Table S1 List of the genes included in the GeneRead™ DNAseq Targeted Panels V2 Human Comprehensive Cancer Panel (QIAGEN)

ABL1
AKT1
AKT2
ALK
AMER1
APC
AR
ARID1A
ARID2
ASXL1
ATM
ATRX
BAP1
BCL6
BCOR
BRAF
BRCA1
BRCA2
BRIP1
BTK
BUB1B
CARD11
CBL
CBLB
CD79A
CD79B
CDC73
CDH1
CDK12
CDK4
CDKN2A
CHEK2
CIC
CREBBP
CRLF2
CSF1R
CTNNB1
CYLD
DAXX
DDB2
DDR2
DICER1
DNMT3A
ECT2L
EGFR
EP300
EPCAM
ERBB2
ERBB3
ERBB4
ERCC5
ESR1
EZH2
FAM46C
FANCA
FANCD2
FANCE
FAS
FBXO11
FBXW7
FGFR2
FGFR3
FH
FLCN
FLT3
FUBP1
GATA1
GATA2
GATA3
GNA11
GNAQ
GNAS
GPC3
GRIN2A
H3F3A
HIST1H3B
HNF1A
HRAS
HSPH1
IDH1
IDH2
IKZF1
IL6ST
IL7R
JAK1
JAK2
JAK3
KDM6A
KDR
KIT
KLF6
KMT2D
KRAS
MAP2K1
MAP2K2
MAP2K4
MAP3K1
MAP4K3
MDM2
MED12
MEN1
MET
MLH1
MSH2
MSH6
MTOR
MUTYH
MYC
MYD88
NF1
NF2
NFE2L2
NFKBIA
NOTCH1
NOTCH2
NPM1
NRAS
PALB2
PAX5
PBRM1
PDGFRA
PHF6
PIK3CA
PIK3R1
PMS2
PPP2R1A
PRDM1
PRKAR1A
PTCH1
PTEN
PTPN11
PAC1
RB1
RET
ROS1
SDHB
SETD2
SF3B1
SLC7A8
SMAD4
SMARCA4
SMARCB1
SMO
SPOP
SRC
STK11
SUFU
TERT
TNFAIP3
TNFRSF14
TP53
TSC1
TSC2
TSHR
U2AF1
VHL
WT1
XPC
ZNF2
ZRSR2

Table S2 The sequences for reverse transcriptase-PCR

ASCL1	F	GGTGCGAATGGACTTTGGAA
	R	GGCATGCCTCGCTTAGTTG
CSF1R	F	CCAGCACGAGAACATCGTCAA
	R	AGACGGTCGCCATAGCAACAG
JAK1	F	TGCCCACCTAACTGTCCAGATG
	R	TGAAAGCTTGTCCGATTGGATG
MAP2K2	F	GGCCATCTTTGAACTCCTGGACTA
	R	AACACACCGTTGGGCAGCTTA
MTOR	F	GGCCTGGATGGCAACTACAGA
	R	TGACTGGCCAGCAGAGTAGGAA
NOTCH1	F	AAGCTGCATCCAGAGGCAAAC
	R	TGGCATACACACTCCGAACACA
NOTCH2	F	CCTGGGCTATACTGGGAGCTACTG
	R	ACACCCTGATAGCCTGGGACAC
GAPDH	F	GCACCGTCAAGGCTGAGAAC
	R	TGGTGAAGACGCCAGTGGA

Abbreviations: F, forward primer; R, reverse primer.

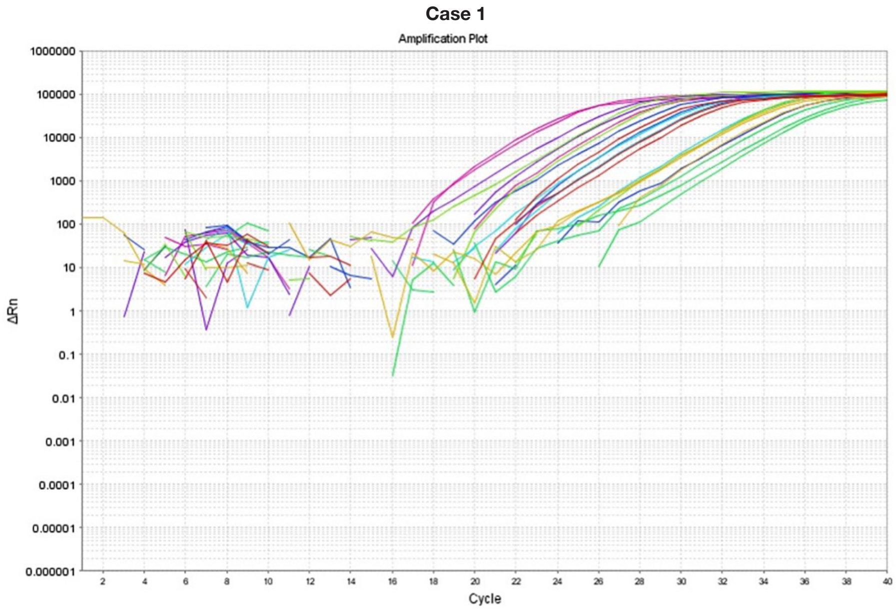

Figure S1 Real-time reverse transcriptase-PCR curve for case 1.

