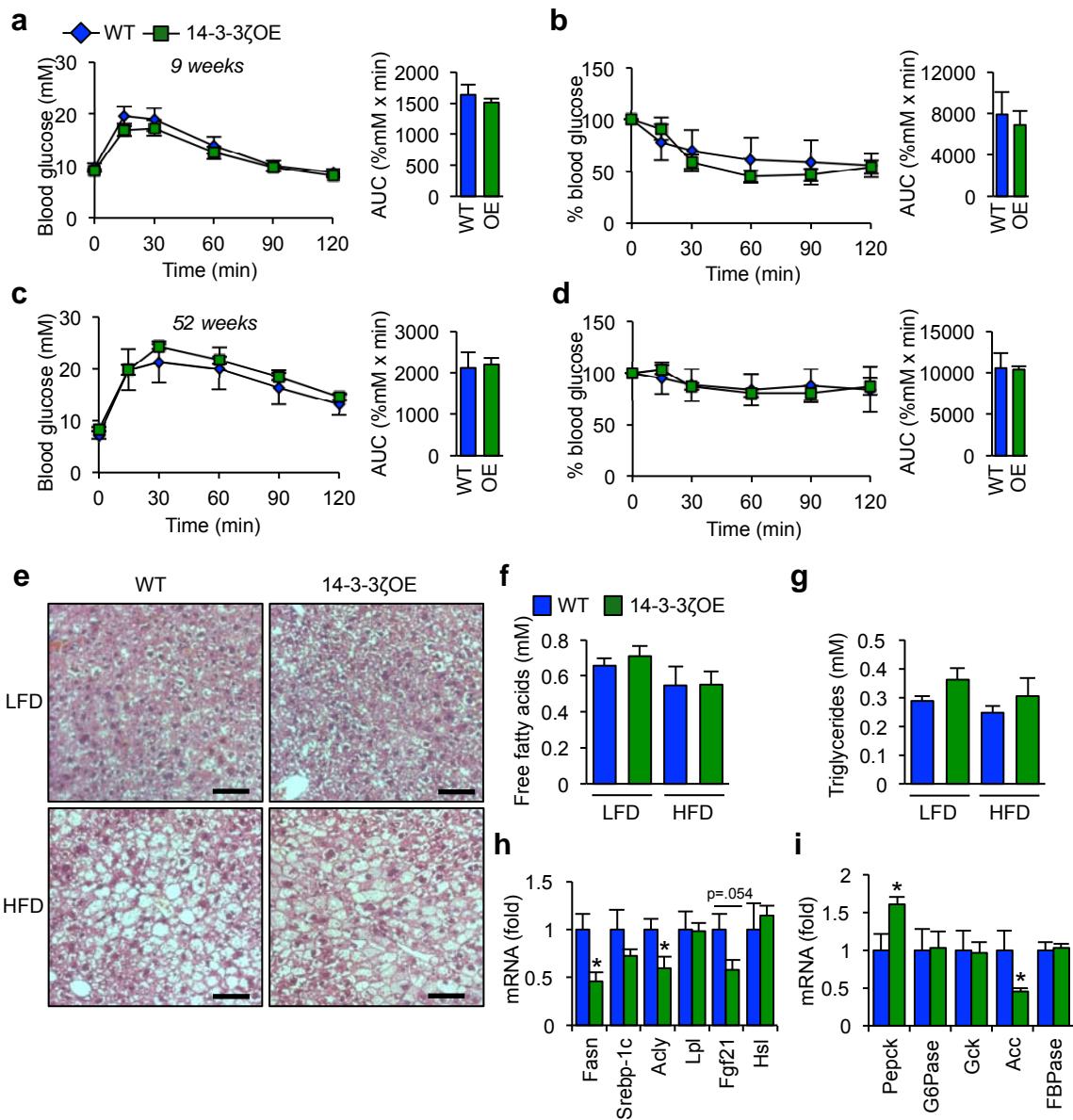


**Supplementary Figure 1. 14-3-3ζKO mice display mild perturbations in glucose homeostasis and insulin sensitivity.** (a-c) Images of 14-3-3ζKO embryos at e19.5 (a), mice at 3 weeks of age (b), and 24 weeks of age (c). (d) View of gonadal fat pads from WT and 14-3-3ζKO mice (representative of n=4 per genotype). (e) Fasting and random-fed plasma leptin, free fatty acid, and triglyceride levels from 32 week-old mice (n=5-7 per group). (f) Wild-type (WT) and 14-3-3ζKO mice were allowed to acclimate for 1 week prior to placement in metabolic cages to measure energy expenditure and food intake. Data were averaged from the last two full light: dark cycles (n=5-7). (g) Histological examination of livers showed marked steatosis in 14-3-3ζKO mice (representative of n = 6 mice per genotype). (h,i) Isolated RNA was subjected to quantitative PCR analysis of lipogenic (h) and gluconeogenic (i) genes between wildtype and 14-3-3ζKO mice (n=6 per genotype). (j) Akt phosphorylation, as measured by immunoblotting, 5 minutes after an *i.p.* bolus of insulin (5 U/kg) in liver samples from overnight-fasted WT and 14-3-3ζKO mice (n=6 per genotype). Significant differences, as assessed by Student's t-test or ANOVA, are indicated by \*: p<0.05. Error bars represent S.E.M.

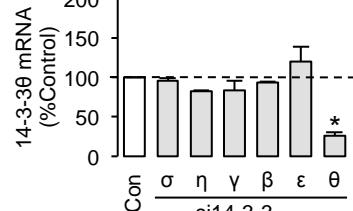
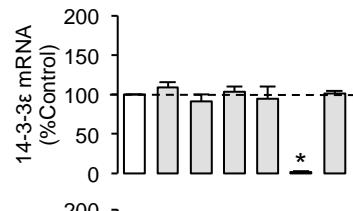
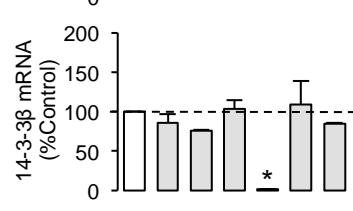
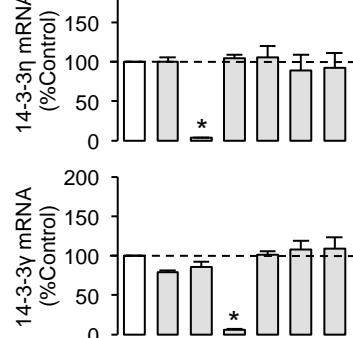
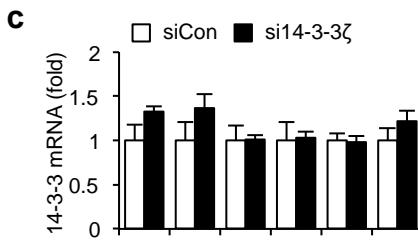
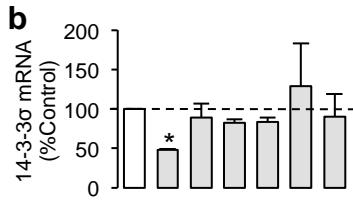


**Supplementary Figure 2. Modest over-expression of 14-3- $\zeta$  has minor effects on the liver.** (a-d) Glucose tolerance (a,c) and insulin tolerance (b,d) tests were administered to WT and 14-3- $\zeta$ OE mice at 9 (a,b) and 52 (c,d) weeks of age (n=4-9 per group). (e) Liver histology of wild-type (WT) and 14-3- $\zeta$  over-expressing (14-3- $\zeta$ OE) mice fed low-fat (LFD, 10%) or high-fat (HFD, 60%) diets for 8 weeks (representative images of n=4 mice per group, scale bars= 100  $\mu$ m). (f,g) Circulating fasting plasma free fatty acids (f) and triglycerides (g) from WT and 14-3- $\zeta$ OE mice (n=4-9 per group). (h,i) Isolated liver RNA was subjected to quantitative PCR analysis for lipogenic (h) and gluconeogenic (i) genes between WT and 14-3- $\zeta$ OE mice (n=4-9 per group). Significant differences, as assessed by Student's t-test, are indicated by \*: p<0.05. Error bars represent S.E.M.

