

Supplemental Table S1. Data sources and statistical comparisons

Name	Tissue	Source	Comparison
Fig. 2A – Comparison of LKB1 associations from various datasets			
MSKCC	lung adeno	Chitale et al, 2009	t-test: LKB1 mut (16) vs LKB1 WT (75)
UNC	lung adeno	GSE26939	t-test: LKB1 mut (n=6) vs LKB1 WT (n=75)
Wash U	lung adeno	GSE12667	t-test: LKB1 mut (n=7) vs LKB1 WT (n=34)
Michigan	lung adeno	Shedden et al, 2008	Linear regression with LKB1 probeset 41657_at (n=178)
TCGA	lung adeno	https://confluence.broadinstitute.org/display/GDAC/Home (LUAD RNAseqv2 Level3 RSEM downloaded 2013/07/15)	t-test: LKB1 mut (n=67) vs LKB1 WT (n=339)
MSKCC2	lung adeno	Chitale et al, 2009	t-test: LKB1 mut (n=12) vs LKB1 WT (n=90)
USC	lung adeno	GSE32861	t-test: LKB1 mut (n=8) vs LKB1 WT (n=48)
Sanger	NSCLC cell lines	www.broadinstitute.org/cgi-bin/cancer/datasets.cgi (Sanger_Cell_Line_Project_Affymetrix_QCed_Data_n798.gct)	t-test: LKB1 mut (n=25) vs LKB1 WT (n=44)
CCLL	NSCLC cell lines	www.broadinstitute.org/ccle/home (CCLE_Expression_2012-09-29.res)	t-test: LKB1 mut (n=34) vs LKB1 WT (n=46)
A549	NSCLC cell line	GSE51266	avg diff: LKB1 WT (n=3) vs pBABE vector (n=3)
H2122	NSCLC cell line	GSE51266	avg diff: LKB1 WT (n=3) vs pBABE vector (n=2)
Ji (A)	Mouse lung adeno	GSE6135	t-test: LKB1/KRAS primary adeno (n=5) vs KRAS primary adeno (n=5)
Ji (B)	Mouse lung adeno	GSE6135	t-test: LKB1/KRAS primary adeno (n=5) vs KRAS/p53 primary adeno (n=5)
Carretero	Mouse lung adeno	GSE21581	t-test: LKB1/KRAS primary adeno (n=9) vs KRAS primary adeno (n=9)
Carretero Mets	Mouse lung adeno	GSE21581	t-test: LKB1/KRAS metastases (n=17) vs LKB1/KRAS primary (n=9)

Supplementary Table S3 – Associations with the mTOR/Mitochondria cluster

Mitochondrial localization	http://www.broadinstitute.org/pubs/MitoCarta/	MITOCARTA_LIST
ELK1	http://www.broadinstitute.org/gsea/msigdb	SCGGAAGY_V\$ELK1_02
SF1	http://www.broadinstitute.org/gsea/msigdb	V\$SF1_Q6
NRF1	http://www.broadinstitute.org/gsea/msigdb	RCGCANGCGY_V\$NRF1_Q6
MYC	http://www.broadinstitute.org/gsea/msigdb	CACGTG_V\$MYC_Q2

Supplemental Table S1. Data sources and statistical comparisons (cont.)

