



Supporting Online Material for

Frequent Mutations of Chromatin Remodeling Gene *ARID1A* in Ovarian Clear Cell Carcinoma

Siân Jones, Tian-Li Wang, Ie-Ming Shih, Tsui-Lien Mao, Kentaro Nakayama, Richard Roden, Ruth Glas, Dennis Slamon, Luis A. Jr. Diaz, Bert Vogelstein, Kenneth W. Kinzler,* Victor E. Velculescu,* Nickolas Papadopoulos*

*To whom correspondence should be addressed. E-mail: npapado1@jhmi.edu (N.P.); kinzlike@jhmi.edu (K.W.K.); velculescu@jhmi.edu (V.E.V.)

Published 8 September 2010 on *Science Express*
DOI: 10.1126/science.1196333

This PDF file includes:

Materials and Methods
Tables S1 to S5
References

Supporting Online Material

Materials and Methods

Immunoaffinity isolation of ovarian clear cell carcinoma cells

Because the sensitivity of mutation detection in tumor tissues can be affected by the purity of the tumor DNA analyzed, we affinity purified tumor cells using Epi-CAM antibody coated beads from freshly collected ovarian clear cell carcinoma samples. Briefly, tumors were minced to small fragments (1 mm x 1 mm x 1 mm) and digested with collagenase I (1 mg/ml in RPMI1640 supplemented with 10%FBS) at 37°C for 40 min. The cells were washed and incubated with 300-500 ml of Epi-CAM conjugated Dynal® (cat no: 162-03, Invitrogen) beads for 30 minutes at 2-8°C. Tumor cells that bound to the beads were separated from non-tumor cell population by a magnet and repeated sorting. Tumor cells (~2X10⁶-10⁷ cells) were then collected and their genomic DNA purified using a Qiagen DNA purification kit. The source of normal DNA was primary fibroblast culture, frozen colon mucosa, frozen myometrium, or peripheral blood mononuclear cells from the same individual.

Preparation of Illumina Genomic DNA library

DNA samples were obtained from patients after informed consent as described (1, 2). Genomic DNA libraries were prepared following Illumina's (Illumina, San Diego, CA) suggested protocol with the following modifications. **(1)** 3 micrograms (µg) of genomic DNA from tumor or normal cells in 100 microliters (µl) of TE was fragmented in a Covaris sonicator (Covaris, Woburn, MA) to a size of 100-500 bp. DNA was purified with a PCR purification kit (Cat # 28104, Qiagen, Valencia, CA) and eluted in 35 µl of elution buffer included in the kit. **(2)** Purified, fragmented DNA was mixed with 40 µl of H₂O, 10 µl of 10 x T4 ligase buffer with 10 mM ATP, 4 µl of 10 mM dNTP, 5 µl of T4 DNA polymerase, 1 µl of Klenow Polymerase, and 5 µl of T4 polynucleotide Kinase. All reagents used for this step and those described below were from New England Biolabs (NEB, Ipswich, MA) unless otherwise specified. The 100 µl end-repair mixture was incubated at 20°C for 30 min, purified by a PCR purification kit (Cat # 28104, Qiagen) and eluted with 32 µl of elution buffer (EB). **(3)** To A-tail, all 32 µl of end-repaired DNA was mixed with 5 µl of 10 x Buffer (NEB buffer 2), 10 µl of 1 mM dATP and 3 µl of Klenow (exo-). The 50 µl mixture was incubated at 37°C for 30 min before DNA was purified with a MinElute PCR purification kit (Cat # 28004, Qiagen). Purified DNA was eluted with 12.5 µl of 70°C EB and obtained with 10 µl of EB. **(4)** For adaptor ligation, 10 µl of A-tailed DNA was mixed with 10 µl of PE-adaptor (Illumina), 25 µl of 2x Rapid ligase buffer and 5 µl of Rapid Ligase. The ligation mixture was incubated at room temperature (RT) or 20°C for 15 min. **(5)** To purify adaptor- ligated DNA, 50 µl of ligation mixture from step (4) was mixed with 200 µl of NT buffer from NucleoSpin Extract II kit (cat# 636972, Clontech, Mountain View, CA) and loaded into NucleoSpin column. The column was centrifuged at 14000 g in a desktop centrifuge for 1 min, washed once with 600 µl of wash buffer (NT3 from Clontech), and centrifuged again for 2 min to dry completely. DNA was eluted in 50 µl elution buffer included in the kit. **(6)** To obtain an amplified library, ten PCRs of 25 µl each were set up, each including 13.25 µl of H₂O, 5 µl of 5 x Phusion HF buffer, 0.5 µl of a dNTP mix containing 10 mM of each dNTP, 0.5 µl of Illumina PE primer #1, 0.5 µl of Illumina PE primer #2, 0.25 µl of Hotstart Phusion polymerase, and 5 µl of the DNA from step (5). The PCR program used was: 98°C 1 minute; 6 cycles of 98°C for 20 seconds, 65°C for 30 seconds, 72°C for 30 seconds; and 72°C for 5 min. To purify the PCR product, 250 µl PCR mixture (from the ten PCR reactions) was mixed with 500 µl NT buffer from a NucleoSpin Extract II kit and purified as described in step (5).

Library DNA was eluted with 70°C-warm elution buffer and the DNA concentration was estimated by absorption at 260 nm.

Exome and targeted subgenomic DNA capture

Human exome capture was performed following a protocol from Agilent's SureSelect Paired-End version 2.0 Human Exome Kit (Agilent, Santa Clara, CA) with the following modifications. **(1)** A hybridization mixture was prepared containing 25 µl of SureSelect Hyb # 1, 1 µl of SureSelect Hyb # 2, 10 µl of SureSelect Hyb # 3, and 13 µl of SureSelect Hyb # 4. **(2)** 3.4 µl (0.5 µg) of the PE-library DNA described above, 2.5 µl of SureSelect Block #1, 2.5 µl of SureSelect Block #2 and 0.6 µl of Block #3; was loaded into one well in a 384-well Diamond PCR plate (cat# AB-1111, Thermo-Scientific, Lafayette, CO), sealed with microAmp clear adhesive film (cat# 4306311; ABI, Carlsbad, CA) and placed in GeneAmp PCR system 9700 thermocycler (Life Sciences Inc., Carlsbad CA) for 5 minutes at 95°C, then held at 65°C (with the heated lid on). **(3)** 25-30 µl of hybridization buffer from step (1) was heated for at least 5 minutes at 65°C in another sealed plate with heated lid on. **(4)** 5 µl of SureSelect Oligo Capture Library, 1 µl of nuclease-free water, and 1 µl of diluted RNase Block (prepared by diluting RNase Block 1: 1 with nuclease-free water) were mixed and heated at 65°C for 2 minutes in another sealed 384-well plate. **(5)** While keeping all reactions at 65°C, 13 µl of Hybridization Buffer from Step (3) was added to the 7 µl of the SureSelect Capture Library Mix from Step (4) and then the entire contents (9 µl) of the library from Step (2). The mixture was slowly pipetted up and down 8 to 10 times. **(6)** The 384-well plate was sealed tightly and the hybridization mixture was incubated for 24 hours at 65°C with a heated lid.

After hybridization, five steps were performed to recover and amplify captured DNA library: **(1)** Magnetic beads for recovering captured DNA: 50 µl of Dynal M-280 Streptavidin magnetic beads (Cat # 112-05D, Invitrogen) was placed in a 1.5 ml microfuge tube and vigorously resuspended on a vortex mixer. Beads were washed three times by adding 200 µl SureSelect Binding buffer, mixed on a vortex for five seconds, then removing and discarding supernatant after placing the tubes in a Dynal magnetic separator. After the third wash, beads were resuspended in 200 µl of SureSelect Binding buffer. **(2)** To bind captured DNA, the entire hybridization mixture described above (29 µl) was transferred directly from the thermocycler to the bead solution and mixed gently; the hybridization mix /bead solution was rotated for 30 minutes at room temperature. **(3)** To wash the beads, the supernatant was removed from beads after applying a Dynal magnetic separator and the beads was resuspended in 500 µl SureSelect Wash Buffer #1 by mixing on vortex mixer for 5 seconds and incubated for 15 minutes at room temperature. Wash Buffer#1 was then removed from beads after magnetic separation. The beads were further washed three times, each with 500 µl pre-warmed SureSelect Wash Buffer #2 after incubation at 65°C for 10 minutes. After the final wash, SureSelect Wash Buffer #2 was completely removed. **(4)** To elute captured DNA, the beads were suspended in 50 µl SureSelect Elution Buffer, vortex-mixed and incubated for 10 minutes at room temperature. The supernatant was removed after magnetic separation, collected in a new 1.5 ml microcentrifuge tube, and mixed with 50 µl of SureSelect Neutralization Buffer. DNA was purified with a Qiagen MinElute column and eluted in 17 µl of 70°C EB to obtain 15 µl of captured DNA library. **(5)** The captured DNA library was amplified in the following way: 15 PCR reactions each containing 10.25 µl of H₂O, 3 µl of 5 x Phusion HF buffer, 0.3 µl of 10 mM dNTP, 0.15 µl of Illumina PE primer #1, 0.15µl of Illumina PE primer #2, 0.15 µl of Hotstart Phusion polymerase, and 1 µl of captured exome library were set up. The PCR program used was: 98°C for 30 seconds; 14 cycles of 98°C for 10 seconds, 65°C for 30 seconds, 72°C for 30 seconds; and 72°C for 5 min. To purify PCR products, 225µl PCR mixture (from 15 PCR reactions) was mixed with 450 µl NT buffer from NucleoSpin Extract II kit and purified as described above. The final library DNA was eluted with 30 µl of 70°C elution buffer and DNA concentration was estimated by OD260 measurement. The

concentration of the library was determined by real time quantitative PCR using KAPA sybr fast qPCR kit (KAPA biosystems, Cape Town, SA) for iCycler and primers specific for Illumina libraries.

