SUPPLEMENT TABLE 1: Antibody information

	IHC			Western Blot		
Target	**Company**	**Cat #**	**Dilution**	**Company**	**Cat #**	**Dilution**
RB1	Cell Signaling	9309	1:1600	Cell Signaling	9309	1:1000
INSM1	Santa Cruz	sc-271408	1:400	Santa Cruz	sc-271408	1:500
YAP1	Cell Signaling	14074	1:400	Cell Signaling	4912	1:1000
ASCL1 (MASH1)	BD Pharmingen	556604	1:100	BD Pharmingen	556604	1:100
NEUROD1	Abcam	205300	1:500	Cell Signaling	4373	1:1000
POU2F3	Sigma	HPA019652	1:800	Sigma	HPA019652	1:500
ACTB				Sigma	A5441	1:10k
CCND1				Cell Signaling	55506	1:1000
CDK2				Santa Cruz	6248	1:1000
CDK4				Cell Signaling	12790	1:1000
CDK6				Cell Signaling	3136	1:1000
E2F1				Santa Cruz	251	1:1000
CDKN2A				Cell Signaling	4824	1:1000
pRB1-Ser780				Cell Signaling	8180	1:1000

SUPPLEMENT TABLE 2 : *RB1* LOF signature genes from Chen et al (reference 23)

Low expression in *RB1* -loss: **Enriched in wt *RB1***	High expression in *RB1* -loss: **Low in wt *RB1***
ALDH18A1	ACYP1
APOBEC3C	AKAP5
ARAP3	BTF3L4
ARPC1B	CAMK2N2
ARPC2	CAND2
AUP1	CCNE2
BAZ2A	CDKAL1
BECN1	CDKN2A
BMS1	CDKN2C
CAB39L	CLSPN
CCND1	COCH
CDADC1	CPE
CDK6	DAND5
CIB1	DCHS1
COG3	DEK
CTSB	DONSON
DDX21	EID2B
DDX54	ELF2
DGKA	FAM111B
DNAJA2	FANCL
DNPEP	FBLN7
DYRK4	GKAP1
E2F4	GLRB
ECD	GPR137C
EDEM1	H2AFV
EEF1D	HSD17B6
EIF3A	ID4
EIF3D	IQCC
ELF1	JAKMIP1
EPB41L2	KCND2
ESD	KCTD16
ETV4	KIAA1841
FNDC3A	KLHL2
GHITM	LHX2
GLUD1	MESP1
GSTO1	MNS1
GTF2F2	NEURL1B
H6PD	OSCP1
HIF1AN	PCSK1
HMGA2	PDIK1L
HMGXB3	PIK3R3
HOXB13	POU4F1
HPS6	RAD1
IGF2BP2	RIBC2

IKBKE	RNASEH2A
IMP4	RTN3
INTS6	SH3GL2
ITM2B	SLC36A4
KPNA3	SPSB4
LDB1	STMN1
LIF	TCTEX1D2
LRCH1	TEX9
M6PR	TIGD7
MCCC2	TTLL7
MED4	TXNDC16
MIPEP	UBR7
MMS19	UCHL1
MPG	USP1
MRPL35	ZBTB8A
MRPS31	ZNF254
MTHFD1L	ZNF347
MTRF1	ZNF367
NAB2	ZNF43
NADSYN1	ZNF528
NEK3	ZNF606
NIP7	ZNF610
NOB1	ZSCAN16
NOP16	ZSCAN18
NPAS2	
NUDT15	
NUFIP1	
OAF	
OGFR	
PDCD6IP	
PDE12	
PHF11	
PLD2	
POLD4	
POMP	
PUS1	
PVT1	
RB1	
RBM19	
RFT1	
RHBDF2	
RNF123	
RNF6	
RPL22L1	
SEC23IP	
SEC24C	