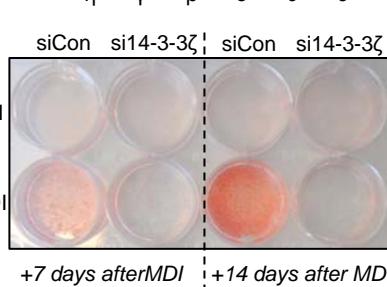
**a**

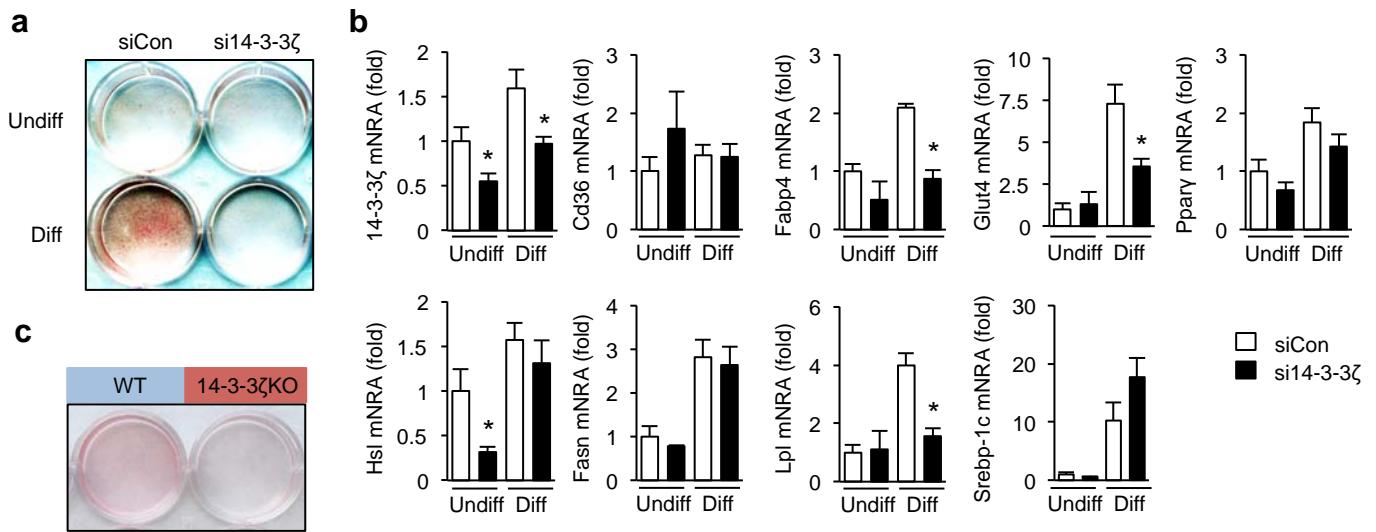
mRNA (Fold change)

MDI (hr)	14-3-3 $\sigma$	14-3-3 $\eta$	14-3-3 $\gamma$	14-3-3 $\beta$	14-3-3 $\varepsilon$	14-3-3 $\theta$	14-3-3 $\zeta$
0	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1
24	0.8 ± 0.2	1.2 ± 0.1	1.4 ± 0.2	1.2 ± 0.2	1.8 ± 0.2*	1.8 ± 0.2*	1.6 ± 0.2*
48	1.1 ± 0.3	0.9 ± 0.4	1.5 ± 0.4	1.3 ± 0.1	1.0 ± 0.1	1.1 ± 0.1	1.6 ± 0.1*

siCon       $\sigma$        $\eta$        $\gamma$        $\beta$        $\varepsilon$        $\theta$       si14-3-3

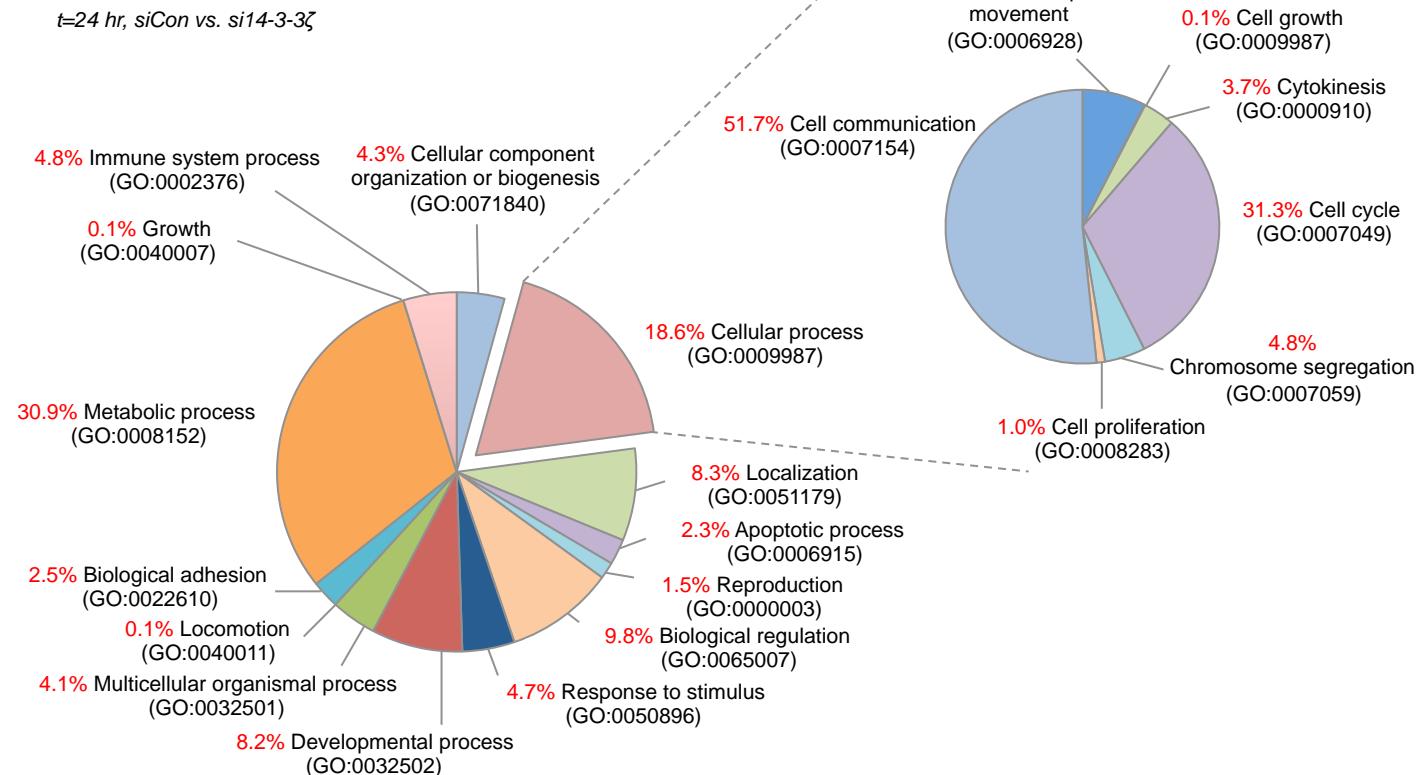
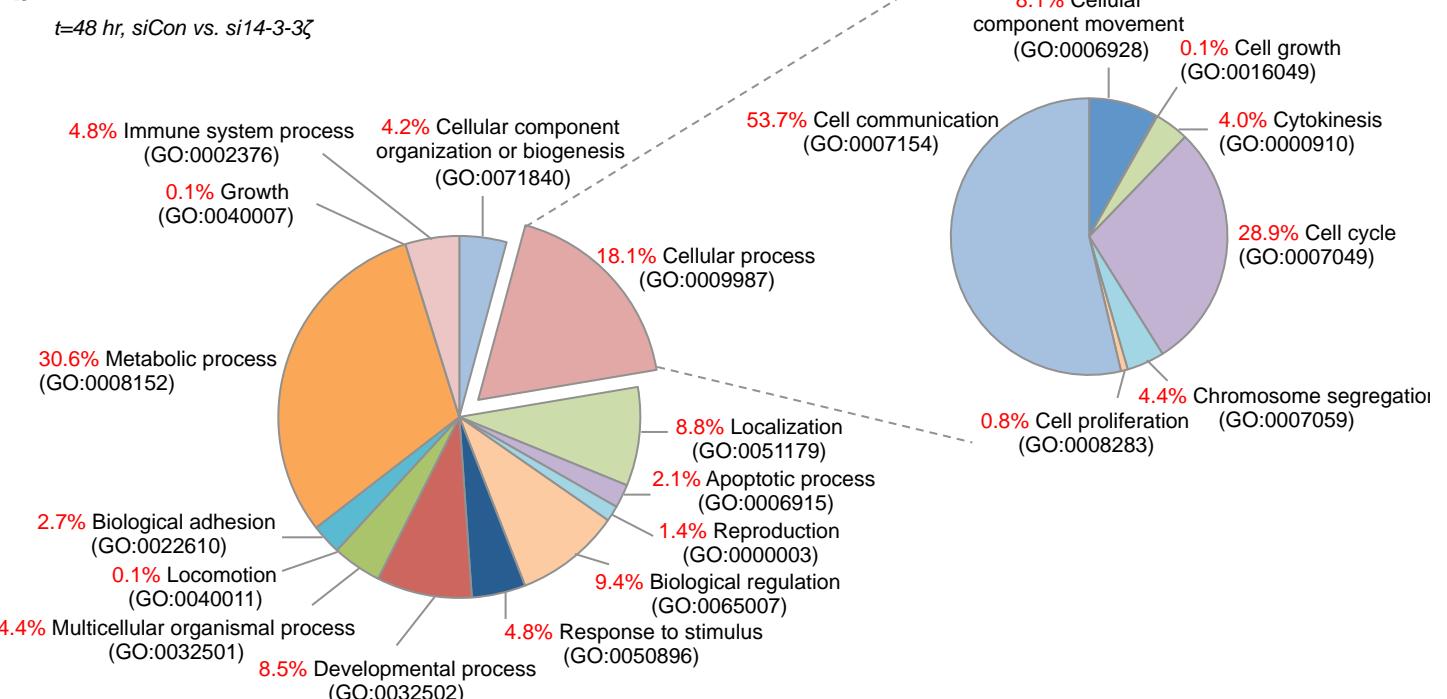
**Supplementary Figure 3. Knockdown of 14-3-3 $\zeta$  does not affect the expression of other isoforms in 3T3-L1 pre-adipocytes.** (a) Expression profile of all 14-3-3 isoforms in 3T3-L1 pre-adipocytes during the first 48 hours of differentiation (n=4 independent experiments; \*: p<0.05 when compared to undifferentiated cells, as assessed by one-way ANOVA). (b) 3T3-L1 pre-adipocytes were transfected with siRNA to knock down each mammalian 14-3-3 isoform. 48 hours after transfection, RNA was isolated, cDNA synthesized, and quantitative PCR was performed. All data were normalized to HPRT and quantified by the  $2^{-\Delta C(t)}$  method (n=3 biological replicates, \*: p<0.05 when compared to siCon, as assessed by Student's t-test). (c) Quantitative PCR analysis of remaining 14-3-3 isoforms from 14-3-3 $\zeta$ -depleted 3T3-L1 pre-adipocytes (n=3 independent experiments). (d) Following transfection with siRNA and induction of differentiation with MDI, 3T3-L1 cells were maintained in insulin-containing media for 7 or 14 days (representative of n=3 experiments). Error bars represent S.E.M.





