

Figure S1

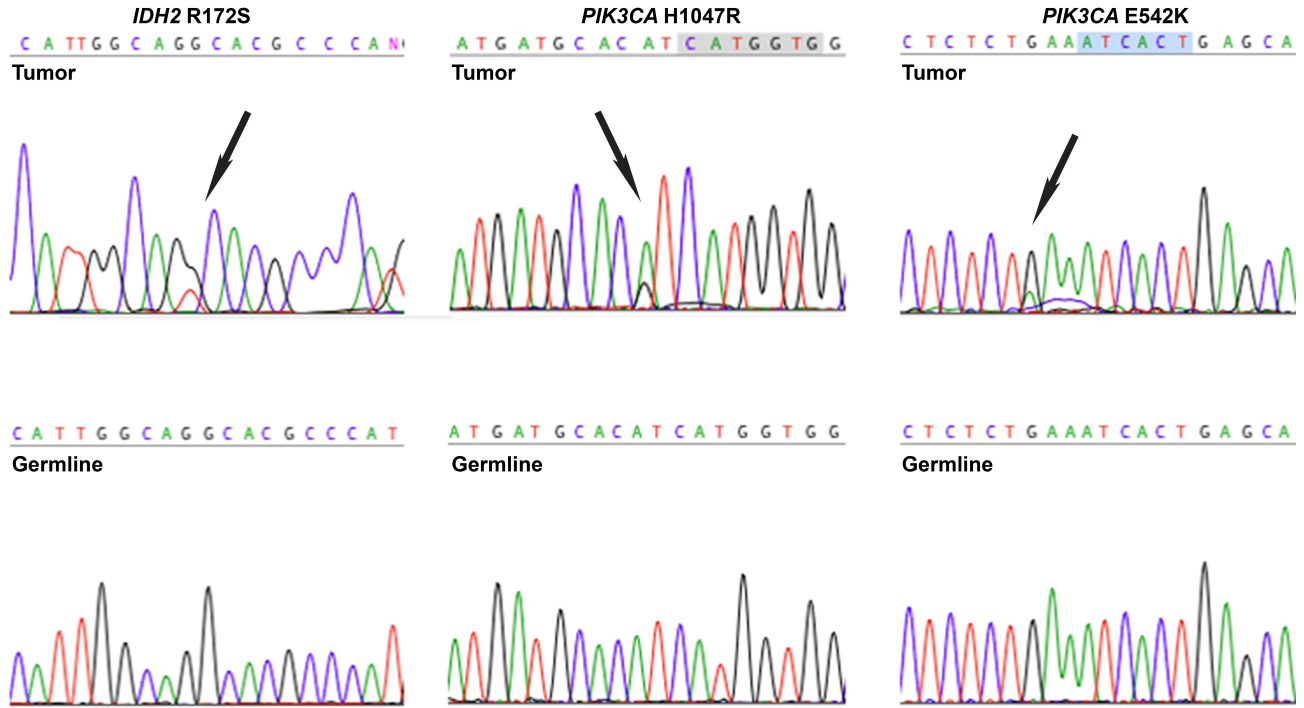


Figure S2

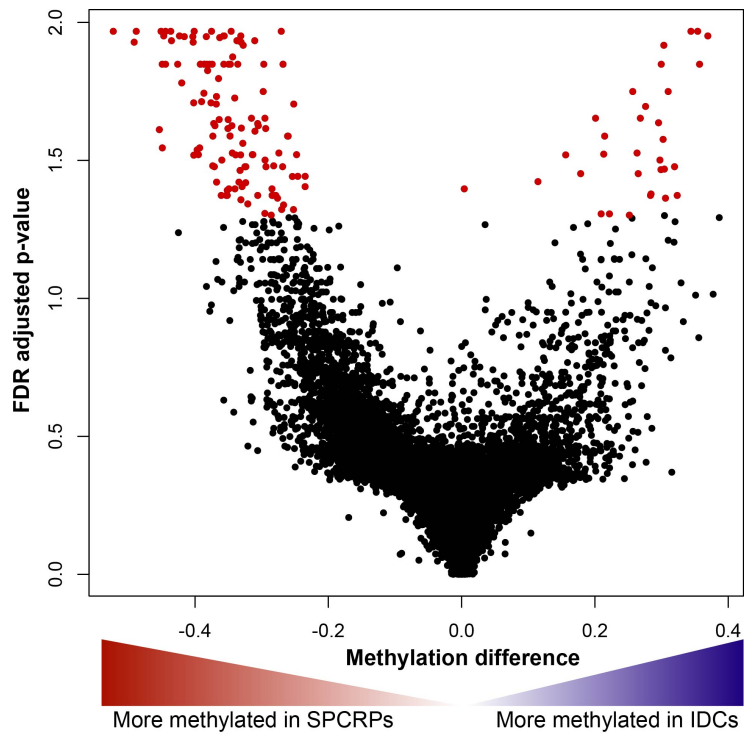


