Case Report

Mutation profiles of synchronous colorectal cancers from a patient with Lynch syndrome suggest distinct oncogenic pathways

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Abstract: Patients with Lynch syndrome often present with multiple synchronous or metachronous colorectal cancers (CRCs). The presence of multiple CRCs with distinct genetic profiles and driver mutations could complicate treatment as each cancer may respond differently to therapy. Studies of sporadic CRCs suggested that synchronous tumors have distinct etiologies, but could not rule out differences in genetic background. The presence of multiple cancers in a patient with a predisposing mutation provides an opportunity to profile synchronous cancers in the same genetic background. Here, we describe the case of a patient with Lynch syndrome that presented with six synchronous CRCs. Microsatellite instability (MSI) and genomic profiling indicated that each lesion had a unique pattern of instability and a distinct profile of affected genes. These findings support the idea that in Lynch syndrome, synchronous CRCs can develop in parallel with distinct mutation profiles and that these differences may inform treatment decisions.

Keywords: Colorectal neoplasms; hereditary nonpolyposis; medical oncology; neoplasms; multiple primary; molecular targeted therapy

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Introduction

Due to the high risk of synchronous and metachronous colorectal cancers (CRCs), the recommended treatment for CRC in patients with Lynch syndrome is colectomy (1). However, as the use of targeted therapies increases, including VEGF and EGFR inhibitors, an understanding of the molecular profiles of synchronous CRCs will be crucial in determining the most effective courses of treatment. If synchronous cancers are clonally derived, treatment may be relatively uniform. However, if they are distinct, each with a different oncogenic history, a treatment plan may need to include additional agents or therapeutic regimens.

In unselected patient populations with synchronous or metachronous CRCs, it is thought that different cancerous lesions in the same patient may follow distinct pathways of progression (2-4). Studies of matched synchronous CRCs suggested that exposure to different toxins at various locations within the colon were associated with distinct progression profiles (5,6). However, the effects of genetic background and environmental variation are confounding aspects in studying initiation and progression in sporadic cancers from different patients. Patients with Lynch syndrome frequently present with multiple synchronous or metachronous cancers (1,7,8). The presence of synchronous cancers arising in a single patient with a predisposing genetic mutation presents an opportunity to study the oncogenic pathways that lead to CRC while minimizing the effects of genetic background. In this study, we examined microsatellite instability (MSI) and genomic profiling in synchronous CRCs from a Lynch syndrome patient.

Materials and Methods

Pathology review and DNA extraction

Specimens were formaldehyde fixed, paraffin embedded and hematoxylin and eosin (H&E) stained. Representative sections were reviewed by a pathologist (CS) for histologic subtype, grade, staging and percent tumor burden. Sections

were macrodissected to increase the representation of tumor DNA in the total DNA extracted from the specimen. DNA was isolated following cell lysis and proteinase K treatment using the QiaQuick extraction method (Qiagen, VHilden Germany).

Analysis of microsatellite instability (MSI)

DNA from normal and tumor specimens was amplified using the MSI analysis system version 1.2 (Promega, Madison WI, USA) according to the manufacturer's instructions. Amplicons were detected using capillary electrophoresis on an ABI 3130xl Genetic Analyzer (Life Technologies, Carlsbad CA, USA) and the results were analyzed using GeneMapper V3.7 software (Life Technologies, Carlsbad CA, USA). The presence of instability in two, or more, of the five loci (>30%) was considered MSI-high (MSI-H).

SNaPshot mutation profiling

A SNaPshot single base extension assay was used to assess the mutation status of 62 loci in 7 genes (*AKT1*, *BRAF*, *KRAS*, *NRAS*, *PIK3CA*, *PTEN* and *SMAD4*) associated with CRC prognosis and treatment (9). SNaPshot products were separated using an ABI 3130xl Genetic Analyzer (Life Technologies, Carlsbad CA, USA) and compared to positive and normal controls for interpretation.

Massively parallel DNA sequencing

Multiplex amplicon-based sequencing libraries were prepared using the GeneRead DNA-seq Human Comprehensive Cancer Panel NGHS-501X (Qiagen, Hilden Germany) following the manufacturer's instructions. This panel targets coding and UTR regions of 124 commonly mutated genes in multiple cancer types. Once prepared, libraries were sequenced using a MiSeq 300 cycle V2 reagent kit (Illumina, San Diego CA, USA) with MiSeq Control software V2.3.0.3 and RTA software V1.18.42.0. Variant analysis was performed using the CLCbio genomics workbench (Qiagen, Hilden Germany).

Results

An 81-year-old Egyptian male presented with weight loss, upper quadrant abdominal and rectal pain and blood streaked stools. The medical history was significant for cancer including a tumor of unreported origin removed by a partial small bowel resection in his 50's, renal cell carcinoma removed by nephrectomy in his 60's and prostate cancer treated with implantation of radioactive seeds in his 70's. The family history was also significant for cancer. Two first-degree relatives had colon cancer, 2 first-degree relatives had kidney cancer and a first-degree relative had an unspecified lymph node/head and neck cancer.

After total proctocolectomy, 6 lesions were identified. These included 5 colonic and 1 rectal lesion. Lesion 1 (medullary carcinoma, 5 cm in greatest dimension, T4N0M0) was located in the left colon near to the splenic flexure (*Figure 1A*). Lesion 2 (moderately differentiated invasive adenocarcinoma, 6 cm, T3N0M0) was located in the right colon near to the hepatic flexure (*Figure 1B*). The colon also contained 3 early invasive carcinomas (T1N0M0) arising from tubulovillous adenomas that, from proximal to distal, were 1cm (lesion 3, *Figure 1C*), 1.3 cm (lesion 4) and 1.2 cm (lesion 5). Lesion 6 was identified in the rectum (invasive mucinous adenocarcinoma with clusters of signet ring cells, 6.5 cm, 8 of 15 lymph nodes involved, T3N2bM0) (*Figure 1D*).

MSI was detected in all lesions. However, the character of MSI was different in each (*Figure 2*). Differences included the number of unstable loci and the pattern and extent of instability. Each lesion was also screened for a panel of 62 hot-spot variants in 7 genes related to prognosis and treatment in colon cancer (9). *BRAF* V600E was not detected in any of the lesions (data not shown) suggesting Lynch syndrome rather than sporadic CRC (10). Other identified variants included *KRAS* G12D in lesion 1 and *KRAS* G13D in lesion 6 (data not shown). To identify potential Lynch syndrome-related germline variants, *MLH1*, *MSH2*, *MSH6* and *PMS2* were examined in DNA isolated from peripheral blood. A frameshift variant was detected in *MSH2*, c.2082delT (p.Phe694Leufs*16). This variant was previously reported in patients with CRC and established a diagnosis of Lynch syndrome in this patient (11). Taken together, these findings suggest that each lesion arose from a unique event in a background predisposing to cancer.