SETDB2	
SFT2D1	
SLC12A9	
SLC25A15	
SLC25A30	
SMAD3	
SMO	
SMURF1	
SMYD5	
SNHG4	
SPRY4	
STAT6	
SUCLA2	
SUGT1	
TBC1D22A	
TCOF1	
THG1L	
TM9SF3	
TNFRSF10B	
TOP1MT	
TPCN2	
TPT1	
TRADD	
WBP4	
WDFY2	
WDR59	
XPNPEP1	
XPO4	

SUPPLEMENT TABLE 3: H scores for all SCLC cases analyzed by IHC*

	PID	# cores	Site	RB	INSM1	ASCL1	NEUROD1	POU2F3	YAP1
TMA 0035	326	2	node	120	50	50	na	na	120
	553	4	brain	0	190	60	35	0	60
	551	2	node	5	180	40	na	na	0
	425	2	node	0	190	0	na	na	0
	424	2	node	0	190	170	20	na	10
	550	2	node	10	190	160	0	0	5
	549	2	lung	180	190	180	0	0	0
	548	2	brain	0	190	160	na	na	0
	543	2	lung	0	180	170	0	0	0
	541	2	lung	140	10	0	10	?	160
	458	2	lung	0	120	0	na	na	5
	519	2	lung	5	180	190	0	0	0
	556	2	lung	0	160	140	15	0	0
	482	2	lung	5	190	190	0	0	10
	557	2	pleura	0	190	20	na	na	0
	558	2	spine	0	20	5	0	0	0
	559	2	pleura	120	190	190	na	na	0
	475	2	brain	0	90	0	na	0	0
	555	4	brain	0	190	180	20	0	0
TMA 0047	48	1	lung	0	0	na	na	na	na
	277	2	trachea	na	na	na	na	na	na
	217	2	node	0	3	0	0	na	0
	?	2	node	0	270	270	60	30	3
	420	2	node	0	0	15	150	0	90
	246	4	mediastinum	180	0	90	240	0	0
	200	2	lung	0	10	na	na	na	na
	243	2	lung	90	240	0	0	0	0
	268	2	lung	0	150	na	na	na	na
	270	2	neck	0	240	225	0	0	0
	302	2	lung	0	120	na	na	na	na
	408	2	bronchus	0	40	na	na	0	0
	343	2	node	0	5	na	na	na	na
	374	2	bronchus	0	5	na	na	na	na
	394	2	lung	0	60	0	0	0	0
	283	2	node	0	0	0	na	0	0
	340	4	node	0	60	0	10	0	0
	508	2	diaphragm	3	240	na	na	na	na
	598	2	adrenal	0	240	270	15	3	60
	636	2	pleura	100	270	160	255	0	0
	639	4	node	0	285	na	na	na	na

	Cases		
Positives (H Score at least 20)	**#**	**total evaluable**	**%**
RB1	9	62	14.5
INSM1	51	62	82.2
ASCL1	36	51	70.5
NEUROD1	16	41	39
POU2F3	1	42	2.3
YAP1	7	53	20.7
RB1/YAP1	3	9	33.3
RB1/INSM1	7	9	77.7
RB1/ASCL1	7	9	77.7
RB1/NEUROD1	3	7	42.8
ASCL1/NEUROD1	13	31	41.9

Site	
brain	20
lung	16
node	13
bronchus	4
pleura	3
spine	2
trachea	1
mediastinum	1
neck	1
diaphragm	1
adrenal	1
liver	1

	649	2	bronchus	0	225	na	na	na	na
	665	2	brain	0	210	195	1	0	1
	669	2	brain	0	285	294	75	0	0
	671	2	lung	0	180	na	na	na	na
	677	2	bronchus	15	120	20	0	0	0
	693	2	lung	0	255	35	10	0	0
	697	2	lung	0	270	0	na	na	0
	703	2	spine	0	180	270	40	0	0
	662	2	node	0	60	0	0	0	0
	737	2	liver	na	na	195	2	0	0
TMA 0048	?	4	brain	0	180	na	160	6	0
	?	2	brain	0	0	0	30	0	0
	527	4	brain	15	50	110	0	0	2
	?	2	brain	0	0	na	na	0	0
	776	4	brain	225	120	40	0	15	6
	?	4	brain	0	70	40	285	0	0
	?	6	brain	10	270	270	240	0	0
	603	2	brain	0	85	180	0	0	70
	655	6	brain	0	270	285	3	0	4
Multiple TMAs	552	2	brain	5	190	180	0	0	0
	471	6	brain	180	285	270	270	0	40
	554	8	brain	5	255	270	0	0	0
	589	6	brain	0	270	190	285	6	30
	460	4	brain	0	240	180	180	0	0
	* All RB1 positives case highlighted in yellow								
	na = no tissue available for analysis								