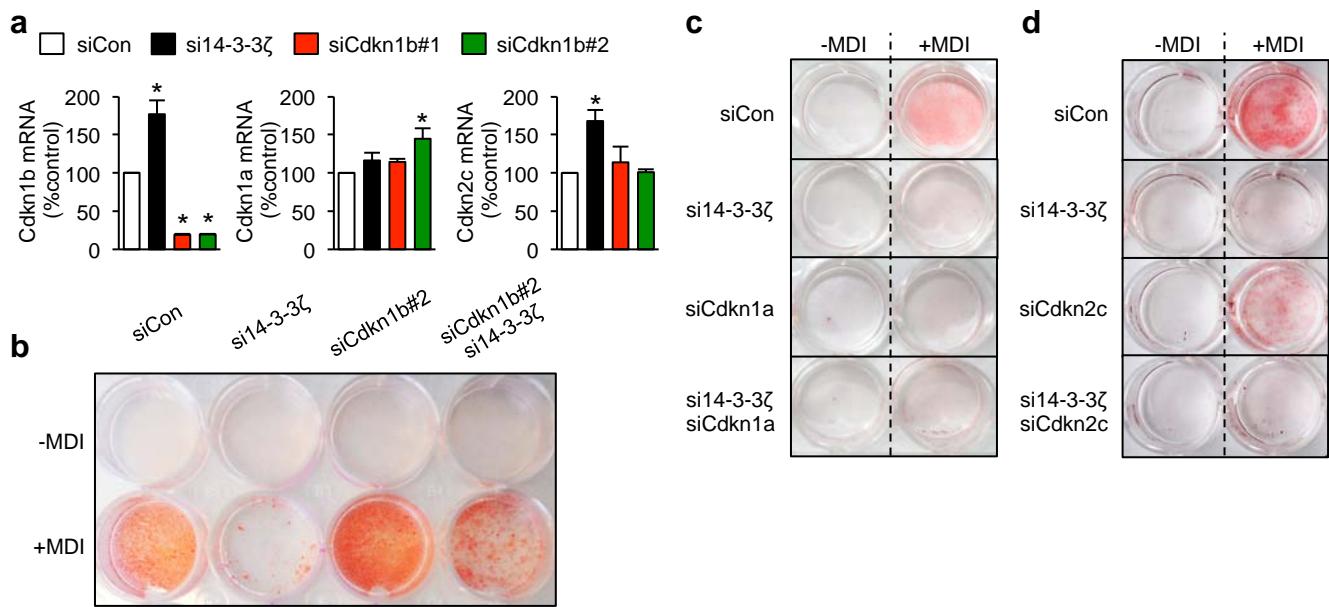
**Supplementary Figure 4. Role of 14-3-3 $\zeta$  in adipogenesis can be reproduced in 3T3-F442A cells and mouse embryonic fibroblasts.**

(a) 3T3-F442A cells were transfected with siRNA against 14-3-3 $\zeta$  or the scrambled control (siCon) 24 hours prior to differentiation. Seven days after differentiation, cells were stained with Oil Red O (representative of n=3 independent experiments). (b) Quantitative PCR for mature adipocyte markers was performed on isolated RNA from transfected 3T3-F442A cells seven days following differentiation (n=4 biological replicates). (c) Differentiation of mouse embryonic fibroblasts derived from WT and 14-3-3 $\zeta$ KO mice into adipocytes (representative of n=4 independent experiments). Significant differences between siCon vs. si14-3-3 $\zeta$ , as assessed by Student's t-test, are indicated by \*: p<0.05. Error bars represent S.E.M.

**a****b**

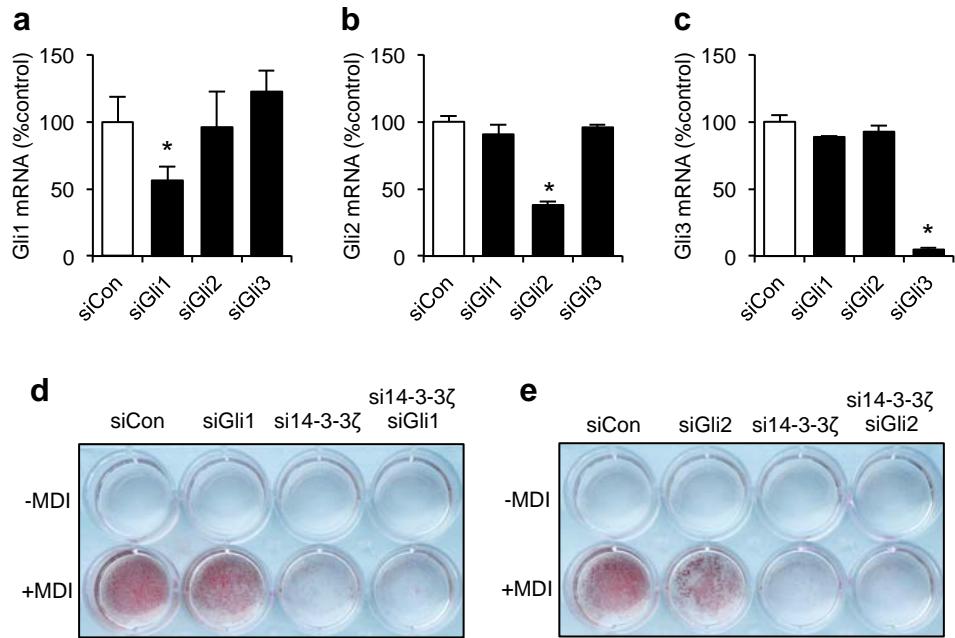
**Supplementary Figure 5. Knockdown of 14-3-3 $\zeta$  alters the transcriptome of differentiating 3T3-L1 adipocytes at 24 and 48 hours. (a-b)**

Panther gene ontology analysis was used to categorize transcriptome results of differentially expressed genes from 3T3-L1 adipocytes after 24 (a) and 48 (b) hours after differentiation. (RNA-Seq data were derived from n=5-6 mice per genotype).

