

Supplementary Table S1. Antibody sources for Western blot, IP, IF and IHC.

Antibody for	Brand & Catalog No.	Dilution
Western blot		
β -actin	#66009-1-Ig, Proteintech	1/5000
GAPDH	#60004-1-Ig, Proteintech	1/5000
Human LKB1	#3050, Cell Signaling Technology	1/1000
Mouse LKB1	#10746-1-AP, Proteintech	1/1000
Skp2	#2652, Cell Signaling Technology	1/1000
p-AMPK	#2535, Cell Signaling Technology	1/1000
AMPK	#5831, Cell Signaling Technology	1/1000
Human PD-L1	#ab205921, Abcam	1/1000
Mouse PD-L1	#66248-1-Ig, Proteintech	1/1000

Myc tag	#A02060, Abbkine	1/2000
Flag tag	#A02010, Abbkine	1/2000
His tag	#A02050, Abbkine	1/2000
HA tag	#A02040, Abbkine	1/2000
Ub	#MAB701, R&D	1/1000
HRP-Rabbit IgG	#7074, Cell Signaling Technology	1/2000
HRP-Mouse IgG	#7076, Cell Signaling Technology	1/2000
Antibody for IP	Brand & Catalog No.	Dilution
Myc tag	#A02060, Abbkine	1/500
Flag tag	#F3165, Sigma	1/500
HA tag	#A02040, Abbkine	1/500
LKB1	#3050, Cell Signaling Technology	1/100

Skp2	#2652, Cell Signaling Technology	1/50
PD-L1	#ab237726, Abcam	1/30
Antibody for IHC	Brand & Catalog No.	Dilution
LKB1	#10746-1-AP, Proteintech	1/200
Skp2	# ab183039, Abcam	1/50
Human PD-L1	#ab237726, Abcam	1/100
Mouse PD-L1	#66248-1-Ig, Proteintech	1/300
Human CD8	#ab245118, Abcam	1/100
Mouse CD8	#98941, Cell Signaling Technology	1/200
Granzyme B	#ab255598, Abcam	1/2000
Ki67	#ab15580, Abcam	1/300

Supplementary Table S2. Enrichment analysis *LKB1* co-mutant genes.

Event: Indicates whether gene1 and gene2 are co-mutated or mutually exclusive.

pValue: The *P*-value indicating the probability of this event.

oddsRatio: The odds ratio supporting this event.

00: The number of samples where neither of the two genes is mutated.

11: The number of samples where both genes are mutated.

01: The number of samples where gene1 is not mutated, but gene2 is mutated.

10: The number of samples where gene2 is not mutated, but gene1 is mutated.

event_ratio: Co-mutated samples / mutually exclusive samples for the two genes.

Gene1	Gene 2	pValue	oddsRatio	00	11	01	10	Event	Gene pair	event_ratio
BRAF	KRAS	0.000688313	0	97	0	83	13	Mutually_Exclusive	BRAF, KRAS	0/96
TP53	KRAS	0.000706995	0.356738755	36	35	48	74	Mutually_Exclusive	KRAS, TP53	35/122
FLT1	TLR4	0.000970009	11.48029144	170	5	12	6	Co_Occurence	FLT1, TLR4	5/18
MUC16	TP53	0.001119085	2.970755931	67	47	62	17	Co_Occurence	MUC16, TP53	47/79
RET	ZFH3	0.001147328	10.74572154	170	5	7	11	Co_Occurence	RET, ZFH3	5/18