Name	Tissue	Source	Comparison
Supplemental Table S3 (cont.)			
LY-294002	HL60	www.broadinstitute.org/cmap/#	avg diff: 10uM LY-294002 (n=9) vs DMSO
LY-294002	MCF7	www.broadinstitute.org/cmap/#	avg diff: 10uM LY-294002 (n=18) vs DMSO
LY-294002	PC3	www.broadinstitute.org/cmap/#	avg diff: 10uM LY-294002 (n=6) vs DMSO
Sirolimus	HL60	www.broadinstitute.org/cmap/#	avg diff: 100nM sirolimus (n=9) vs DMSO
Sirolimus	MCF7	www.broadinstitute.org/cmap/#	avg diff: 100nM sirolimus (n=19) vs DMSO
Sirolimus	PC3	www.broadinstitute.org/cmap/#	avg diff: 100nM sirolimus (n=6) vs DMSO
PD0325901	multiple	GSE10087	paired t-test: 12 cell lines treated 8hr with 50nM PD-0325901 (n=1 rep each) vs DMSO
Supplementary Table S4 - Associations with the NRF2 cluster			
AP1		http://www.broadinstitute.org/gsea/msigdb	TGANTCA_V\$AP1_C
NRF2		http://www.broadinstitute.org/gsea/msigdb	V\$NRF2_Q4
15dPGJ2	MCF7	www.broadinstitute.org/cmap/#	avg diff: 10uM 15-delta prostaglandin J2 (n=5) vs DMSO
15dPGJ2	HL60	www.broadinstitute.org/cmap/#	avg diff: 10uM 15-delta prostaglandin J2 (n=3) vs DMSO
15dPGJ2	PC3	www.broadinstitute.org/cmap/#	avg diff: 10uM 15-delta prostaglandin J2 (n=2) vs DMSO
keap1-/-	mouse liver	GSE11287	avg diff: KEAP1-/- liver (n=3) vs control
KEAP1 mut	LUSQ	https://tcga-data.nci.nih.gov/tcga/	t-test: KEAP1 mut (n=22) vs KEAP1/NRF2 WT (n=171)
NRF2 mut	LUSQ	https://tcga-data.nci.nih.gov/tcga/	t-test: NRF2 mut (n=24) vs KEAP1/NRF2 WT (n=171)
Supplemental Table S5 - Associations with the FOX/CREB cluster			
CREB		http://www.broadinstitute.org/gsea/msigdb	V\$CREB_01
Colforsin	MCF7	www.broadinstitute.org/cmap/#	avg diff: MCF7; 0.5uM (n=1) or 50uM (n=1) vs DMSO
Colforsin	PC3	www.broadinstitute.org/cmap/#	avg diff: PC3; 0.5uM (n=2) vs DMSO
Forskolin	PC12	GSE2071	avg diff: PC12; 10uM forskolin (n=4) vs DMSO
CREB regulated	Human Islet cells	natural.salk.edu/CREB/	Table S5: Islet

Supplemental Table S1. Data sources and statistical comparisons (cont.)

Name	Tissue	Source	Comparison
Supplemental Table S5 (cont)			
CREB regulated	MIN6	natural.salk.edu/CREB/	Table S5: MIN6
CREB regulated	HEK293T	natural.salk.edu/CREB/	Table S5: HEK293T
FOXO1/3/4		www.broadinstitute.org/gsea/msigdb	TTGTTT_V\$FOXO4_01
induction by CA-FOXO3	DLD1	E-MEXP-3262	With constitutively active, tamoxifen inducible FOXO3: avg diff: 24h tamoxifen induction (n=3) vs control (n=3)
induction by CA-FOXO3	HuVEC	GSE16573	With constitutively active, tamoxifen inducible FOXO3: avg diff: 12h tamoxifen induction (n=3) vs control (n=3)
induction by CA-FOXO3	RCC4	GSE23926	With constitutively active, tamoxifen inducible FOXO3: avg diff: 12h tamoxifen induction (n=1) vs control (n=1)
induction by CA-FOXO3	UMRC2	GSE23926	With constitutively active, tamoxifen inducible FOXO3: avg diff: 12h tamoxifen induction (n=1) vs control (n=1)
Prochlorperazine induction	HL60	www.broadinstitute.org/cmap/#	avg diff: 10uM Prochlorperazine (n=4) vs DMSO
Prochlorperazine induction	MCF7	www.broadinstitute.org/cmap/#	avg diff: 10uM Prochlorperazine (n=9) vs DMSO
Prochlorperazine induction	PC3	www.broadinstitute.org/cmap/#	avg diff: 10uM Prochlorperazine (n=3) vs DMSO
Thioridazine induction	HL60	www.broadinstitute.org/cmap/#	avg diff: 10uM Thioridazine (n=4) vs DMSO
Thioridazine induction	MCF7	www.broadinstitute.org/cmap/#	avg diff: 10uM Thioridazine (n=11) vs DMSO
Thioridazine induction	PC3	www.broadinstitute.org/cmap/#	avg diff: 10uM Thioridazine (n=5) vs DMSO
Trifluoperazine induction	HL60	www.broadinstitute.org/cmap/#	avg diff: 10uM Trifluoperazine (n=4) vs DMSO
Trifluoperazine induction	MCF7	www.broadinstitute.org/cmap/#	avg diff: 10uM Trifluoperazine (n=9) vs DMSO
Trifluoperazine induction	PC3	www.broadinstitute.org/cmap/#	avg diff: 10uM Trifluoperazine (n=3) vs DMSO
FOXA2/HNF3		www.broadinstitute.org/gsea/msigdb	TGTTTGY_V\$HNF3_Q6
Promoter occupancy	A549	http://genome.ucsc.edu/ENCODE/	'broadPeak' file used to determine ChIP-seq peaks within 1000 bp of gene start codon
Promoter occupancy	HEPG2	http://genome.ucsc.edu/ENCODE/	'broadPeak' file used to determine ChIP-seq peaks within 1000 bp of gene start codon
Promoter occupancy	Human Liver	GSE25836	'Bed' file used to determine ChIP-seq peaks within 1000 bp of gene start codon