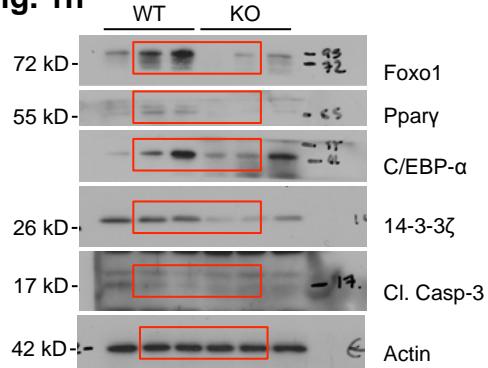
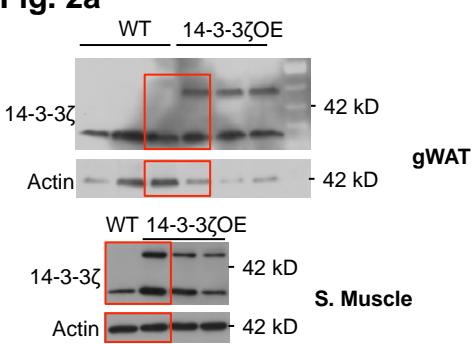
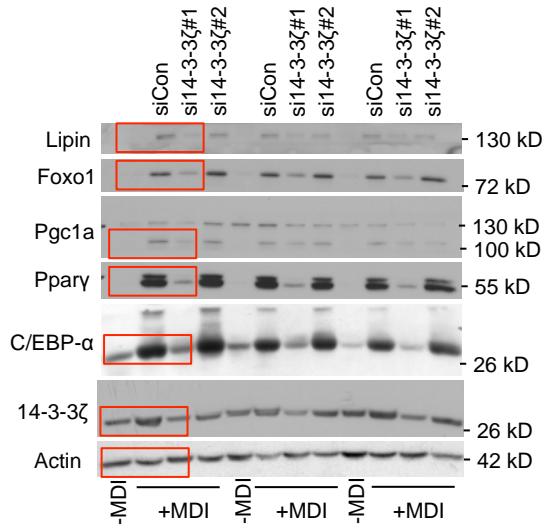
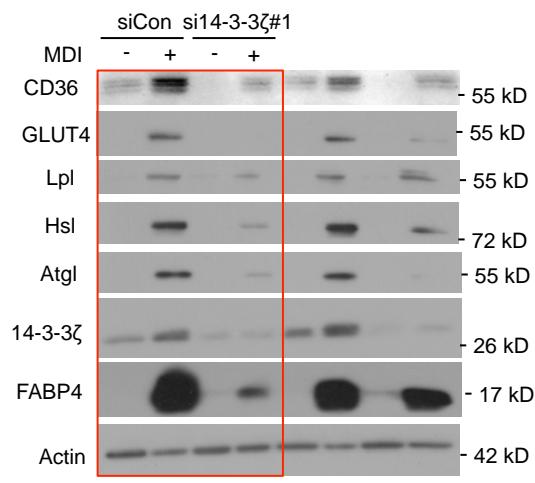


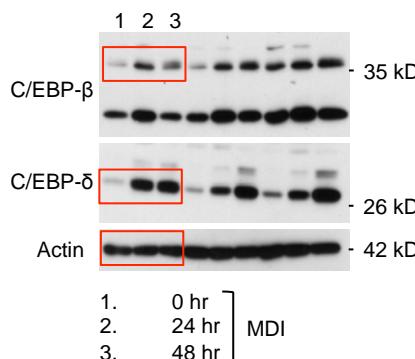
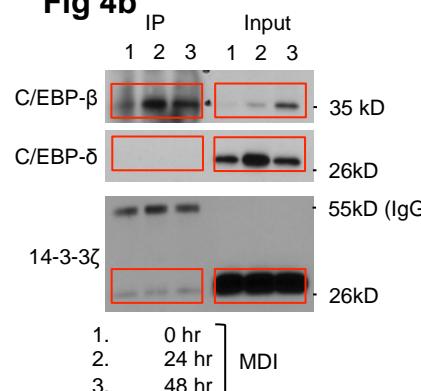
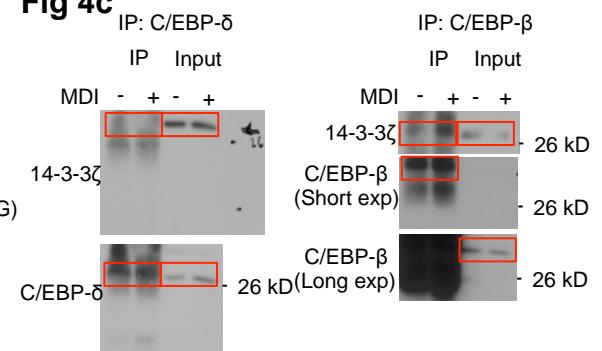
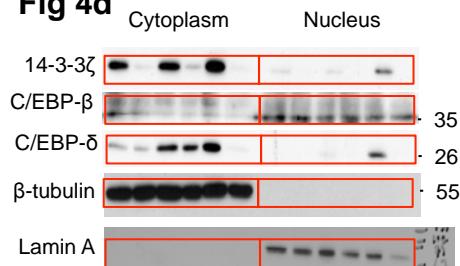
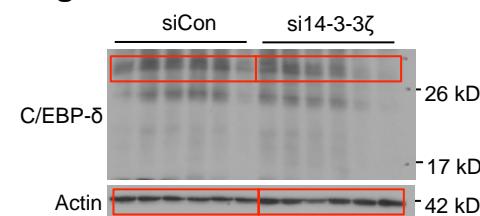
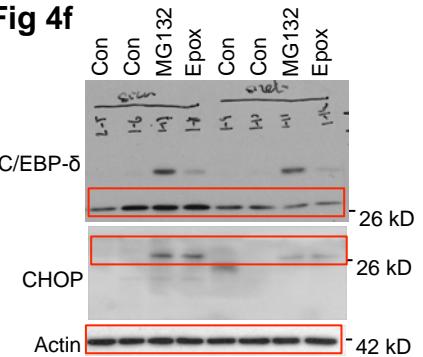
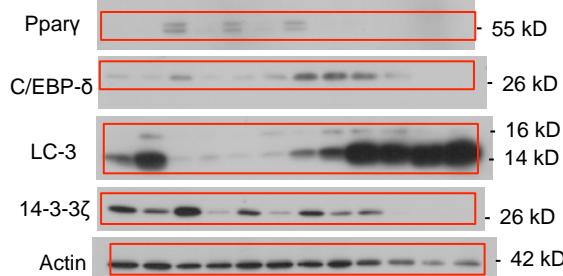
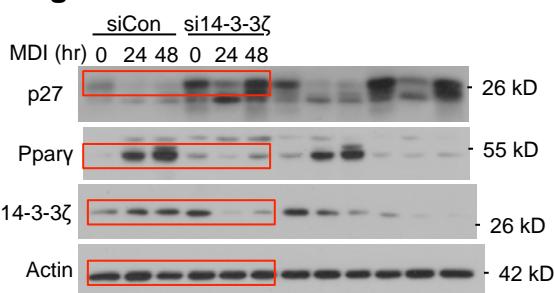
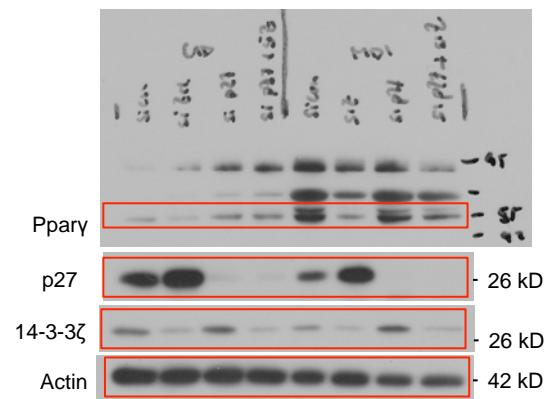
**Supplementary Figure 6. Knockdown of only *Cdkn1b/p27<sup>Kip1</sup>* was able to rescue the defect in differentiation of 14-3-3 $\zeta$ -depleted cells.**