SUPPLEMENT TABLE 4: PATIENT CHARACTERISTICS OF IHC (N=64) COHORT (8 missing)

	RB1: Positive (N=9)	RB1: Negative (N=47)	p-value
Age: mean (STD)	64.8 (4.1)	67.7 (9.9)	0.454
Sex: Male/Female (0 missing)	6/3	26/21	0.529
Race: White/Black (1 missing)	7/2	36/10	0.974
Smoking: No/Yes (0 missing)	2/7	1/46	0.014
Stage: Extensive/Limited (2 missing)	6/3	37/8	0.29
Stage: (6 missing)			
1,2	2	3	
3	1	2	0.285
4	6	36	

SUPPLEMENT TABLE 5: PATIENT CHARACTERISTICS OF GENOMIC (N=122) COHORT

	RB1: WT (N=37)	RB1: Mutant (N=85)	p-value
Age: mean (STD)	62.2 (11.4)	65.9 (9.4)	0.089
Sex: Male/Female (0 missing)	21/16	36/49	0.143
Race: White/Black (8 missing)	21/14	61/18	0.059
Smoking: No/Yes (3 missing)	3/33	5/78	0.644
Stage: Extensive/Limited (1 missing)	30/6	61/24	0.178
Stage: (22 missing)			
1,2	0	4	
3	2	7	0.283
4	30	57	