CUX1	ATR	0.001305241	10.22288165	170	5	9	9	Co_Occurence	ATR, CUX1	5/18
MUC16	RBM10	0.00205786	4.047898504	120	15	9	49	Co_Occurence	MUC16, RBM10	15/58
KMT2C	BRIP1	0.002232273	9.070471296	167	5	6	15	Co_Occurence	BRIP1, KMT2C	5/21
ARID2	FGFR3	0.00228572	12.0424247	174	4	7	8	Co_Occurence	ARID2, FGFR3	4/15
TLR4	CREBBP	0.002417262	8.557221856	168	5	8	12	Co_Occurence	CREBBP, TLR4	5/20
CUX1	RET	0.002618145	8.301570062	168	5	11	9	Co_Occurence	CUX1, RET	5/20
FAT1	KRAS	0.00264191	0.136159399	93	2	81	17	Mutually_Exclusive	FAT1, KRAS	2/98
FLT1	KRAS	0.002737654	0	99	0	83	11	Mutually_Exclusive	FLT1, KRAS	0/94
TLR4	NAV3	0.002790574	5.701793445	157	7	19	10	Co_Occurence	NAV3, TLR4	7/29
GRIN2A	CREBBP	0.003201321	10.67660567	173	4	9	7	Co_Occurence	CREBBP, GRIN2A	4/16
RB1	ATR	0.003555598	7.577081961	167	5	9	12	Co_Occurence	ATR, RB1	5/21
GNAS	FLT1	0.003580687	7.928823769	165	5	6	17	Co_Occurence	FLT1, GNAS	5/23
TSHZ3	KMT2D	0.00471881	6.962775578	166	5	13	9	Co_Occurence	KMT2D, TSHZ3	5/22
TSHZ3	NTRK3	0.00471881	6.962775578	166	5	13	9	Co_Occurence	NTRK3, TSHZ3	5/22
NF1	KRAS	0.004769093	0.14619267	94	2	81	16	Mutually_Exclusive	KRAS, NF1	2/97
FLT1	PTPRT	0.005744366	8.676366235	171	4	11	7	Co_Occurence	FLT1, PTPRT	4/18

GNAS	TLR4	0.005944145	5.376851456	160	6	11	16	Co_Occurence	GNAS, TLR4	6/27
MUC16	GRIN2A	0.006919396	5.938487492	126	8	3	56	Co_Occurence	GRIN2A, MUC16	8/59
RET	GRIN2A	0.007424408	7.921622161	170	4	7	12	Co_Occurence	GRIN2A, RET	4/19
ARID1A	MGA	0.007424408	7.921622161	170	4	7	12	Co_Occurence	ARID1A, MGA	4/19
APC	MUC16	0.008281195	3.989379627	122	12	52	7	Co_Occurence	APC, MUC16	12/59
RB1	TP53	0.008543571	6.492710816	82	15	94	2	Co_Occurence	RB1, TP53	15/96
RB1	KRAS	0.008550557	0.157561175	95	2	81	15	Mutually_Exclusive	KRAS, RB1	2/96
TSHZ3	CREBBP	0.008620579	7.401090166	170	4	9	10	Co_Occurence	CREBBP, TSHZ3	4/19
NAV3	TP53	0.009726072	3.747457559	79	21	88	5	Co_Occurence	NAV3, TP53	21/93
ARID1A	LRRK2	0.010562947	6.907062905	169	4	8	12	Co_Occurence	ARID1A, LRRK2	4/20
MUC16	KDR	0.010921563	5.06567048	125	9	4	55	Co_Occurence	KDR, MUC16	9/59
MUC16	SETBP1	0.010921563	5.06567048	125	9	4	55	Co_Occurence	MUC16, SETBP1	9/59
MUC16	KMT2C	0.011054597	3.464759795	121	12	8	52	Co_Occurence	KMT2C, MUC16	12/60
KEAP1	TP53	0.01107906	0.457312863	43	33	76	41	Mutually_Exclusive	KEAP1, TP53	33/117
SETBP1	POLQ	0.011295562	6.700601092	169	4	11	9	Co_Occurence	POLQ, SETBP1	4/20
NTRK3	FLT1	0.011725997	6.730922879	168	4	7	14	Co_Occurence	FLT1, NTRK3	4/21

