Table SI. Primers for SYBR green allele-specific quantitative PCR.

A, Case 1

Gene	Temperature	Primer name	Oligonucleotide DNA sequence (5'-3')
RRM1	60˚C	Wild-type	ggtcaatttacatgttaattacatttg
		Mutation	ggtcaatttacatgttaattacatttt
		Counter	TTGTCAAACATGACTCGTTC
CDH1	60˚C	Wild-type	tctacCTGAACCAGGTTTTT
		Mutation	tctacCTGAACCAGGTTTTTT
		Counter	TTGCTCACATTTCCCAACT
PIK3CA	65˚C	Wild-type	GTTGTCCAGCCACCATGAT
		Mutation	GTTGTCCAGCCACCATGAA
		Counter	CATTCGAAAGACCCTAGCCTTAG
RALGDS	65˚C	Wild-type	CTGGTCACAGGACTTGGAG
		Mutation	CTGGTCACAGGACTTGGAA
		Counter	taagccaactcttcaccca
AKT1	68˚C	Wild-type	CCGCCAGGTCTTGATGTACTC
		Mutation	CCGCCAGGTCTTGATGTACTT
		Counter	tgtcctggcacacccagt

B, Case 2

Gene	Temperature	Primer name	Oligonucleotide DNA sequence (5'-3')
PIK3CA	65˚C	Wild-type	CCATAGAAAATCTTTCTCCTGCTC
		Mutation	CCATAGAAAATCTTTCTCCTGCTT
		Counter	ctctggattcacagatgatttacag
KMT2C	65˚C	Wild-type	AGGGATTGATGGTGAATCAG
		Mutation	AGGGATTGATGGTGAATCA
		Counter	CAAATGGGGCAGGTTTTAC
CDH1	65˚C	Wild-type	GTCTCCTCTTGGCTCTGCC
		Mutation	GTCTCCTCTTGGCTCTGCT
		Counter	CACCGTGAACGTGTAGCTCT
TIMP3	65˚C	Wild-type	TTGATGGTGTAGACCAGCG
		Mutation	TTGATGGTGTAGACCAGCC
		Counter	ctgagatgctgttcctgatgt

Temperature, Annealing temperature; Capital letters, Exonic base; Small letters, Intronic base.

Table SII. PCR primers for case 2.

A, DNA amplification

Gene	Oligonucleotide DNA sequence (5'-3')
PIK3CA	Forward: gcaatgtaaaatttattgaaaatgtattt
	Reverse: aacagagaatctccattttagcac
KMT2C	Forward: GATTTTATGCAACCTCTAGGACC
	Reverse: GCTTCACAGAAGAAAAATTTGG
CDH1	Forward: agtcacccggttccatctac
	Reverse: GGACGCGGCCTCTCT
TIMP3	Forward: taagagtgcaattccaggctc
	Reverse: ccagggtgatgacattacctac

B, Direct sequencing

Gene	Oligonucleotide DNA sequence (5'-3')
CDH1	Forward: TGCTCATTTCCCAACTCC
	Reverse: ccctcccagagaaacagaga
KMT2C	Forward: GATTTTATGCAACCTCTAGGACC
	Reverse: GCTTCACAGAAGAAAAATTTGG

Capital letters, Exonic bases; Small letters, Intronic bases.

Table SIII. Frequency of genetic mutations detected by the comprehensive cancer panel.

A, Case 1 genetic mutations

Gene	Locus	Type	Genotype	RefSeq	Location	Function	Protein	dbSNP
PIK3CA	chr3:178952085	SNV	A/T	NM_006218.4	Exon	Missense	p.His1047Leu	s121913279
RALGDS	chr9:135977481	SNV	G/A	NM_001271775.1	Exon	Synonymous	p.(=)	-
RRM1	chr11:4123150	SNV	G/T	NM_001033.3	Intron	-	-	-
AKT1	chr14:105246550	INDEL	TC/TT	NM_001014431.1	Exon	Missense	p.Glu17Lys	rs121434592: rs34409589
CDH1	chr16:68842455	SNV	T/T	ANM_004360.3	Exon	Frameshift insertion	p.Asn174fs	-