To understand better how these cancers developed, sequencing of 124 cancer-related genes was performed. Only lesions 1, 2 and 3 had an adequate amount of high quality DNA for this analysis. The majority of variants (48.7%, 186/382) including substitutions, insertions and deletions were identified in all 3 lesions. In the absence of normal DNA to use for comparison, the common variants are a good estimate of the patient's germline

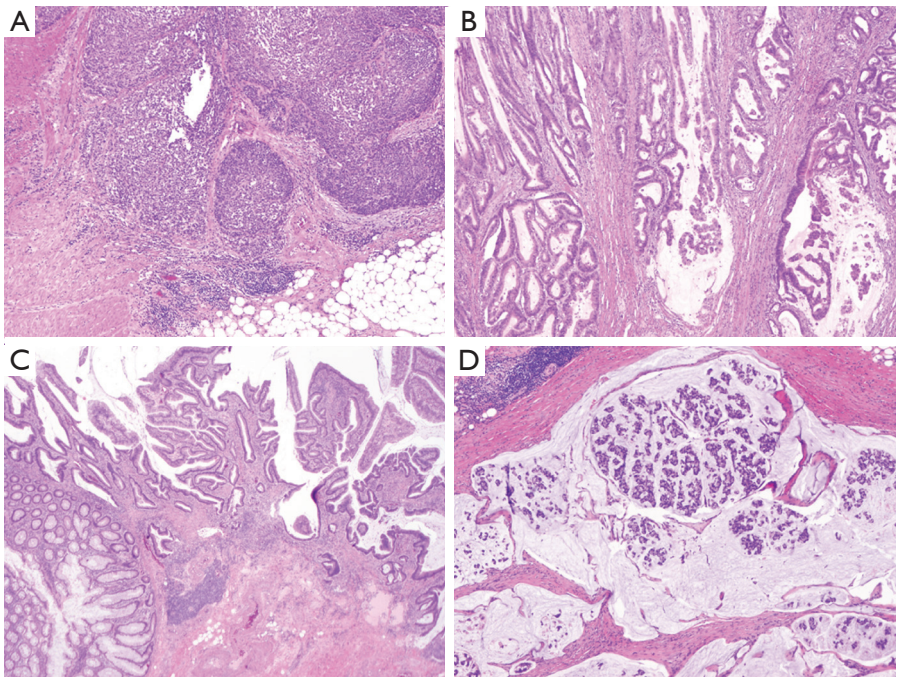

Figure 1 The morphology of synchronous CRCs (H&E, 40×). (A) Lesion 1: left-sided colonic lesion showing poorly differentiated medullary carcinoma (T4N0M0); (B) lesion 2: right-sided colonic lesion showing moderately differentiated invasive adenocarcinoma (T3N0M0); (C) lesion 3: a representative section of one of 3 tubulovillous adenoma with early invasion in the submucosa (T1N0M0); (D) lesion 6 is a rectal lesion consisting of invasive mucinous adenocarcinoma with clusters of signet ring cells (T3N2bM0). CRCs, colorectal cancer.

variation. However, some of these variants may also be hot-spot mutations that occurred independently in each lesion. Germline variants have an expected frequency of approximately 50% (heterozygous) or 100% (homozygous). Of the presumed germline variants identified in the patient's CRCs, 89.2% have a variant frequency that is indicative of a heterozygous (58.6% with a variant frequency of 40–60%) or homozygous (30.6% with a variant frequency of 90–100%) state. Presumed germline variants were found in 61 genes, all with low or moderate impact predictions (*Tables S1*,*S2*). The single high impact variant observed in all lesions was the previously identified c.2082delT in the *MSH2* gene.

To determine the lesion-specific variants, the presumed germline variants were subtracted from each lesion. After subtraction, the percent of variants in each lesion that met the criteria for homozygous or heterozygous state was drastically reduced: 8.1% in lesion 1, 11.8% in lesion 2 and 2.2% in lesion 3. These values are significantly different from the values in the presumed germline variation suggesting that the majority of variants ascribed to the lesions are the result of somatic mutation. Respectively, lesions 1, 2 and 3 had 96, 74 and 46 somatic variants with similar distributions of types (*Table 1*). To compare the mutational landscape between lesions, similarities and differences in affected genes were examined (*Figure 3*, *Table 2*). All 3 lesions had somatic variants in two genes, *SMARCA4* and *ALK*. For *SMARCA4*, each lesion contained distinct high impact variants: lesion 1 had a non-synonymous coding variant, lesion 2 had a frameshift and lesion 3 had two distinct non-synonymous coding variants. In *ALK*, lesion 2 contained a C-terminal deletion while lesions 1 and 3 contained the same N-terminal deletion. These data suggest an important role for loss of function of these genes in the development of these lesions. Additionally, as expected, all 3 lesions had different combinations of variants in WNT pathway genes including *APC*, *ARID1A*, *CTNNB1*, and *FBXW7*.

There were also significant differences between the lesions. Thirteen genes had variants in 2 lesions and 34 genes had variants in only a single lesion indicating significant differences between lesions. Lesion 1 had variants in 18 unique genes involved in Notch, RAS, and NF2 signaling (*Table 2*). In addition, a variant in *MSH2*

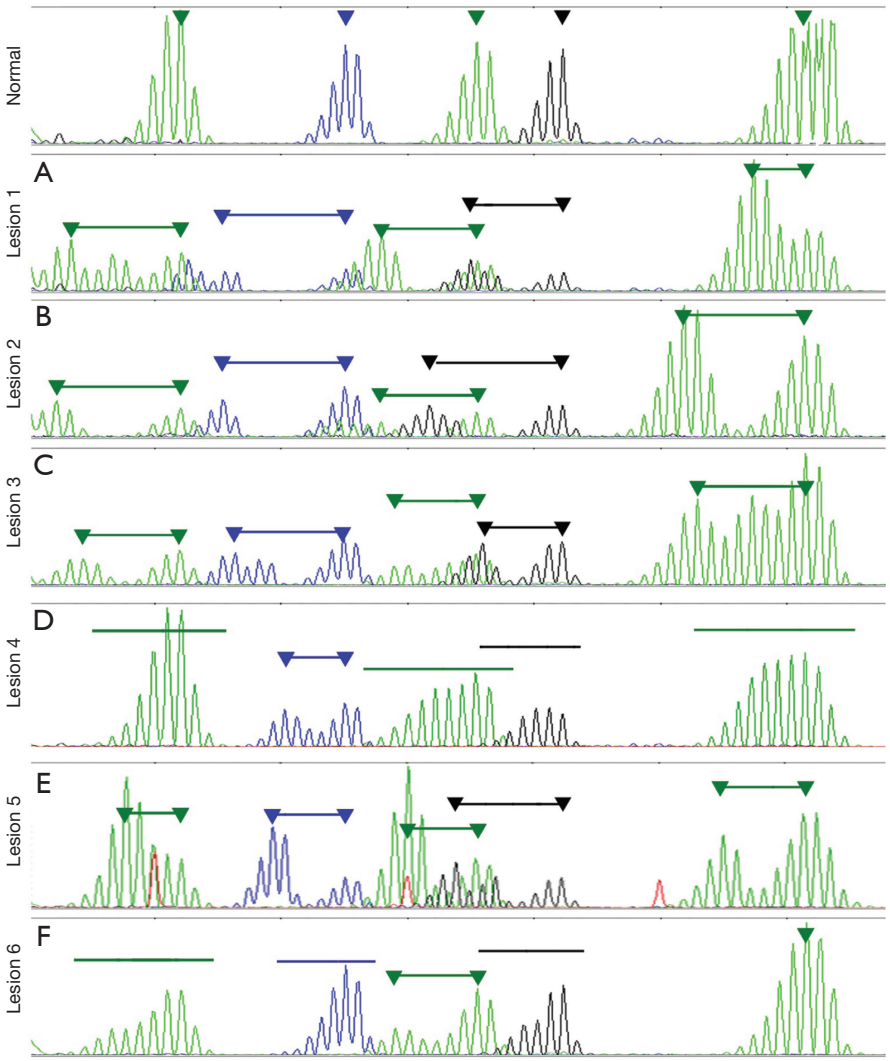

Figure 2 MSI patterns. Each lesion showed an MSI-H phenotype with a unique pattern of peaks indicating differences in repeat number or deletion size for each locus. Arrowheads connected by a bar indicate the size difference between the highest peak in the spread for the normal and the instability alleles for each locus. Bars without arrowheads indicate larger spreads of peaks that are considered instability alleles, but do not have an obvious second allele size. Lesions 1-6, show instability at all 5 loci compared to the normal. MSI, microsatellite instability; MSI-H, MSI-high.