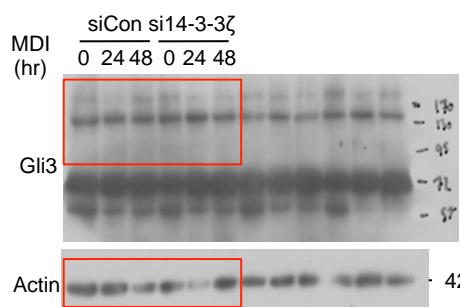
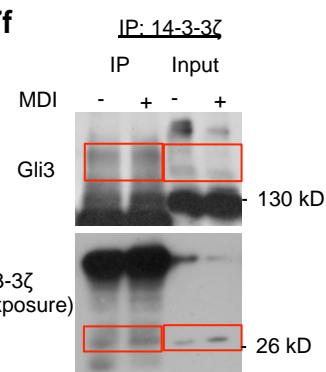
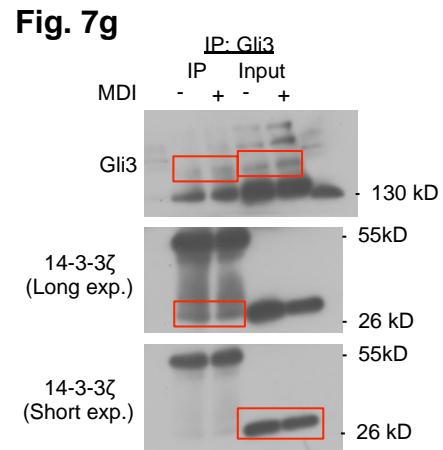
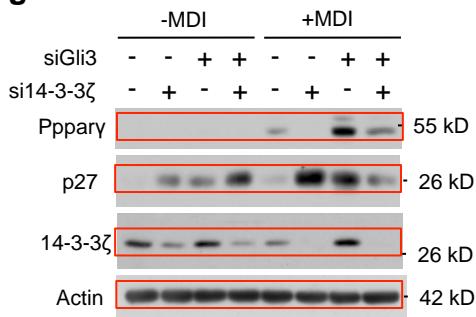
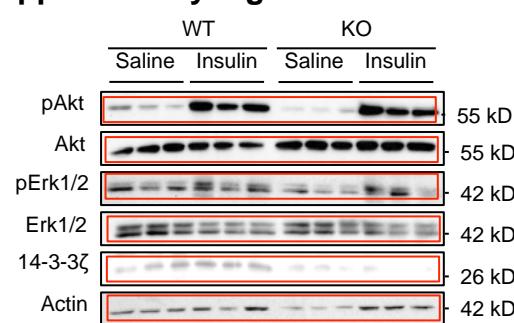
(a) Two distinct siRNA duplexes were used to knockdown *Cdkn1b* in 3T3-L1 pre-adipocytes. Due to off-target effects on siCdkn1b#2 on *Cdkn1a* expression, only siCdkn1b#1 was used (n=4 per group, \*: p<0.05 when compared to siCon). (b) Co-transfection of siRNA against 14-3-3 $\zeta$  and p27<sup>Kip1</sup> (siCdkn1b#2) was used to examine if knockdown of both proteins could restore differentiation, as determined by Oil Red-O staining (h). (n=4 independent experiments). (c,d) Co-transfection of siRNA against 14-3-3 $\zeta$  and (c) *Cdkn1a/p21* or (d) *Cdkn2c/p18* was used to examine if knockdown of both proteins could restore differentiation, as determined by Oil Red-O staining (n=4 independent experiments). Significant differences were assessed by one-way ANOVA and are indicated by \*: p<0.05. Error bars represent S.E.M.



**Supplementary Figure 7. Knockdown of Gli1 or Gli2 was unable to restore differentiation in 14-3-3 $\zeta$ -depleted cells.** (a-c) 3T3-L1 pre-adipocytes were transfected with siRNA against Gli1 (a), Gli2 (b), and Gli3 (c), followed by RNA isolation, and qPCR to measure transfection efficiencies (n=4 per group). (d,e) Co-transfection of siRNA against 14-3-3 $\zeta$  and (d) Gli1 or (e) Gli2 was used to examine if knockdown of both proteins could restore differentiation, as determined by Oil Red-O staining (n=4 independent experiments). . Significant differences, as assessed by one-way ANOVA, are indicated by \*: p<0.05. Error bars represent S.E.M.

**Fig. 1h****Fig. 2a****Fig. 3c****Fig. 3d****Supplementary Figure 8. Original Scans of Western Blots**

**Fig 4a****Fig 4b****Fig 4c****Fig 4d****Fig 4e****Fig 4f****Fig 4h****Fig. 6F****Fig. 6G****Supplementary Figure 8. Original Scans of Western Blots (Con)**

**Fig. 7e****Fig. 7f****Fig. 7g****Fig. 7i****Supplementary Figure 1i****Supplementary Figure 8. Original Scans of Western Blots (Con)**

**Supplementary Table 1: Fasting plasma hormone concentrations in wild-type and 14-3-3 $\zeta$ KO mice**

	<b>WT</b>	<b>14-3-3<math>\zeta</math>KO</b>
<b>Insulin</b> (ng/ ml)	0.34 ± 0.07	0.46 ± 0.06 *
<b>Total adiponectin</b> ( $\mu$ g/ ml)	4.08 ± 0.20	3.72 ± 0.21
<b>HMW adiponectin</b> ( $\mu$ g/ ml)	2.34 ± 0.12	2.11 ± 0.33
<b>Corticosterone</b> (ng/ ml)	337.01 ± 102.52	492.72 ± 106.03

n=5-7 per genotype

\*: p<0.05 when compared to control

**Supplementary Table 2: Top and bottom 25 most changed genes after 48 hours of differentiation relative to siCon-transfected cells**

		siCon			siZeta		
		0	24	48	0	24	48
1	Krt15	1	103.110918	497.311385	2.66051696	106.477924	145.796555
2	Fam83a	1	46.9124964	368.012974	13.9652891	16.5395541	31.0906177
3	Krt13	1	127.748073	164.971274	2.10433604	81.8750183	45.9900747
4	2310014L17F	1	1.41740611	88.8011892	0.48230434	0.93882377	1.18106303
5	Nog	1	32.6942053	85.9266531	1.4719336	25.3915159	41.8079214
6	G0s2	1	8.61711945	84.4316184	0.35808763	1.04070388	5.65038824
7	Ren1	1	11.4951963	82.4971445	0	2.50361952	25.099235
8	Retn	1	9.39441789	63.502244	0.78129008	4.25782917	5.98152364
9	Klra17	1	0.25956822	45.3978432	2.8325008	0.18471283	13.8490692
10	Wnt4	1	15.9620244	45.3354564	0.76280073	24.8068077	45.1882186
11	Fam107a	1	3.09442691	44.2671316	0.47626856	6.86753891	89.1542819
12	Ramp3	1	135.193704	44.0992625	1.60991663	48.1753458	13.8392369
13	Cidec	1	6.49830578	40.2399565	0.44840159	1.500989	3.58758375
14	Arxes1	1	3.02212458	37.401903	0.9221424	5.72310422	8.75339344
16	Wfdc12	1	3.51105395	27.2384208	1.12254452	4.75851608	5.40723019
17	Sprr1b	1	89.5338408	23.7858685	0	27.95191	2.29093426
18	2210020M01	1	6.13623433	23.0792172	0.61979871	3.01962916	7.39391541
19	Sema3g	1	11.1457743	22.8030941	0.34652529	10.4947652	8.8418583
20	Gpd1	1	1.31666881	21.5113343	1.07285388	1.18917206	4.2092994
21	Rasd1	1	3.87338682	20.9617456	1.31982267	6.70150905	8.04514435
22	Ear2	1	8.46312165	20.706659	0	4.16784271	4.34382435
23	Cfd	1	1.50353483	20.5678042	0.7495344	0.23013684	1.74720513
24	Gm12347,Krl	1	23.300067	18.3841511	0.63432479	22.6639369	12.0704546
25	Mcam	1	5.38954757	18.2322709	2.55386429	3.34622458	5.3578282
9221	Apol9b	1	0.08373423	0.01948934	0.60923863	0.06082538	0.02648439
9222	Zbp1	1	0.0742234	0.01943856	0.41698993	0.02447823	0.0173708
9223	Oas3	1	0.07558769	0.01918292	0.47856067	0.01535832	0.01746165
9224	Ifi47,Olfr56	1	0.04992641	0.0163962	0.59134299	0.02718881	0.02831703
9225	BC023105	1	0.06714218	0.01464959	0.3617296	0.04433502	0.11591034
9226	Pde1b	1	0.02099799	0.01344245	1.13107782	0.02510594	0.00967196
9227	Gpr176	1	0.02035509	0.01135962	0.93039992	0.02116034	0.01790346
9228	Mmp13	1	0.02023406	0.01093638	0.27693908	0.00582188	0.00528267
9229	Serpinb9g	1	0.26502259	0.0107546	0.29989923	0.11016691	0.03022964
9230	Ces1a	1	0.05015896	0.01048362	0.81041207	0.04175486	0.01681023
9231	Vnn3	1	0.08024184	0.01027809	0.42577837	0.00669902	0.02750213
9232	Ubd	1	0.00266743	0.00997673	1.67059581	0.01285738	0.01558555
9233	Il1a	1	0.01260677	0.00964124	0.49442405	0.00619738	0.01258758
9234	Nov	1	0.03553023	0.00944395	1.42627053	0.12325194	0.14244752
9235	Rsd2	1	0.08694472	0.00941971	0.26700663	0.04735587	0.01091572
9236	Mamdc2	1	0.02190166	0.00847977	0.58208341	0.02056469	0.01430511
9237	Dlgap2	1	0.27744687	0.00742684	0.93054361	0.09900994	0.05647909
9238	Siglecg	1	0.07252997	0.00722883	0.93852424	0.02480858	0.0091241
9239	Gm12185,Tg	1	0.03304194	0.00669948	0.55308361	0.04808998	0.0012725
9240	Gm4070	1	0.02262252	0.00616123	0.31498816	0.00391003	0.00578352
9241	Mpeg1	1	0.03792581	0.00586986	0.25259452	0.01251313	0.00637423
9242	Mmp8	1	0.04044817	0.00553258	0.33967777	0.02070749	0.01046043
9243	I830012O16F	1	0.02556889	0.00407705	0.33324216	0.00908203	0.00616297
9244	Ifit3	1	0.03142822	0.00382907	0.31572258	0.01235294	0.00424276
9245	Tgtp2	1	0.01567832	0.0009063	0.3673668	0.02448039	0.00620549