B, Case 2 genetic mutations

Gene	Locus	Type	Genotype	RefSeq	Location	Function	Protein	dbSNP
MSH6	chr2:48032885	SNV	T/A	NM_000179.2	Intron	-	-	-
PIK3CA	chr3:178936091	INDEL	G/A	NM_006218.2	Exon	Missense	p.Glu545Lys	763:27133: 295672:125370
KMT2C	chr7:151860111	SNV	AG/A	NM_170606.2	Exon	Frameshift deletion	p.Pro3517fs	-
FGFR1	chr8:38272357	SNV	T/A	NM_001174067.1	Exon	Synonymous	p.(=)	-
KAT6A	chr8:41790824	SNV	G/A	NM_006766.3	Exon	Synonymous	p.(=)	-
RECQL4	chr8:145740605	SNV	T/G	NM_004260.3	Exon	Missense	p.Gln471Pro	-
MLLT10	chr10:22019877	SNV	C/T	NM_001195626.1	Exon	Synonymous	p.(=)	-
EP400	chr12:132547096	SNV	G/A	NM_015409.4	Exon	Synonymous	p.(=)	1360187
CDH1	chr16:68772218	SNV	C/T	NM_004360.3	Exon	Nonsense	p.Gln23Ter	19503
NF1	chr17:29676364	SNV	G/A	NM_001042492.2	Intron	-	-	-
RNF213	chr17:78319102	SNV	C/T	NM_001256071.1	Exon	Nonsense	p.Gln2323Ter	-
TIMP3	chr22:33245493	SNV	C/G	NM_003490.3|NM_000362.4	Intron|exon	Missense	|p.Thr59Arg	-
CYP2D6	chr22:42523890	SNV	C/A	NM_000106.5	Exon	Synonymous	p.(=)	-
BCYRN1	chrX:70674652	SNV	A.G	NR_001568.1|NM_004606.4	Intron_nc|exon	Missense	|p.Glu1648Gly	-
KDM5C	chrX:53223568	SNV	G/A	NM_004187.3	Exon	Missense	p.Ala1264Val	-

C, Variant frequencies in Case 1

		EMNT			DCIS2			IDC			ILC		
Gene	Locus	Total	Variant	Frequency	Total	Variant	Frequency	Total	Variant	Frequency	Total	Variant	Frequency
PIK3CA	chr3:178952085	145	0	0.00	159	17	0.11	No	No	No	No	No	No
RALGDS	chr9:135977481	No	No	No	373	89	0.24	No	No	No	No	No	No

Table SIII. Continued.

C, Variant frequencies in Case 1

Gene	Locus	EMNT			DCIS2			IDC			ILC		
		Total	Variant	Frequency	Total	Variant	Frequency	Total	Variant	Frequency	Total	Variant	Frequency
RRM1	chr11:4123150	No	No	No	No	No	No	No	No	No	267	58	0.22
AKT1	chr14:105246550	No	No	No	552	164	0.30	No	No	No	No	No	No
CDH1	chr16:68842455	No	No	No	No	No	No	177	30	0.17	65	30	0.46

D, Variant frequencies in Case 2

Gene	Locus	EMNT			NB			FEA			IDC			LCIS		
		Total	Variant	Frequency	Total	Variant	Frequency	Total	Variant	Frequency	Total	Variant	Frequency	Total	Variant	Frequency
MSH6	chr2:48032885	No	No	No	No	No	No	No	No	No	359	35	0.10	382	38	0.10
PIK3CA	chr3:178936091	893	0	0.00	1,097	33	0.03	826	131	0.16	921	439	0.48	0	791	0.00
KMT2C	chr7:151860111	No	No	No	No	No	No	No	No	No	1,596	810	0.51	No	No	No
FGFR1	chr8:38272357	537	39	0.07	879	101	0.11	613	68	0.11	568	64	0.11	628	60	0.10
KAT6A	chr8:41790824	214	17	0.08	303	22	0.07	409	43	0.11	278	28	0.10	325	31	0.10
RECQL4	chr8:145740605	170	12	0.07	127	9	0.07	220	11	0.05	175	17	0.10	157	18	0.11
MLLT10	chr10:22019877	262	21	0.08	425	55	0.13	470	64	0.14	364	24	0.07	477	46	0.10
EP400	chr12:132547096	No	No	No	No	No	No	No	No	No	No	No	No	112	14	0.13
CDH1	chr16:68772218	No	No	No	No	No	No	No	No	No	No	No	No	575	178	0.31
NF1	chr17:29676364	204	10	0.05	230	23	0.10	346	41	0.12	257	26	0.10	343	39	0.11
RNF213	chr17:78319102	1,013	84	0.08	1,294	90	0.07	1,903	140	0.07	1,037	74	0.07	1,282	126	0.10
TIMP3	chr22:33245493	No	No	No	No	No	No	988	142	0.14	618	199	0.32	No	No	No
CYP2D6	chr22:42523890	383	14	0.04	No	No	No	586	57	0.10	395	21	0.05	No	No	No
BCYRN1	chrX:70674652	273	61	0.22	573	63	0.11	628	88	0.14	464	39	0.08	296	37	0.13
KDM5C	chrX:53223568	703	71	0.10	579	64	0.11	824	134	0.16	603	85	0.14	731	72	0.10

Chr, chromosome; SNV, single nucleotide variant; SNP, single nucleotide polymorphism; p.(=), protein has not been analyzed but no change is expected; INDEL, -, the cells that do not have the relevant information; insertion or deletion; EMNT, extramammary non-neoplastic tissue; FEA, flat epithelial atypia; NB, normal breast; DCIS, ductal carcinoma *in situ*; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LCIS, lobular carcinoma *in situ*; No, no call; Total, total coverage; Variant, variant coverage; Frequency, variant frequency=Variant/Total