Table 1 Identified variants by location and predicted effect

Variant type	Germline	Lesion 1	Lesion 2	Lesion 3
Frameshift	0.5% (1/186)	7.3% (7/96)	10.8% (8/74)	6.5% (3/46)
Non-synonymous coding	16.7% (31/186)	29.2% (28/96)	23.8% (25/74)	32.6% (15/46)
Splice site	0.0% (0/186)	3.1% (3/96)	0.0% (0/74)	0.0% (0/46)
Stop codon gained	0.0% (0/186)	0.0% (0/96)	2.7% (2/74)	0.0% (0/46)
Intron	38.7% (72/186)	43.8% (42/96)	33.8% (25/74)	37.0% (17/46)
Synonymous coding	37.6% (70/186)	13.5% (13/96)	17.6% (13/74)	17.4% (8/46)
Upstream	1.1% (2/186)	0.0% (0/96)	0.0% (0/74)	2.2% (1/46)
UTR	5.4% (10/186)	3.1% (3/96)	1.4% (1/74)	4.3% (2/46)
Total	186	96	74	46

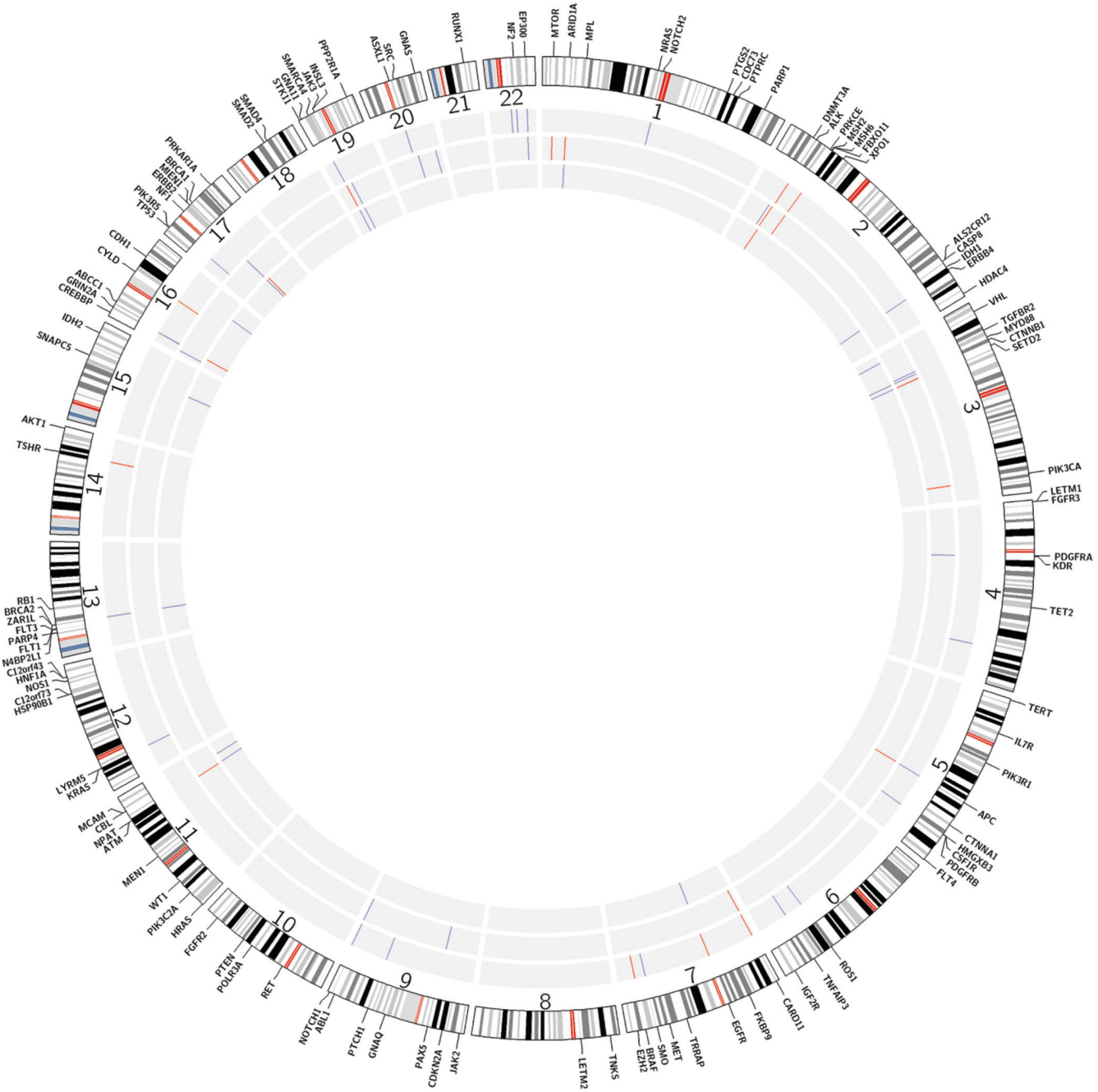

Figure 3 Comparison of variants by lesion. The outer wheel of this Circos plot depicts each chromosome with sequenced genes labeled. The inner wheels depict the variants identified in lesion 1 (outermost of inner wheels), lesion 2 (middle) and lesion 3 (innermost). Colored lines in the inner wheels indicate variants identified in the corresponding gene. Colors indicate high (red) and moderate (blue) predicted effect on gene function as categorized by SnpEff (12).

Table 2 Genes in each lesion with at least one identified variant

Lesion 1	Lesion 2	Lesion 3
ALK	ALK	ALK
AMER1	x	x
APC	APC	x
x	ARID1A	ARID1A
ASXL1	x	x
x	ATM	ATM
BRAF	x	x
x	x	BRCA1
BRCA2	x	BRCA2
CARD11	CARD11	x
x	x	CBL
x	x	CDH1
x	CREBBP	x
CSF1R	x	x
x	CTNNB1	CTNNB1
CYLD	x	x
x	DNMT3A	x
EGFR	x	EGFR
EP300	x	x
x	ERBB2	x
ERBB4	x	ERBB4
FBXW7	x	x
x	GNAS	x
GRIN2A	x	GRIN2A
x	JAK3	x
x	KIT	x
KRAS	x	x
x	x	MAP2K1
MAP2K4	x	x
MET	x	x
MSH2	x	x
x	MSH6	x
x	MTOR	x
x	MYD88	x
NF2	x	x
NOTCH1	NOTCH1	x
NOTCH2		x
PAX5	PAX5	x
x	PIK3CA	x
PTCH1	x	x
ROS1	x	x
x	SETD2	SETD2
SMARCA4	SMARCA4	SMARCA4
SMARCB1	x	x
SMO	x	x
x	SRC	x
TNFAIP3	x	x
TSHR	x	TSHR
x	x	VHL

(c.2634+1G>A) is described as pathogenic in ClinVar because it interrupts a canonical splice site and is likely the second MSH2 inactivating event (13). Lesion 2 had variants in 11 unique genes involved in the EGFR, KIT, MTOR and SRC signaling pathways and transcriptional regulation (*CREBBP*, *DNMT3A*, *MYD88*, *PAX5*) (*Table 2*). Of note, a frameshift mutation was identified in *MSH6* (c.3205delG, p.G1070fs*9). Heterozygosity of both partners in the MSH2/MSH6 heterodimer may result in reduced function. Lesion 3 was the least advanced of the cancers studied (T1N0M0) and had the smallest number genes containing variants. Identified variants did not correspond to obvious signaling molecules, but were present in genes involved in DNA repair, gene expression and proteasome function. These data, like the MSI data, indicate distinct oncogenic histories for each lesion.