Figure S3

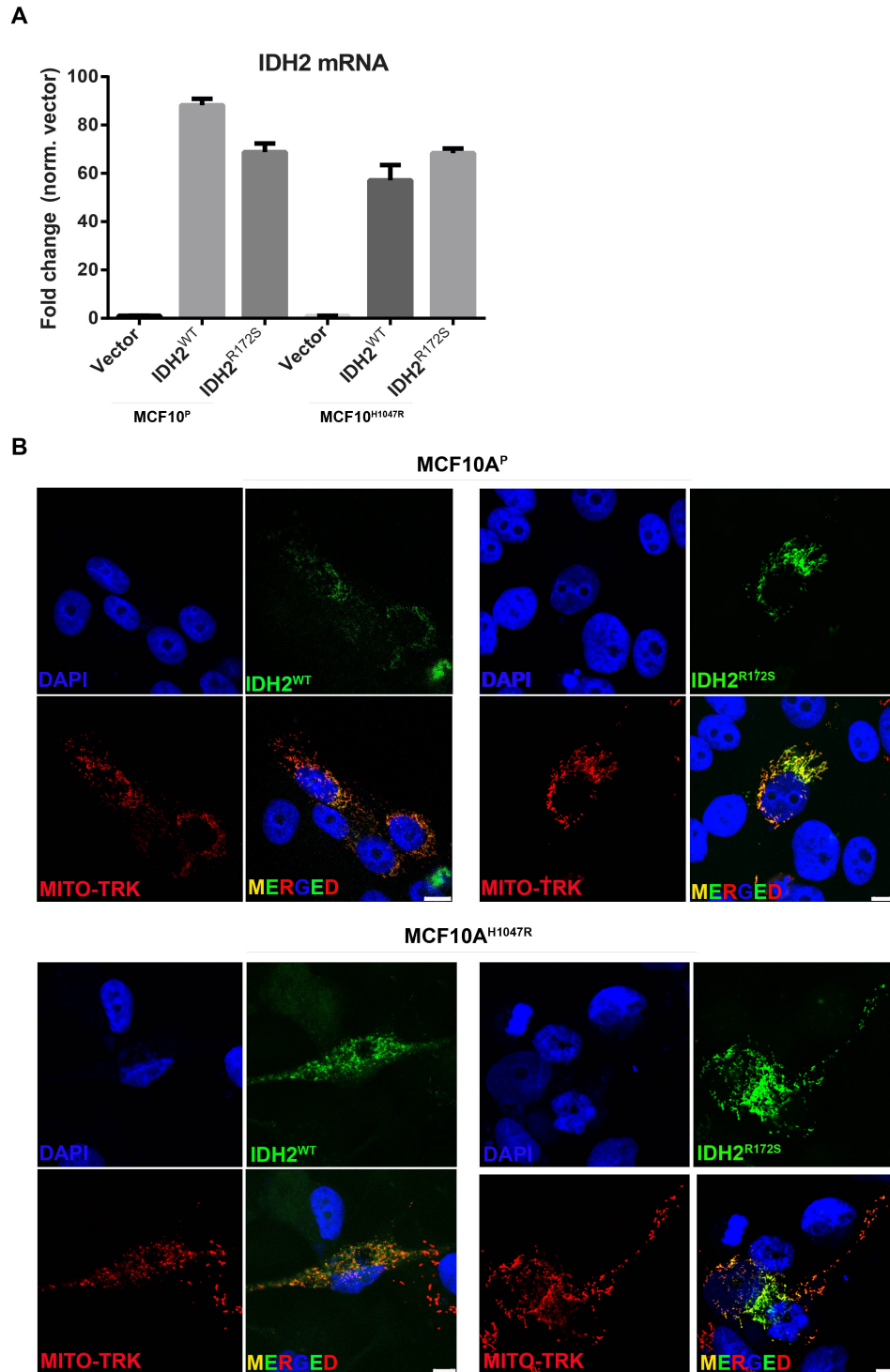


Figure S4

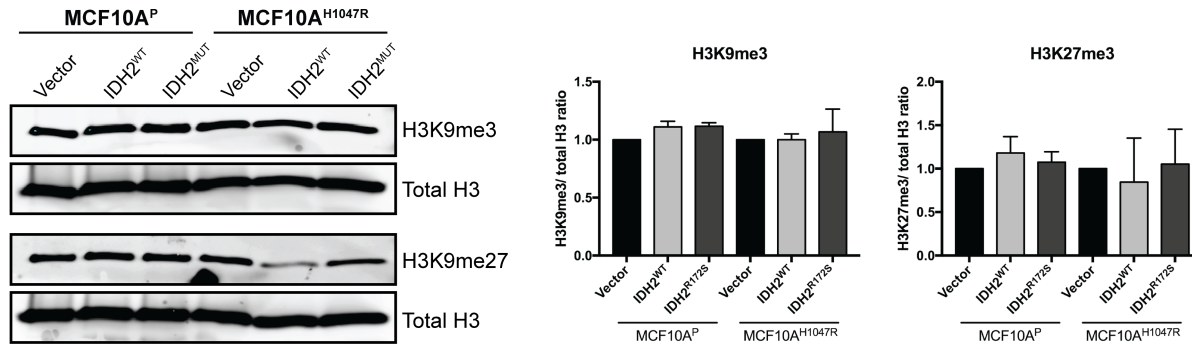