Supplemental Table S2. Number of overlapping LKB1-associated genes across datasets, and associated P-values

	Resected lung adenocarcinomas						NSCLC cell lines					Murine model lung adenocarcinomas			
	MSKCC	UNC	Wash U	Michigan	TCGA	MSKCC2	USC	Sanger	CCLC	A549*	H2122*	Ji (A)	Ji (B)	Carretero	Carretero mets
MSKCC	200	2	3	3	2	0	3	3	2	4	2	1	2	1	2
UNC	2	200	5	13	23	16	21	8	12	9	13	0	1	1	5
Wash U	3	5	200	34	35	27	30	26	32	14	14	6	7	5	1
Michigan	3	13	34	200	55	44	35	28	33	26	25	4	5	2	1
TCGA	2	23	35	55	200	82	54	35	44	27	38	1	3	6	4
MSKCC2	0	16	27	44	82	200	35	26	30	21	26	4	8	3	2
USC	3	21	30	35	54	35	200	20	27	17	16	2	5	1	2
Sanger	3	8	26	28	35	26	20	200	81	47	49	2	6	7	0
CCLC	2	12	32	33	44	30	27	81	200	46	45	5	3	5	2
A549*	4	9	14	26	27	21	17	47	46	200	49	2	6	8	1
H2122*	2	13	14	25	38	26	16	49	45	49	200	2	8	7	2
Ji (A)	1	0	6	4	1	4	2	2	5	2	2	200	56	42	5
Ji (B)	2	1	7	5	3	8	5	6	3	6	8	56	200	65	17
Carretero	1	1	5	2	6	3	1	7	5	8	7	42	65	200	10
Carretero mets	2	5	1	1	4	2	2	0	2	1	2	5	17	10	200
	MSKCC	UNC	Wash U	Michigan	TCGA	MSKCC2	USC	Sanger	CCLC	A549*	H2122*	Ji (A)	Ji (B)	Carretero	Carretero mets
MSKCC	0	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
UNC	NS	0	NS	3.1E-06	2.3E-14	1.4E-08	3.5E-12	0.004	1.1E-05	0.0016	4.4E-06	NS	NS	NS	NS
Wash U	NS	NS	0	1.6E-27	2.7E-28	2.1E-19	2.8E-22	2.6E-18	4.2E-25	4.4E-07	4.4E-07	NS	0.02	NS	NS
Michigan	NS	3.1E-06	1.6E-27	0	2.4E-55	1.5E-40	3.3E-28	1.7E-20	2.7E-26	5.1E-18	5.7E-17	NS	NS	NS	NS
TCGA	NS	2.3E-14	2.7E-28	2.4E-55	0	1.6E-101	7.0E-53	8.6E-28	2.2E-40	2.6E-18	7.1E-31	NS	NS	NS	NS
MSKCC2	NS	1.4E-08	2.1E-19	1.5E-40	1.6E-101	0	3.2E-28	2.6E-18	9.2E-23	4.3E-13	3.8E-18	NS	0.006	NS	NS
USC	NS	3.5E-12	2.8E-22	3.3E-28	7.0E-53	3.2E-28	0	4.8E-12	8.0E-20	6.7E-09	3.9E-08	NS	NS	NS	NS
Sanger	NS	0.0041	2.6E-18	1.7E-20	8.6E-28	2.6E-18	4.8E-12	0	3.2E-101	2.8E-44	3.8E-47	NS	NS	0.018	NS
CCLC	NS	1.1E-05	4.2E-25	2.7E-26	2.2E-40	9.2E-23	8.0E-20	3.2E-101	0	1.9E-43	5.0E-42	NS	NS	NS	NS
A549*	NS	0.0016	4.4E-07	5.1E-18	2.6E-18	4.3E-13	6.7E-09	2.8E-44	1.9E-43	0	2.1E-46	NS	NS	0.0085	NS
H2122*	NS	4.4E-06	4.4E-07	5.7E-17	7.1E-31	3.8E-18	3.9E-08	3.8E-47	5.0E-42	2.1E-46	0	NS	0.006163049	0.013	NS
Ji (A)	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	0	7.6E-46	2.6E-31	NS
Ji (B)	NS	NS	0.02	NS	NS	0.006	NS	NS	NS	NS	0.0061	7.6E-46	0	1.1E-62	1.0E-06
Carretero	NS	NS	NS	NS	NS	NS	NS	0.018	NS	0.0085	0.014	2.6E-31	1.1E-62	0	0.0051
Carretero mets	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	1.0E-06	0.0051	0