SUPPLEMENT TABLE 6: Gene Alterations in Genomic Cohort

Patient ID (PID)	Platform	RB1	RB1 Gene Alteration	TP53	TP53 Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration	Gene	Gene Alteration
433	Foundation	RB1	ND	TP53	E336*	APC	L592fs*12	MYST3	amplfication																
459	Foundation	RB1	S834*	TP53	splice site 672+1G>A																				
474	Foundation	RB1	splice site 1390_1G>T	TP53	G245V	ATR	R849*	CREBBP	Q881* subclonal																
475	Foundation	RB1	splice site 1332+2T>A	TP53	R175F	AR	Q58L	ARID1A	Q1519fs*13	CREBBP	S437fs*34	ERG	V440M	LRP1B	splice site 10414+1G>A	MLH1	H727fs*30+	MLL2	P647fs*283	MLL2	R4282*				
476	Foundation	RB1	splice site 539+1G>A	TP53	Q104*	DNMT3A	S770L	DNMT3A	splice site 1123-1G>A	FGFR1	amplification	KEAP1	E218*												
477	Foundation	RB1	loss, exons 2-27	TP53	Y220C	BCL2L2	amplification- equivocal	EGFR	L747_S752del	FBXW7	E192A	MCL1	amplification- equivocal	NFKB1A	amplification- equivocal	NKX2-1	amplification- equivocal	PIK3CA	E545K						
478	Foundation	RB1	ND	TP53	R181P	TP53	E258K	CDC73	R330L																
479	Foundation	RB1	ND	TP53	loss	KDR	amplification- equivocal	KIT	amplification	KIT	Y553C	MAP2K1	amplification	NOTCH2	splice	PDGFRA	amplification								
480	Foundation	RB1	ND	TP53	R273C	TP53	R158L	CTNNB1	S37C	FGFR1	amplification	MLL2	Q1755*	MYST3	amplification	NFE2L2	R18Q	ZNF703	amplification						
481	Foundation	RB1	loss, exons 18-23	TP53	L35fs*9	AKT2	amplification- equivocal	CCNE1	amplification	CRKL	amplification	JAK2	amplification- equivocal												
482	Foundation	RB1	Q384*	TP53	Y126fs*44	EP300	splice site 730-1G>T	MYCL1	amplification	PTEN	splice site 635-1G>A	SETD2	E33*												
483	Foundation	RB1	E268fs*18	TP53	K305*	CREBBP	R1173*	GATA3	loss	LRP1B	Q2329fs*3	MLL2	E1658*	MYC	amplification										
484	Foundation	RB1	splice site 138-1G>T	TP53	splice site 673-2A>G																				
485	Foundation	RB1	ND	TP53	H168R	FAM46C	V69I	FGF10	amplification- equivocal	RICTOR	amplification- equivocal														
486	Foundation	RB1	R445*	TP53	ND	ATRX	G175*	AXL	R295W																
487	Foundation	RB1	R544fs*11	TP53	R65fs*58	CREBBP	P858S	FBXW7	C533*																
488	Foundation	RB1	Q471*	TP53	G154fs*16	GATA3	T108S	KDM6A	G653fs*38	PTCH1	E1242K														
489	Foundation	RB1	ND	TP53	ND	SMARCA4	splice site 1761+1G>A																		
490	Foundation	RB1	E53*	TP53	H179Y																				
491	Foundation	RB1	P371fs*11	TP53	C141Y	CREBBP	R1446H	FGF10	amplification	RICTOR	amplification														
492	Foundation	RB1	ND	TP53	P128fs*42	ERBB2	T733I																		
493	Foundation	RB1	loss, exons 18-27	TP53	H178fs*1																				
495	Foundation	RB1	S829*	TP53	C141W	KRAS	G12D	MLL2	P647fs*283																
496	Foundation	RB1	ND	TP53	ND	EWSR1	EWSR1-FLI1 fusion																		
497	Foundation	RB1	ND	TP53	R248P	MCL1	amplification	PTEN	loss																
498	Foundation	RB1	R579*	TP53	Q317fs*19	MTOR	amplification	MYCL1	amplification	NTRK1	M375I														
499	Foundation	RB1	ND	TP53	V272L	ARID1A	G285*	CD274	amplification	MLL2	M3161fs*32	MYCN	amplification	PDCD1LG2	amplification										
500	Foundation	RB1	splice site 2107-1G>C	TP53	Q136*	PTEN	splice site 1027-2A>T																		
501	Foundation	RB1	loss	TP53	R282W	APC	E991*	APC	C1410fs*1	BRAF	V600E- subclonal	ERBB3	G284R	KRAS	G12S	SUFU	loss, exon 12								