Figure S5

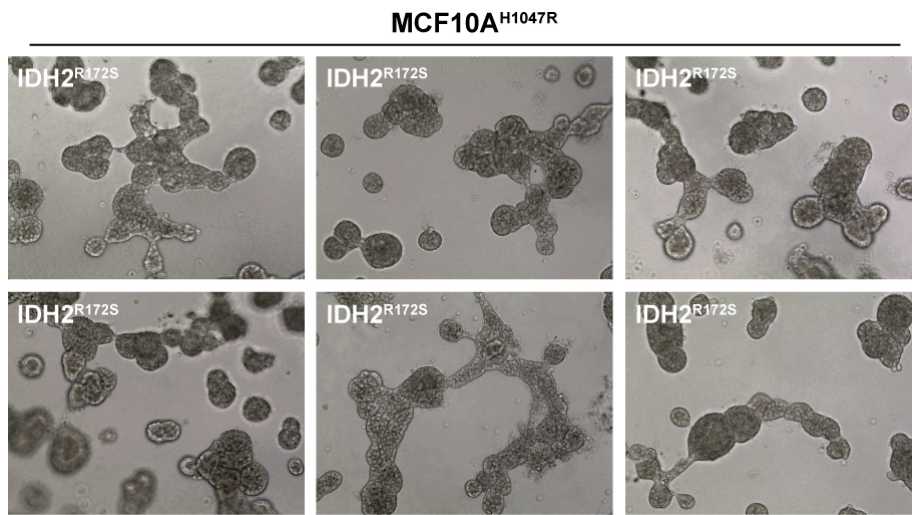


Table S1. Antibodies used for immunohistochemistry.