P-value determined by hypergeometric test. Only genes represented by probesets in the Affymetrix U133A array platform were included in this analysis (n=13211). When comparisons were made between different platforms, only genes included in both platforms were considered for statistical calculations. Raw P-values are presented, without adjustment for multiple hypothesis testing.

Supplemental Table S3. Selected results for gene sets significantly associated with mitochondria/mTOR gene cluster.

	Tissue/Cell line	P-value*
Mitochondrial Localization (MitoCarta)		3.6e-22
ELK1 Transcription Factor Predicted promoter elements (msigDB)		2.2e-13
Splicing Factor 1 Transcription Factor Predicted promoter elements (msigDB)		1.1e-9
NRF1 Transcription Factor Predicted promoter elements (msigDB)		3.9e-7
MYC Transcription Factor Predicted promoter elements (msigDB)		4.2e-7
LY-294002 Repression	HL60	1.1e-8
	MCF7	2.2e-17
	PC3	3.0e-12
Sirolimus Repression	HL60	3.0e-12
	MCF7	1.2e-19
	PC3	1.2e-19
PD0325901 Repression	Multiple	1.9e-24
PGC1A Induction	C2C12	1.3e-10

*P-value determined by hypergeometric test for the significance of overlap between top 200 genes associated with mitochondria/mTOR cluster (Supplementary data 1) compared to the indicated gene set. For pre-determined genesets, these are used as downloaded. For associations derived from other studies, the top 200 associated genes are used for comparison.

Supplemental Table S4. Selected results for gene sets significantly associated with NRF2 gene cluster.

	Tissue/Cell line	P-value*
AP1Transcription Factor		
Predicted promoter elements (msigDB)		6.2e-12
NRF2 Transcription Factor		
Predicted promoter elements (msigDB)		5.2e-11
dmPGJ2 induction	HL60	1.2e-19
	PC3	5.5e-22
	MCF7	1.0e-39
KEAP1 -/-	Mouse liver	8.8e-8
KEAP1 mutant	Lung SqCC	1.7e-62
NRF2 mutant	Lung SqCC	9.6e-69
siNRF2 repressed	A549	2.9e-24

*P-value determined by hypergeometric test for the significance of overlap between top 200 genes associated with NRF2 cluster (Supplementary data 1) compared to the indicated gene set. For pre-determined genesets, these are used as downloaded. For associations derived from other studies, the top 200 associated genes are used for comparison.

Supplemental Table S5. Selected results for gene sets significantly associated with the FOX/ CREB gene cluster.

