	1	Inhibited	biased	-2	9.08E-04	5.90E-03	4 (1)	1
SREBF2	transcription	1		biased	-1.633	9.77E-04	1.29E-02	6 (1)	1
PTTG1	transcription	2		biased	1.941	9.90E-04	2.71E-02	13 (2)	2
RB1	transcription	1		biased	-1.732	1.00E-03	3.18E-02	12 (1)	1
RET	kinase	1			0.577	1.03E-03	2.70E-03	3 (1)	1
TADA3	transcription	3			-1.069	1.03E-03	2.88E-02	14 (4)	4
GNA11	enzyme	2			-1.147	1.08E-03	4.88E-02	19 (4)	4
TAS1R3	G-protein co	2		biased	0.535	1.11E-03	3.69E-02	14 (5)	4
FOXO3	transcription	1	Inhibited	biased	-2.646	1.16E-03	1.31E-02	7 (1)	1
PADI4	enzyme	1		biased	1.414	1.34E-03	1.39E-02	2 (1)	1
PTPMT1	phosphatase	1		biased	1.414	1.34E-03	6.10E-03	2 (1)	1
Gcn5l	group	1		biased	-1.414	1.34E-03	1.34E-02	2 (1)	1
LCOR	transcription	1		biased	1.414	1.34E-03	9.20E-03	2 (1)	1
FHIT	enzyme	1		biased	-1.414	1.34E-03	1.32E-02	2 (1)	1
LRP5	transmembra	2		biased	0.775	1.37E-03	3.42E-02	15 (5)	4
CRY1	enzyme	1		biased	1.732	1.39E-03	1.49E-02	3 (1)	1
ACVR1	kinase	2		biased	-1.732	1.39E-03	5.10E-03	3 (2)	2
SULF2	enzyme	2			1.387	1.53E-03	4.34E-02	13 (4)	3
CTNNB1	transcription	1	Inhibited	biased	-2.496	1.59E-03	3.66E-02	13 (1)	1
AHR	ligand-depen	1			0	1.74E-03	4.21E-02	12 (1)	1
KDM5A	transcription	1	Activated	biased	3	1.78E-03	2.37E-02	9 (1)	1
UGCG	enzyme	1		biased	1.732	1.82E-03	1.17E-02	3 (1)	1
BMPR2	kinase	2		biased	-1.604	1.84E-03	3.17E-02	14 (5)	5
FABP2	transporter	1			1.732	2.33E-03	3.20E-03	3 (1)	1
CHD4	enzyme	1		biased	1.342	2.34E-03	9.10E-03	5 (1)	1
BCAS2	other	1		biased	1.414	2.63E-03	2.69E-02	2 (1)	1
NLN	peptidase	1		biased	1.414	2.63E-03	4.00E-03	2 (1)	1
SMAD1/5	group	1		biased	-1.414	2.63E-03	5.10E-03	2 (1)	1
BAG6	enzyme	1		biased	-1.414	2.63E-03	2.59E-02	2 (1)	1

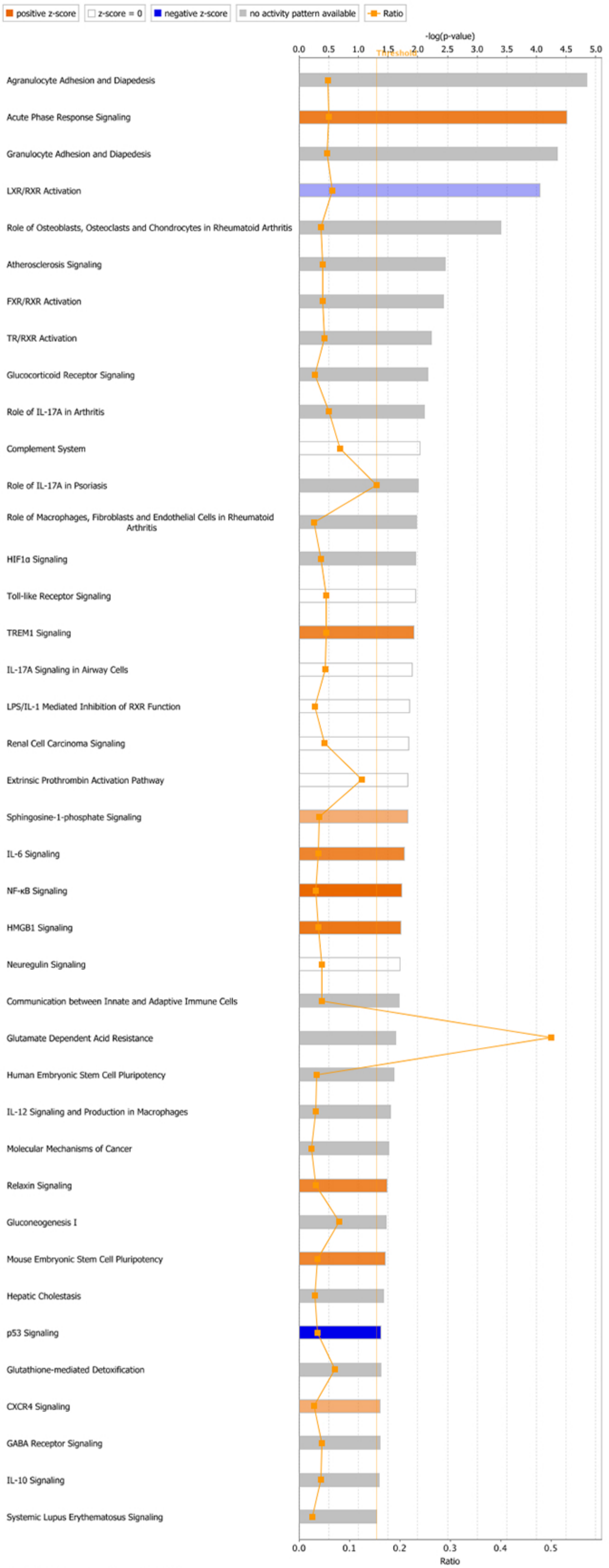
CTNNBIP1	other	1		biased	0	2.63E-03	1.84E-02	2 (1)	1
ACVR2A	kinase	1		biased	-1.414	2.63E-03	3.40E-03	2 (1)	1