KMT2D	GRIN2A	0.011725997	6.730922879	168	4	7	14	Co_Occurence	GRIN2A, KMT2D	4/21
RET	FAT1	0.011743682	5.216902144	163	5	14	11	Co_Occurence	FAT1, RET	5/25
RET	MUC16	0.012986147	3.767110327	123	10	54	6	Co_Occurence	MUC16, RET	10/60
TP53	FAT1	0.013292832	4.613813522	81	16	3	93	Co_Occurence	FAT1, TP53	16/96
ARID1A	KDR	0.014470227	6.115513577	168	4	9	12	Co_Occurence	ARID1A, KDR	4/21
BACH2	TP53	0.014727621	5.512612502	82	13	96	2	Co_Occurence	BACH2, TP53	13/98
NAV3	GNAS	0.015054021	3.698060666	152	7	15	19	Co_Occurence	GNAS, NAV3	7/34
TSHZ3	PTPRT	0.015062831	6.005765524	168	4	11	10	Co_Occurence	PTPRT, TSHZ3	4/21
KMT2D	MUC16	0.01544021	3.590621828	122	11	53	7	Co_Occurence	KMT2D, MUC16	11/60
CUX1	MUC16	0.016313276	4.025372494	124	9	55	5	Co_Occurence	CUX1, MUC16	9/60
BACH2	GNAS	0.016930871	4.675419237	161	5	17	10	Co_Occurence	BACH2, GNAS	5/27
RELN	MUC16	0.017091938	3.013726996	119	13	51	10	Co_Occurence	MUC16, RELN	13/61
GLI1	PTPRD	0.017270065	4.845445014	158	5	23	7	Co_Occurence	GLI1, PTPRD	5/30
GRIN2A	FGFR3	0.017822325	7.968507182	174	3	8	8	Co_Occurence	FGFR3, GRIN2A	3/16
GRIN2A	FLT1	0.017822325	7.968507182	174	3	8	8	Co_Occurence	FLT1, GRIN2A	3/16
PIK3CG	MGA	0.017822325	7.968507182	174	3	8	8	Co_Occurence	MGA, PIK3CG	3/16

ATR	RBM10	0.018099265	4.620572704	160	5	19	9	Co_Occurence	ATR, RBM10	5/28
CREBBP	RB1	0.018178832	5.619112679	167	4	13	9	Co_Occurence	CREBBP, RB1	4/22
SETBP1	TLR4	0.018178832	5.619112679	167	4	13	9	Co_Occurence	SETBP1, TLR4	4/22
RET	ATR	0.01921106	5.480350865	167	4	10	12	Co_Occurence	ATR, RET	4/22
NAV3	KMT2D	0.020002178	3.836351784	155	6	12	20	Co_Occurence	KMT2D, NAV3	6/32
KMT2D	FAT1	0.020190248	4.370300505	161	5	14	13	Co_Occurence	FAT1, KMT2D	5/27
CREBBP	KMT2D	0.022451855	5.192815127	166	4	14	9	Co_Occurence	CREBBP, KMT2D	4/23
PIK3CA	KMT2D	0.022451855	5.192815127	166	4	14	9	Co_Occurence	KMT2D, PIK3CA	4/23
SETBP1	KMT2D	0.022451855	5.192815127	166	4	14	9	Co_Occurence	KMT2D, SETBP1	4/23
KDR	NF1	0.022451855	5.192815127	166	4	14	9	Co_Occurence	KDR, NF1	4/23
CREBBP	NTRK3	0.022451855	5.192815127	166	4	14	9	Co_Occurence	CREBBP, NTRK3	4/23
KMT2D	TP53	0.022563881	4.280597078	81	15	94	3	Co_Occurence	KMT2D, TP53	15/97
EPPK1	GLI1	0.023001193	7.058733377	173	3	9	8	Co_Occurence	EPPK1, GLI1	3/17
GRIN2A	LRRK2	0.023001193	7.058733377	173	3	9	8	Co_Occurence	GRIN2A, LRRK2	3/17
RB1	TSHZ3	0.024028125	5.034690925	166	4	10	13	Co_Occurence	RB1, TSHZ3	4/23
PTPRT	RBM10	0.024830676	4.137921608	159	5	19	10	Co_Occurence	PTPRT, RBM10	5/29