	Tissue/Cell line	P-value*
CREB Transcription Factor		
Predicted promoter elements (msigDB)		3.1E-04
Colforsin induction	MCF7	2.2E-17
	PC3	2.6E-28
	PC12	1.6E-05
CREB regulated	Islet Cells	2.0E-14
	MIN6	4.5E-09
	HEK293T	6.5E-06
FOXO1/3/4 Transcription Factor		
Predicted promoter elements (msigDB)		9.5E-05
Induction by CA-FOXO3	DLD1	5.4E-11
	HuVEC	1.4E-05
	RCC4	4.2E-07
	UMRC2	3.3E-08
Prochlorperazine induction	HL60	1.6E-03
	MCF7	2.0E-06
	PC3	9.2E-03
Thioridazine induction	HL60	7.2E-05
	MCF7	1.5E-17
	PC3	7.2E-13
Trifluoperazine induction	HL60	6.0E-14
	MCF7	4.5E-10
	PC3	2.0E-06
FOXA2 Transcription Factor (HNF3B)		
Predicted promoter element (msigDB)		2.0E-04
Promoter occupancy (ChIP-Seq)	A549	7.1E-09
	HEPG2	4.4E-05
	Human Liver	1.1E-04

*P-value determined by hypergeometric test for the significance of overlap between top 200 genes associated with NRF2 cluster (Supplementary data 1) compared to the indicated gene set. For pre-determined genesets, these are used as downloaded. For associations derived from other studies, the top 200 associated genes are used for comparison.

Supplemental Table S6. Comparison of LKB1-associated gene expression profiles from this work to those from previously studies.

		200 genes overexpressed in LKB1 mutant lung adenocarcinomas (TCGA; 67 mutants vs 339 WT)			200 genes with decreased expression in A549 with pBABE-LKB1 (present work)			200 genes with decreased expression in H2122 with pBABE-LKB1 (present work)		
		Overlap (n)	Odds Ratio	P-value ^a	Overlap (n)	Odds Ratio	P-value ^a	Overlap (n)	Odds Ratio	P-value ^a
Current work										
LKB1 score ^b	TCGA	101	62	1.1e-128	35	13	2.3e-28	39	15.3	2.0e-33
LKB1 score ^b	Michigan	138	130	1.1e-223	34	12	4.2e-26	41	15.2	8.9e-35
Previous LKB1 associations in studies of resected tumors										
Fernandez	Fig 2b ^c	0	0	NS	1	6	NS	0	0	NS
Wilkerson	Magnoid ^d	10	3.0	0.0007	4	1.2	NS	7	2.3	0.014
Previous studies of effects of LKB1 add-back on gene expression in cell lines										
Jimenez	A549 (Table 1)	1	2.3	NS	4	9.7	3.9e-05	4	9.7	3.9e-05
Ji	A549	21	6.8	2.3e-12	60	25	5.6e-64	35	13	5.5e-28
Ji	H2126	12	3.7	3.5e-05	7	2.2	0.016	12	3.9	2.2e-05
Lin-Marq	HeLa	9	3.4	0.0004	20	8.3	1.5e-13	18	7.4	1.4e-11

a: P-values determined by hypergeometric test

b: 200 genes most strongly overexpressed by lung adenocarcinomas classified by the LKB1-loss score as LKB1-deficient.

c: 200 genes most strongly overexpressed by lung adenocarcinomas (GSE26939) classified by Wilkerson et al as ‘magnoid’ subtype.

d: 10 genes reported to be overexpressed by LKB1 mutant tumors (n=5) compared to LKB1 wild-type tumors (n=14).

Supplemental Table S7. Association of LKB1 loss with copy number alterations in lung adenocarcinoma.

Chromosomal region	Alteration	Cancer genes in region	P-value	Q-value
Lower copy number values in LKB1-deficient lung adenocarcinomas				
19p13.2	Deletion	KEAP1	5.2E-13	4.1E-11
19p13.3	Deletion	STK11	1.8E-08	7.0E-07
5p15.33	Amplification	TERT	6.3E-07	1.7E-05
7p21.1	Amplification		2.6E-06	5.2E-05
3q29	Deletion		5.6E-06	8.8E-05
4q35.1	Deletion		5.7E-06	7.5E-05
1p36.13	Deletion		1.9E-05	2.2E-04
1p13.2	Deletion		6.5E-05	6.4E-04
7p11.2	Amplification	EGFR	5.1E-04	0.0033
Higher copy number values in LKB1-deficient lung adenocarcinomas				
10q26.3	Deletion		5.1E-07	4.0E-06
10p15.1	Amplification		2.7E-05	1.9E-04
15q11.2	Deletion		2.8E-04	1.9E-03
12q24.33	Deletion		7.9E-04	0.0048

*P-value determined by Student's t-test comparing continuous variable copy number data reported for TCGA lung adenocarcinomas expressing LKB1 loss signature (n=149) to adenocarcinomas expressing LKB1 WT signature (n=295). Q-values represent adjustment for multiple-hypothesis testing of 79 regions of amplification or deletion determined by TCGA GISTIC analysis.