Supplementary Table 4: Gene Set Enrichment Analysis for highly enriched genes in si14-3-37-transfected 3T3-L1 cells at t=0 hr of differentiation

Term ID	Description	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MAX	LEADING EDGE
GO:0007049	cell cycle	528	-0.3056521	-7.94206	0	0	0	8955	tags=57%, list=27%, signal=77%
GO:0006259	DNA metabolic process	401	-0.2489749	-5.759177	0	0	0	8904	tags=51%, list=27%, signal=69%
GO:0018193	peptidyl-amino acid modification	410	-0.2426255	-5.5757174	0	0	0	8902	tags=51%, list=27%, signal=68%
GO:0007059	chromosome segregation	107	-0.4349217	-5.3092785	0	0	0	8893	tags=70%, list=27%, signal=95%
GO:0055086	nucleobase-containing small molecule metabolic process	515	-0.2022069	-5.2696376	0	0	0	8942	tags=47%, list=27%, signal=63%
GO:0016192	vesicle-mediated transport	489	-0.1954034	-4.900353	0	0	0	8967	tags=46%, list=27%, signal=62%
GO:0051338	regulation of transferase activity	502	-0.1830628	-4.857795	0	0	0	8777	tags=44%, list=26%, signal=59%
GO:0010608	posttranscriptional regulation of gene expression	312	-0.2196499	-4.4571986	0	0	0	9072	tags=49%, list=27%, signal=67%
GO:0016071	mRNA metabolic process	179	-0.2810754	-4.451542	0	0	0	8910	tags=55%, list=27%, signal=74%
GO:0043009	chordate embryonic development	565	-0.1618644	-4.417902	0	0	0	9188	tags=44%, list=28%, signal=59%
GO:0030334	regulation of cell migration	446	-0.1811758	-4.3825593	0	0	0	8894	tags=45%, list=27%, signal=60%
GO:0023014	signal transduction by phosphorylation	160	-0.2971594	-4.335813	0	0	0	8456	tags=55%, list=25%, signal=73%
GO:0006396	RNA processing	234	-0.2419045	-4.2817945	0	0	0	8924	tags=51%, list=27%, signal=69%
GO:0080135	regulation of cellular response to stress	306	-0.208088	-4.1767898	0	0	0	8902	tags=47%, list=27%, signal=64%
GO:0007167	enzyme linked receptor protein signaling pathway	372	-0.1805735	-4.079011	0	0	0	8902	tags=45%, list=27%, signal=60%
GO:0007507	heart development	375	-0.1787231	-4.0699983	0	0	0	8756	tags=44%, list=26%, signal=59%
GO:0010639	negative regulation of organelle organization	159	-0.2807691	-4.0543103	0	0	0	8904	tags=55%, list=27%, signal=74%
GO:0006508	proteolysis	341	-0.1930983	-4.023275	0	0	0	8858	tags=46%, list=27%, signal=62%
GO:0044772	mitotic cell cycle phase transition	85	-0.3715078	-3.988436	0	0	0	6848	tags=58%, list=21%, signal=72%
GO:0032886	regulation of microtubule-based process	110	-0.3330276	-3.9558992	0	0	0	8915	tags=60%, list=27%, signal=82%
GO:0007264	small GTPase mediated signal transduction	102	-0.3345701	-3.9269848	0	0	0	8144	tags=58%, list=24%, signal=76%
GO:0032259	methylation	135	-0.2895593	-3.9095492	0	0	0	8885	tags=56%, list=27%, signal=76%
GO:0061024	membrane organization	354	-0.1763437	-3.8309417	0	0	0	8947	tags=44%, list=27%, signal=60%
GO:0010563	negative regulation of phosphorus metabolic process	291	-0.1954303	-3.827398	0	0	0	8300	tags=44%, list=25%, signal=59%
GO:0051960	regulation of nervous system development	543	-0.1384103	-3.6872585	0	0	0	8946	tags=41%, list=27%, signal=55%
GO:0035295	tube development	417	-0.1529209	-3.675426	0	0	0	9094	tags=42%, list=27%, signal=58%
GO:0007163	establishment or maintenance of cell polarity	91	-0.3233953	-3.656385	0	0	0	6451	tags=52%, list=19%, signal=64%
GO:0040008	regulation of growth	461	-0.1448446	-3.5984418	0	0	0	8884	tags=41%, list=27%, signal=55%
GO:0032844	regulation of homeostatic process	282	-0.1829575	-3.5802863	0	0	0	9062	tags=45%, list=27%, signal=62%
GO:0016197	endosomal transport	101	-0.2962198	-3.4776554	0	0	0	8947	tags=56%, list=27%, signal=77%
GO:0034329	cell junction assembly	62	-0.3737445	-3.4713187	0	0	0	8513	tags=63%, list=26%, signal=84%
GO:0016311	dephosphorylation	185	-0.2183339	-3.466415	0	0	0	8958	tags=49%, list=27%, signal=66%
GO:0042176	regulation of protein catabolic process	170	-0.2244362	-3.4592838	0	0	0	8811	tags=49%, list=26%, signal=69%
GO:2001234	negative regulation of apoptotic signaling pathway	146	-0.2411573	-3.4360778	0	0	0	8871	tags=51%, list=27%, signal=69%
GO:0022610	biological adhesion	360	-0.1547073	-3.4122567	0	0	0	8675	tags=41%, list=26%, signal=55%
GO:0009125	nucleoside monophosphate catabolic process	173	-0.2177962	-3.3851202	0	0	0	8942	tags=49%, list=27%, signal=66%
GO:0009725	response to hormone stimulus	363	-0.1510749	-3.3512826	0	0	0	8956	tags=42%, list=27%, signal=57%
GO:0002009	morphogenesis of an epithelium	358	-0.1555922	-3.3489702	0	0	0	9094	tags=43%, list=27%, signal=58%
GO:0006260	DNA replication	85	-0.3097296	-3.3088357	0	0	0	8887	tags=58%, list=27%, signal=79%
GO:0006397	mRNA processing	118	-0.2591716	-3.3041995	0	0	0	8885	tags=53%, list=27%, signal=71%
GO:0001501	skeletal system development	338	-0.1541148	-3.2663224	0	0	0	9095	tags=43%, list=27%, signal=58%
GO:0005975	carbohydrate metabolic process	291	-0.1595047	-3.2057004	0	0	0	8570	tags=42%, list=26%, signal=56%
GO:0044723	single-organism carbohydrate metabolic process	279	-0.1594094	-3.0918698	0	0	0	8570	tags=42%, list=26%, signal=56%
GO:0044782	cilium organization	118	-0.2346532	-2.9884195	0	3.53E-06	0.001	8852	tags=50%, list=27%, signal=68%
GO:0030010	establishment of cell polarity	63	-0.3180787	-2.978343	0	3.50E-06	0.001	6862	tags=52%, list=21%, signal=66%
GO:0034330	cell junction organization	99	-0.2523095	-2.9613662	0	3.44E-06	0.001	8766	tags=52%, list=26%, signal=70%
GO:0061061	muscle structure development	339	-0.1393739	-2.9450989	0	3.41E-06	0.001	8950	tags=41%, list=27%, signal=55%
GO:0001655	urogenital system development	222	-0.1711532	-2.9394283	0	3.40E-06	0.001	7379	tags=39%, list=22%, signal=50%
GO:0042110	T cell activation	203	-0.1657692	-2.7623887	0	5.70E-05	0.019	11558	tags=51%, list=35%, signal=78%
GO:0007389	pattern specification process	373	-0.1253858	-2.7555656	0	5.68E-05	0.019	9518	tags=41%, list=29%, signal=57%
GO:0031669	cellular response to nutrient levels	77	-0.2605761	-2.7249963	0	6.44E-05	0.022	9062	tags=53%, list=27%, signal=73%
GO:0045444	fat cell differentiation	69	-0.2736957	-2.7130942	0	6.68E-05	0.023	7304	tags=49%, list=22%, signal=63%
GO:0040029	regulation of gene expression, epigenetic	126	-0.2059611	-2.7013478	0	7.26E-05	0.025	7957	tags=44%, list=24%, signal=58%
GO:0003002	regionalization	272	-0.1414191	-2.6830518	0	7.77E-05	0.026	9518	tags=43%, list=29%, signal=59%
GO:0050678	regulation of epithelial cell proliferation	221	-0.1583128	-2.6724598	0	7.96E-05	0.027	9517	tags=44%, list=29%, signal=62%