Antibody	Clone/Source	Dilution
Calponin	CALP/ DAKO	1:250
SMMHC	SMMS-1/ DAKO	RTU
p63	BC4A4/ BIOCARE	1:200
CK AE1/AE3	AE1/AE3 /DAKO	RTU
CK7	OV-TL12/30/ DAKO	RTU
CK5/6	D5/16B4/ DAKO	RTU
CK 34 β E12	34 β E12/ DAKO	RTU
E-cadherin	36B5/ Leica	RTU
H3K27me3	C36B11/ CST	1:100
MUC1	MA552/ Leica	1:50
ER	SP1/ Thermo Scientific	1:50
PR	PgR636 /DAKO	RTU
AR	AR441/ DAKO	1:50
HER2	HercepTest/ DAKO	RTU
Mammaglobin	304-1A5/ DAKO	RTU
GCDFP-15	23A3/ DAKO	RTU
TTF-1	SPT24/ LEICA	1:25
Thyroglobulin	R-Polyclonal /DAKO	RTU

AR, androgen receptor; CK, cytokeratin; ER, estrogen receptor; GCDFP-15, gross cystic disease fluid protein-15; PR, progesterone receptor; RTU, ready to use; SMMHC, smooth muscle myosin heavy chain; TTF-1, thyroid transcription factor-1.

Table S2. SNaPshot tumor genotyping assay.

Gene	Amino acid - cDNA residue	Gene	Amino acid - cDNA residue	Gene	Amino acid - cDNA residue
AKT1	E17 - 49G	HRAS	G12 - 35G	PIK3CA	E545-1634A
APC	R1114 - 3340C	HRAS	G13 - 37G	PIK3CA	Q546 - 1636C
APC	Q1338 - 4012C	HRAS	G13 - 38G	PIK3CA	Q546 - 1637A
APC	R1450 - 4348C	HRAS	Q61 - 181C	PIK3CA	H1047 - 3139C
APC	T1556fs*3 - 4666_667insA	HRAS	Q61 - 182A	PIK3CA	H1047 - 3140A
BRAF	G466 - 1397G	HRAS	Q61 - 183A	PIK3CA	G1049 - 3145G
BRAF	G469 - 1406G	IDH1	R132 - 394C	PTEN	R130 - 388C
BRAF	L597 - 1789C	IDH1	R132 - 395G	PTEN	R173 - 517C
BRAF	V600 - 1798G	IDH2	R140 - 418G	PTEN	R233 - 697C
BRAF	V600 - 1799T	IDH2	R140 - 419G	PTEN	K267fs* - 800delA
CTNNB1	D32 - 94G	IDH2	R172 - 514A	RET	M918 - 2753T
CTNNB1	D32 - 95A	IDH2	R172 - 515G	TP53	R175-524G
CTNNB1	S33 - 98C	IDH2	R172 - 516G	TP53	G245 - 733G
CTNNB1	G34 - 101G	KIT	D816 - 2447A	TP53	R248 - 742C
CTNNB1	S37 - 109T	KRAS	G12 - 34G	TP53	R248 - 743G
CTNNB1	S37 - 110C	KRAS	G12 - 35G	TP53	R273-817C
CTNNB1	T41 - 121A	KRAS	G13 - 38G	TP53	R273 - 818G
CTNNB1	T41 - 122C	KRAS	G13 - 37G	TP53	R306 - 916C
CTNNB1	S45 - 133T	KRAS	Q61 - 181C		
CTNNB1	S45 - 134C	KRAS	Q61 - 182A	Sizing assay:	
EGFR	G719 - 2155G	KRAS	A146 - 436G	EGFR	exon 19 deletions
EGFR	G719 - 2156G	KRAS	A146 - 437C	EGFR	exon 20 insertions/deletions
EGFR	T790 - 2369C	MAP2K1	Q56 - 167A	ERBB2	exon 20 insertions
EGFR	L858 - 2573T	MAP2K1	K57 - 171G		
EGFR	L861 - 2582T	MAP2K1	D67 - 199G		
EGFR	E746_A750 - 2235_2249del	NOTCH1	L1575 - 4724T		
EGFR	E746_A750 - 2236_2250del	NOTCH1	L1601 - 4802T		
EML4-ALK	L1996 - 4493C	NRAS	G12 - 35G		
FGFR3	R248 - 742C	NRAS	G12 - 35G		
FGFR3	S249 - 746C	NRAS	G13 - 37G		
FGFR3	G370 - 1108C	NRAS	G13 - 38G		
FGFR3	Y373 - 1118A	NRAS	Q61 - 181C		
GNA11	Q209 - 626A	NRAS	Q61 - 183G		
GNAQ	Q209 - 626A	NRAS	Q61 - 183A		
GNAS	R201 - 601C	PIK3CA	R88 - 263G		
GNAS	R201 - 602G	PIK3CA	E542 - 1624G		
HRAS	G12 - 34G	PIK3CA	E545 - 1633G		