502	Foundation	RB1	ND	TP53	ND	CCND1	amplification	CDK4	amplification	FGF19	amplification	FGF3	amplification	FGF4	amplification	MDM2	amplification								
503	Foundation	RB1	R355fs*12	TP53	A159P	BRD4	splice site 3283-2A>G	FBXW7	S427*	FGFR1	amplification	MYC	amplification- equivocal	NFE2L2	E63Q										
504	Foundation	RB1	P777fs*33	TP53	V157F	CREBBP	F280fs*14	FAT1	A2456T- subclonal	IRF4	G202S	MLL2	A1105fs*14	PTEN	loss	SPTA1	E2320*								
505	Foundation	RB1	ND	TP53	R181H- subclonal	TP53	R110L	TET2	Q1389*																
506	Foundation	RB1	R73fs*36	TP53	R249S	PIK3R1	splice site 1746-2A>T	PREX2	V537I	SPTA1	splice site 532-2A>T														
508	Foundation	RB1	loss, exons 9-11	TP53	M246I	CTNNB1	S45F	KRAS	G12C																
509	Foundation	RB1	ND	TP53	G245S																				
510	Foundation	RB1	splice site 137+1G>T	TP53	R158L	BRCA1	Q1756fs*74	FBXW7	R505fs*19	FBXW7	R479*	PTEN	loss, exons 3-5- equivocal												
511	Foundation	RB1	R7fs*24	TP53	splice site 376-1G>T	TP53	T118fs*5																		
512	Foundation	RB1	ND	TP53	E298*	FGF10	amplification	FGFR1	amplification	KEAP1	rearrangement, exon 3	PRDM1	E743K	PTCH1	T1064M	RICTOR	amplification	SPEN	truncation, exon 11	STK11	K64*	ZNF703	amplification		
513	Tempus	RB1	ND	TP53	P190L	KMT2D	E122*																		
534	Foundation	RB1	loss, exons 25-26	TP53	Q167*	FGFR1	amplification	LRP1B	G683*	LYN	amplification- equivocal														
563	Foundation	RB1	E747_E748>D*	TP53	C176fs*71	CREBBP	loss, exons 1-11																		
583	Foundation	RB1	splice site 1216-1G>C	TP53	N247_R249>K	PIK3R2	splice site 902-2A>T																		
592	Foundation	RB1	S634*	TP53	R249W	ATM	E672*	KRAS	amplification	MCL1	amplification- equivocal	STK11	E199fs*88												
604	Foundation	RB1	loss, exons 3-17	TP53	R248W	AXIN1	A526V	BCOR	splice site 4072-1G>C	NF1	G2392fs*4														
606	Foundation	RB1	Q62*	TP53	splice site 97-2A>T	CCNE1	amplification	GATA6	amplification																
607	Foundation	RB1	splice site 2212-2A>G	TP53	loss, exons 10-11																				
610	Foundation	RB1	R73fs*36	TP53	R282P	CD274	amplification	JAK2	amplification	KDR	Q1344H	MYST3	amplification	PDCD1LG2	amplification	STK11	K96fs*6								
616	Foundation	RB1	ND	TP53	E287*	CDKN2A	P114L	NF1	splice site 5268+1G>T	STAT3	D661V- subclonal														
624	Foundation	RB1	E554*	TP53	R158L	LRP1B	Q3888*	SMAD2	splice site 236+2T>C																
626	Foundation	RB1	K341*	TP53	splice site 560-2A>C	MLL2	G3775fs*55	SPTA1	E216*																
627	Foundation	RB1	R579*	TP53	V173G																				
630	Foundation	RB1	ND	TP53	E51*	ARID1A	R1722*	PARK2	C337*																
632	Foundation	RB1	splice site 138-2A>C	TP53	Q144P	NF1	Q853fs*20																		
634	Foundation	RB1	splice site 2490-2A>G	TP53	C135fs*35	AKT2	amplification	CCND3	amplification	CCNE1	amplification	FAT1	G4065fs*141	KEL	E134*	MTOR	L1907F	SPTA1	E284*- subclonal	VEGFA	amplification				
636	Foundation	RB1	RB1-USP24 fusion	TP53	G245S																				
639	Foundation	RB1	R467*	TP53	V157fs*13	EPHB1	D848Y	KDM5C	M1V	NOTCH1	Y662fs*1														
642	Foundation	RB1	loss, exons 3-6	TP53	G245R	ATR	A2043fs*5	BRCA1	E1038G	BRCA2	splice site 9117G>A														
643	Foundation	RB1	A17fs*3	TP53	splice site 375G>T	EGFR	amplification- equivocal	MLL2	T2195fs*69	MYC	amplification- equivocal														