Table S3 Genetic alterations about PIK3 and AKT

Case	additive/lost	Gene Name	Chrom	Position GRCh37	COSMIC ID	Reference	Variant	Variant Type	Codon Change	Amino Acid Change	snpEff effect
1	additive	PIK3CA	chr3	178916573	-	T	<DEL>	CNV	-	-	Splice site donor
	lost	PIK3R1	chr5	67576349	-	C	T	SNP			INTRON
		AKT1	chr14	105239146	-	C	G	SNP			INTRON
		AKT1	chr14	105239192	-	T	C	SNP			INTRON
		AKT1	chr14	105239610	-	G	A	SNP	c.935C>T	p.T312I	NON_SYNONYMOUS_CODING
		AKT1	chr14	105239612	-	G	A	SNP	c.933C>T	p.G311	SYNONYMOUS_CODING
		AKT1	chr14	105243220	-	G	A	SNP			INTRON
		AKT1	chr14	105246325	-	T	A	SNP			INTRON
		AKT1	chr14	105246407	-	G	A	SNP			INTRON
		AKT2	chr19	40740892	-	C	<DUP>	CNV			INTRON
		AKT2	chr19	40741991	-	A	G	SNP	c.981T>C	p.Y327	SYNONYMOUS_CODING
		AKT2	chr19	40742079	-	G	A	SNP			INTRON
2	additive	PIK3R1	chr5	67589343	-	G	A	SNP	-	-	INTRON
		PIK3R1	chr5	67590959	-	G	A	SNP	-	-	INTRON
		AKT1	chr14	105236654	-	C	T	SNP	-	-	UTR_3_PRIME
		AKT1	chr14	105239611	-	T	C	SNP	c.934A>G	p.T312A	NON_SYNONYMOUS_CODING
		AKT1	chr14	105241997	-	G	A	SNP	c.427C>T	p.H143Y	NON_SYNONYMOUS_CODING
		AKT1	chr14	105246373	-	G	A	SNP	-	-	INTRON
		AKT2	chr19	40741103	-	T	A	SNP	-	-	INTRON
		AKT2	chr19	40741302	-	G	A	SNP	-	-	INTRON
		AKT2	chr19	40741743	-	G	A	SNP	-	-	INTRON
		AKT2	chr19	40742145	-	C	T	SNP	-	-	INTRON
		AKT2	chr19	40742361	-	C	T	SNP	-	-	INTRON
		AKT2	chr19	40743834	-	G	A	SNP	-	-	INTRON
		AKT2	chr19	40744956	-	G	A	SNP	-	-	INTRON
		AKT2	chr19	40747984	-	G	A	SNP	-	-	INTRON
		AKT2	chr19	40771143	-	C	T	SNP	c.32G>A	p.W11*	STOP_GAINED
		AKT2	chr19	40771178	-	G	A	SNP	-	-	UTR_5_PRIME
		AKT2	chr19	40771190	-	C	T	SNP	-	-	UTR_5_PRIME
	lost	PIK3R1	chr5	67522481	-	T	<DUP>	CNV			UTR_5_PRIME
		PIK3R1	chr5	67522722	-	C	T	SNP	c.219C>T	p.Y73	SYNONYMOUS_CODING
		AKT2	chr19	40741991	-	A	G	SNP	c.981T>C	p.Y327	SYNONYMOUS_CODING
3	additive	PIK3R1	chr5	67522481	-	T	<DUP>	CNV	-	-	UTR_5_PRIME
		AKT1	chr14	105236653	-	T	<DUP>	CNV	-	-	UTR_3_PRIME
	lost	PIK3CA	chr3	178916573	-	T	<DEL>	CNV			SPLICE_SITE_DONOR
		PIK3CA	chr3	178948034	-	C	T	SNP	c.2806C>T	p.H936Y	NON_SYNONYMOUS_CODING
		AKT1	chr14	105239610	-	G	A	SNP	c.935C>T	p.T312I	NON_SYNONYMOUS_CODING
		AKT1	chr14	105258972	-	G	A	SNP	c.9C>T	p.D3	SYNONYMOUS_CODING
		AKT2	chr19	40741991	-	A	G	SNP	c.981T>C	p.Y327	SYNONYMOUS_CODING

Table S4 Comparison of copy number variation between adenocarcinoma and small-cell carcinoma

Case	Gene name	chr No.	copy number		
			adenocarcinoma	small cell carcinoma	remainder
1	*KLF6*	chr10	4.16	1.53	–2.63
	HRAS	chr11	15.03	4.33	–10.7
	NFKBIA	chr14	20.79	9.72	–11.07
	GNAS.1	chr20	21.52	12.65	–8.87
	RB1	chr13	2.48	2.9	0.42
	TP53	chr17	2.76	2.26	–0.5
2	*KLF6*	chr10	2.91	5.8	2.89
	HRAS	chr11	6.7	21.6	14.9
	NFKBIA	chr14	7.88	43.74	35.86
	GNAS.1	chr20	5.32	12.39	7.07
	RB1	chr13	0.97	0.7	–0.27
	TP53	chr17	2.59	4.67	2.08
3	*KLF6*	chr10	4.9	1.27	–3.63
	HRAS	chr11	9.76	2.67	–7.09
	NFKBIA	chr14	8.51	3.32	–5.19
	GNAS.1	chr20	17.35	2.08	–15.27
	RB1	chr13	1.39	1.92	0.53
	TP53	chr17	2.71	1.81	–0.9

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