Table S3. Primers used for Sanger sequencing analysis.

Sanger sequencing primers <i>IDH2</i> and <i>PIK3CA</i> hotspots		
	Forward	Reverse
IDH2 R172	GGTGCCCAGGTCAGTGGAT	GCTGTGTTGTTGCTTGGGGT
IDH2 R140	CGTGCCTGCCAATGGTGAT	TCAAATTCTGGTTGAAAGATGGC
PIK3CA	CTGTGAATCCAGAGGGGAAA	GCACTTACCTGTGACTCCATAGAA
PIK3CA H1047	TGGAATCCAGAGTGAGCTTTC	CTCAATGATGCTTGGCTCTG
TET2_AA23/24	ATGGCCCCGAAGCAAGCC	ACTTGGTGTCTCCATTTACTTCTG
TET2_AA268	ATCCAGATTGTGTTTCCATTGC	CATTATCAGCATCATCAGCATCA
TET2_AA429	ACCACCACCACCATCACAAT	GTAGATGGATTAGGACTCTGGGA

Sanger sequencing primers plasmid genotyping		
	Forward	Reverse
IDH2 R172	AGTTCAAGCTGAAGAAGATGT	CTCGTCGGTGTTGTACATGC

Table S4. Whole exome and targeted capture massively parallel sequencing statistics.

Sample	Sample Type	Sequencing Type	Target Territory	Total Reads	PCT Selected Bases	Mean Target Coverage	PCT TARGET BASES 2X	PCT TARGET BASES 10X	PCT TARGET BASES 20X	PCT TARGET BASES 30X	PCT TARGET BASES 40X	PCT TARGET BASES 50X	PCT TARGET BASES 100X
SPCRP10 N	Normal	Whole exome	51542852	89737793	90.04%	111.4	91.45%	85.88%	81.18%	77.25%	73.55%	69.91%	49.62%
SPCRP10 T	Tumor	Whole exome	51542852	120904304	86.11%	142.0	92.33%	87.86%	83.80%	80.47%	77.43%	74.52%	59.69%
SPCRP13 N	Normal	Whole exome	51542852	196656130	58.62%	112.5	94.95%	91.31%	88.66%	85.34%	81.42%	77.10%	51.35%
SPCRP13 T	Tumor	Whole exome	51542852	271215295	76.55%	211.5	94.66%	91.87%	90.19%	88.42%	86.49%	84.41%	73.10%
SPCRP5 T	Tumor	MSK-IMPACT 410	1362579	34470791	85.42%	734.3	99.32%	99.10%	98.97%	98.86%	98.76%	98.63%	97.78%
SPCRP11 T	Tumor	MSK-IMPACT 410	1362579	57985946	63.85%	572.7	99.51%	99.37%	99.24%	99.14%	99.02%	98.92%	98.41%

Table S5. Non-synonymous somatic single nucleotide variants and small insertion/deletions identified in SPCRps subjected to whole-exome and targeted massively parallel sequencing.