644	Foundation	RB1	splice site 2107-2A>T	TP53	splice site 993+1G>A	ATRX	R1135W	BCORL1	E952*	FGFR1	amplification	LRP1B	splice site 13659+1G>T	ZNF703	amplification										
649	Foundation	RB1	ND	TP53	E298*	EZH2	S538L- subclonal	MLL2	Q152fs*56	SLIT2	R1427S	TET2	T970fs*2												
652	Foundation	RB1	loss, exon 12	TP53	M246V	AKT2	E17K- subclonal	CREBBP	K1588*	KDR	amplification	KIT	amplification												
653	Foundation	RB1	splice site 607+1G>T	TP53	G244V	ERBB4	Y268C	HRAS	G13C	NOTCH3	V483fs*116	TET2	Q1274E- subclonal												
657	Foundation	RB1	ND	TP53	splice site 375+1G>A	AKT1	E17K																		
660	Foundation	RB1	splice site 1498+1G>A	TP53	P142fs*28	AKT2	amplification	AXL	amplification	BCOR	E1708*	BRAF	G469V	CCND2	amplification- equivocal	DNMT3A	splice site 639+1G>T	KDM5A	amplification	LRP1B	splice site 3521-1G>T	NOTCH1	G546*	PTEN	R41*
664	Foundation	RB1	I274fs*2	TP53	M246V	CCNE1	amplification	NFE2L2	D13N																
673	Foundation	RB1	G435*	TP53	R273H	MYCL1	amplification- equivocal	STAG2	K225fs*2																
674	Foundation	RB1	ND	TP53	E285V	ATRX	splice site 189+1G>T	AURKA	amplification	BRCA2	S195*	CCNE1	amplification	GNAS	amplification	KIT	amplification	PDGFRA	amplification	ZNF217	amplification				
676	Foundation	RB1	loss	TP53	S106R	BRIP1	G677fs*11	NKX2-1	amplification- equivocal	SOX2	amplification- equivocal														
677	Foundation	RB1	ND	TP53	D259Y	C17orf39	amplification	FANCC	truncation, exon 3	NFKB1A	amplification	NKX2-1	amplification	STK11	splice site 598-1G>A										
679	Foundation	RB1	ND	TP53	R248L	CCND1	amplification	CDKN2A/B	loss	FGF19	amplification	FGF4	amplification	MYC	amplification	SPTA1	V1233I								
683	Foundation	RB1	L60*	TP53	splice site 375G>T	MLL2	splice site 15921+1G>C	PIK3CA	E545A- subclonal																
687	Foundation	RB1	ND	TP53	V157F	MYCN	amplification																		
693	Foundation	RB1	G617fs*6	TP53	K319*	BCORL1	P699fs*5	EP300	splice site 3671+1G>A- subclonal	LRP1B	splice site 8850+1G>T														
695	Foundation	RB1	splice site 2326-1G>T	TP53	Q331H	FBXW7	L417*	MYC	amplification- equivocal																
699	Foundation	RB1	E166*	TP53	G293*																				
700	Foundation	RB1	splice site 1215+1G>T	TP53	R175G	CD274	amplification	CHD4	splice site 100+2T>C	MYC	amplification	PIK3CA	E542K												
706	Foundation	RB1	ND	TP53	splice site 993+1G>T	SPTA1	L1267M																		
712	Foundation	RB1	Y756fs*9	TP53	splice site 375G>T	CHD4	A2fs*23	PBRM1	loss, exons 24-30																
713	Foundation	RB1	R445*	TP53	L111P	CCND2	amplification- equivocal	FGF23	amplification- equivocal	FGF6	amplification- equivocal	KDM5A	amplification	MLL2	P2539fs*4	NOTCH1	E493*								
716	Foundation	RB1	L769fs*41	TP53	M40fs*75	ATM	splice site 663-2A>T	MAP2K1	Q56P	MLL2	Q4228*														
719	Foundation	RB1	R500*	TP53	C135G	CREBBP	I1084fs*3																		
736	Foundation	RB1	splice site 1215+1G>A	TP53	G266V	ABL1	L248_G250del	MLH1	R325Q	NSD1	R1054T														
750	Foundation	RB1	R358*	TP53	M237I	CREBBP	R1446L	RBM10	splice site 664-1G>T																
754	Foundation	RB1	loss	TP53	ND	CDKN1B	K96fs*29	MDM2	amplification																
755	Foundation	RB1	ND	TP53	L194R	STK11	loss, exon 12																		
762	Foundation	RB1	loss, exons 5-20	TP53	P190fs*57	CREBBP	R1672fs*70	PIK3R1	S652fs*8																