Supplemental Table S8. Association of LKB1 loss with differences in microRNA expression in lung adenocarcinoma.

miRNA species	Average expression (log2)	Fold difference (log2)	P-value	Q-value
Increased expression in LKB1-deficient lung adenocarcinomas				
hsa-mir-582	7.7	1.3	9.2E-19	7.9E-17
hsa-mir-148b	7.5	0.6	2.8E-18	1.6E-16
hsa-mir-141	10.2	0.9	9.2E-14	4.0E-12
hsa-mir-203	11.7	1.1	7.4E-12	2.6E-10
hsa-mir-375	13.9	1.3	1.2E-11	3.4E-10
hsa-mir-629	6.7	0.6	2.6E-10	5.7E-09
hsa-mir-200c	13.1	0.6	2.7E-10	5.2E-09
hsa-mir-192	8.9	1.3	3.3E-10	5.7E-09
hsa-mir-194-1	6.7	1.1	2.2E-08	2.7E-07
hsa-mir-107	6.5	0.3	3.6E-08	3.6E-07
hsa-mir-194-2	6.9	1.1	7.7E-08	7.4E-07
hsa-mir-330	5.3	0.4	2.2E-07	1.9E-06
hsa-mir-181d	4.4	0.5	3.1E-07	2.6E-06
hsa-mir-1307	10.2	0.6	4.1E-07	3.3E-06
hsa-mir-17	9.3	0.4	8.3E-07	6.2E-06
hsa-mir-181c	6.6	0.4	9.0E-07	6.5E-06
hsa-mir-128-2	5.8	0.4	1.0E-06	7.0E-06
Decreased expression in LKB1-deficient lung adenocarcinomas				
hsa-mir-146b	10.3	-0.9	7.3E-20	6.3E-18
hsa-mir-222	6.1	-0.6	1.2E-10	2.9E-09
hsa-mir-221	8.0	-0.6	1.7E-09	2.7E-08
hsa-mir-378	7.9	-0.6	2.5E-09	3.6E-08
hsa-mir-224	4.8	-1.0	1.6E-08	2.2E-07
hsa-mir-452	6.1	-0.8	2.2E-08	2.6E-07
hsa-mir-146a	7.1	-0.6	3.2E-08	3.4E-07
hsa-mir-30c-2	8.7	-0.5	1.5E-07	1.3E-06

***P-value determined by Student's t-test comparing miRNAseq expression (log2 values) for TCGA lung adenocarcinomas expressing LKB1 loss signature (n=125) to adenocarcinomas expressing LKB1 WT signature (n=249). Analysis was limited to miRNA species with average expression values greater than 4.0; Q-values represent adjustment for multiple-hypothesis testing of 173 miRNA species.**

Supplementary Table S9. Proteins and phosphorylated proteins differentially expressed in LKB1-deficient lung adenocarcinomas