BACH2	RET	0.024840348	4.959538148	166	4	12	11	Co_Occurence	BACH2, RET	4/23
BRIP1	TP53	0.024874062	8.317799507	83	10	99	1	Co_Occurence	BRIP1, TP53	10/100
FLT1	TP53	0.024874062	8.317799507	83	10	99	1	Co_Occurence	FLT1, TP53	10/100
PTPRD	KDR	0.025185445	4.219390286	157	5	8	23	Co_Occurence	KDR, PTPRD	5/31
NTRK3	ATM	0.02531295	4.057416858	160	5	15	13	Co_Occurence	ATM, NTRK3	5/28
NF1	KMT2C	0.02531295	4.057416858	160	5	15	13	Co_Occurence	KMT2C, NF1	5/28
MET	KRAS	0.02624258	0.203009389	98	2	81	12	Mutually_Exclusive	KRAS, MET	2/93
APC	KDR	0.027315776	4.82280825	165	4	9	15	Co_Occurence	APC, KDR	4/24
PAK5	EPPK1	0.028941155	6.330001852	172	3	8	10	Co_Occurence	EPPK1, PAK5	3/18
CREBBP	FLT1	0.028941155	6.330001852	172	3	8	10	Co_Occurence	CREBBP, FLT1	3/18
SETBP1	FLT1	0.028941155	6.330001852	172	3	8	10	Co_Occurence	FLT1, SETBP1	3/18
BRAF	GRIN2A	0.028941155	6.330001852	172	3	8	10	Co_Occurence	BRAF, GRIN2A	3/18
PAK5	MGA	0.028941155	6.330001852	172	3	8	10	Co_Occurence	MGA, PAK5	3/18
FGFR3	RELN	0.028972868	4.837657668	163	4	19	7	Co_Occurence	FGFR3, RELN	4/26
GRIN2A	RELN	0.028972868	4.837657668	163	4	19	7	Co_Occurence	GRIN2A, RELN	4/26
MGA	RELN	0.028972868	4.837657668	163	4	19	7	Co_Occurence	MGA, RELN	4/26

KMT2D	CUX1	0.029545073	4.65251295	165	4	10	14	Co_Occurence	CUX1, KMT2D	4/24
RET	ARID1A	0.031402579	4.524726408	165	4	12	12	Co_Occurence	ARID1A, RET	4/24
ATM	CREBBP	0.032792928	4.498408408	164	4	9	16	Co_Occurence	ATM, CREBBP	4/25
RET	CDKN2A	0.03303007	3.742380839	158	5	19	11	Co_Occurence	CDKN2A, RET	5/30
PAK5	MUC16	0.033164921	3.517056614	124	8	56	5	Co_Occurence	MUC16, PAK5	8/61
CDKN2A	FLT1	0.033676349	4.571237836	162	4	7	20	Co_Occurence	CDKN2A, FLT1	4/27
RBM10	MGA	0.033676349	4.571237836	162	4	7	20	Co_Occurence	MGA, RBM10	4/27
NAV3	PTPRT	0.034898477	3.701681868	157	5	10	21	Co_Occurence	NAV3, PTPRT	5/31
ATR	FGFR3	0.035649112	5.73175199	171	3	8	11	Co_Occurence	ATR, FGFR3	3/19
MET	FGFR3	0.035649112	5.73175199	171	3	8	11	Co_Occurence	FGFR3, MET	3/19
TSHZ3	FGFR3	0.035649112	5.73175199	171	3	8	11	Co_Occurence	FGFR3, TSHZ3	3/19
CUX1	GRIN2A	0.035649112	5.73175199	171	3	8	11	Co_Occurence	CUX1, GRIN2A	3/19
CUX1	MGA	0.035649112	5.73175199	171	3	8	11	Co_Occurence	CUX1, MGA	3/19
MET	MGA	0.035649112	5.73175199	171	3	8	11	Co_Occurence	MET, MGA	3/19
TSHZ3	MGA	0.035649112	5.73175199	171	3	8	11	Co_Occurence	MGA, TSHZ3	3/19
TSHZ3	PIK3CG	0.035649112	5.73175199	171	3	8	11	Co_Occurence	PIK3CG, TSHZ3	3/19