Discussion

The presence of multiple synchronous cancers in this patient allowed for a unique analysis of genetic diversity among CRCs without the confounding effects of genetic background. Taken together, these results provide a diverse picture of colon carcinogenesis with distinct histology, MSI patterns and gene mutation profiles.

Two genes had variants identified in all 3 sequenced lesions. Both SMARCA4 and ALK are involved in other cancer types, but neither was identified at significant levels in the survey of CRCs performed by The Cancer Genome Atlas (14). *SMARCA4* encodes a subunit of the SWI/SNF complex and mutations could alter transcriptional regulation through that mechanism (15). Outside of childhood neuroblastoma, ALK mutations have not been widely identified, although ALK fusions are involved in the development of multiple cancer types (16). It is possible that the development of variants in these genes is unique to this patient or to patients with Lynch syndrome. Comprehensive DNA sequencing studies of cancers in patients with Lynch syndrome are needed to identify genes that may be particularly susceptible to mutation in this patient population.

The analysis of MSI is usually focused on the interpretation: stable, low or high. However, when studying the relatedness of cancerous lesions, the pattern of errors observed can act as a genetic fingerprint. This is because MSI assesses the accumulation of replication errors during the clonal expansion of cancer cells. Therefore, independent cancers should have different patterns of errors owing to their unique oncogenic

history and the randomness of the errors. In this study, each synchronous lesion had a distinct pattern of errors indicating distinct oncogenic histories. The genetic differences implied by the MSI analyses were observed in the SNaPshot and sequencing data as each lesion had a unique set of variants affecting a unique set of genes. Therefore, it may be possible to use MSI analysis as a screening tool to determine the relatedness of synchronous of metastatic lesions.

It is estimated that approximately 4% of unselected patients presenting with CRCs have a synchronous cancer and the 5-year survival rate for both synchronous and single lesion CRC was approximately 50% (17,18). These studies, while comprehensive, examined data from patients collected up until 2004 prior to the wide-spread use of targeted agents in CRC therapy. Targeted therapies have shown positive effects on progression free and overall survival, but the presence of multiple cancers complicates the choice of targeted therapies (19). In the current study, 2 of 6 lesions harbored activating KRAS mutations and all 3 sequenced lesions had either EGFR, ERBB2 or ERBB4 variants identified. EGFR antibody therapy is unlikely to be effective for the lesions with KRAS mutations and the variants in ERBB2 and ERBB4 may affect the efficiency of agents targeted to those molecules. These findings suggest that for patients with synchronous cancers, surgical resection may still be the best option as each tumor can have a different response to targeted agents. Further, when targeted therapies are considered, multiple lesions should be profiled, to reveal the complexity of disease and to optimize treatment.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Table S1 Identified somatic variants