LIMA1	other	1		biased	0	2.63E-03	8.70E-03	2 (1)	1
DDB1	other	1		biased	1.414	2.63E-03	2.35E-02	2 (1)	1
DVL1	other	2			1.265	2.64E-03	2.87E-02	10 (5)	4
PPARGC1B	transcription	1	Inhibited	biased	-2	3.15E-03	1.57E-02	4 (1)	1
STAT6	transcription	1			0.632	3.28E-03	4.97E-02	10 (1)	1
VWC2	other	2	Activated	biased	2.646	3.29E-03	2.66E-02	7 (3)	2
ITGAL	transmembran	2		biased	-0.905	3.42E-03	4.71E-02	11 (3)	2
SMAD4	transcription	1	Inhibited	biased	-2.646	3.49E-03	4.98E-02	7 (1)	1
MLXIPL	transcription	2		biased	0	3.58E-03	2.31E-02	4 (2)	2
NUMB	other	2		biased	1.667	3.75E-03	4.56E-02	9 (3)	3
HOXA10	transcription	1		biased	1.89	3.94E-03	3.63E-02	7 (1)	1
FGF21	growth facto	1	Inhibited	biased	-2	4.04E-03	1.19E-02	4 (1)	1
SPDEF	transcription	1		biased	0.447	4.11E-03	2.81E-02	5 (1)	1
RASSF6	other	1		biased	-1.414	4.33E-03	1.35E-02	2 (1)	1
NUBPL	other	1		biased	-1.414	4.33E-03	1.02E-02	2 (1)	1
UBR5	enzyme	1		biased	1.414	4.33E-03	2.32E-02	2 (1)	1
BMPER	other	2	Activated	biased	2	4.54E-03	2.68E-02	4 (3)	2
APLNR	G-protein co	2			0.707	4.61E-03	3.42E-02	8 (3)	3
SLC29A1	transporter	1		biased	-0.577	5.21E-03	2.77E-02	3 (1)	1
GPS2	transcription	1		biased	1	5.66E-03	4.21E-02	4 (1)	1
KLF15	transcription	1	Inhibited	biased	-2	5.66E-03	2.88E-02	4 (1)	1
UCP1	transporter	1	Inhibited	biased	-2.121	5.86E-03	3.88E-02	8 (1)	1
BST1	enzyme	2		biased	1.414	5.86E-03	4.92E-02	8 (3)	2
UBE2I	enzyme	1			-0.577	6.16E-03	2.11E-02	3 (1)	1
RASSF3	other	1		biased	-1.414	6.40E-03	1.64E-02	2 (1)	1
AMER1	other	1		biased	0	6.40E-03	3.33E-02	2 (1)	1
MDM4	enzyme	1		biased	1.414	6.40E-03	1.49E-02	2 (1)	1
ERCC1	enzyme	1		biased	0	6.40E-03	2.67E-02	2 (1)	1

MECOM	transcription	1		biased	-1.414	6.40E-03	3.53E-02	2 (1)	1
RPL22	other	1		biased	1.414	6.40E-03	2.53E-02	2 (1)	1
PPP5C	phosphatase	1			1.414	6.40E-03	4.61E-02	2 (1)	1