Tumor Sample	Effect	Gene	AA	Tumor Depth	Normal Depth	Tumor MAF	Normal MAF	CHROM	POS	REF	ALT	Mutation Tester	CHASM	FATHMM	EXAC Frequency	Cancer Gene Census	Kandath et al (127 genes)	Lawrence et al (6000+ genes)
SPCRP13	missense_variant	NBPF1	p.Ser891Asn	27	28	18.50%	0.00%	1	16893841	C	T		Passenger		0.1105			TRUE
SPCRP13	stop_gained	RNF1C3	p.Ser111*	327	208	38.80%	0.00%	1	180868724	C	G	A	Passenger					
SPCRP13	missense_variant	NBPF10	p.Tyr35Ser	16	8	37.50%	0.00%	1	145253628	G	C	N	Passenger		0.0836			
SPCRP13	missense_variant	LMOD1	p.Val11Glu	456	167	3.30%	0.00%	1	201915437	A	T	D	Passenger	PASSENGER/OTHER				
SPCRP13	frameshift_variant	BIRC6	p.Ile3500fs	184	124	33.52%	0.00%	2	32738151	ATTCT								
SPCRP13	missense_variant	B3GALT1	p.Arg214Trp	305	176	38.40%	0.00%	2	188726189	C	T	D	Passenger	PASSENGER/OTHER	8.24E-06			
SPCRP13	missense_variant	NWAP2	p.Ala307Thr	407	261	3.20%	0.00%	2	226447352	G	A	D	Passenger	PASSENGER/OTHER	8.33E-06			
SPCRP13	missense_variant	PKNOX3	p.Asn421Thr	89	74	10.10%	1.40%	3	138433350	T	G	D	Passenger	CANCER				
SPCRP13	missense_variant	TECLR	p.Leu214Val	116	58	30.20%	0.00%	4	65175661	A	C	N	Passenger	PASSENGER/OTHER				
SPCRP13	frameshift_variant	PKCIR1	p.Glu300fs	84	68	29.01%	0.00%	5	67578817	AAC	A					TRUE	TRUE	TRUE
SPCRP13	missense_variant	PCDHGA11	p.Val627Gly	191	97	41.40%	1.00%	5	140802874	T	G	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	HST1H2AH	p.Leu404Arg	275	197	52.80%	0.00%	6	27115088	T	G	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	AK9	p.Leu1333His	234	125	77.00%	0.00%	6	108531127	A	T	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	ADGB	p.Ile245Leu	69	59	13.00%	1.70%	6	146985457	A	C	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	PLOD3	p.Val238Met	178	100	36.50%	0.00%	7	100856453	C	T	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	MGAM	p.Ala1260Ser	70	44	12.90%	2.30%	7	141758807	G	T	N	Passenger	PASSENGER/OTHER	0.0001573			
SPCRP13	missense_variant	IRNAE2	p.Gly2188Ser	303	228	39.40%	0.00%	9	7932628	C	T	N	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	APBB1P	p.Ala78Ser	341	251	34.30%	0.00%	10	26789819	G	T	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	PLA2G12B	p.Asp130Gly	383	209	4.20%	0.00%	10	74701004	T	C	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	CALHM3	p.Arg72Tyr	59	53	37.30%	0.00%	10	105238576	G	A	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	INP9F	p.Ser909Phe	441	272	11.80%	0.00%	10	121586607	C	T	D	Passenger	PASSENGER/OTHER				
SPCRP13	frameshift_variant	AF3A2	p.His309fs	274	146	29.62%	0.68%	11	980921	A	ACG							