GO:0070646	protein modification by small protein removal	75	0.28339273	2.9289825	0	1.77E-05	0.004	9218	tags=56%, list=28%, signal=77%
GO:0051321	meiotic cell cycle	101	0.24785416	2.9274647	0	1.76E-05	0.004	8573	tags=50%, list=26%, signal=68%
GO:0006323	DNA packaging	54	0.3365832	2.9004579	0	2.59E-05	0.006	8530	tags=59%, list=26%, signal=80%
GO:0043414	macromolecule methylation	117	0.23143785	2.886418	0	2.58E-05	0.006	8530	tags=49%, list=26%, signal=65%
GO:0010498	proteasomal protein catabolic process	110	0.23338087	2.8803222	0	3.81E-05	0.009	8588	tags=49%, list=26%, signal=66%
GO:0051302	regulation of cell division	115	0.22380655	2.871471	0	3.77E-05	0.009	8775	tags=49%, list=26%, signal=66%
GO:0006275	regulation of DNA replication	92	0.25450647	2.863415	0	3.75E-05	0.009	8547	tags=51%, list=26%, signal=69%
GO:00071478	cellular response to radiation	79	0.27556917	2.861568	0	3.73E-05	0.009	7694	tags=51%, list=23%, signal=66%
GO:0009725	response to hormone stimulus	363	0.13235202	2.846107	0	3.70E-05	0.009	10211	tags=44%, list=31%, signal=63%
GO:0001824	blastocyst development	72	0.28723127	2.843375	0	3.68E-05	0.009	8942	tags=56%, list=27%, signal=76%
GO:0071805	potassium ion transmembrane transport	121	0.22129007	2.8198617	0	3.64E-05	0.009	19324	tags=80%, list=58%, signal=191%
GO:0007517	muscle organ development	194	0.17131089	2.8195271	0	3.62E-05	0.009	10619	tags=49%, list=32%, signal=72%
GO:0015850	organic hydroxy compound transport	74	0.27273202	2.8060503	0	3.98E-05	0.01	8475	tags=53%, list=25%, signal=71%
GO:0030198	extracellular matrix organization	143	0.19884458	2.763261	0	5.94E-05	0.015	8530	tags=45%, list=26%, signal=61%
GO:0048610	cellular process involved in reproduction	337	0.1302919	2.755669	0	7.08E-05	0.018	9623	tags=42%, list=29%, signal=58%
GO:0071705	nitrogen compound transport	272	0.14023651	2.7311828	0	8.10E-05	0.021	8577	tags=40%, list=26%, signal=53%
GO:0043062	extracellular structure organization	144	0.19568029	2.7120702	0	8.71E-05	0.023	8530	tags=45%, list=26%, signal=60%
GO:0006813	potassium ion transport	132	0.19992867	2.7055109	0	9.42E-05	0.025	19324	tags=78%, list=58%, signal=186%
GO:0043484	regulation of RNA splicing	59	0.2925913	2.7033465	0	9.75E-05	0.026	8322	tags=54%, list=25%, signal=72%
GO:0034599	cellular response to oxidative stress	112	0.21821173	2.7014441	0	9.71E-05	0.026	7909	tags=46%, list=24%, signal=60%
GO:0052547	regulation of peptidase activity	272	0.13863705	2.6739967	0	1.30E-04	0.035	6796	tags=34%, list=20%, signal=43%
GO:0042593	glucose homeostasis	121	0.2034039	2.667982	0	1.41E-04	0.038	9199	tags=48%, list=28%, signal=66%
GO:1901698	response to nitrogen compound	501	0.10092685	2.6494074	0	1.46E-04	0.04	8574	tags=36%, list=26%, signal=47%
GO:0050888	lipid homeostasis	77	0.254814	2.6454492	0	1.55E-04	0.042	9683	tags=55%, list=29%, signal=77%
GO:0014706	striated muscle tissue development	240	0.14914125	2.624339	0	1.91E-04	0.051	8792	tags=41%, list=26%, signal=56%
GO:0021782	glial cell development	59	0.29089195	2.6229906	0	1.90E-04	0.051	8942	tags=56%, list=27%, signal=76%
GO:0001890	placenta development	134	0.19077103	2.6223893	0	1.89E-04	0.051	8570	tags=45%, list=26%, signal=60%
GO:0051241	negative regulation of multicellular organismal process	318	0.12669249	2.6156278	0	2.06E-04	0.056	8479	tags=38%, list=25%, signal=51%
GO:0048871	multicellular organismal homeostasis	159	0.17659664	2.614055	0	2.05E-04	0.056	8585	tags=43%, list=26%, signal=58%
GO:0033500	carbohydrate homeostasis	121	0.2034039	2.610297	0	2.15E-04	0.059	9199	tags=48%, list=28%, signal=66%
GO:0050878	regulation of body fluid levels	161	0.17227031	2.5730689	0	2.63E-04	0.074	9995	tags=47%, list=30%, signal=67%
GO:0044262	cellular carbohydrate metabolic process	84	0.23767315	2.532458	0	3.55E-04	0.101	8346	tags=49%, list=25%, signal=65%
GO:0061136	regulation of proteasomal protein catabolic process	81	0.23715718	2.529238	0	3.60E-04	0.103	8553	tags=49%, list=26%, signal=66%
GO:0061458	reproductive system development	223	0.1438763	2.5220964	0	3.79E-04	0.108	8667	tags=40%, list=26%, signal=54%
GO:0048520	positive regulation of behavior	101	0.2162302	2.5184104	0	3.87E-04	0.11	7646	tags=45%, list=23%, signal=58%
GO:0044242	cellular lipid catabolic process	97	0.22352554	2.5120099	0	3.99E-04	0.114	8357	tags=47%, list=25%, signal=63%
GO:0071214	cellular response to abiotic stimulus	131	0.1853334	2.5080063	0	4.07E-04	0.117	8329	tags=44%, list=25%, signal=58%
GO:0016042	lipid catabolic process	117	0.20235017	2.5050256	0	4.12E-04	0.119	8357	tags=45%, list=25%, signal=60%
GO:0006066	alcohol metabolic process	164	0.16332719	2.5041996	0	6.05E-04	0.179	8585	tags=42%, list=26%, signal=56%
GO:0006639	acylglycerol metabolic process	57	0.27350664	2.442612	0	6.11E-04	0.183	8421	tags=53%, list=25%, signal=70%
GO:0003018	vascular process in circulatory system	77	0.23805712	2.438942	0	6.37E-04	0.19	7216	tags=45%, list=22%, signal=58%
GO:0048872	homeostasis of number of cells	169	0.1612845	2.4382162	0	6.38E-04	0.19	8633	tags=42%, list=26%, signal=56%
GO:0016050	vesicle organization	88	0.22332267	2.4247236	0	7.01E-04	0.21	8463	tags=48%, list=25%, signal=64%
GO:0045637	regulation of myeloid cell differentiation	139	0.17408213	2.4218872	0	6.99E-04	0.211	8588	tags=43%, list=26%, signal=58%
GO:0006006	glucose metabolic process	75	0.23719203	2.414232	0	7.23E-04	0.218	8534	tags=49%, list=26%, signal=66%
GO:0007548	sex differentiation	204	0.1470891	2.412705	0	7.24E-04	0.219	8667	tags=41%, list=26%, signal=55%
GO:0007610	behavior	462	0.09530542	2.3805897	0	8.61E-04	0.257	10549	tags=41%, list=32%, signal=59%
GO:0051604	protein maturation	160	0.16269946	2.3752468	0	8.93E-04	0.267	9994	tags=46%, list=30%, signal=66%
GO:0044744	protein targeting to nucleus	74	0.23053376	2.3656347	0.002079	9.59E-04	0.286	8527	tags=49%, list=26%, signal=65%