Variables	Chrom	Pos GRCh37	Confidence	Ref	Variant	Gene name	Variant type	Transcript ID	Codon change	AA change	Filtered coverage	Allele coverage	Allele frequency	Variant frequency	P value	SNPEff effect	SNPEff impact	Filter	SIFT score	Interpro domain	UniProt	PolyPhen score	COSMIC sample count	Somatic mutation assay	Variant clinical significance
Lesion 1	chr1	11167007	Higher	C	A	*MTOR*	SNP	NM_004958.3			2491	C =1752 A =735	C =0.703 A =0.295	0.295	0.00001	Utr_3_prime	Modifier	Utr_3_prime	0.18						N/A
Lesion 1	chr1	11259520	Higher	A	C	*MTOR*	SNP	NM_004958.3			929	A =838 C =91	A =0.902 C =0.098	0.098	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr1	120459166	Higher	C	T	*NOTCH2*	SNP	NM_024408.3	c.6179G > A	p.R2060H	671	C =604 T =67	C =0.9 T =0.1	0.1	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.04	Ankyrin_repeat-containing_domain_(3),	Q04721	0.451			N/A
Lesion 1	chr1	120465437	Higher	A	ATCTCGG	*NOTCH2*	INS	NM_024408.3			207	A =55 ATCTCGG =140	A =0.266 ATCTCGG =0.676	0.676	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr2	29446184	Higher	C	G	*ALK*	SNP	NM_004304.4			44	C =16 G =28	C =0.364 G =0.636	0.636	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr2	30143051	Higher	CG	C	*ALK*	DEL	NM_004304.4		p.-158	300	CG =225 C =75	CG =0.75 C =0.25	0.25	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 1	chr2	47708011	Higher	G	A	*MSH2*	SNP	NM_001258281.1			30	G =10 A =20	G =0.333 A =0.667	0.667	0.00001	Splice_site_donor	High	Utr_3_prime							N/A
Lesion 1	chr2	48032740	Higher	ATT	A,AT	*MSH6*	DEL	NM_000179.2			236	ATT =0 A =23 AT =71	ATT =0.0 A =0.097 AT =0.301	0.301	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr2	48033551	Higher	C	G	*MSH6*	SNP	NM_000179.2			30	C =12 G =18	C =0.4 G =0.6	0.6	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr2	212543924	Higher	A	G	*ERBB4*	SNP	NM_005235.2			136	A =57 G =79	A =0.419 G =0.581	0.581	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr2	212578379	Higher	TAAAA	T	*ERBB4*	DEL	NM_005235.2			58	TAAAA =22 T =18	TAAAA =0.379 T =0.31	0.31	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr2	212587202	Higher	C	T	*ERBB4*	SNP	NM_005235.2	c.799G > A	p.V267I	258	C =169 T =88	C =0.655 T =0.341	0.341	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.57	Growth_factor,_receptor_(1),Furin-like_cysteine-rich_domain_(1),	Q15303-4,Q15303-2,Q53QS8,Q15303-3,Q15303	0.008,0.013,0.016,0.008,0.016			N/A
Lesion 1	chr2	212989680	Higher	C	T	*ERBB4*	SNP	NM_005235.2			173	C =140 T =33	C =0.809 T =0.191	0.191	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr3	37070427	Higher	C	T	*MLH1*	SNP	NM_001258274.1			629	C =438 T =191	C =0.696 T =0.304	0.304	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr3	37089021	Higher	G	A	*MLH1*	SNP	NM_001258271.1	c.1743G > A	p.P581	537	G =410 A =127	G =0.764 A =0.236	0.236	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chr3	178921639	Higher	C	A	*PIK3CA*	SNP	NM_006218.2			26	C =6 A =20	C =0.231 A =0.769	0.769	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr4	1807894	Higher	G	A	*FGFR3*	SNP	NM_001163213.1	c.1959G > A	p.T653	94	G =0 A =94	G =0.0 A =1.0	1	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chr4	153268158	Higher	C	T	*FBXW7*	SNP	NM_001013415.1	c.296G > A	p.G99D	2412	C =1732 T =678	C =0.718 T =0.281	0.281	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.11		B7Z2C8,Q969H0,Q969H0-4,Q969H0-2	0.01,0.145,0.003,0.787			N/A
Lesion 1	chr5	1280477	Higher	G	A	*TERT*	SNP	NM_198253.2			402	G =1 A =401	G =0.002 A =0.998	0.998	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr5	35873563	Higher	A	ATACATTG	*IL7R*	INS	NM_002185.3			25	A =8 ATACATTG =17	A =0.32 ATACATTG =0.68	0.68	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr5	67576330	Higher	CTTTT	C	*PIK3R1*	DEL	NM_181523.2			76	CTTTT =26 C =27	CTTTT =0.342 C =0.355	0.355	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr5	112178805	Higher	G	A	*APC*	SNP	NM_001127510.2	c.7514G > A	p.R2505Q	499	G =348 A =150	G =0.697 A =0.301	0.301	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime		Adenomatous_polyposis_coli_protein_basic_domain_(1),	Q4LE70,P25054	0.961,0.961			N/A
Lesion 1	chr5	149435631	Higher	C	T	*CSF1R*	SNP	NM_005211.3	c.2512G > A	p.V838I	811	C =746 T =64	C =0.92 T =0.079	0.079	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.01	Serine-threonine/tyrosine-protein_kinase_(1),Protein_kinase-like_domain_(1),Tyrosine-protein_kinase,_catalytic_domain_(1),Protein_kinase,_catalytic_domain_(1),	P07333	0.476	1		N/A
Lesion 1	chr6	117686421	Higher	T	C	*ROS1*	SNP	NM_002944.2			33	T =24 C =9	T =0.727 C =0.273	0.273	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr6	117686943	Higher	A	T	*ROS1*	SNP	NM_002944.2			36	A =15 T =21	A =0.417 T =0.583	0.583	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr6	117714346	Higher	C	G	*ROS1*	SNP	NM_002944.2			24	C =12 G =12	C =0.5 G =0.5	0.5	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr6	117714448	Higher	C	T	*ROS1*	SNP	NM_002944.2	c.1201G > A	p.E401K	1002	C =720 T =280	C =0.719 T =0.279	0.279	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.23		P08922	0.005			N/A
Lesion 1	chr6	138202346	Higher	G	A	*TNFAIP3*	SNP	NM_006290.3	c.2263G > A	p.E755K	164	G =118 A =46	G =0.72 A =0.28	0.28	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.26		P21580	0.008			N/A
Lesion 1	chr7	2968322	Higher	CG	C	*CARD11*	DEL	NM_032415.4		p.-555	2174	CG =1607 C =551	CG =0.739 C =0.253	0.253	0.00001	Frame_shift	High	Utr_3_prime					5		N/A
Lesion 1	chr7	2984084	Higher	C	T	*CARD11*	SNP	NM_032415.4	c.446G > A	p.R149H	1539	C =1200 T =338	C =0.78 T =0.22	0.22	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.17		Q9BXL7	0.006			N/A
Lesion 1	chr7	55228053	Higher	A	T	*EGFR*	SNP	NM_201284.1			40	A =0 T =40	A =0.0 T =1.0	1	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr7	55268879	Higher	AG	A	*EGFR*	DEL	NM_005228.3			2496	AG =1955 A =541	AG =0.783 A =0.217	0.217	0.00001	Splice_site_acceptor	High	Utr_3_prime							N/A
Lesion 1	chr7	128850274	Higher	C	A	*SMO*	SNP	NM_005631.4	c.1537C > A	p.P513T	529	C =373 A =155	C =0.705 A =0.293	0.293	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0		A4D1K5,Q99835	0.999,0.999			N/A
Lesion 1	chr7	140434620	Higher	A	AAAG	*BRAF*	INS	NM_004333.4			792	A =398 AAAG =238	A =0.503 AAAG =0.301	0.301	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr7	140500283	Higher	T	C	*BRAF*	SNP	NM_004333.4			363	T =253 C =110	T =0.697 C =0.303	0.303	0.00001	Splice_site_acceptor	High	Utr_3_prime							N/A
Lesion 1	chr9	21971220	Higher	A	G	*CDKN2A*	SNP	NM_058197.4			25	A =15 G =4	A =0.6 G =0.16	0.16	0.00098	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr9	36840623	Higher	G	A	*PAX5*	SNP	NM_016734.1	c.1110C > T	p.Y370	393	G =0 A =393	G =0.0 A =1.0	1	0.00001	Synonymous_coding	Low	Utr_3_prime	0.07		E7ERW5,E7EQT0	0.0,0.001			N/A