CUX1	FAT1	0.035787105	4.320446481	164	4	15	10	Co_Occurence	CUX1, FAT1	4/25
PIK3CA	ZFH3	0.037049674	5.605788359	171	3	9	10	Co_Occurence	PIK3CA, ZFH3	3/19
POLQ	NF1	0.037866725	4.209455235	164	4	14	11	Co_Occurence	NF1, POLQ	4/25
BRAF	SMARCA4	0.038705703	3.666985701	154	5	26	8	Co_Occurence	BRAF, SMARCA4	5/34
KDR	SMARCA4	0.038705703	3.666985701	154	5	26	8	Co_Occurence	KDR, SMARCA4	5/34
RET	RB1	0.038931606	4.15606774	164	4	13	12	Co_Occurence	RB1, RET	4/25
LRRK2	RELN	0.03995627	4.214089542	162	4	19	8	Co_Occurence	LRRK2, RELN	4/27
KRAS	PTPRD	0.040775709	0.392130417	89	7	21	76	Mutually_Exclusive	KRAS, PTPRD	7/97
GNAS	TP53	0.041246401	2.905007931	79	17	92	5	Co_Occurence	GNAS, TP53	17/97
CDKN2A	EGFR	0.042789048	3.412117779	157	5	12	19	Co_Occurence	CDKN2A, EGFR	5/31
CDKN2A	TLR4	0.042789048	3.412117779	157	5	12	19	Co_Occurence	CDKN2A, TLR4	5/31
POLQ	BRIP1	0.043125298	5.23089262	170	3	8	12	Co_Occurence	BRIP1, POLQ	3/20
BACH2	FLT1	0.043125298	5.23089262	170	3	8	12	Co_Occurence	BACH2, FLT1	3/20
PTPRT	MGA	0.043125298	5.23089262	170	3	8	12	Co_Occurence	MGA, PTPRT	3/20
MUC16	FGFR3	0.043545913	3.807844536	125	7	4	57	Co_Occurence	FGFR3, MUC16	7/61
MUC16	FLT1	0.043545913	3.807844536	125	7	4	57	Co_Occurence	FLT1, MUC16	7/61

MUC16	PIK3CG	0.043545913	3.807844536	125	7	4	57	Co_Occurence	MUC16, PIK3CG	7/61
CUX1	GLI1	0.045453049	5.074832119	170	3	9	11	Co_Occurence	CUX1, GLI1	3/20
ATR	LRRK2	0.045453049	5.074832119	170	3	9	11	Co_Occurence	ATR, LRRK2	3/20
ATR	ZFH3	0.045453049	5.074832119	170	3	9	11	Co_Occurence	ATR, ZFH3	3/20
NTRK3	RELN	0.045635061	3.32475966	157	5	18	13	Co_Occurence	NTRK3, RELN	5/31
GLI1	CDKN2A	0.046236192	3.981647599	161	4	20	8	Co_Occurence	CDKN2A, GLI1	4/28
SETBP1	BRAF	0.046242316	5.024286541	170	3	10	10	Co_Occurence	BRAF, SETBP1	3/20
PAK5	CREBBP	0.046242316	5.024286541	170	3	10	10	Co_Occurence	CREBBP, PAK5	3/20
SETBP1	CREBBP	0.046242316	5.024286541	170	3	10	10	Co_Occurence	CREBBP, SETBP1	3/20
PAK5	KDR	0.046242316	5.024286541	170	3	10	10	Co_Occurence	KDR, PAK5	3/20
MUC16	KRAS	0.046513478	0.529491218	67	21	62	43	Mutually_Exclusive	KRAS, MUC16	21/105
RET	FLT1	0.051363966	4.806460192	169	3	8	13	Co_Occurence	FLT1, RET	3/21
BRAF	RELN	0.053063534	3.728114925	161	4	19	9	Co_Occurence	BRAF, RELN	4/28
PAK5	RELN	0.053063534	3.728114925	161	4	19	9	Co_Occurence	PAK5, RELN	4/28
ATR	SMARCA4	0.053260888	3.242087596	153	5	26	9	Co_Occurence	ATR, SMARCA4	5/35
MET	SMARCA4	0.053260888	3.242087596	153	5	26	9	Co_Occurence	MET, SMARCA4	5/35