Somatic mutation identification by Illumina GAIIX sequencing and Sanger sequencing

All captured DNA libraries were sequenced with Illumina GAIIX Genome Analyzer, yielding 75 base pairs from the final library fragments. All sequencing reads were analyzed and aligned to human genome hg18 with the Eland algorithm of CASAVA 1.6 software (Illumina). The reads that passed the chastity filter of the BaseCall software of Illumina were used for subsequent analysis. Point mutations and indels were called by the ELANDv2 algorithm of CASAVA 1.6 software (Illumina). Mismatches of known polymorphisms were removed from the analysis. A mismatched base was identified as a somatic mutation only when (i) it has a QS score greater than 20; (ii) it was identified by more than four distinct tags; (iii) the number of distinct tags containing a particular mismatched base was at least 20% of the total distinct tags; and (iv) it was not present in >0.5% of the tags in the matched normal sample.

All somatic mutations identified by the first round of exome sequencing were subjected to conventional Sanger sequencing. PCR amplification and sequencing were performed following protocols described previously (3) using the primers listed in table S4. SNP search databases included <http://www.ncbi.nlm.nih.gov/projects/SNP/> and <http://browser.1000genomes.org/index.html>.

Evaluation of genes in additional tumors and matched normal controls, and cell lines.

For the *ARID1A*, *PPP2R1A*, *PIK3CA*, and *KRAS* genes, the coding region was sequenced in a series of additional ovarian clear cell carcinomas and matched controls. PCR and Sanger sequencing were performed as described above using the primers listed in table S4.

table S1. Characteristics of Human Ovarian Clear Cell Carcinoma

Sample	Patient age (years)	Tissue derivation	Stage	Sample type	Screen*	ARID1A Mutation	PPP2R1A Mutation	PIK3CA Mutation	KRAS Mutation
OCC01PT	39	Primary tumor	IV	Immunopurified	Discovery	Y	N	Y	N
OCC02PT	47	Primary tumor	IIIC	Immunopurified	Discovery	Y	N	Y	N
OCC03PT	58	Primary tumor	IC	Immunopurified	Discovery	Y	N	N	N
OCC04PT	32	Primary tumor	IV	Immunopurified	Discovery	N	N	N	Y
OCC05PT	55	Primary tumor	IC	Immunopurified	Discovery	N	Y	N	Y
OCC06PT	46	Recurrent tumor ^s	na**	Immunopurified	Discovery	N	N	Y	N
OCC07PT	52	Primary tumor	IIIC	Immunopurified	Discovery	Y	Y	N	N
OCC08PT	53	Primary tumor	IC	Immunopurified	Discovery	Y	N	Y	N
OCC09PT	38	Primary tumor	IC	Immunopurified	Validation	N	N	Y	N
OCC10PT	47	Primary tumor	IA	Immunopurified	Validation	Y	N	Y	N
OCC11PT	53	Primary tumor	IIIC	Immunopurified	Validation	Y	N	Y	N
OCC12PT	56	Primary tumor	IV	Bulk tumor, >80% tumor cells	Validation	N	N	N	N
OCC13PT	49	Recurrent tumor	na	Immunopurified	Validation	Y	N	Y	N
OCC14PT	46	Primary tumor	IIIC	Immunopurified	Validation	Y	N	N	N
OCC15PT	54	Primary tumor	IIIC	Immunopurified	Validation	Y	N	Y	N
OCC16PT	82	Primary tumor	IIB	Immunopurified	Validation	Y	N	N	N
OCC17PT	56	Primary tumor	IA	Bulk tumor, >80% tumor cells	Validation	N	N	N	N
OCC18PT	63	Primary tumor	IA	Bulk tumor, >80% tumor cells	Validation	Y	N	N	N
OCC19PT	45	Primary tumor	IC	Bulk tumor, >80% tumor cells	Validation	N	N	N	N
OCC20PT	62	Primary tumor	IC	Immunopurified	Validation	Y	N	Y	N
OCC21PT	63	Primary tumor	IC	Bulk tumor, >80% tumor cells	Validation	N	N	N	N
OCC22PT	38	Primary tumor	IC	Bulk tumor, >70% tumor cells	Validation	Y	N	Y	N
OCC23PT	40	Primary tumor	IC	Bulk tumor, >70% tumor cells	Validation	Y	N	Y	N
OCC24PT	50	Primary tumor	IC	Bulk tumor, >70% tumor cells	Validation	Y	N	N	N
OCC25PT	52	Primary tumor	IC	Bulk tumor, >70% tumor cells	Validation	N	N	N	N

OCC26PT	47	Primary tumor	IC	Bulk tumor, >70% tumor cells	Validation	N	N	N	N
OCC27PT	51	Primary tumor	IIIC	Bulk tumor, >70% tumor cells	Validation	Y	N	Y	N
OCC28PT	62	Primary tumor	IC	Bulk tumor, >70% tumor cells	Validation	N	N	N	N
OCC29PT	60	Primary tumor	IV	Immunopurified	Validation	N	N	N	N
OCC30PT	53	Primary tumor	IC	Immunopurified	Validation	Y	N	Y	N
OCC31PT	52	Primary tumor	IC	Immunopurified	Validation	N	N	N	N
OCC32PT	42	Primary tumor	IC	Immunopurified	Validation	Y	N	N	N
OCC33PT	55	Primary tumor	IIIC	Immunopurified	Validation	N	N	N	N
OCC34PT	47	Recurrent tumor	na	Immunopurified	Validation	Y	N	N	N
OCC35PT	46	Primary tumor	IC	Immunopurified	Validation	N	N	Y	N
OCC36PT	37	Primary tumor	IC	Immunopurified	Validation	Y	Y	Y	N
OCC37PT	57	Primary tumor	IC	Immunopurified	Validation	N	N	N	N
OCC38PT	53	Primary tumor	IC	Immunopurified	Validation	N	N	N	N
OCC39PT	70	Primary tumor	IIA	Bulk tumor, >70% tumor cells	Validation	Y	N	N	N
OCC40PT	47	Primary tumor	IC	Bulk tumor, >70% tumor cells	Validation	N	N	N	N
OCC41PT	57	Primary tumor	IC	Bulk tumor, >70% tumor cells	Validation	Y	N	N	N
OCC42PT	51	Primary tumor	IIIC	Bulk tumor, >70% tumor cells	Validation	Y	N	Y	N

* Discovery: the eight samples used to capture and sequence all the ~18,000 genes. Validation: additional samples used to determine the sequence of *PIK3CA*, *KRAS*, *PPP21R1A*, and *ARID1A* by Sanger sequencing.

[§]Sample from patient with recurrent tumor previously treated with 3 cycles of cisplatin and cyclophosphamide.

**na indicates not available.

table S2. Summary of sequence analysis of clear cell ovarian cancers

	Average	OCC01		OCC02		OCC03		OCC04		OCC05		OCC06		OCC07		OCC08	
		Normal	Tumor	Normal	Tumor	Normal	Tumor	Normal	Tumor	Normal	Tumor	Normal	Tumor	Normal	Tumor	Normal	Tumor
Bases in target region	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033	37,806,033
Bases sequenced (after quality filtering)	6,511,999,219	5,869,322,400	6,039,432,975	7,743,998,175	5,887,057,800	4,927,758,075	5,350,539,525	5,481,781,050	4,796,809,725	8,072,903,325	6,098,389,650	8,784,608,625	10,792,972,200	5,876,999,250	7,251,704,925	5,324,268,750	5,893,441,050
Bases mapped to genome	5,061,611,963	4,697,337,900	4,752,944,850	6,092,898,975	4,526,013,900	3,560,079,675	4,074,495,075	4,294,296,450	3,835,246,875	6,609,351,825	4,836,418,575	7,064,921,250	7,611,497,100	4,593,099,375	5,707,748,925	4,159,913,325	4,572,727,650
Bases mapped to targeted region	3,161,943,119	2,951,410,606	2,905,106,291	3,938,277,117	2,787,699,744	2,372,698,851	2,347,615,071	2,789,190,294	2,415,146,056	4,205,386,161	2,944,517,632	4,405,093,249	4,716,682,489	2,984,229,243	3,561,297,932	2,652,614,272	2,914,230,335
Average # of reads per targeted base	84	78.1	76.8	104.2	73.7	62.8	62.1	73.8	63.9	111.2	77.9	116.5	124.8	78.9	94.7	70.2	77.1
Targeted bases with at least 10 reads (%)	92.7%	93.5%	91.7%	94.5%	91.7%	89.6%	89.4%	93.1%	90.7%	94.0%	92.8%	95.1%	93.5%	93.0%	93.6%	93.1%	93.7%
Known SNPs identified in targeted region	20,037	19,703	19,519	19,800	19,504	19,551	18,998	19,524	19,266	21,391	21,240	18,907	18,632	22,946	18,765	24,318	18,523
Somatic mutations identified in targeted region	20 (excluding OCC06)		20		19		23		13		24		125		20		24