**Supplementary Table 8: Gene Set Enrichment Analysis for highly enriched genes in si14-3-3 $\zeta$ -transfected 3T3-L1 cells at t=48 hr of differentiation**

Term ID	Description	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MAX	LEADING EDGE
GO:0016192	vesicle-mediated transport	489	-0.2361505	-6.080085	0	0	0	8720	tags=49%, list=26%, signal=66%
GO:0051338	regulation of transferase activity	502	-0.2227057	-5.769673	0	0	0	8671	tags=48%, list=26%, signal=64%
GO:0030029	actin filament-based process	273	-0.2970658	-5.734875	0	0	0	8718	tags=56%, list=26%, signal=75%
GO:0051726	regulation of cell cycle	527	-0.2115478	-5.602441	0	0	0	8663	tags=47%, list=26%, signal=62%
GO:0040012	regulation of locomotion	497	-0.2185218	-5.5083847	0	0	0	8633	tags=47%, list=26%, signal=63%
GO:0044087	regulation of cellular component biogenesis	355	-0.231789	-5.1717477	0	0	0	8674	tags=49%, list=26%, signal=66%
GO:0009118	regulation of nucleoside metabolic process	322	-0.2468043	-5.038128	0	0	0	8603	tags=50%, list=26%, signal=67%
GO:0016265	death	558	-0.1833818	-4.9549775	0	0	0	8665	tags=44%, list=26%, signal=59%
GO:0043009	chordate embryonic development	565	-0.1818715	-4.8722143	0	0	0	8946	tags=45%, list=27%, signal=60%
GO:0051674	localization of cell	578	-0.1724396	-4.7479477	0	0	0	8634	tags=43%, list=26%, signal=57%
GO:0044782	cilium organization	118	-0.3615969	-4.6650243	0	0	0	8591	tags=62%, list=26%, signal=83%
GO:0035295	tube development	417	-0.1997826	-4.6648045	0	0	0	7954	tags=44%, list=24%, signal=57%
GO:0001934	positive regulation of protein phosphorylation	497	-0.18468	-4.659271	0	0	0	8671	tags=44%, list=26%, signal=59%
GO:0051960	regulation of nervous system development	543	-0.1740141	-4.6578426	0	0	0	8700	tags=43%, list=26%, signal=58%
GO:0022610	biological adhesion	360	-0.2121174	-4.626606	0	0	0	8634	tags=47%, list=26%, signal=63%
GO:0061024	membrane organization	354	-0.2132091	-4.554719	0	0	0	8016	tags=45%, list=24%, signal=59%
GO:0006508	proteolysis	341	-0.2123188	-4.5170197	0	0	0	8713	tags=47%, list=26%, signal=63%
GO:0001501	skeletal system development	338	-0.2123708	-4.515681	0	0	0	8850	tags=48%, list=27%, signal=64%
GO:0007155	cell adhesion	353	-0.2043017	-4.414575	0	0	0	8634	tags=46%, list=26%, signal=62%
GO:0007017	microtubule-based process	310	-0.2080735	-4.350895	0	0	0	8700	tags=47%, list=26%, signal=63%
GO:0040008	regulation of growth	461	-0.1722964	-4.171805	0	0	0	8633	tags=43%, list=26%, signal=57%
GO:0007167	enzyme linked receptor protein signaling pathway	372	-0.1899223	-4.163928	0	0	0	8684	tags=45%, list=26%, signal=60%
GO:0016197	endosomal transport	101	-0.3430935	-4.123549	0	0	0	8710	tags=60%, list=26%, signal=82%
GO:0060627	regulation of vesicle-mediated transport	247	-0.2212148	-4.033931	0	0	0	8720	tags=48%, list=26%, signal=65%
GO:0051052	regulation of DNA metabolic process	226	-0.2233231	-4.0264244	0	0	0	8663	tags=48%, list=26%, signal=65%
GO:0043069	negative regulation of programmed cell death	540	-0.1510924	-3.964681	0	0	0	8544	tags=41%, list=26%, signal=54%
GO:0007018	microtubule-based movement	106	-0.3364804	-3.9404993	0	0	0	8611	tags=59%, list=26%, signal=80%
GO:0007033	vacuole organization	51	-0.4419144	-3.7341652	0	0	0	8149	tags=69%, list=25%, signal=91%
GO:0001822	kidney development	154	-0.2531526	-3.7174761	0	0	0	8680	tags=51%, list=26%, signal=69%
GO:0009607	response to biotic stimulus	419	-0.1559732	-3.7136965	0	0	0	8768	tags=42%, list=26%, signal=56%
GO:0001655	urogenital system development	222	-0.2193321	-3.6954725	0	0	0	6237	tags=41%, list=19%, signal=50%
GO:0006914	autophagy	50	-0.4356172	-3.6658747	0	0	0	8149	tags=68%, list=25%, signal=90%
GO:0007389	pattern specification process	373	-0.1595423	-3.6485147	0	0	0	9019	tags=43%, list=27%, signal=58%
GO:0043207	response to external biotic stimulus	407	-0.1559459	-3.641813	0	0	0	8768	tags=42%, list=26%, signal=56%
GO:0048736	appendage development	144	-0.2459476	-3.5145888	0	0	0	8946	tags=51%, list=27%, signal=70%
GO:0034330	cell junction organization	99	-0.2973587	-3.4823043	0	0	0	8616	tags=56%, list=26%, signal=75%
GO:0090066	regulation of anatomical structure size	220	-0.1897631	-3.3558002	0	0	0	8545	tags=45%, list=26%, signal=60%
GO:0019953	sexual reproduction	447	-0.1385429	-3.3028207	0	0	0	8623	tags=40%, list=26%, signal=53%
GO:0003002	regionalization	272	-0.1743102	-3.2917876	0	0	0	9289	tags=45%, list=28%, signal=62%
GO:0005975	carbohydrate metabolic process	291	-0.1645853	-3.2805629	0	0	0	8174	tags=41%, list=25%, signal=54%
GO:0006650	glycerophospholipid metabolic process	124	-0.2504226	-3.271072	0	0	0	8331	tags=50%, list=25%, signal=66%
GO:0032970	regulation of actin filament-based process	199	-0.1993976	-3.2358994	0	0	0	8616	tags=46%, list=26%, signal=61%
GO:0030855	epithelial cell differentiation	347	-0.1482942	-3.1943257	0	0	0	8633	tags=41%, list=26%, signal=54%
GO:0009611	response to wounding	353	-0.1447205	-3.1915536	0	0	0	8616	tags=40%, list=26%, signal=54%
GO:0006366	transcription from RNA polymerase II promoter	381	-0.1405681	-3.1911757	0	0	0	8559	tags=40%, list=26%, signal=53%
GO:0050776	regulation of immune response	342	-0.144324	-3.116725	0	0	0	8766	tags=41%, list=26%, signal=55%
GO:0007224	smoothened signaling pathway	60	-0.3347433	-3.0625434	0	0	0	7733	tags=57%, list=23%, signal=74%
GO:0001503	ossification	142	-0.2161579	-3.0522537	0	0	0	8065	tags=46%, list=24%, signal=60%
GO:0071396	cellular response to lipid	195	-0.1862987	-3.0480232	0	0	0	15840	tags=66%, list=48%, signal=126%
GO:0050678	regulation of epithelial cell proliferation	221	-0.1739182	-3.0351386	0	0	0	9152	tags=45%, list=28%, signal=61%
GO:0009636	response to toxic substance	79	-0.2923874	-3.0161343	0	3.69E-06	0.001	7559	tags=52%, list=23%, signal=67%
GO:0071495	cellular response to endogenous stimulus	510	-0.1144523	-2.990661	0	3.63E-06	0.001	8446	tags=37%, list=25%, signal=48%
GO:0000910	cytokinesis	62	-0.3168415	-2.9571779	0	7.00E-06	0.002	7720	tags=55%, list=23%, signal=71%