BRIP1	KEAP1	0.053670733	0.150362595	109	1	73	10	Mutually_Exclusive	BRIP1, KEAP1	1/83
KMT2D	CDKN2A	0.054173101	3.132011468	156	5	19	13	Co_Occurence	CDKN2A, KMT2D	5/32
KMT2C	POLQ	0.054340659	3.644347249	162	4	11	16	Co_Occurence	KMT2C, POLQ	4/27
ATM	PTPRT	0.054340659	3.644347249	162	4	11	16	Co_Occurence	ATM, PTPRT	4/27
KMT2C	PTPRT	0.054340659	3.644347249	162	4	11	16	Co_Occurence	KMT2C, PTPRT	4/27
LRRK2	BACH2	0.05476405	4.630623372	169	3	12	9	Co_Occurence	BACH2, LRRK2	3/21
LRRK2	PTPRT	0.05476405	4.630623372	169	3	12	9	Co_Occurence	LRRK2, PTPRT	3/21
APC	RELN	0.056891334	3.070411702	156	5	18	14	Co_Occurence	APC, RELN	5/32
PTPRD	MGA	0.057066836	3.724933753	158	4	7	24	Co_Occurence	MGA, PTPRD	4/31
RB1	KMT2D	0.058313266	3.525449332	162	4	14	13	Co_Occurence	KMT2D, RB1	4/27
TLR4	KMT2D	0.058313266	3.525449332	162	4	14	13	Co_Occurence	KMT2D, TLR4	4/27
TLR4	NTRK3	0.058313266	3.525449332	162	4	14	13	Co_Occurence	NTRK3, TLR4	4/27
FLT1	EGFR	0.06035402	4.441957835	168	3	14	8	Co_Occurence	EGFR, FLT1	3/22
GRIN2A	RB1	0.06035402	4.441957835	168	3	14	8	Co_Occurence	GRIN2A, RB1	3/22
GRIN2A	TLR4	0.06035402	4.441957835	168	3	14	8	Co_Occurence	GRIN2A, TLR4	3/22
NF1	MUC16	0.062272562	2.78442092	121	10	54	8	Co_Occurence	MUC16, NF1	10/62

TP53	POLQ	0.062557493	3.321698229	81	12	3	97	Co_Occurence	POLQ, TP53	12/100
ARID2	ARID1A	0.064964305	4.254369268	168	3	13	9	Co_Occurence	ARID1A, ARID2	3/22
ZFH3	ARID1A	0.064964305	4.254369268	168	3	13	9	Co_Occurence	ARID1A, ZFH3	3/22
LRRK2	RET	0.064964305	4.254369268	168	3	13	9	Co_Occurence	LRRK2, RET	3/22
CDKN2A	FAT1	0.067220619	2.891827955	155	5	14	19	Co_Occurence	CDKN2A, FAT1	5/33
RET	ATM	0.067499908	3.323754597	161	4	16	12	Co_Occurence	ATM, RET	4/28
BRAF	BACH2	0.067804597	4.149258771	168	3	12	10	Co_Occurence	BACH2, BRAF	3/22
KDR	BACH2	0.067804597	4.149258771	168	3	12	10	Co_Occurence	BACH2, KDR	3/22
RELN	ATR	0.06830437	3.33769667	160	4	10	19	Co_Occurence	ATR, RELN	4/29
RELN	MET	0.06830437	3.33769667	160	4	10	19	Co_Occurence	MET, RELN	4/29
TLR4	FAT1	0.069709701	3.273109617	161	4	15	13	Co_Occurence	FAT1, TLR4	4/28
EPPK1	KMT2D	0.070079625	4.125552485	167	3	15	8	Co_Occurence	EPPK1, KMT2D	3/23
FLT1	KMT2D	0.070079625	4.125552485	167	3	15	8	Co_Occurence	FLT1, KMT2D	3/23
FGFR3	NF1	0.070079625	4.125552485	167	3	15	8	Co_Occurence	FGFR3, NF1	3/23
GRIN2A	NTRK3	0.070079625	4.125552485	167	3	15	8	Co_Occurence	GRIN2A, NTRK3	3/23
MGA	NTRK3	0.070079625	4.125552485	167	3	15	8	Co_Occurence	MGA, NTRK3	3/23