table S3. Mutations identified in the discovery screen

Sample	Gene	Transcript Accession	Nucleotide (genomic)*	Nucleotide (cDNA)	Amino acid (protein)	Mutation type
OCC06PT	<i>ABCC10</i>	CCDS4896.1	g.chr6:43523575T>G	c.3797T>G	p.F1266C	Missense
OCC06PT	<i>ABCD4</i>	CCDS59828.1	g.chr14:73823213C>T	c.1696G>A	p.G566S	Missense
OCC06PT	<i>ACADVL</i>	CCDS11090.1	g.chr17:7067740G>C	c.1236G>C	p.Q412H	Missense
OCC04PT	<i>ADAM7</i>	CCDS6045.1	g.chr8:24414262G>A	c.2072G>A	p.R691H	Missense
OCC08PT	<i>ADNP2</i>	CCDS32853.1	g.chr18:75994633C>T	c.346C>T	p.Q116X	Nonsense
OCC06PT	<i>AFF4</i>	CCDS4164.1	g.chr5:132260486G>C	c.1735C>G	p.R579G	Missense ^S
OCC01PT	<i>AICDA</i>	CCDS41747.1	g.chr12:8648681G>A	c.532C>T	p.R178C	Missense
OCC08PT	<i>AMPD1</i>	CCDS876.1	g.chr1:115017346delT	c.2154delA	fs	Indel
OCC06PT	<i>ANKDD1A</i>	CCDS10197.2	g.chr15:63021732C>G	c.883C>G	p.L295V	Missense
OCC02PT	<i>ARHGAP5</i>	CCDS32062.1	g.chr14:31631490G>A	c.1864G>A	p.E622K	Missense [#]
OCC01PT	<i>ARID1A</i>	CCDS285.1	g.chr1:26972561_26972562insA	c.3854_3855insA	fs	Indel
OCC02PT	<i>ARID1A</i>	CCDS285.1	g.chr1:26896034C>T	c.553C>T	p.Q185X	Nonsense
OCC02PT	<i>ARID1A</i>	CCDS285.1	g.chr1:26978879-26978880dupGT	c.903_904dupGT	fs	Indel
OCC03PT	<i>ARID1A</i>	CCDS285.1	g.chr1:26972009_26972034delTGATGGGGCGATGCTCTATGAGCCA (hom)	c.3659_3684delTGATGGGGCGATGCTCTATGAGCCA	fs	Indel
OCC07PT	<i>ARID1A</i>	CCDS285.1	g.chr1:26896066C>A	c.585C>A	p.Y195X	Nonsense
OCC08PT	<i>ARID1A</i>	CCDS285.1	g.chr1:26970389delC	c.3391delC	fs	Indel
OCC02PT	<i>ARID1B</i>	CCDS5251.1	g.chr6:157570517dupC	c.6500dupC	fs	Indel
OCC06PT	<i>ARPC2</i>	CCDS2410.1	g.chr2:218822398G>A	c.743G>A	p.R248Q	Missense
OCC06PT	<i>ASB2</i>	CCDS9915.1	g.chr14:93487138C>G	c.696G>C	p.Q232H	Missense
OCC02PT	<i>ATP4A</i>	CCDS12467.1	g.chr19:40737917C>T	c.2317G>A	p.V773M	Missense
OCC06PT	<i>ATP6V0C</i>	CCDS10470.1	g.chr16:2509574G>A	c.295G>A	p.V99M	Missense
OCC06PT	<i>B3GALT</i>	CCDS9341.1	g.chr13:30687235C>T	c.118C>T	p.Q40X	Nonsense
OCC07PT	<i>B4GALNT3</i>	CCDS5804.1	g.chr12:537114_537118delCAACA	c.2460_2464delCAACA	fs	Indel
OCC06PT	<i>BCL11A</i>	CCDS1862.1	g.chr2:60542953C>G	c.598G>C	p.E200Q	Missense
OCC06PT	<i>BMF</i>	CCDS10052.1	g.chr15:38185428delG	c.154delC	fs	Indel
OCC06PT	<i>BZW2</i>	CCDS5362.1	g.chr7:16704324C>G	c.1096C>G	p.L366V	Missense
OCC06PT	<i>C10orf90</i>	CCDS31310.1	g.chr10:128183143G>A	c.616C>T	p.R206W	Missense
OCC08PT	<i>C10orf91</i>	CCDS7668.1	g.chr10:134111295C>G	c.178C>G	p.Q60E	Missense
OCC03PT	<i>C13orf35</i>	CCDS9526.1	g.chr13:112381800G>T	c.106G>T	p.D36Y	Missense
OCC06PT	<i>C14orf43</i>	CCDS9819.1	g.chr14:73255795G>C	c.3100C>G	p.Q1034E	Missense
OCC06PT	<i>C16orf70</i>	CCDS10828.1	g.chr16:65731955C>T	c.836C>T	p.S279L	Missense
OCC06PT	<i>C17orf61</i>	CCDS11102.1	g.chr17:7247227G>C	c.224C>G	p.T75R	Missense
OCC06PT	<i>C1orf168</i>	CCDS30729.1	g.chr1:56989372C>G	c.1320G>C	p.M440I	Missense
OCC06PT	<i>C2CD3</i>	CCDS31636.1	g.chr11:73481254C>G	c.3372G>C	p.Q1124H	Missense
OCC01PT	<i>C2orf16</i>	CCDS42666.1	g.chr2:27654243G>A	c.1300G>A	p.V434I	Missense
OCC06PT	<i>CC2D1B</i>	CCDS30714.1	g.chr1:52593147C>G	c.2310G>C	p.K770N	Missense
OCC06PT	<i>CCT2</i>	CCDS8991.1	g.chr12:68267579G>T	c.172G>T	p.D58Y	Missense
OCC06PT	<i>CCT8L1</i>	ENST00000021776	g.chr7:151774819C>A	c.1325C>A	p.A442D	Missense
OCC06PT	<i>CD97</i>	CCDS32929.1	g.chr19:14374516G>T	c.1291G>T	p.E431X	Nonsense
OCC06PT	<i>CDH11</i>	CCDS10803.1	g.chr16:63584411G>A	c.551C>T	p.S184L	Missense
OCC06PT	<i>CDK19</i>	CCDS5085.1	g.chr6:111243029C>T	c.4G>A	p.D2N	Missense
OCC05PT	<i>CELF5</i>	CCDS12106.1	g.chr19:3233451C>T	c.994C>T	p.P332S	Missense
OCC03PT	<i>CELSR3</i>	CCDS2775.1	g.chr3:48660374G>A	c.7033C>T	p.R2345C	Missense
OCC03PT	<i>CHD4</i>	CCDS8552.1	g.chr12:6567814T>C	c.3376A>G	p.T1126A	Missense
OCC06PT	<i>CHD5</i>	CCDS57.1	g.chr1:6110824C>G	c.3772G>C	p.D1258H	Missense
OCC06PT	<i>CLCN1</i>	CCDS5881.1	g.chr7:142746776G>C	c.1522G>C	p.D508H	Missense
OCC08PT	<i>CLEC4C</i>	CCDS8583.1	g.chr12:7785340T>C	c.179A>G	p.E60G	Missense [#]
OCC04PT	<i>COL22A1</i>	CCDS6376.1	g.chr8:139761041C>A	IVS39+1G>T	Splice site	Splice site
OCC04PT	<i>CRMP1</i>	CCDS33950.1	g.chr4:5881160G>A	c.1760C>T	p.A587V	Missense
OCC06PT	<i>CSMD2</i>	CCDS380.1	g.chr1:33844067A>G	c.6332T>C	p.L2111P	Missense
OCC03PT	<i>CSMD3</i>	CCDS6315.1	g.chr8:113718308G>A	c.3629C>T	p.S1210L	Missense
OCC03PT	<i>CSNK1D</i>	CCDS11805.1	g.chr17:77802635T>C	c.794A>G	p.D265G	Missense
OCC06PT	<i>CYP11A</i>	CCDS10268.1	g.chr15:72800116C>G	c.1306G>C	p.D436H	Missense
OCC03PT	<i>CYP4F22</i>	CCDS12331.1	g.chr19:15509730G>A	c.597G>A	p.M199I	Missense
OCC05PT	<i>DCAF12L1</i>	CCDS14610.1	g.chrX:125513117T>A	c.1156A>T	p.R386X	Nonsense
OCC06PT	<i>DDHD1</i>	CCDS9714.1	g.chr14:52610215C>G	c.1390G>C	p.D464H	Missense
OCC07PT	<i>DDX52</i>	CCDS35214.1	g.chrX:22929339G>A	c.1244G>A	p.R415H	Missense
OCC02PT	<i>DIS3L2</i>	CCDS42834.1	g.chr2:232811498G>A	c.1216G>A	p.V406M	Missense
OCC05PT	<i>DMRTB1</i>	CCDS581.1	g.chr1:53697826G>A	c.112G>A	p.E38K	Missense ^S
OCC03PT	<i>DNAH8</i>	CCDS4838.1	g.chr6:38971909G>A	c.8219G>A	p.R2740H	Missense
OCC05PT	<i>DNAJC13</i>	CCDS33857.1	g.chr3:133703893C>T	c.4607C>T	p.T1536I	Missense
OCC06PT	<i>DNAJC14</i>	CCDS8894.1	g.chr12:54507891G>C	c.819C>G	p.L273M	Missense
OCC03PT	<i>DPP8</i>	CCDS10207.1	g.chr15:63526323G>C	c.2649C>G	p.Y883X	Nonsense
OCC06PT	<i>DSC2</i>	CCDS11892.1	g.chr18:26903091G>T	c.2275C>A	p.Q759K	Missense
OCC03PT	<i>DYRK1A</i>	CCDS42925.1	g.chr21:37799751C>T	c.1535C>T	p.S512L	Missense ^S
OCC06PT	<i>EIF5B</i>	CCDS42721.1	g.chr2:99347175G>A	c.1147G>A	p.E383K	Missense