IL34	other	2		biased	-1	6.95E-03	3.30E-02	4 (3)	2
GBF1	other	2		biased	-1	6.95E-03	3.30E-02	4 (3)	2
NAPA	transporter	2		biased	-1	7.67E-03	3.30E-02	4 (3)	2
AURKB	kinase	1		biased	1.732	8.33E-03	4.74E-02	3 (1)	1
Cbp/p300	group	2			1.732	8.33E-03	3.28E-02	3 (2)	2
ZBTB33	other	1		biased	-1.414	8.84E-03	4.17E-02	2 (1)	1
miR-542-3p (m	mature micro	1		biased	1.414	8.84E-03	8.80E-03	2 (1)	1
TGFB1I1	transcription	1		biased	0	8.84E-03	3.35E-02	2 (1)	1
GREM1	other	2			0	8.84E-03	2.96E-02	2 (2)	2
BMP6	growth facto	1	Inhibited	biased	-2	9.24E-03	3.19E-02	4 (1)	1
GDF2	growth facto	1		biased	-1.732	9.57E-03	2.88E-02	3 (1)	1
Pde3	group	2			0.577	9.57E-03	4.36E-02	3 (4)	3
Vegf	group	1			-0.447	1.09E-02	3.46E-02	5 (1)	1
LTBP4	growth facto	1		biased	1.414	1.16E-02	1.81E-02	2 (1)	1
PPM1D	phosphatase	1		biased	1.414	1.16E-02	2.43E-02	2 (1)	1
RGS19	other	1		biased	1.414	1.16E-02	3.39E-02	2 (1)	1
CTBP1	enzyme	1		biased	0	1.16E-02	4.84E-02	2 (1)	1
AIFM1	enzyme	1		biased	-1.414	1.16E-02	2.46E-02	2 (1)	1
KMT2D	transcription	1	Inhibited	biased	-3	1.20E-02	2.69E-02	9 (1)	1
GNL3	other	1		biased	1.732	1.24E-02	4.88E-02	3 (1)	1
CEACAM6	other	2		biased	-0.447	1.24E-02	3.49E-02	5 (3)	2
PVR	other	2		biased	0	1.30E-02	3.87E-02	4 (4)	3
SDC3	other	2		biased	-0.447	1.40E-02	3.73E-02	5 (3)	2
mir-221	microRNA	1		biased	1.414	1.47E-02	2.78E-02	2 (1)	1
RXRG	ligand-depen	1		biased	-1.414	1.47E-02	4.27E-02	2 (1)	1
GUCY2D	kinase	2		biased	-0.577	1.55E-02	3.54E-02	3 (3)	3
NRF1	transcription	1		biased	-1.732	1.73E-02	4.99E-02	3 (1)	1

SLC51A	transporter	1		biased	0	1.82E-02	4.95E-02	2 (1)	1
ZFHX3	transcription	1		biased	-1.414	1.82E-02	4.45E-02	2 (1)	1
LMX1A	transcription	1		biased	-1.414	1.82E-02	3.95E-02	2 (1)	1
PAX3	transcription	1		biased	-1.414	1.82E-02	4.37E-02	2 (1)	1
DDAH2	enzyme	1		biased	-1	2.13E-02	2.74E-02	1 (1)	1