Lesion 1	chr9	80343587	Higher	GAAAA	G	*GNAQ*	DEL	NM_002072.3			24	GAAAA =15 G =8	GAAAA =0.625 G =0.333	0.333	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr9	98231165	Higher	G	C	*PTCH1*	SNP	NM_000264.3	c.2118C > G	p.S706R	22	G =16 C =6	G =0.727 C =0.273	0.273	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.27		Q13635-4,Q13635-3,Q13635-2,Q13635	0.474,0.394,0.495,0.016			N/A
Lesion 1	chr9	98231322	Higher	G	A	*PTCH1*	SNP	NM_000264.3	c.1961C > T	p.T654M	2472	G =1763 A =708	G =0.713 A =0.286	0.286	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.02		Q13635-4,Q13635-3,Q13635-2,Q13635	0.991,0.983,0.978,0.98			N/A
Lesion 1	chr9	133738320	Higher	G	A	*ABL1*	SNP	NM_007313.2	c.777G > A	p.T259	2498	G =1691 A =805	G =0.677 A =0.322	0.322	0.00001	Synonymous_coding	Low	Utr_3_prime	0						N/A
Lesion 1	chr9	133759792	Higher	C	T	*ABL1*	SNP	NM_007313.2	c.2172C > T	p.G724	51	C =34 T =17	C =0.667 T =0.333	0.333	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chr9	139391898	Higher	C	T	*NOTCH1*	SNP	NM_017617.3	c.6293G > A	p.R2098H	68	C =44 T =24	C =0.647 T =0.353	0.353	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0	Ankyrin_repeat-containing_domain_(3),	P46531	0.939			N/A
Lesion 1	chr9	139397682	Higher	C	T	*NOTCH1*	SNP	NM_017617.3	c.5119G > A	p.A1707T	44	C =34 T =10	C =0.773 T =0.227	0.227	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.07	Notch,_NODP_domain_(1),	P46531	0.959			N/A
Lesion 1	chr9	139407932	Higher	A	G	*NOTCH1*	SNP	NM_017617.3	c.2265T > C	p.N755	2481	A =1147 G =1333	A =0.462 G =0.537	0.537	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chr9	139410209	Higher	G	GAGAAC	*NOTCH1*	INS	NM_017617.3			53	G =2 GAGAAC =18	G =0.038 GAGAAC =0.34	0.34	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr9	139411880	Higher	G	A	*NOTCH1*	SNP	NM_017617.3			73	G =26 A =47	G =0.356 A =0.644	0.644	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr11	108213912	Higher	CT	C	*ATM*	DEL	NM_000051.3			342	CT =256 C =86	CT =0.749 C =0.251	0.251	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr12	25398284	Higher	C	T	*KRAS*	SNP	NM_004985.3	c.35G > A	p.G12D	950	C =679 T =271	C =0.715 T =0.285	0.285	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0	Small_GTP-binding_protein_domain_(1),	P01116-2,P01116	0.257,0.361	10487		N/A
Lesion 1	chr13	32900363	Higher	CT	C	*BRCA2*	DEL	NM_000059.3			399	CT =272 C =109	CT =0.682 C =0.273	0.273	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr13	32906652	Higher	A	C	*BRCA2*	SNP	NM_000059.3	c.1037A > C	p.N346T	40	A =26 C =14	A =0.65 C =0.35	0.35	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.2		P51587,A1YBP1	0.001,0.01			N/A
Lesion 1	chr13	32912050	Higher	T	A	*BRCA2*	SNP	NM_000059.3	c.3558T > A	p.V1186	123	T =105 A =18	T =0.854 A =0.146	0.146	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chr13	32915005	Higher	G	C	*BRCA2*	SNP	NM_000059.3	c.6513G > C	p.V2171	200	G =0 C =200	G =0.0 C =1.0	1	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chr14	81422039	Higher	C	CT	*TSHR*	INS	NM_001142626.2		p.-6?	2255	C =1358 CT =894	C =0.602 CT =0.396	0.396	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 1	chr14	81609696	Higher	A	AGAGGTCTACAG	*TSHR*	INS	NM_000369.2		p.-432EVY?	27	A =10 AGAGGTCTACAG =16	A =0.37 AGAGGTCTACAG =0.593	0.593	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 1	chr14	81609728	Higher	C	T	*TSHR*	SNP	NM_000369.2	c.1326C > T	p.S442	1670	C =1196 T =471	C =0.716 T =0.282	0.282	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chr15	90628215	Higher	C	CATGT	*IDH2*	INS	NM_002168.2			38	C =17 CATGT =21	C =0.447 CATGT =0.553	0.553	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr16	3808052	Higher	TAAA	T,TAA	*CREBBP*	DEL	NM_004380.2			160	TAAA =0 T =6 TAA =36	TAAA =0.0 T =0.037 TAA =0.225	0.225	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr16	9857680	Higher	G	A	*GRIN2A*	SNP	NM_001134408.1	c.3721C > T	p.R1241W	454	G =315 A =139	G =0.694 A =0.306	0.306	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime		Glutamate_[NMDA]_receptor,_epsilon_subunit,_C-terminal_(1),	F5GZ52,Q17RZ6,Q12879	0.944,0.967,0.96			N/A
Lesion 1	chr16	9916303	Higher	A	AAG	*GRIN2A*	INS	NM_001134408.1			1220	A =590 AAG =619	A =0.484 AAG =0.507	0.507	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr16	10032075	Higher	C	T	*GRIN2A*	SNP	NM_000833.3	c.748G > A	p.G250R	1854	C =1334 T =520	C =0.72 T =0.28	0.28	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime		Extracellular_ligand-binding_receptor_(1),	F5GZ52,Q17RZ6,Q12879	0.933,0.978,1.0	1		N/A
Lesion 1	chr16	50813646	Higher	G	GTTTA	*CYLD*	INS	NM_015247.2		p.-404F?	25	G =6 GTTTA =19	G =0.24 GTTTA =0.76	0.76	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 1	chr17	12028656	Higher	C	T	*MAP2K4*	SNP	NM_003010.2	c.859C > T	p.R287C	332	C =219 T =111	C =0.66 T =0.334	0.334	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0	Serine/threonine-protein_kinase-like_domain_(1),Serine/threonine-protein_kinase,_catalytic__domain_(1),Protein_kinase-like_domain_(1),Protein_kinase,_catalytic_domain_(1),	B7ZA62,P45985-2,P45985	1.0,0.979,0.988			N/A
Lesion 1	chr17	41231419	Higher	G	A	*BRCA1*	SNP	NR_027676.1			2461	G =2181 A =280	G =0.886 A =0.114	0.114	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr17	41231432	Higher	A	T	*BRCA1*	SNP	NR_027676.1			2143	A =1901 T =242	A =0.887 T =0.113	0.113	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr17	41267834	Higher	G	GTCATAACA	*BRCA1*	INS	NR_027676.1			28	G =20 GTCATAACA =8	G =0.714 GTCATAACA =0.286	0.286	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr17	66526385	Higher	A	ACAC	*PRKAR1A*	INS	NM_212472.2			35	A =0 ACAC =35	A =0.0 ACAC =1.0	1	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr17	66526387	Higher	T	TTCAAATC	*PRKAR1A*	INS	NM_212472.2			35	T =0 TTCAAATC =35	T =0.0 TTCAAATC =1.0	1	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr17	66526400	Higher	C	CACGTTCAA	*PRKAR1A*	INS	NM_212472.2			61	C =39 CACGTTCAA =22	C =0.639 CACGTTCAA =0.361	0.361	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr19	11136215	Higher	C	G	*SMARCA4*	SNP	NM_003072.3			82	C =37 G =45	C =0.451 G =0.549	0.549	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr19	11144816	Higher	C	T	*SMARCA4*	SNP	NM_003072.3	c.3891C > T	p.P1297	1279	C =908 T =368	C =0.71 T =0.288	0.288	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chr19	11172481	Higher	G	A	*SMARCA4*	SNP	NM_001128849.1	c.5029G > A	p.E1677K	2487	G =1753 A =734	G =0.705 A =0.295	0.295	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.24		B1A8Z6,B1A8Z4,B1A8Z7,Q9HBD4,B1A8Z5,P51532	0.028,0.028,0.028,0.028,0.028,0.028			N/A