NTRK3	NF1	0.070454355	3.2565703	161	4	14	14	Co_Occurence	NF1, NTRK3	4/28
ARID2	TP53	0.071094776	4.115873569	82	10	99	2	Co_Occurence	ARID2, TP53	10/101
NAV3	MUC16	0.071572545	2.263990454	116	13	51	13	Co_Occurence	MUC16, NAV3	13/64
GLI1	KRAS	0.072678029	0.248418764	100	2	81	10	Mutually_Exclusive	GLI1, KRAS	2/91
KEAP1	EGFR	0.073096587	0.318517776	105	3	14	71	Mutually_Exclusive	EGFR, KEAP1	3/85
CDKN2A	KEAP1	0.073233286	0.383105612	100	5	69	19	Mutually_Exclusive	CDKN2A, KEAP1	5/88
GLI1	EGFR	0.076028988	3.931356703	167	3	14	9	Co_Occurence	EGFR, GLI1	3/23
ARID2	RB1	0.076028988	3.931356703	167	3	14	9	Co_Occurence	ARID2, RB1	3/23
LRRK2	RB1	0.076028988	3.931356703	167	3	14	9	Co_Occurence	LRRK2, RB1	3/23
CDKN2A	KRAS	0.077137977	0.400009448	92	6	77	18	Mutually_Exclusive	CDKN2A, KRAS	6/95
RELN	TP53	0.078145449	2.392015368	78	17	92	6	Co_Occurence	RELN, TP53	17/98
CUX1	CDKN2A	0.078345391	3.153296568	159	4	20	10	Co_Occurence	CDKN2A, CUX1	4/30
MET	CDKN2A	0.078345391	3.153296568	159	4	20	10	Co_Occurence	CDKN2A, MET	4/30
CREBBP	NAV3	0.07925177	3.165206351	158	4	22	9	Co_Occurence	CREBBP, NAV3	4/31
PIK3CA	NAV3	0.07925177	3.165206351	158	4	22	9	Co_Occurence	NAV3, PIK3CA	4/31
SMARCA4	EPPK1	0.079564913	3.252861976	155	4	7	27	Co_Occurence	EPPK1, SMARCA4	4/34

RET	BRAF	0.080112528	3.811776861	167	3	10	13	Co_Occurrence	BRAF, RET	3/23
ARID1A	PAK5	0.080112528	3.811776861	167	3	10	13	Co_Occurrence	ARID1A, PAK5	3/23
RET	PAK5	0.080112528	3.811776861	167	3	10	13	Co_Occurrence	PAK5, RET	3/23
ARID1A	PIK3CA	0.080112528	3.811776861	167	3	10	13	Co_Occurrence	ARID1A, PIK3CA	3/23
KMT2D	KRAS	0.080192318	0.348938493	96	4	79	14	Mutually_Exclusive	KMT2D, KRAS	4/93
MGA	APC	0.080520757	3.848288536	166	3	16	8	Co_Occurrence	APC, MGA	3/24
FGFR3	FAT1	0.080520757	3.848288536	166	3	16	8	Co_Occurrence	FAT1, FGFR3	3/24
FLT1	FAT1	0.080520757	3.848288536	166	3	16	8	Co_Occurrence	FAT1, FLT1	3/24
GRIN2A	FAT1	0.080520757	3.848288536	166	3	16	8	Co_Occurrence	FAT1, GRIN2A	3/24
RBM10	ATM	0.081942819	2.683467012	154	5	15	19	Co_Occurrence	ATM, RBM10	5/34
KMT2C	RB1	0.082231862	3.051599009	160	4	13	16	Co_Occurrence	KMT2C, RB1	4/29
NTRK3	SMARCA4	0.083540727	0	144	0	31	18	Mutually_Exclusive	NTRK3, SMARCA4	0/49
KMT2D	APC	0.083858116	3.022783472	160	4	15	14	Co_Occurrence	APC, KMT2D	4/29
BRAF	KEAP1	0.084707369	2.74837454	114	8	66	5	Co_Occurrence	BRAF, KEAP1	8/71
NAV3	SMARCA4	0.085043744	0.183670873	137	1	30	25	Mutually_Exclusive	NAV3, SMARCA4	1/55
ARID2	KMT2D	0.087927713	3.65016456	166	3	15	9	Co_Occurrence	ARID2, KMT2D	3/24