SPCRP13	missense_variant	ORS1B4	p.Leu154Phe	417	309	7.70%	0.33%	11	6322715	C	A	N	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	C11orf85	p.Val72Leu	90	50	12.20%	2.00%	11	64717836	C	A	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	KRTAP5-7	p.Val59Ile	97	45	5.20%	0.00%	11	71238461	G	A	N	Passenger	PASSENGER/OTHER	0.001803			
SPCRP13	missense_variant	CR3	p.Glu61Lys	43	51	18.60%	2.00%	11	8808242	C	T	D	Passenger	PASSENGER/OTHER	2.56E-05			
SPCRP13	missense_variant	HTRF8	p.Arg332His	291	137	4.10%	0.73%	11	119815382	A	G	N	Passenger	PASSENGER/OTHER	1.65E-05			
SPCRP13	missense_variant	DEPDC4	p.Ala73Val	124	106	43.90%	0.00%	12	100657611	G	A	N	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	RILPL2	p.Ser150Ala	93	40	44.60%	0.00%	12	123815098	A	C	N	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	OR6S1	p.His247Asp	339	202	43.40%	0.50%	14	21109112	G	C	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	MIR625	p.Pro121Leu	290	162	3.80%	0.62%	14	23326260	C	T	N	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	ADAM21	p.Pro685Leu	336	245	40.90%	0.00%	14	70929270	C	T	N	Passenger	PASSENGER/OTHER	4.96E-05			
SPCRP13	missense_variant	ZFYVE1	p.Ile169Phe	139	80	17.30%	2.50%	14	73485002	T	A	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	ALKBH1	p.His176Asn	264	130	36.90%	0.77%	14	78146243	G	D	Passenger	PASSENGER/OTHER					
SPCRP13	missense_variant	SCAPER	p.Ser232Glu	222	137	60.50%	0.73%	15	77057276	C	T	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	PLA2G1B	p.Asn146Ser	170	85	14.70%	0.00%	15	14765691	A	C	D	Passenger	PASSENGER/OTHER	8.28E-06			
SPCRP13	missense_variant	MFG8E	p.Val54Met	225	125	4.00%	0.00%	15	89453095	C	T	N	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	IDH2	p.Arg172Ser	323	146	54.30%	0.00%	15	90631837	C	G	D	Driver	CANCER		TRUE	TRUE	TRUE
SPCRP13	missense_variant	TMC5	p.Ile933Leu	224	87	5.80%	1.10%	16	19503521	A	C	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	KCTD13	p.Gly1Arg	289	88	30.10%	0.00%	16	29937174	C	T	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	p.Ser744Phe		303	157	40.20%	0.00%	16	14816309	A	C	D	Passenger	PASSENGER/OTHER		TRUE		
SPCRP13	missense_variant	NINL	p.Asp1147Glu	165	64	5.50%	0.00%	20	25443160	A	T	N	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	BPIFA1	p.Phe197Leu	90	64	13.30%	0.00%	20	13829199	C	N	Passenger	PASSENGER/OTHER					
SPCRP13	missense_variant	TOMM34	p.Leu132Asp	124	92	20.20%	1.10%	20	43580629	A	C	D	Passenger	PASSENGER/OTHER				
SPCRP13	missense_variant	URD1	p.Tyr180Cys	128	84	42.20%	1.60%	21	3375759	T	C	N	Passenger	PASSENGER/OTHER				
SPCRP10	stop_gained	AHC1	p.Lys190*	178	180	33.00%	0.00%	1	2781939	G	A							
SPCRP10	splice_acceptor_variant/intron_variant	GPD2	p.Gln390*	200	160	26.00%	0.00%	2	157425336	G	A	D						
SPCRP10	missense_variant	CRTPA	p.Ala166Thr	34	32	32.40%	0.00%	3	33181860	G	A	D	Passenger	PASSENGER/OTHER	4.12E-05			