Protein	P-value	Q-value	Protein	P-value	Q-value
Increased expression in lung adenocarcinomas with LKB1 loss			Decreased expression in lung adenocarcinomas with LKB1 loss		
Claudin-7	2.5E-19	4.6E-17	AMPK pT172	4.3E-14	2.6E-12
c-Kit	1.6E-17	1.5E-15	PKC alpha pS657	3.4E-10	1.3E-08
Tau	3.2E-13	1.5E-11	Annexin I	2.0E-07	5.2E-06
AMPK alpha	1.6E-07	5.0E-06	Axl	1.8E-06	3.3E-05
TIGAR	1.3E-06	3.0E-05	PKC alpha	2.1E-06	3.6E-05
HER3	1.7E-06	3.5E-05	KEAP1	3.2E-06	4.9E-05
IGFBP2	8.6E-06	1.1E-04	STAT5 alpha	4.1E-06	5.8E-05
Rab11	9.3E-06	1.1E-04	NF-kB p65 pS536	8.3E-06	1.1E-04
AR	1.2E-05	1.3E-04	p38 MAPK	2.6E-05	2.7E-04
CDK1	5.5E-05	4.9E-04	NF2	3.5E-05	3.5E-04
Nrf2	1.7E-04	0.0014	Dvl3	4.2E-05	3.9E-04
LCN2a	2.1E-04	0.0016	PDK1 pS241	1.2E-04	0.0010
Bim	2.4E-04	0.0017	ERK2	2.1E-04	0.0016
CD31	5.6E-04	0.0035	TSC2	3.1E-04	0.0021
E-Cadherin	0.0010	0.0060	p70S6K	4.4E-04	0.0029
N-Cadherin	0.0014	0.0070	PI3K p110	4.7E-04	0.0030
14-3-3 epsilon	0.0018	0.0088	PI3K p85	6.1E-04	0.0036
Caspase-9 cleaved	0.0026	0.012	Syk	0.0011	0.0060
Rab25	0.0031	0.014	Pea-15	0.0011	0.0059
HER3 pY1289	0.0050	0.021	EGFR pY1068	0.0011	0.0059
p90RSK pT359 S363	0.0054	0.022	PKC delta pS664	0.0015	0.0074
Notch3	0.0072	0.029	XIAP	0.0020	0.0095
Cyclin D1	0.0078	0.030	ACC pS79	0.0036	0.016
Beclin	0.0090	0.034	LKB1	0.0046	0.020
RPS6	0.0095	0.035	EGFR	0.0049	0.021
IGF1R beta	0.010	0.038	MIG-6	0.013	0.044
Mre11	0.011	0.039	CD49b	0.016	0.055
STAT3 pY705	0.017	0.057	MACC1	0.016	0.054
Chk2 pT68	0.021	0.062	MSH2	0.017	0.056
cIAP	0.024	0.069	Bad pS112	0.018	0.057
alpha-Catenin	0.026	0.075	Akt	0.018	0.056
XRCC1	0.027	0.075	c-Jun pS73	0.018	0.056
Chromogranin A	0.030	0.079	Fibronectin	0.019	0.059
Smad4	0.031	0.079	Akt pS473	0.020	0.061
PARP	0.035	0.089	AIB1	0.023	0.066
MEK1 pS217 S221	0.036	0.090	INPP4B	0.028	0.078
eIF4E	0.037	0.090	ER alpha	0.029	0.079
Chk1	0.038	0.091	4E-BP1	0.031	0.080
			C-Raf	0.032	0.082
			ATM	0.039	0.094
			Rad50	0.043	0.102
			GSK3 pS9	0.043	0.101

*P-value determined by Student's t-test comparing RPPA expression values (arbitrary units) for TCGA lung adenocarcinomas expressing LKB1 loss signature (n=80) to adenocarcinomas expressing LKB1 WT signature (n=153). Q-values represent adjustment for multiple-hypothesis testing of 186 total RPPA targets.

Supplemental Table S10. Association of LKB1 loss with clinical variables in lung adenocarcinoma.

	LKB1-loss classifier		Fisher test	
	Number of Samples (LKB1 loss / total)	Fraction LKB1 loss (%)	Odds Ratio (95% C.I.)	P-value
TCGA Lung Adenocarcinomas				
Stage I	71 / 217	32.7	NA	NA
Stage II	32 / 88	36.4	1.2 (0.67, 2.0)	0.59
Stage III	22 / 64	34.4	1.1 (0.57, 2.0)	0.88
Stage IV	9 / 20	45	1.7 (0.59 4.7)	0.32
Never smoker	13 / 55	23.6	0.48 (0.22, 0.97)	0.031
Ever smoker	96 / 245	39.2		
Pooled Analysis Lung Adenocarcinomas				
Stage I	153 / 476	32.1	NA	NA
Stage II	51 / 148	34.5	1.1 (0.68 1.7)	0.62
Stage III	31 / 118	26.3	0.73 (0.43, 1.2)	0.27
Stage IV	2 / 10	20	0.52 (0.052, 2.7)	0.51
Never smoker	12 / 116	10.3	0.20 (0.010, 0.38)	6.50E-09
Ever smoker	200 / 553	36.2		