OCC06PT	<i>ELP2</i>	CCDS11918.1	g.chr18:31976873C>G	c.742C>G	p.Q248E	Missense
OCC05PT	<i>EML3</i>	CCDS8023.2	g.chr11:62129695_62129698delGGTC	c.del1906-1909delGACC	fs	Indel
OCC08PT	<i>EPHA1</i>	CCDS5884.1	g.chr7:142801541G>C	c.2370C>G	p.I790M	Missense
OCC05PT	<i>ETV6</i>	CCDS8643.1	g.chr12:11796732C>T	c.115C>T	p.R39X	Nonsense
OCC06PT	<i>EXOC3L2</i>	CCDS12657.1	g.chr19:50426910G>C	c.41C>G	p.S14C	Missense
OCC02PT	<i>FAM13C</i>	CCDS7255.1	g.chr10:60699701G>A	c.767C>T	p.S256L	Missense
OCC06PT	<i>FAM40A</i>	CCDS30798.1	g.chr1:110387874G>A	c.1159G>A	p.D387N	Missense
OCC01PT	<i>FAM71B</i>	CCDS4335.1	g.chr5:156522716T>C	c.1138A>G	p.I380V	Missense
OCC01PT	<i>FAT4</i>	CCDS3732.2	g.chr4:126631378A>G	c.13780A>G	p.I4594V	Missense
OCC06PT	<i>FBXO34</i>	CCDS32086.1	g.chr14:54887408G>T	c.547G>T	p.G183C	Missense
OCC06PT	<i>FILIP1</i>	CCDS4984.1	g.chr6:76081298G>C	c.970C>G	p.Q324E	Missense
OCC06PT	<i>FLG2</i>	CCDS30861.1	g.chr1:150590126C>A	c.6760G>T	p.G2254C	Missense [#]
OCC03PT	<i>FNDC3B</i>	CCDS3217.1	g.chr3:173578891C>T	c.3146C>T	p.T1049I	Missense
OCC06PT	<i>FOLH1</i>	CCDS7946.1	g.chr11:49154047C>T	c.959G>A	p.R320K	Missense [#]
OCC06PT	<i>GADD45A</i>	CCDS640.1	g.chr1:67925936_67925937delCA	c.389_390delCA	fs	Indel
OCC02PT	<i>GAL3ST3</i>	CCDS8128.1	g.chr11:65567327C>T	c.523G>A	p.V175I	Missense
OCC03PT	<i>GALNT8</i>	CCDS8533.1	g.chr12:4724019G>A	c.752G>A	p.R251Q	Missense
OCC02PT	<i>GARNL3</i>	CCDS8689.1	g.chr9:129159326G>A	c.1889G>A	p.C630Y	Missense
OCC01PT	<i>GATA3</i>	CCDS31143.1	g.chr10:8155905G>T	c.1248G>T	p.M416I	Missense
OCC06PT	<i>GBA2</i>	CCDS6589.1	g.chr9:35730929T>G	c.919A>C	p.N307H	Missense
OCC06PT	<i>GCN1L1</i>	CCDS41847.1	g.chr12:119063135C>T	c.5905G>A	p.E1969K	Missense
OCC06PT	<i>GFI1B</i>	CCDS6957.1	g.chr9:134856217G>A	c.952G>A	p.D318N	Missense
OCC02PT	<i>GIMAP8</i>	CCDS34777.1	g.chr7:149805569G>A	c.1766G>A	p.R589H	Missense
OCC06PT	<i>GOPC</i>	CCDS5117.1	g.chr6:118006855T>G	c.351A>C	p.K117N	Missense [#]
OCC06PT	<i>GPR22</i>	CCDS5744.1	g.chr7:106903043G>C	c.1302G>C	p.X434Y	Missense
OCC08PT	<i>GPR3</i>	CCDS303.1	g.chr1:27593530C>A	c.641C>A	p.A214D	Missense [#]
OCC06PT	<i>GPRIN3</i>	CCDS34030.1	g.chr4:90389594C>G	c.691G>C	p.E231Q	Missense
OCC01PT	<i>GPT</i>	CCDS6430.1	g.chr8:145702267G>A	c.901G>A	p.A301T	Missense
OCC01PT	<i>GRN</i>	CCDS11483.1	g.chr17:39782410G>A	c.229G>A	p.V77I	Missense
OCC06PT	<i>H3F3B</i>	CCDS11729.1	g.chr17:71286367G>C	c.315C>G	p.F105L	Missense
OCC05PT	<i>HAO2</i>	CCDS901.1	g.chr1:119729197A>T	c.559A>T	p.K187X	Nonsense
OCC06PT	<i>HDAC2</i>	CCDS43493.1	g.chr6:114384509C>G	c.607G>C	p.E203Q	Missense
OCC06PT	<i>HEATR4</i>	CCDS9815.1	g.chr14:73059203A>C	c.266T>G	p.V89G	Missense
OCC07PT	<i>HECTD1</i>	CCDS41939.1	g.chr14:30645942delA	c.6887delA	fs	Indel
OCC06PT	<i>HIBADH</i>	CCDS5414.1	g.chr7:27655756G>C	c.113C>G	p.S38X	Nonsense
OCC06PT	<i>HIST1H4B</i>	CCDS4572.1	g.chr6:26135340C>A	c.120G>T	p.R40S	Missense
OCC06PT	<i>HIST1H4B</i>	CCDS4572.1	g.chr6:26135341C>A	c.119G>T	p.R40M	Missense
OCC08PT	<i>HSP90B1</i>	CCDS9094.1	g.chr12:102851919G>A	c.467G>A	p.R156K	Missense
OCC05PT	<i>HSPA14</i>	CCDS7103.1	g.chr10:14937857A>C	c.902A>C	p.E301A	Missense
OCC05PT	<i>IGSF10</i>	CCDS3160.1	g.chr3:152647246delC	c.3213delG	fs	Indel
OCC01PT	<i>IL1RAP</i>	CCDS3298.1	g.chr3:191804683A>T	c.137A>T	p.K46M	Missense
OCC06PT	<i>ITGA1</i>	CCDS3955.1	g.chr5:52269009C>T	c.2986C>T	p.P996S	Missense
OCC06PT	<i>ITGB2</i>	CCDS13716.1	g.chr21:45136197C>T	c.1367G>A	p.R456H	Missense
OCC06PT	<i>KCNT2</i>	CCDS1384.1	g.chr1:194843995C>A	c.68G>T	p.G23V	Missense [#]
OCC03PT	<i>KCNV2</i>	CCDS6447.1	g.chr9:2707998G>A	c.259G>A	p.E87K	Missense
OCC06PT	<i>KCTD3</i>	CCDS1515.1	g.chr1:213818978G>A	c.410G>A	p.R137H	Missense [#]
OCC01PT	<i>KIAA0247</i>	CCDS9796.1	g.chr14:69195186dupT	IVS1+2dupT	Splice site	Splice site
OCC06PT	<i>KIAA0649</i>	CCDS6988.1	g.chr9:137516929A>C	c.752A>C	p.K251T	Missense [#]
OCC07PT	<i>KIAA1109</i>	CCDS43267.1	g.chr4:123387357C>T	c.5254C>T	p.H1752Y	Missense
OCC05PT	<i>KIAA1539</i>	CCDS6578.1	g.chr9:35097703_35097704delAA	c.568_569delTT	fs	Indel
OCC06PT	<i>KIAA1715</i>	CCDS33332.1	g.chr2:176520535C>G	c.625G>C	p.E209Q	Missense
OCC01PT	<i>KLHL28</i>	CCDS9680.1	g.chr14:44484193C>T	c.689G>A	p.S230N	Missense
OCC04PT	<i>KRAS</i>	CCDS8703.1	g.chr12:25289551C>T	c.35G>A	p.G12D	Missense
OCC05PT	<i>KRAS</i>	CCDS8703.1	g.chr12:25289551C>G	c.35G>C	p.G12A	Missense
OCC01PT	<i>LAMA5</i>	CCDS33502.1	g.chr20:60332924C>A	c.5611G>T	p.D1871Y	Missense
OCC07PT	<i>LECT1</i>	CCDS9437.1	g.chr13:52175897C>T	c.839G>A	p.G280E	Missense
OCC06PT	<i>LGALS4</i>	CCDS12521.1	g.chr19:43984294C>A	c.922G>T	p.D308Y	Missense
OCC06PT	<i>LIFR</i>	CCDS3927.1	g.chr5:38566445_38566452dupCTCATTCT	c.55_62dupAGAATGT	fs	Indel [#]
OCC05PT	<i>LRP1B</i>	CCDS2182.1	g.chr2:141175867G>A	c.6320C>T	p.S2107F	Missense
OCC05PT	<i>LRP1B</i>	CCDS2182.1	g.chr2:141175868A>T	c.6319T>A	p.S2107T	Missense
OCC06PT	<i>LRRRC7</i>	CCDS645.1	g.chr1:70277630G>A	c.3421G>A	p.D1141N	Missense
OCC08PT	<i>LRRK2</i>	CCDS31774.1	g.chr12:38995283G>A	c.4741G>A	p.V1581I	Missense
OCC06PT	<i>MARCH6</i>	CCDS34135.1	g.chr5:10447235G>A	c.808G>A	p.E270K	Missense [#]
OCC03PT	<i>MARK1</i>	CCDS31029.2	g.chr1:218892093G>A	c.1714G>A	p.G572S	Missense
OCC03PT	<i>MARK3</i>	CCDS41993.1	g.chr14:103039093C>T	c.1966C>T	p.R656C	Missense
OCC08PT	<i>MAS1</i>	CCDS5272.1	g.chr6:160248330C>T	c.353C>T	p.T118M	Missense
OCC02PT	<i>MCF2L2</i>	CCDS3243.1	g.chr3:184408211C>T	c.2591G>A	p.R864Q	Missense
OCC06PT	<i>MDGA2</i>	CCDS41948.1	g.chr14:46413127C>A	c.1570G>T	p.G524C	Missense
OCC06PT	<i>MED13L</i>	CCDS9177.1	g.chr12:115159803G>T	c.163C>A	p.P55T	Missense