766	Foundation	RB1	K462fs*16	TP53	E298*	ACVR1B	G214V	BAP1	S520fs*51	NOTCH1	E756*														
772	Foundation	RB1	loss, exons 11-17	TP53	R158L	AKT2	amplification	AXL	amplification	CCNE1	amplification	ERBB2	amplification	RBM10	E829fs*18	SOX2	amplification- equivocal	TERT	promoter -124C>T						
774	Foundation	RB1	loss, exons 25-26	TP53	R273fs*71	BRCA2	Q1802*	SMAD4	E330K																
775	Foundation	RB1	loss, exons 18-27	TP53	R282W	EGFR	G719C	FGF14	amplification- equivocal	IRS2	amplification- equivocal	PIK3CA	E545K												
776	Foundation	RB1	ND	TP53	ND	ARID1A	T433fs*182	CTNNB1	S37F	KRAS	G12D	PIK3CA	E545K												
777	Foundation	RB1	ND	TP53	ND	ATM	R1086L	CHEK2	E501*	KRAS	G12C	NFKB1A	amplification	NKX2-1	amplification	PTPRO	V233I	RAD21	amplification	SMAD2	G379fs*4	STK11	D237Y		
778	Foundation	RB1	ND	TP53	ND	CDKN1B	Q20*	CDKN1B	R113fs*2- subclonal																
790	Foundation	RB1	splice site 1154_1215+33del95	TP53	R342*	JAK1	M828I																		
832	Foundation	RB1	K420*	TP53	Y234fs*13																				
837	Foundation	RB1	splice site 1960+1G>C	TP53	ND																				
842	Foundation	RB1	I172fs*13	TP53	R273G	AKT2	amplification	FBXW7	R339*																
843	Foundation	RB1	ND	TP53	H179R	SDHA	R554Q																		
846	Foundation	RB1	splice site 382-2A>G	TP53	R248W	CUL4A	amplification	ERBB4	R838Q	FGF14	amplification	FGFR1	amplification	IRS2	amplification	NFKB1A	amplification	NKX2-1	amplification	NSD3	amplification	ZNF703	amplification		
892	Foundation	RB1	E837*	TP53	splice site 673-2A>T	CCNE1	amplification	EP300	Y1414C	KDR	amplification	KIT	amplification	NF1	E196*	NSD3	A41T	PBRM1	E1097*	PDGFRA	amplification	PTEN	Q214*		
896	Foundation	RB1	ND	TP53	K132N																				
898	Tempus	RB1	splice site 1128-1G>C	TP53	S241F	KDM6A	K987*	KRAS	G12D																
899	Foundation	RB1	K844fs*11	TP53	R249T	CDH1	rearrangement exon 2	SOX2	amplification																
906	Foundation	RB1	ND	TP53	R273L	APC	loss	CCNE1	amplification	FAS	K100*	NF1	G910*	PIK3R1	Y463_D464insEY	STK11	loss								
918	Foundation	RB1	S576*	TP53	C275F	BRIP1	splice site 1340+1G>A	NOTCH1	G1215C																
931	Foundation	RB1	K791*	TP53	E56*	ATR	splice site 3580_3581+12del14	FOXL2	C134W																
938	Tempus	RB1	N290fs	TP53	V157F	KMT2D	R2410*	PIK3CA	E453K	PIK3CA	G118D														
939	Foundation	RB1	Y529fs*26	TP53	R272P	BCL2L1	amplification	CREBBP	R370*	EED	R414*	IKZF1	K48*	MYCL1	amplification	SOX2	amplification								
941	Foundation	RB1	Q689*	TP53	splice site 376-2A>T	APC	S2631F	BRCA1	S1007*	CREBBP	splice site 1317_1330+11del25	CREBBP	Q355*	MLL2	V1561fs*1	TNFRSF14	G193*								
942	Foundation	RB1	ND	TP53	C124R	BCL2	amplification	CREBBP	M783fs*21	GATA6	amplification	SOX2	amplification												
947	Foundation	RB1	P23fs*40	TP53	D208V	C17orf39	amplification	CCNE1	amplification	EP300	N1126S	FANCC	splice site 844-1G>C												
948	Tempus	RB1	loss	TP53	G245D																				
957	Tempus	RB1	E748*	TP53	R342*	APC	loss	NCOR1	Y1693*																
958	Tempus	RB1	K720*	TP53	TE170*	FAT1	loss																		
964	Tempus	RB1	G509*	TP53	splice site 375+1G>T	KMT2D	Q277*	KMT2D	E1838*																
975	Tempus	RB1	ND	TP53	E298*	GPS2	L88fs																		
979	Tempus	RB1	splice site 265-1G>A	TP53	V173L	ING1	M1?	SETD2	T2037A																