GLI1	KMT2D	0.087927713	3.65016456	166	3	15	9	Co_Occurrence	GLI1, KMT2D	3/24
ZFH3	KMT2D	0.087927713	3.65016456	166	3	15	9	Co_Occurrence	KMT2D, ZFH3	3/24
ARID2	NF1	0.087927713	3.65016456	166	3	15	9	Co_Occurrence	ARID2, NF1	3/24
LRRK2	NF1	0.087927713	3.65016456	166	3	15	9	Co_Occurrence	LRRK2, NF1	3/24
LRRK2	NTRK3	0.087927713	3.65016456	166	3	15	9	Co_Occurrence	LRRK2, NTRK3	3/24
FAT1	SMARCA4	0.090851736	2.732314763	149	6	25	13	Co_Occurrence	FAT1, SMARCA4	6/38
KEAP1	KMT2C	0.091075301	0.369545517	103	4	16	70	Mutually_Exclusive	KEAP1, KMT2C	4/86
EPPK1	ATM	0.091653728	3.602471835	165	3	17	8	Co_Occurrence	ATM, EPPK1	3/25
FLT1	ATM	0.091653728	3.602471835	165	3	17	8	Co_Occurrence	ATM, FLT1	3/25
FGFR3	KMT2C	0.091653728	3.602471835	165	3	17	8	Co_Occurrence	FGFR3, KMT2C	3/25
MUC16	GNAS	0.092756586	2.216401185	118	11	11	53	Co_Occurrence	GNAS, MUC16	11/64
RB1	BRAF	0.093384035	3.521278029	166	3	10	14	Co_Occurrence	BRAF, RB1	3/24
TLR4	BRAF	0.093384035	3.521278029	166	3	10	14	Co_Occurrence	BRAF, TLR4	3/24
TLR4	PAK5	0.093384035	3.521278029	166	3	10	14	Co_Occurrence	PAK5, TLR4	3/24
TLR4	ROS1	0.093384035	3.521278029	166	3	10	14	Co_Occurrence	ROS1, TLR4	3/24
RB1	SETBP1	0.093384035	3.521278029	166	3	10	14	Co_Occurrence	RB1, SETBP1	3/24

BACH2	MUC16	0.094012673	2.476908576	122	8	56	7	Co_Occurence	BACH2, MUC16	8/63
ATR	ARID1A	0.09672202	3.448229568	166	3	13	11	Co_Occurence	ARID1A, ATR	3/24
KMT2C	TP53	0.096825	2.509959939	79	15	94	5	Co_Occurence	KMT2C, TP53	15/99
PTPRT	POLQ	0.097845171	3.424529438	166	3	12	12	Co_Occurence	POLQ, PTPRT	3/24
NTRK3	KMT2C	0.098494408	2.818304928	159	4	16	14	Co_Occurence	KMT2C, NTRK3	4/30
MET	TP53	0.098848254	3.014952026	81	11	98	3	Co_Occurence	MET, TP53	11/101
TSHZ3	TP53	0.098848254	3.014952026	81	11	98	3	Co_Occurence	TP53, TSHZ3	11/101

Supplementary Table S3. Enrichment analysis of CNVs in *LKB1* WT and *LKB1* mutant NSCLC.

<i>LKB1</i> WT (5809 samples)		<i>LKB1</i> mutant (193 samples)	
Gene	Ratio	Gene	Ratio
TERC	10.21%	MYC	17.10%
EGFR	6.23%	MCL1	13.47%
MDM2	5.70%	TERC	8.29%
MYC	5.47%	LYN	4.66%
MCL1	5.04%	RIT1	3.63%
SOX2	4.36%	MDM2	3.11%
TERT	4.01%	CCNE1	3.11%
CDK4	3.89%	GNAS	3.11%
RAC1	2.91%	KRAS	3.11%
BCL6	2.51%	RAC1	2.59%
PIK3CA	2.39%	EGFR	2.59%
PRKCI	2.32%	PAK1	2.59%
CCND1	2.26%	BCL9	2.59%
MAP3K13	2.00%	SOX2	2.59%
ETV5	1.95%	CRKL	2.59%
FGF4	1.79%	RICTOR	2.07%
FGF19	1.76%	MET	2.07%

FGF3	1.72%	FGF3	2.07%
RICTOR	1.65%	FGF4	2.07%
FGFR1	1.62%	CDK4	2.07%

Supplementary Table S4. Analysis of TMB in *LKB1* WT and *LKB1* mutant NSCLC.

TMB	≥ 20 Muts/Mb (%)	< 20 Muts/Mb (%)
<i>LKB1</i> mutant	27 (14.59%)	158 (85.41%)
<i>LKB1</i> WT	234 (4.14%)	5419 (95.86%)

Supplementary Table S5. The usage of anti-PD-1/PD-L1 immunotherapy.

Anti-PD-1/PD-L1 agents	Number of receipts	Lines of treatment
Sintilimab	7	6 patients in 1L 1 patient in 3L
Camrelizumab	10	8 patients in 1L 1 patient in 2L 1 patient in 3L
Pembrolizumab	6	5 patients in 1L 1 patient in 2L
Durvalumab	1	1 patient in 1L
Tislelizumab	13	13 patients in 1L
Toripalimab	3	1 patient in 1L 2 patients in 2L