SLC17A7	transporter	1		biased	-1	2.13E-02	3.25E-02	1 (1)	1
KREMEN1	other	1		biased	1	2.13E-02	4.50E-02	1 (1)	1
NAP1L2	other	1		biased	-1	2.13E-02	4.18E-02	1 (1)	1
CCDC8	other	1		biased	-1	2.13E-02	3.86E-02	1 (1)	1
Raet1a	other	1		biased	1	2.13E-02	4.14E-02	1 (1)	1
Raet1b	other	1		biased	1	2.13E-02	4.14E-02	1 (1)	1
PAM	enzyme	1		biased	-1	2.13E-02	3.57E-02	1 (1)	1
miR-616-3p (m	mature micro	1		biased	1	2.13E-02	3.68E-02	1 (1)	1
miR-23a-5p (a	mature micro	1		biased	1	2.13E-02	3.24E-02	1 (1)	1
KREMEN2	other	1		biased	1	2.13E-02	4.50E-02	1 (1)	1
H60a	other	1		biased	1	2.13E-02	4.14E-02	1 (1)	1
MLK	group	1		biased	-1	2.13E-02	4.38E-02	1 (1)	1
Raet1d/Raet1e	other	1		biased	1	2.13E-02	4.14E-02	1 (1)	1
SERPINB3	other	1		biased	-1	2.13E-02	3.69E-02	1 (1)	1
ZNF613	other	1		biased	1	2.13E-02	3.73E-02	1 (1)	1
MAG	other	1		biased	1	2.13E-02	1.29E-02	1 (1)	1
SRPK2	kinase	1		biased	-1	2.13E-02	3.76E-02	1 (1)	1
SNRPD1	other	1		biased	1	2.13E-02	3.61E-02	1 (1)	1
Pln	other	1		biased	-1	2.13E-02	4.43E-02	1 (1)	1
LYL1	transcription	1			-1.414	2.19E-02	4.36E-02	2 (1)	1
BMPR2	kinase	1		biased	-1.414	2.59E-02	4.13E-02	2 (1)	1
LGR5	transmembr	1			1	4.21E-02	3.11E-02	1 (1)	1
ACTC1	enzyme	1		biased	1	4.21E-02	4.43E-02	1 (1)	1
HIST1H1C	other	1		biased	1	4.21E-02	4.50E-02	1 (1)	1
PDIA3	peptidase	1		biased	-1	4.21E-02	4.52E-02	1 (1)	1

CTCF	transcription	1		biased	-1	4.21E-02	3.99E-02	1 (1)	1
CDK11B	kinase	1			1	4.21E-02	3.23E-02	1 (1)	1
Hist1h1e	other	1		biased	1	4.21E-02	4.50E-02	1 (1)	1
DACT3	other	1		biased	1	6.25E-02	4.50E-02	1 (1)	1
LAMTOR2	other	1		biased	-1	6.25E-02	4.76E-02	1 (1)	1
BRCA2	transcription	1		biased	1	6.25E-02	3.86E-02	1 (1)	1
MAP3K11	kinase	1			-1	8.24E-02	4.38E-02	1 (1)	1
ZMIZ2	transcription	1		biased	-1	1.02E-01	4.50E-02	1 (1)	1
JAK	group	1		biased	1	1.58E-01	4.66E-02	1 (1)	1





# Supplemental Figure S1