OCC08PT	<i>MFSD5</i>	CCDS8851.1	g.chr12:51933584C>G	c.698C>G	p.S233X	Nonsense
OCC06PT	<i>MLL3</i>	CCDS5931.1	g.chr7:151509027G>T	c.6851C>A	p.S2284X	Nonsense
OCC06PT	<i>MLL3</i>	CCDS5931.1	g.chr7:151522533G>A	c.4432C>T	p.Q1478X	Nonsense
OCC05PT	<i>MR11</i>	CCDS32923.1	g.chr19:13740712A>G	c.799A>G	p.I267V	Missense
OCC06PT	<i>MTO1</i>	CCDS4979.1	g.chr6:74246564C>T	c.1123C>T	p.Q375X	Nonsense
OCC06PT	<i>MYH11</i>	CCDS10565.1	g.chr16:15777493C>T	c.832G>A	p.E278K	Missense
OCC03PT	<i>MYO16</i>	CCDS32008.1	g.chr13:108502685C>A	c.2843C>A	p.S948X	Nonsense
OCC04PT	<i>MYO1G</i>	CCDS34629.1	g.chr7:44971978G>A	c.2164C>T	p.R722W	Missense
OCC06PT	<i>MYO3B</i>	CCDS42773.1	g.chr2:170764100_170764101delAA	c.139_140delAA	fs	Indel
OCC01PT	<i>MYO5B</i>	CCDS42436.1	g.chr18:45660823G>A	c.3046C>T	p.R1016X	Nonsense
OCC06PT	<i>MYST3</i>	CCDS6124.1	g.chr8:41919512C>G	c.2392G>C	p.E798Q	Missense
OCC07PT	<i>NDRG2</i>	CCDS59565.1	g.chr14:20558829A>G	c.422T>C	p.I141T	Missense
OCC06PT	<i>NDUF4F4</i>	CCDS5037.1	g.chr6:97445894C>T	c.335G>A	p.G112D	Missense [#]
OCC06PT	<i>NFKBIL2</i>	CCDS34968.1	g.chr8:145630246C>T	c.2833G>A	p.D945N	Missense
OCC06PT	<i>NFKBIL2</i>	CCDS34968.1	g.chr8:145630291C>T	c.2788G>A	p.E930K	Missense
OCC06PT	<i>NGRN</i>	CCDS32329.1	g.chr15:88615882G>C	c.734G>C	p.R245T	Missense
OCC06PT	<i>NIPBL</i>	CCDS3920.1	g.chr5:37007894C>A	c.862C>A	p.P288T	Missense
OCC04PT	<i>NLGN4X</i>	CCDS14126.1	g.chrX:5837139C>A	c.767G>T	p.G256V	Missense
OCC06PT	<i>NLRP3</i>	CCDS1632.1	g.chr1:245654152C>T	c.784C>T	p.R262X	Nonsense
OCC06PT	<i>NOS1</i>	CCDS41842.1	g.chr12:116142349C>T	c.4084G>A	p.D1362N	Missense
OCC06PT	<i>NR1I2</i>	CCDS2995.1	g.chr3:121014470G>A	c.884G>A	p.S295N	Missense
OCC02PT	<i>NR2F2</i>	CCDS10375.1	g.chr15:94681704T>C	c.1094T>C	p.L365P	Missense
OCC03PT	<i>NR6A1</i>	CCDS35137.1	g.chr9:126326955C>G	c.1220G>C	p.S407T	Missense
OCC08PT	<i>NUP98</i>	CCDS7746.1	g.chr11:3671072G>C	c.4277C>G	p.S1426C	Missense
OCC02PT	<i>OR4D1</i>	CCDS42365.1	g.chr17:53587855dupT	c.342dupT	fs	Indel
OCC05PT	<i>OR5I12</i>	CCDS31383.1	g.chr11:5431563G>A	c.269G>A	p.R90H	Missense
OCC05PT	<i>OR5J3</i>	CCDS31370.1	g.chr11:5024450C>T	c.119C>T	p.A40V	Missense
OCC06PT	<i>OR5D16</i>	CCDS31512.1	g.chr11:55363314C>T	c.511C>T	p.H171Y	Missense
OCC05PT	<i>OR6C75</i>	CCDS31820.1	g.chr12:54045519C>T	c.358C>T	p.R120C	Missense [#]
OCC05PT	<i>OXCT1</i>	CCDS3937.1	g.chr5:41843189C>A	IVS8+1G>T	Splice site	Splice site
OCC06PT	<i>PALMD</i>	CCDS758.1	g.chr1:99927932G>A	c.1528G>A	p.E510K	Missense
OCC07PT	<i>PAPSS1</i>	CCDS3676.1	g.chr4:108794150G>A	c.1183C>T	p.Q395X	Nonsense
OCC04PT	<i>PCDH10</i>	CCDS34063.1	g.chr4:134303647A>C	c.2863A>C	p.M955L	Missense
OCC06PT	<i>PCDH17</i>	CCDS31986.1	g.chr13:57105042G>C	c.361G>C	p.E121Q	Missense
OCC04PT	<i>PCDHA3</i>	CCDS34248.1	g.chr5:140162411C>T	c.1445C>T	p.A482V	Missense [#]
OCC07PT	<i>PCDHA7</i>	CCDS34252.1	g.chr5:140195657G>A	c.1505G>A	p.R502H	Missense [#]
OCC07PT	<i>PCDHA8</i>	CCDS34253.1	g.chr5:140202604C>T	c.1514C>T	p.S505L	Missense [#]
OCC06PT	<i>PCDHB7</i>	CCDS4249.1	g.chr5:140534794C>T	c.2194C>T	p.R732X	Missense [#]
OCC01PT	<i>PDE4DIP</i>	CCDS30824.1	g.chr1:143590779C>T	c.4028G>A	p.R1343Q	Missense [#]
OCC06PT	<i>PDE9A</i>	CCDS13690.1	g.chr21:43058674G>C	IVS15+1G>C	Splice site	Splice site
OCC05PT	<i>PDZD7</i>	CCDS31269.1	g.chr10:102773205A>G	c.520T>C	p.F174L	Missense
OCC06PT	<i>PEPD</i>	CCDS42544.1	g.chr19:38594443G>A	c.793C>T	p.R265X	Nonsense
OCC02PT	<i>PFKM</i>	CCDS8760.1	g.chr12:46817867C>T	c.1033C>T	p.R345C	Missense
OCC05PT	<i>PGM1</i>	CCDS625.1	g.chr1:63886821C>T	c.1190C>T	p.A397V	Missense
OCC06PT	<i>PHF3</i>	CCDS4966.1	g.chr6:64480931G>C	c.5488G>C	p.G1830R	Missense
OCC06PT	<i>PHLPP2</i>	CCDS32479.1	g.chr16:70270185C>T	c.1242G>A	p.M414I	Missense
OCC06PT	<i>PIAS2</i>	CCDS32824.1	g.chr18:42649287G>T	c.1672C>A	p.P558T	Missense
OCC01PT	<i>PIK3CA</i>	CCDS43171.1	g.chr3:180418788C>A	c.1636C>A	p.Q546K	Missense
OCC02PT	<i>PIK3CA</i>	CCDS43171.1	g.chr3:180418776G>A	c.1624G>A	p.E542K	Missense
OCC06PT	<i>PIK3CA</i>	CCDS43171.1	g.chr3:180418785G>A	c.1633G>A	p.E545K	Missense
OCC08PT	<i>PIK3CA</i>	CCDS43171.1	g.chr3:180418785G>A	c.1633G>A	p.E545K	Missense
OCC06PT	<i>PKD1L1</i>	CCDS34633.1	g.chr7:47835604G>A	c.6679C>T	p.R2227C	Missense
OCC06PT	<i>PLD5</i>	CCDS1621.1	g.chr1:240343918T>G	c.691A>C	p.S231R	Missense
OCC08PT	<i>PLEKHA6</i>	CCDS1444.1	g.chr1:202484579G>A	c.1817C>T	p.A606V	Missense
OCC06PT	<i>PLIN2</i>	CCDS6490.1	g.chr9:19116246G>T	c.92C>A	p.S31X	Nonsense
OCC06PT	<i>PLS1</i>	CCDS3125.1	g.chr3:143885798G>T	c.759G>T	p.L253F	Missense
OCC07PT	<i>PMFBP1</i>	CCDS32483.1	g.chr16:70727871T>G	c.1180A>C	p.K394Q	Missense [#]
OCC06PT	<i>PMM1</i>	CCDS14020.1	g.chr22:40315716C>G	c.40G>C	p.V14L	Missense
OCC07PT	<i>POLRMT</i>	CCDS12036.1	g.chr19:572222C>G	c.2476G>C	p.E826Q	Missense [#]
OCC08PT	<i>PPL</i>	CCDS10526.1	g.chr16:4875813C>G	c.2844G>C	p.E948D	Missense
OCC06PT	<i>PPP1R12C</i>	CCDS12916.1	g.chr19:60315966C>T	c.331A>G	p.D111N	Missense
OCC05PT	<i>PPP2R1A</i>	CCDS12849.1	g.chr19:57407794C>G	c.547G>G	p.R183G	Missense
OCC07PT	<i>PPP2R1A</i>	CCDS12849.1	g.chr19:57407794C>T	c.547C>T	p.R183W	Missense
OCC07PT	<i>PTPRM</i>	CCDS11840.1	g.chr18:7945226C>G	c.946C>G	p.R316G	Missense
OCC06PT	<i>R3HDM2</i>	CCDS8937.1	g.chr12:55935044G>C	c.1693C>G	p.Q565E	Missense
OCC06PT	<i>RABBB</i>	CCDS10183.1	g.chr15:61328957G>A	c.246G>A	p.M82I	Missense
OCC04PT	<i>RAI2</i>	CCDS14183.1	g.chrX:17729307G>A	c.745C>T	p.P249S	Missense
OCC06PT	<i>RCBTB1</i>	CCDS9418.1	g.chr13:49006380A>C	c.1475T>G	p.F492C	Missense
OCC06PT	<i>RETSAT</i>	CCDS1972.1	g.chr2:85431542C>G	c.469G>C	p.V157L	Missense