SPCRP10	missense_variant	TMPRSS11B	p.Gly368Arg	68	48	25.00%	0.00%	4	69003778	C	T	D	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	SILCA4	p.Asp291Val	165	124	31.50%	0.00%	4	7230367	A	T	D	Passenger	PASSENGER/OTHER				TRUE
SPCRP10	missense_variant	GAU1	p.Gln120Ser	172	154	44.20%	0.00%	4	17416039	A	T	D	Passenger	PASSENGER/OTHER				
SPCRP10	frameshift_variant	PKCIR1	p.Gln455fs	16	34	31.20%	0.00%	5	67595959	TCA	A							TRUE
SPCRP10	missense_variant	DLK2	p.Cys7Tyr	65	63	12.30%	0.00%	6	43422544	C	T	D	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	MUC3A	p.Thi530Ala	51	265	41.20%	4.70%	7	100551007	A	G							0.003414
SPCRP10	frameshift_variant	CFTR	p.Leu1258fs	124	79	24.90%	0.00%	7	117229241	C	CT							
SPCRP10	missense_variant	PW12	p.Met835Leu	106	88	34.90%	0.00%	11	12375998	A	C	D	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	EMC2	p.Asp170Glu	76	60	22.40%	0.00%	8	10948811	C	D	Passenger	PASSENGER/OTHER					
SPCRP10	missense_variant	VPS13A	p.Leu1318Pro	118	102	33.90%	0.00%	9	79917965	T	C	D	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	G1QTNF4	p.Ser232Glu	77	57	6.50%	0.00%	11	47812274	G	A	D	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	TME142B	p.Pro148Ser	106	88	15.10%	0.00%	11	12375998	A	C	D	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	TLN2	p.Ala195Tyr	81	68	43.20%	0.00%	15	6304966	G	A	D	Passenger	PASSENGER/OTHER	5.88E-05			
SPCRP10	missense_variant	IDH2	p.Arg172Gly	129	107	28.90%	0.94%	15	90631839	T	C	D	Driver	CANCER		TRUE	TRUE	TRUE
SPCRP10	missense_variant	STAT3	p.Phe384Leu	112	104	54.00%	0.00%	17	40441653	A	T	D	Passenger	PASSENGER/OTHER		TRUE		
SPCRP10	missense_variant	C3	p.Asn760Asp	139	96	6.50%	0.00%	19	6702558	T	C	N	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	CUL2	p.Asp202Gly	79	62	34.20%	0.00%	19	1963370	G	A	N	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	ZNF524	p.Arg44Tyr	160	128	21.90%	0.78%	19	56113608	C	T	N	Passenger	PASSENGER/OTHER	1.09E-05			
SPCRP10	missense_variant	ZC3H7B	p.Asp493Gly	184	157	40.00%	0.00%	22	41742025	A	G	D	Passenger	PASSENGER/OTHER	4.12E-05			
SPCRP10	missense_variant	NROB1	p.Ile444Thr	119	102	14.30%	0.00%	X	30322778	A	G	D	Passenger	PASSENGER/OTHER				
SPCRP10	missense_variant	CCDC120	p.Ser2AAsn	23	29	21.70%	0.00%	X	48920089	G	A	N	Passenger	PASSENGER/OTHER				TRUE
SPCRP5	missense_variant	MPL	p.Phe105Leu	541	271	46.40%	0.00%	1	4383413	T	C	N	Passenger	PASSENGER/OTHER	0.0001153	TRUE	TRUE	TRUE
SPCRP5	missense_variant	PK3CA	p.Cys420Asp	111	157	24.32%	0.64%	3	17892790	T	C	D	Passenger	CANCER		TRUE	TRUE	TRUE
SPCRP5	missense_variant	ATM	p.Ser49Cys	159	292	49.00%	0.00%	11	10809576	C	G	N	Passenger	CANCER		0.007373	TRUE	TRUE
SPCRP																		