Lesion 1	chr20	31017710	Higher	C	T	*ASXL1*	SNP	NM_015338.5	c.572C > T	p.S191L	987	C =646 T =339	C =0.655 T =0.343	0.343	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.16		Q8IXJ9	0.964			N/A
Lesion 1	chr22	24145583	Higher	G	A	*SMARCB1*	SNP	NM_003073.3	c.602G > A	p.R201Q	1267	G =890 A =376	G =0.702 A =0.297	0.297	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.04		G5E975,Q17S11,Q12824	0.404,0.905,0.53			N/A
Lesion 1	chr22	30074260	Higher	G	A	*NF2*	SNP	NM_181832.2	c.1522G > A	p.D508N	1828	G =1290 A =537	G =0.706 A =0.294	0.294	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime		Moesin_(1),Ezrin/radixin/moesin,_C-terminal_(1),	B7Z4B6,P35240-8,P35240-5,P35240,P35240-2,P35240-6,P35240-4,P35240-3	0.73,0.453,0.531,0.73,0.721,0.819,0.862,0.894			N/A
Lesion 1	chr22	30077541	Higher	A	T	*NF2*	SNP	NM_181832.2	c.1688A > T	p.N563I	117	A =107 T =10	A =0.915 T =0.085	0.085	0.00011	Non_synonymous_coding	Moderate	Utr_3_prime		Moesin_(1),Ezrin/radixin/moesin,_C-terminal_(1),	B7Z4B6,P35240-8,P35240-5,P35240,P35240-2,P35240-6,P35240-4,P35240-3	0.866,0.554,0.653,0.812,0.812,0.701,0.531,0.72			N/A
Lesion 1	chr22	41537234	Higher	G	T	*EP300*	SNP	NM_001429.3			26	G =0 T =26	G =0.0 T =1.0	1	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chr22	41573200	Higher	C	T	*EP300*	SNP	NM_001429.3	c.5485C > T	p.R1829C	803	C =570 T =230	C =0.71 T =0.286	0.286	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0		Q09472	0.028	2		N/A
Lesion 1	chrX	44938563	Higher	G	A	*KDM6A*	SNP	NM_021140.2	c.3111G > A	p.Q1037	40	G =0 A =40	G =0.0 A =1.0	1	0.00001	Synonymous_coding	Low	Utr_3_prime					1		N/A
Lesion 1	chrX	44949951	Higher	GTT	G	*KDM6A*	DEL	NM_021140.2			138	GTT =56 G =76	GTT =0.406 G =0.551	0.551	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chrX	48650639	Higher	CA	C	*GATA1*	DEL	NM_002049.3			402	CA =132 C =194	CA =0.328 C =0.483	0.483	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 1	chrX	63410536	Higher	G	T	*AMER1*	SNP	NM_152424.3	c.2631C > A	p.G877	93	G =78 T =14	G =0.839 T =0.151	0.151	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 1	chrX	63412937	Higher	C	T	*AMER1*	SNP	NM_152424.3	c.230G > A	p.R77Q	554	C =225 T =328	C =0.406 T =0.592	0.592	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.01		Q5JTC6	0.998			N/A
Lesion 1	chr1	120465428	Lower	G	A	*NOTCH2*	SNP	NM_024408.3			250	G =129 A =116	G =0.516 A =0.464	0.464	0.00084	Intron	Modifier	Hap_Score_More_Than_200							N/A
Lesion 1	chr2	25457094	Lower	T	A	*DNMT3A*	SNP	NM_175629.2			687	T =623 A =61	T =0.907 A =0.089	0.089	0.00001	Utr_3_prime	Modifier	Fs_More_Than_60							N/A
Lesion 1	chr4	55124928	Lower	C	CAAGGAACT	*PDGFRA*	INS	NM_006206.4			362	C =256 CAAGGAACT =106	C =0.707 CAAGGAACT =0.293	0.293	0.00001	Utr_5_prime	Modifier	Fs_More_Than_200							N/A
Lesion 1	chr7	116399473	Lower	A	AGGTTCTTT	*MET*	INS	NM_001127500.1		p.-783GS?	565	A =447 AGGTTCTTT =118	A =0.791 AGGTTCTTT =0.209	0.209	0.00001	Frame_shift	High	Fs_More_Than_200							N/A
Lesion 1	chr7	116411586	Lower	A	ACCCAAGT	*MET*	INS	NM_001127500.1		p.-940PK?	363	A =258 ACCCAAGT =105	A =0.711 ACCCAAGT =0.289	0.289	0.00001	Frame_shift	High	Fs_More_Than_200							N/A
Lesion 1	chr9	36966572	Lower	T	G	*PAX5*	SNP	NM_016734.1	c.754A > C	p.T252P	462	T =142 G =316	T =0.307 G =0.684	0.684	0.00001	Non_synonymous_coding	Moderate	Hap_Score_More_Than_200	0.01		C0KTF8,C0KTF7,C0KTF9,C0KTF6,C0KTE2,E7ERW5,E7EQT0,Q6S730,Q6S731,Q02548	0.146,0.001,0.818,0.202,0.719,0.005,0.493,0.202,0.207,0.202			N/A
Lesion 1	chr9	36966581	Lower	T	G	*PAX5*	SNP	NM_016734.1	c.745A > C	p.I249L	435	T =372 G =27	T =0.855 G =0.062	0.062	0.00001	Non_synonymous_coding	Moderate	Hap_Score_More_Than_200	0.05		C0KTF8,C0KTF7,C0KTF9,C0KTF6,C0KTE2,E7ERW5,E7EQT0,Q6S730,Q6S731,Q02548	0.0,0.003,0.209,0.001,0.801,0.044,0.109,0.001,0.456,0.456			N/A
Lesion 1	chr9	36966584	Lower	C	G	*PAX5*	SNP	NM_016734.1	c.742G > C	p.D248H	409	C =322 G =17	C =0.787 G =0.042	0.042	0.00001	Non_synonymous_coding	Moderate	Hap_Score_More_Than_200	0		C0KTF8,C0KTF7,C0KTF9,C0KTF6,C0KTE2,E7ERW5,E7EQT0,Q6S730,Q6S731,Q02548	0.667,0.452,0.998,0.667,0.998,0.832,0.923,0.667,0.99,0.667			N/A
Lesion 1	chr16	9857291	Lower	G	T	*GRIN2A*	SNP	NM_001134407.1	c.4110C > A	p.S1370	917	G =844 T =72	G =0.92 T =0.079	0.079	0.00001	Synonymous_Coding	Low	Fs_More_Than_60							N/A
Lesion 1	chr16	9916338	Lower	G	T	*GRIN2A*	SNP	NM_001134408.1			875	G =614 T =260	G =0.702 T =0.297	0.297	0.00001	Intron	Modifier	Fs_More_Than_60							N/A
Lesion 1	chr16	9916340	Lower	G	T	*GRIN2A*	SNP	NM_001134408.1			873	G =613 T =259	G =0.702 T =0.297	0.297	0.00001	Intron	Modifier	Fs_More_Than_60							N/A
Lesion 1	chr17	7573019	Lower	C	G	*TP53*	SNP	NM_001126118.1			286	C =175 G =40	C =0.612 G =0.14	0.14	0.00001	Intron	Modifier	Hap_Score_More_Than_200							N/A
Lesion 1	chr17	7573025	Lower	C	A	*TP53*	SNP	NM_001126118.1			272	C =178 A =42	C =0.654 A =0.154	0.154	0.00017	Intron	Modifier	Hap_Score_More_Than_200							N/A
Lesion 2	chr1	11294234	Higher	CG	C	*MTOR*	DEL	NM_004958.3		p.-766	1066	CG =794 C =272	CG =0.745 C =0.255	0.255	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 2	chr1	27059206	Higher	G	GC	*ARID1A*	INS	NM_139135.2		p.-615?	1087	G =776 GC =311	G =0.714 GC =0.286	0.286	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 2	chr1	27101219	Higher	C	T	*ARID1A*	SNP	NM_006015.4	c.4501C > T	p.R1501C	527	C =470 T =56	C =0.892 T =0.106	0.106	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.02		O14497-3,O14497,Q4LE49	0.917,0.952,0.828			N/A
Lesion 2	chr2	25463523	Higher	C	T	*DNMT3A*	SNP	NM_175629.2	c.2159G > A	p.R720H	63	C =33 T =30	C =0.524 T =0.476	0.476	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.02		Q9Y6K1,E9PEB8	0.433,0.005			N/A
Lesion 2	chr2	25470497	Higher	C	T	*DNMT3A*	SNP	NM_153759.3	c.410G > A	p.R137H	473	C =354 T =119	C =0.748 T =0.252	0.252	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.1	PWWP_(3),	Q9Y6K1,E9PEB8	0.976,1.0	1		N/A
Lesion 2	chr2	29419591	Higher	G	T	*ALK*	SNP	NM_004304.4			36	G =20 T =16	G =0.556 T =0.444	0.444	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr2	29443611	Higher	TC	T	*ALK*	DEL	NM_004304.4		p.-1202	145	TC =97 T =48	TC =0.669 T =0.331	0.331	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 2	chr2	48030590	Higher	AG	A	*MSH6*	DEL	NM_000179.2		p.-1069	549	AG =377 A =172	AG =0.687 A =0.313	0.313	0.00001	Frame_shift	High	Utr_3_prime					1		N/A