OCC06PT	REV3L	CCDS5091.2	g.chr6:111759634C>G	c.7972G>C	p.D2658H	Missense
OCC08PT	RHBDD3	CCDS13850.1	g.chr22:27986387G>A	c.911C>T	p.S304L	Missense
OCC06PT	RIPK2	CCDS6247.1	g.chr8:90871585G>A	c.1423G>A	p.E475K	Missense
OCC06PT	ROPN1L	CCDS3879.1	g.chr5:10518033G>C	c.667G>C	p.E223Q	Missense [#]
OCC06PT	RPAP2	CCDS740.1	g.chr1:92561809G>T	c.744G>T	p.M248I	Missense [#]
OCC07PT	RRAS	CCDS12774.1	g.chr19:54830656C>T	c.646G>A	p.V216I	Missense
OCC03PT	SAGE1	CCDS14652.1	g.chrX:134818022C>A	c.1268C>A	p.A423D	Missense [#]
OCC03PT	SALL3	CCDS12013.1	g.chr18:74853658C>T	c.679C>T	p.R227C	Missense [#]
OCC06PT	SEL1L2	CCDS42852.1	g.chr20:13798816G>C	c.1138C>G	p.L380V	Missense
OCC06PT	SEN7	CCDS2941.2	g.chr3:102539043G>A	c.2480C>T	p.S827L	Missense
OCC01PT	SERPINB3	CCDS11986.1	g.chr18:59457541G>T	c.626C>A	p.S209Y	Missense
OCC04PT	SFRP1	CCDS34886.1	g.chr8:41285481G>C	c.355C>G	p.P119A	Missense
OCC06PT	SLC12A2	CCDS4144.1	g.chr5:127531402G>C	c.2667G>C	p.K889N	Missense
OCC03PT	SLC12A7	CCDS34129.1	g.chr5:1129308C>T	c.1792G>A	p.V598M	Missense
OCC01PT	SLC18A3	CCDS7231.1	g.chr10:50490297G>A	c.1505G>A	p.R502H	Missense
OCC07PT	SLC30A1	CCDS1499.1	g.chr1:209818351C>A	c.227G>T	p.R76L	Missense
OCC06PT	SLC38A6	CCDS9751.1	g.chr14:60519109G>A	c.236G>A	p.S79N	Missense
OCC02PT	SLC4A3	CCDS2446.1	g.chr2:220212528G>T	c.3185G>T	p.G1062V	Missense
OCC02PT	SLITRK2	CCDS14680.1	g.chrX:144712029G>A	c.394G>A	p.G132S	Missense
OCC07PT	SMAD3	CCDS10222.1	g.chr15:65269917A>G	c.1267A>G	p.S423G	Missense
OCC06PT	SMARCA4	CCDS12253.1	g.chr19:10999550C>G	c.3306C>G	p.F1102L	Missense
OCC04PT	SOC3	CCDS11756.1	g.chr17:73866491C>A	c.281G>T	p.R94L	Missense
OCC06PT	SOLH	CCDS10410.1	g.chr16:539033delC	c.1491delC	fs	Indel
OCC07PT	SON	CCDS13629.1	g.chr21:33848740G>T	c.5333G>T	p.R1778I	Missense
OCC04PT	SPACA3	CCDS11275.1	g.chr17:28348073G>A	c.443G>A	p.R148Q	Missense
OCC06PT	SPARCL1	CCDS3622.1	g.chr4:88622650C>A	c.1618G>T	p.E540X	Missense [#]
OCC08PT	SPATA5L1	CCDS10123.1	g.chr15:43489979G>T	c.1393G>C	p.E465X	Missense [#]
OCC05PT	SPOP	CCDS11551.1	g.chr17:45054368C>T	c.139G>A	p.E47K	Missense
OCC06PT	SPTBN1	CCDS33198.1	g.chr2:54727813C>G	c.4908C>G	p.I1636M	Missense
OCC06PT	ST6GAL2	CCDS2073.1	g.chr2:106825995G>A	c.871C>T	p.R291C	Missense
OCC06PT	STAG3	CCDS34703.1	g.chr7:99637885G>A	c.2549G>A	p.G850E	Missense
OCC06PT	TAF1	CCDS14412.1	g.chrX:70559765C>T	c.4586C>T	p.S1529F	Missense
OCC06PT	TAF1	CCDS14412.1	g.chrX:70559773C>G	c.4594C>G	p.L1532V	Missense
OCC06PT	TANK	CCDS2215.1	g.chr2:161769509G>C	c.286G>C	p.D96H	Missense
OCC06PT	TCERG1	CCDS4282.1	g.chr5:14584332delA	c.2060delA	fs	Indel
OCC05PT	TCN1	CCDS7978.1	g.chr11:59377272C>G	c.1220G>C	p.G407A	Missense
OCC06PT	TCP1L1L2	CCDS9104.1	g.chr12:105239560G>A	c.581G>A	p.R194Q	Missense
OCC05PT	TENC1	CCDS8842.1	g.chr12:51734479G>C	c.539G>C	p.R180P	Missense
OCC06PT	TFAP2A	CCDS4510.1	g.chr6:10518385G>C	c.215C>G	p.P72R	Missense
OCC01PT	THBS1	CCDS32194.1	g.chr15:37666969C>T	c.1250C>T	p.S417L	Missense
OCC06PT	THBS2	CCDS34574.1	g.chr6:169371666C>G	c.2185G>C	p.E729Q	Missense
OCC08PT	TKTL2	CCDS3805.1	g.chr4:164613564G>A	c.773C>T	p.A258V	Missense
OCC01PT	TNNT3	CCDS7727.1	g.chr11:1912711C>T	c.667C>T	p.R223C	Missense
OCC03PT	TOP1	CCDS13312.1	g.chr20:39174872C>T	c.1345C>T	p.R449W	Missense
OCC04PT	TP53	CCDS11118.1	g.chr17:7518978C>A	c.596G>T	p.G199V	Missense
OCC07PT	TPO	CCDS1643.1	g.chr2:1478811C>T	c.2050C>T	p.R684C	Missense
OCC08PT	TRIM7	CCDS4462.1	g.chr5:180555122G>A	c.1186C>T	p.R396W	Missense
OCC03PT	TRPV6	CCDS5874.1	g.chr7:142282824C>T	c.1241G>A	p.R414H	Missense
OCC06PT	TSHZ2	CCDS33490.1	g.chr20:51304068G>A	c.664G>A	p.A222T	Missense
OCC07PT	TXLNB	CCDS34545.1	g.chr6:139651330C>T	c.400G>A	p.E134K	Missense [#]
OCC03PT	UBE3A	CCDS32177.1	g.chr15:23167713T>C	c.641A>G	p.D214G	Missense [#]
OCC01PT	UHRF1BP1L	CCDS31882.1	g.chr12:98990653G>T	c.1477C>A	p.L493I	Missense
OCC06PT	UTRN	CCDS34547.1	g.chr6:144837577C>T	c.3325C>T	p.L1109F	Missense
OCC06PT	VPS33B	CCDS10369.1	g.chr15:89362068C>G	c.148G>C	p.D50H	Missense
OCC02PT	WARS2	CCDS900.1	g.chr1:119377335G>A	c.805C>T	p.R269C	Missense
OCC02PT	YEATS2	CCDS43175.1	g.chr3:184959448G>C	IVS12+1G>C	Splice site	Splice site
OCC08PT	ZHX3	CCDS13315.1	g.chr20:39265364C>G	c.1607G>C	p.R536T	Missense
OCC08PT	ZNF223	CCDS12635.1	g.chr19:49262723C>T	c.902C>T	p.S301L	Missense
OCC08PT	ZNF318	CCDS4895.2	g.chr6:43414988C>A	c.4726G>T	p.G1576C	Missense
OCC06PT	ZNF454	CCDS4441.1	g.chr5:178324711C>T	c.700C>T	p.H234Y	Missense
OCC06PT	ZNF7	CCDS6435.1	g.chr8:146038269C>T	c.973C>T	p.Q325X	Nonsense
OCC08PT	ZP4	CCDS1615.1	g.chr1:236117373G>C	c.665C>G	p.A222G	Missense
OCC06PT	ZSCAN1	CCDS12969.1	g.chr19:63257154G>A	c.1150G>A	p.V384I	Missense
OCC08PT	ZZEF1	CCDS11043.1	g.chr17:3882226A>C	c.6835T>G	p.F2279V	Missense

*All coordinates refer to the human reference genome hg18 release (NCBI 36.1, March 2006).