ND: not detected

SUPPLEMENT TABLE 7: RB1 stained tumor cores with known *RB1* mutation status

TMA	Type SCLC	PID	*RB1* Mut status		Platform	Site	RB1 H score
0035	pure	482	mutant	Q384*	FM	lung	5
0047	pure	636	mutant	RB1-USP24 fusion	FM	pleura	100
	cSCLC	508	mutant	RB1 loss exons 9-11	FM	diaphragm	3
	pure	639	mutant	R467*	FM	node	0
	pure	649	wt		FM	bronchus	0
	pure	677	wt		FM	bronchus	15
	pure	693	mutant	G617fs*6	FM	lung	0
0048	cSCLC	776	wt		FM	brain	225

SUPPLEMENT TABLE 8

	Patient 2: RESPONDER										**Patient 1: NON-RESPONDER**	
Sample	**Biopsy**			**Pre-Rx**			**Post-Rx**				**Biopsy**	
Platform	TEMPUS|xT			TEMPUS|xF			TEMPUS|xF				FOUNDATTION**ONE**®CDx	
Site	Lymph node			Blood			Blood				Lung	
Biologically Relevant	TP53	p.T125T Splice variant- LOF	90.30%	TP53	p.T125T Splice region variant-LOF	62.10%	TP53	p.T124T Splice region variant-LOF	0.40%		TP53	C124R
	KEAP1	p.E493V Missense- LOF	80.50%								CREBBP	M783fs*21 - subclonal
											BCL2	Amp
											GATA6	Amp
											SOX2	Amp- equivocal
VUS	AXIN1	c.1115C>T p.P372L Splice region variant	87.80%	JAK2	c.3158A>G p.K1053R Missense	68.40%	ALK	c.3421G>A p. D1141N Missense	48.60%		AKT1	Amp
	SYNE1	c.1921C>T p.A6406V Missense	81.30%	ALK	c.3421G>A p.D1141N Missense	49.30%	JAK2	c.3158A>G p.K1053R Missense	47.30%		APC	V2781M
	HSPH1	c.211del p.R71fs Frameshift	79.60%	KMT2A (MLL)	c.212G>T p.G71V Missense	35.30%					ATM	G3029D
	GNAQ	c.606-3C>T Splice region variant	72.90%	EGFR	c.478G>C p.E160Q Missense	32.00%					CSF3R	T486M
	ZNF217	c.1260T>A p.C420* Stop gain	54.70%	PTPN11	c.1448-4G>A Splice region variant	31.80%					ESR1	R269C
	KMT2A (MLL)	c.212G>T p.G71V Missense	53.30%	KMT2A (MLL)	c.8041G>C p.D2681H Missense	19.50%					FLT1	K673E
	PTPN11	c.1448-4G>A Splice region variant	51.00%	PDGFRB	c.2919_2920delinsTT p.VD973VY Missense	0.40%					GABRA6	P49S
	EGFR	c.474_478delinsTGTGC p.NVE158NVQ Missense	47.90%								KMT2A (MLL)	P1987T
	AP2M1	c.1012C>T p.P338S Missense	35.80%								MLL2	K287E, V5400C
	TOP2A	c.2645G>C p.G882A Missense	28.30%								MYCN	A220S, I350T
	KMT2A (MLL)	c.8041G>C p.D2681H Missense	23.50%								NOTCH3	F1358V
											RB1	V84_L88del
											ROS1	W2145C
											SMAD2	Amp
											SMAD4	Amp