[§]%,[#]From the 268 mutations, 237 were validated with Sanger sequencing. Of the 31 mutations that were not validated, three (marked by [§] in the Table) were not detectable by Sanger sequencing, while in 28 (marked by [#] in the Table) the PCR failed because the region had an unusually high GC content, because the region was duplicated elsewhere in the genome and primers unique to the region could not be designed, or for unexplained reasons.

table S4. Primers used for PCR amplification and sequencing

Gene Symbol	Transcript IDs	Coding Exon Number	Genomic Region of Interest [*]	M13 PCR primer sequence [†]	PCR primer sequence
<i>ARID1A</i>	ENST00000324856	1	chr1:26895478-26895713	CCCGTTCGAGTTCCTCAGGT	GCAGAAAGCGGAGAGTCACA
<i>ARID1A</i>	ENST00000324856	1	chr1:26895714-26896145	GGGAAAGGAGCTGCAGGA	ACCTCTCGGGGAGCTCAG
<i>ARID1A</i>	ENST00000324856	1	chr1:26896146-26896381	CAGCAGAACTCTCACACCA	CCCACTCAGCTGTGTACCTG
<i>ARID1A</i>	ENST00000324856	1	chr1:26896382-26896622	GAGAAGAGCCAGACAATGGC	ACCCTCAACCAACTGCTCAC
<i>ARID1A</i>	ENST00000324856	2	chr1:26928725-26928945	TTGGAAGCCAAGGATACATTC	AGGTTGGTCTCATTGCTCTTTC
<i>ARID1A</i>	ENST00000324856	3	chr1:26930226-26930491	ACCCTGGGCCTCCTAAGTATG	ATATCTTACTGCGGTGGAGG
<i>ARID1A</i>	ENST00000324856	3	chr1:26930492-26930686	TGCACGTTAGAGAACCCTCTG	ACAACCAGCAAAGTCTCACC
<i>ARID1A</i>	ENST00000324856	4	chr1:26931750-26931874	CAGTCCCATAAACCTTTCACAG	CTGGGCAGGGAGACAGAAC
<i>ARID1A</i>	ENST00000324856	5	chr1:26959930-26960178	GAAACTATGCAGGCATGAGCC	AAAGAACGTGTGTAGTATTTGC
<i>ARID1A</i>	ENST00000324856	6	chr1:26960458-26960555	TTGGCTGGATCTCTTTGTGTG	TTCATGGTCAAACAGCTCTCC
<i>ARID1A</i>	ENST00000324856	7	chr1:26961226-26961401	TCCCAGGATAAGGATGGAGAG	GGACAGCCCTTCTCTACAAG
<i>ARID1A</i>	ENST00000324856	8	chr1:26962047-26962367	TTGAATGACATTGTTGGTGTTC	GGTCCAGAAGCATCTCAATAATC
<i>ARID1A</i>	ENST00000324856	9	chr1:26965295-26965448	ATCATCTCTGGGCTGGCTG	CACAGCACTATTTGGCTCCAG
<i>ARID1A</i>	ENST00000324856	10	chr1:26965531-26965648	GGCTGGGATCTGTCACTCTC	GCCAACAATTCTGCAGGTAAG
<i>ARID1A</i>	ENST00000324856	11	chr1:26966864-26967081	CAAGAGACTTCTGAGCCCTTAGC	CATGGTACCACATGAAGCCAG
<i>ARID1A</i>	ENST00000324856	12	chr1:26970193-26970408	ATCCTTGGCATATCTCTGTTGG	GAATACCTTACAGCCTGATGGG
<i>ARID1A</i>	ENST00000324856	13	chr1:26971574-26971714	AACAAAGGACACGCAGGAGTC	GGCCTTAGGAAGAACTTTCCC
<i>ARID1A</i>	ENST00000324856	14	chr1:26971886-26972069	GGCTGAAGATAAGTGCATGGG	CAAGAACCCTGAGCCATTCTC
<i>ARID1A</i>	ENST00000324856	15	chr1:26972420-26972578	GAAGTCTGAAGAGGGCTCG	AATTGGAGAGGCAGATTGAGC
<i>ARID1A</i>	ENST00000324856	16	chr1:26972654-26972799	CAGAGTGAGGTAAAGCATGCC	CCTTGGGTGGAGAAGCTGATTG
<i>ARID1A</i>	ENST00000324856	17	chr1:26972876-26972980	GTGAGTAAAGCCTGTCTCGG	ATTGAGGACGTGGCTCTCAG
<i>ARID1A</i>	ENST00000324856	18	chr1:26973403-26973673	GGAAAGAAAGAGTGGTGGTTGC	CCAAAGTGAATGGAATTGG
<i>ARID1A</i>	ENST00000324856	18	chr1:26973674-26973835	GGAGATGTACAGCGTCCATA	TCGGTTCACGCCATGATAG
<i>ARID1A</i>	ENST00000324856	18	chr1:26973836-26974028	GCTATGTGCGAGGCAGTACT	GCTCAGCAAGCCACCATGT
<i>ARID1A</i>	ENST00000324856	18	chr1:26974029-26974302	ATTGCATGGCAATGAAGGAG	CCTCCATCTAAGTACCAGCCC
<i>ARID1A</i>	ENST00000324856	19	chr1:26974651-26974789	TGGCTAAAGATGAGACATTCCC	AGACAGAAACTGCCTCCACC
<i>ARID1A</i>	ENST00000324856	20	chr1:26978097-26978514	GTCTTGCTCGAAGTGGGTC	GGAGAACCCTTTGGAAAGGAG
<i>ARID1A</i>	ENST00000324856	20	chr1:26978515-26978778	GGCTTCGAATGGTATTGGACA	CAGGCAAGGACAAGCCAG
<i>ARID1A</i>	ENST00000324856	20	chr1:26978779-26979042	GGCGAGTGAACCAAGGTGTT	GCTAAGAGTTCAGAGGCCATCA
<i>ARID1A</i>	ENST00000324856	20	chr1:26979043-26979306	GCTAAGAGTTCAGAGCCATCA	CCGCATCATGTCCACACTA
<i>ARID1A</i>	ENST00000324856	20	chr1:26979307-26979580	CCTTGGTTACACTGCCAAC	CAGCCGTGATTCTGACAGAGTA
<i>ARID1A</i>	ENST00000324856	20	chr1:26979581-26979838	GAGGTGGAAGGAGGAGAGAGA	CTCAGTGACCCGAAAGAACCC
<i>KRAS</i>	ENST00000311936	1	chr12:25253992-25254116	TCAGTTGCCTGAAGAGAACATAA	TAACAGTCTCGATGGAGCAGG
<i>KRAS</i>	ENST00000395977	1	chr12:25259638-25259765	AGTGGTTGCCACCTGTTACC	GAACAAACCAGGATTCTAGCCC
<i>KRAS</i>	ENST00000395977	2	chr12:25269811-25269978	TGGATTAAGAAGCAATGCCCT	TGGTGTAGTGGAACTAGGAATTACAT
<i>KRAS</i>	ENST00000395977	3	chr12:25271431-25271617	ATGCATGGCATTAGCAAAGAC	CGTCATCTTTGGAGCAGGAAC
<i>KRAS</i>	ENST00000395977	4	chr12:25289471-25289589	TTGAAACCAAGGTACATTTCCAG	TCTTAAGCGTTCGATGGAGGAG
<i>PIK3CA</i>	ENST00000263967	1	chr3:180399304-180399543	TCTGTTTGGGCAACCATAC	CAACAGTTAAGCTTTATGGTTATTTGC
<i>PIK3CA</i>	ENST00000263967	1	chr3:180399544-180399663	GCCTCCGTGAGGCTACATTA	GCAATTTAGAGCAAAGGCAGC
<i>PIK3CA</i>	ENST00000263967	2	chr3:180400168-180400385	AAATCTACAGAGTTCCTGTTTGC	TCAGTATAAGCAGTCCCTGCC
<i>PIK3CA</i>	ENST00000263967	3	chr3:180401768-180402026	TGAATACTGTTGAAATTTCTCCCT	GCAGAGCCTGCAGTGAGC
<i>PIK3CA</i>	ENST00000263967	4	chr3:180404022-180404275	CGGAGATTTGGATGTTCTCCT	TGATTGATCTTGTCTCAACG
<i>PIK3CA</i>	ENST00000263967	5	chr3:180404981-180405074	CAAATCCGACTTCGTGATCC	TTAGTGGATGAAGGCAGCAAC

<i>PIK3CA</i>	ENST00000263967	6	chr3:180410073-180410186	TTGGTTGATCTTTGTCTTCGTG	ATGAACCAAAGCAAGCATGAG
<i>PIK3CA</i>	ENST00000263967	7	chr3:180410664-180410824	TGAATTTTCTTTTGGGAAG	GAGAGAAGGTTTGACTGCCATAA
<i>PIK3CA</i>	ENST00000263967	8	chr3:180410909-180411051	ATGAATGAAGGCAAGCTAGGG	GATTTGCTGAACCTATTGGTG
<i>PIK3CA</i>	ENST00000263967	9	chr3:180418688-180418820	TGCTGAGATCAGCCAAATCA	TCAGCAGTTACTATTCTGTGACTGG
<i>PIK3CA</i>	ENST00000263967	10	chr3:180419674-180419763	AAAGCTAGTAATGTAAGAAGTTGGGA	GGGAAAGATAGTTGTGAATGAGC
<i>PIK3CA</i>	ENST00000263967	11	chr3:180420049-180420221	ATAGACTAATAGTAATATAGTGT	AAGGAAGTTGTATGGATCTAG
<i>PIK3CA</i>	ENST00000263967	12	chr3:180420427-180420538	CGGGAGTTTGACATTGTTCTGA	CGGCCATGCAGAACTGAC
<i>PIK3CA</i>	ENST00000263967	13	chr3:180421464-180421643	GGCCACCTTCTATGTTCCAA	CAAGAAGCATAGGCGTGTGTC
<i>PIK3CA</i>	ENST00000263967	14	chr3:180424559-180424673	TTTGAGGGTAGGAGAATGAGAGA	TCTGAGTGTGCTGCTGTG
<i>PIK3CA</i>	ENST00000263967	15	chr3:180425178-180425307	TCTGTTACCATAGGATAAGAAATGGA	GCTAAATTCATGCATCATAAGCTC
<i>PIK3CA</i>	ENST00000263967	16	chr3:180426440-180426526	CATGTGATGGCGTGATCC	GGTGACACTCCAGAGGCAGTAG
<i>PIK3CA</i>	ENST00000263967	17	chr3:180429750-180429928	GGAAAGGCGATAAAGGTCATGC	GAGGAATACACAAACACCCGACAG
<i>PIK3CA</i>	ENST00000263967	18	chr3:180430482-180430607	TAAATGGAACTTGCACCCTG	AAACAAATGGCACACGTTCTC
<i>PIK3CA</i>	ENST00000263967	19	chr3:180430703-180430862	TACCCAGGCTGTTTTCAATTC	TGGTGAAAGACGATGGACAAG
<i>PIK3CA</i>	ENST00000263967	20	chr3:180434572-180434850	GACATTTGAGCAAAGACCTGAAG	TGGATTGTGCAATTCCTATGC
<i>PPP2R1A</i>	ENST00000322088	1	chr19:57385158-57385243	ATAAGAGACGACGCTGATTG	ACCAAAGAAACGCGAGCTTAG
<i>PPP2R1A</i>	ENST00000322088	2	chr19:57397005-57397103	GCTGACTGGGTTGAGAGCTG	TCCCTTTCACCATCTGTCTCC
<i>PPP2R1A</i>	ENST00000322088	3	chr19:57401024-57401132	GTCCATGTGTTCTGAGCTTGG	TGTTGGATTAAGCGGATGTC
<i>PPP2R1A</i>	ENST00000322088	4	chr19:57406321-57406561	AAGGTCGGGATGGTAATAGG	TGGGAGTGGAGAGAGTTCAGG
<i>PPP2R1A</i>	ENST00000322088	5	chr19:57407747-57407902	TGCTGAGCTCTGGGATTCTC	AACTGCAGAGTCTGTGCTTGC
<i>PPP2R1A</i>	ENST00000322088	6	chr19:57408016-57408179	GGTTCTGCCATGAAAGAG	GATCTTATTGCTCAAACGCC
<i>PPP2R1A</i>	ENST00000322088	7	chr19:57410840-57410962	TTAGCACTGCTTCCAAGGC	TGATGTGCTAGTTCCACCTCC
<i>PPP2R1A</i>	ENST00000322088	8	chr19:57411065-57411143	CTCCACAAGGTCAAAGGTTG	AACTGCTTGAACCCAAGAGC
<i>PPP2R1A</i>	ENST00000322088	9	chr19:57411590-57411732	TCAGCAGATTCCTGGTCAATC	GGGCAGAAGCAGGTTATTGTC
<i>PPP2R1A</i>	ENST00000322088	10	chr19:57414752-57414933	CCACTAAGCCTTCAAAGCCC	AGCTCTTCCATCCTGTCTCTC
<i>PPP2R1A</i>	ENST00000322088	11	chr19:57415250-57415318	GTGTCCGGTCTTTCTAGGGTG	GATCTGTTTCGTCTCTCTCC
<i>PPP2R1A</i>	ENST00000322088	12	chr19:57416040-57416202	GAACCTCTAGCATCCCTCC	TAAGCCATGGTGAGTGTGACC
<i>PPP2R1A</i>	ENST00000322088	13	chr19:57417160-57417310	TGAGTACCCGTATTGCTCAG	CTGACCTGGGCTCTACCTTC
<i>PPP2R1A</i>	ENST00000322088	14	chr19:57420778-57420877	ACAATGCCAAGGTACCTCCC	CTTGAGACTCTCCACCTTG
<i>PPP2R1A</i>	ENST00000322088	15	chr19:57421026-57421050	TGGACAGTGAGACATCTTCCC	CTAGCAGGAGGGTGGACTTTG

Coordinates refer to the human reference genome hg18 release (NCBI 36.1, March 2006).

[†]M13 denotes the universal sequencing primer 5'-GTAAACGACGCCAGT-3'.

table S5. Mutations in *ARID1A*, *KRAS*, *PIK3CA* and *PPP2R1A* in Human Ovarian Clear Cell Carcinoma Cell lines.

Sample	Gene	Transcript Accession	Nucleotide (genomic)*	Nucleotide (cDNA)	Amino acid (protein)	Mutation type
OV207	<i>ARID1A</i>	CCDS285.1	g.chr1:26973940G>A	c.4635G>A	p.W1545X	Nonsense
OVISE	<i>ARID1A</i>	CCDS285.1	g.chr1:26896089dupA	c.608dupA	fs	Indel
OVISE	<i>ARID1A</i>	CCDS285.1	g.chr1:26930505_26930506delGC	c.1626_1627delGC	fs	Indel
OVMANA	<i>ARID1A</i>	CCDS285.1	g.chr1:26972785C>T	c.1332C>T	p.Q1332X	Nonsense
OVMANA	<i>ARID1A</i>	CCDS285.1	g.chr1:26979767C>G	c.6791C>G	p.S2264X	Nonsense
OVTOKO	<i>ARID1A</i>	CCDS285.1	g.chr1:26979601het_delC	c.6625delC	fs	Indel
OVTOKO	<i>ARID1A</i>	CCDS285.1	g.chr1:26895770G>T	c.289C>T	P.E97X	Nonsense
TOV 21G	<i>ARID1A</i>	CCDS285.1	g.chr1:26930529dupC	c.1650dupC	fs	Indel
TOV 21G	<i>ARID1A</i>	CCDS285.1	g.chr1:269611250delC	c.2272delC	fs	Indel
TOV 21G	<i>KRAS</i>	CCDS8703.1	g.chr12:25289549C>A	c.38G>T	p.G13C	Missense
KK	<i>PIK3CA</i>	CCDS43171.1	g.chr3:180418794A>C	c.1634A>C	P.E545A	Missense
OVCA429	<i>PIK3CA</i>	CCDS43171.1	g.chr3:180418793G>A	c.1633G>A	p.E545K	Missense
OVMANA	<i>PIK3CA</i>	CCDS43171.1	g.chr3:180418794A>T	c.1634A>T	p.E545V	Missense
TOV 21G	<i>PIK3CA</i>	CCDS43171.1	g.chr3:180434778C>CT	c.3139C>T	p.H1047Y	Missense
KK	<i>PPP2R1A</i>	CCDS12849.1	g.chr19:57407795G>A	c.548G>A	p.R183Q	Missense
OVISE	<i>PPP2R1A</i>	CCDS12849.1	g.chr19:57407794C>T	c.547C>T	p.R183W	Missense
OVTOKO	<i>PPP2R1A</i>	CCDS12849.1	g.chr19:57407794C>G	c.547C>G	p.R183G	Missense

*Coordinates refer to the human reference genome hg18 release (NCBI 36.1, March 2006).

References

- S1. M. D. Fallin *et al.*, *Am J Hum Genet* **73**, 601 (2003).
- S2. M. D. Fallin *et al.*, *Am J Hum Genet* **77**, 918 (2005).
- S3. T. Sjoblom *et al.*, *Science* **314**, 268 (2006).