Lesion 2	chr2	48032740	Higher	ATTTT	A	*MSH6*	DEL	NM_000179.2			219	ATTTT =67 A =50	ATTTT =0.306 A =0.228	0.228	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr2	48033551	Higher	C	G	*MSH6*	SNP	NM_000179.2			20	C =10 G =10	C =0.5 G =0.5	0.5	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr3	38181460	Higher	C	T	*MYD88*	SNP	NM_002468.4	c.473C > T	p.A158V	1286	C =938 T =346	C =0.729 T =0.269	0.269	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.51		B4DQ72,Q99836,B4DU08,B4E3D6	0.065,0.001,0.025,0.001			N/A
Lesion 2	chr3	41267267	Higher	C	A	*CTNNB1*	SNP	NM_001904.3	c.851C > A	p.A284D	1293	C =976 A =317	C =0.755 A =0.245	0.245	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.63	Armadillo-like_helical_(1),Armadillo-type_fold_(1),	B4DSW9,P35222	0.004,0.004			N/A
Lesion 2	chr3	47084145	Higher	AG	A	*SETD2*	DEL	NM_014159.6		p.-2381	1324	AG =974 A =345	AG =0.736 A =0.261	0.261	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 2	chr3	47127713	Higher	C	T	*SETD2*	SNP	NM_014159.6	c.5369G > A	p.R1790Q	2493	C =1836 T =657	C =0.736 T =0.264	0.264	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.05		F2Z317,Q9BYW2	0.009,0.005			N/A
Lesion 2	chr3	47144879	Higher	C	T	*SETD2*	SNP	NM_014159.6	c.4874G > A	p.R1625H	156	C =111 T =45	C =0.712 T =0.288	0.288	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0	SET_domain_(3),	F2Z317,Q9BYW2	0.999,1.0	2		N/A
Lesion 2	chr3	178916666	Higher	C	T	*PIK3CA*	SNP	NM_006218.2	c.53C > T	p.P18L	1384	C =166 T =1218	C =0.12 T =0.88	0.88	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.24		P42336	0.551	1		N/A
Lesion 2	chr3	178916667	Higher	A	T	*PIK3CA*	SNP	NM_006218.2	c.54A > T	p.P18	1384	A =154 T =1228	A =0.111 T =0.887	0.887	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chr3	178916668	Higher	A	T	*PIK3CA*	SNP	NM_006218.2	c.55A > T	p.R19*	1384	A =156 T =1228	A =0.113 T =0.887	0.887	0.00001	Stop_Gained	High	Utr_3_prime							N/A
Lesion 2	chr3	178921639	Higher	C	A	*PIK3CA*	SNP	NM_006218.2			36	C =16 A =20	C =0.444 A =0.556	0.556	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr4	55595519	Higher	C	T	*KIT*	SNP	NM_000222.2	c.2009C > T	p.T670I	249	C =189 T =60	C =0.759 T =0.241	0.241	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0	Serine-threonine/tyrosine-protein_kinase_(1),Protein_kinase-like_domain_(1),Tyrosine-protein_kinase,_catalytic_domain_(1),Protein_kinase,_catalytic_domain_(1),	D5MAV8,P10721-2,P10721	1.0,1.0,1.0	5		N/A
Lesion 2	chr5	112137024	Higher	C	T	*APC*	SNP	NM_001127510.2	c.778C > T	p.Q260*	218	C =199 T =19	C =0.913 T =0.087	0.087	0.00001	Stop_Gained	High	Utr_3_prime	0.26						N/A
Lesion 2	chr6	117714346	Higher	C	G	*ROS1*	SNP	NM_002944.2			33	C =17 G =15	C =0.515 G =0.455	0.455	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr7	2946355	Higher	C	T	*CARD11*	SNP	NM_032415.4	c.3382G > A	p.V1128I	2499	C =1894 T =605	C =0.758 T =0.242	0.242	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.48		Q9BXL7	0.002	1		N/A
Lesion 2	chr7	2968322	Higher	CG	C	*CARD11*	DEL	NM_032415.4		p.-555	2309	CG =1684 C =614	CG =0.729 C =0.266	0.266	0.00001	Frame_shift	High	Utr_3_prime					5		N/A
Lesion 2	chr7	148512082	Higher	C	T	*EZH2*	SNP	NM_004456.4	c.1596G > A	p.R532	191	C =142 T =49	C =0.743 T =0.257	0.257	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chr7	148523541	Higher	C	T	*EZH2*	SNP	NM_152998.2			768	C =557 T =211	C =0.725 T =0.275	0.275	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr7	148543525	Higher	A	G	*EZH2*	SNP	NM_152998.2			21	A =11 G =10	A =0.524 G =0.476	0.476	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr9	36966706	Higher	G	A	*PAX5*	SNP	NM_016734.1	c.620C > T	p.P207L	888	G =654 A =234	G =0.736 A =0.264	0.264	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.24		C0KTF8,C0KTF7,C0KTF9,C0KTF6,E7ERW5,E7EQT0,Q6S730,Q6S731,Q02548	0.982,0.122,0.996,0.982,0.407,0.82,0.546,0.982,0.982			N/A
Lesion 2	chr9	80343587	Higher	GAAAA	GAAAAA,G	*GNAQ*	INS	NM_002072.3			91	GAAAA =10 GAAAAA =26 G =33	GAAAA =0.11 GAAAAA =0.286 G =0.363	0.363	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr9	133747524	Higher	C	T	*ABL1*	SNP	NM_007313.2	c.888C > T	p.T296	36	C =23 T =13	C =0.639 T =0.361	0.361	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chr9	133759918	Higher	T	C	*ABL1*	SNP	NM_007313.2	c.2298T > C	p.F766	2315	T =2106 C =208	T =0.91 C =0.09	0.09	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chr9	139391184	Higher	C	T	*NOTCH1*	SNP	NM_017617.3	c.7007G > A	p.S2336N	81	C =64 T =17	C =0.79 T =0.21	0.21	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.35		P46531	0.002			N/A
Lesion 2	chr9	139393636	Higher	G	A	*NOTCH1*	SNP	NM_017617.3	c.6010C > T	p.R2004C	2494	G =1809 A =684	G =0.725 A =0.274	0.274	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0	Ankyrin_repeat-containing_domain_(4),	P46531	0.999			N/A
Lesion 2	chr9	139399362	Higher	C	T	*NOTCH1*	SNP	NM_017617.3	c.4781G > A	p.R1594Q	246	C =198 T =48	C =0.805 T =0.195	0.195	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.14	Notch,_NOD_domain_(1),	P46531	1	1		N/A
Lesion 2	chr9	139399937	Higher	C	T	*NOTCH1*	SNP	NM_017617.3	c.4411G > A	p.A1471T	243	C =215 T =28	C =0.885 T =0.115	0.115	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.2	Notch_domain_(5),	P46531	0.818			N/A
Lesion 2	chr9	139410210	Higher	G	GGAT	*NOTCH1*	INS	NM_017617.3			34	G =1 GGAT =17	G =0.029 GGAT =0.5	0.5	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr10	43609110	Higher	C	T	*RET*	SNP	NM_020975.4	c.1866C > T	p.P622	130	C =92 T =38	C =0.708 T =0.292	0.292	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chr11	108121410	Higher	CTTTTTT	C	*ATM*	DEL	NM_000051.3			41	CTTTTTT =7 C =14	CTTTTTT =0.171 C =0.341	0.341	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr11	108123615	Higher	AT	A	*ATM*	DEL	NM_000051.3		p.-625	1690	AT =1151 A =507	AT =0.681 A =0.3	0.3	0.00001	Frame_shift	High	Utr_3_prime					1		N/A
Lesion 2	chr11	108143531	Higher	C	T	*ATM*	SNP	NM_000051.3	c.3236C > T	p.A1079V	1225	C =1100 T =125	C =0.898 T =0.102	0.102	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.26	Armadillo-type_fold_(1),	Q13315	0.144			N/A
Lesion 2	chr11	108180850	Higher	A	T	*ATM*	SNP	NM_000051.3			22	A =12 T =10	A =0.545 T =0.455	0.455	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr13	32915005	Higher	G	C	*BRCA2*	SNP	NM_000059.3	c.6513G > C	p.V2171	90	G =0 C =90	G =0.0 C =1.0	1	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chr13	49051012	Higher	C	T	*RB1*	SNP	NM_000321.2			31	C =0 T =31	C =0.0 T =1.0	1	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr14	105258988	Higher	G	A	*AKT1*	SNP	NM_005163.2			870	G =646 A =224	G =0.743 A =0.257	0.257	0.00001	Utr_5_Prime	Modifier	Utr_3_prime							N/A
Lesion 2	chr15	90628215	Higher	C	CATGT	*IDH2*	INS	NM_002168.2			28	C =21 CATGT =7	C =0.75 CATGT =0.25	0.25	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr16	3779339	Higher	C	T	*CREBBP*	SNP	NM_004380.2	c.5709G > A	p.P1903	139	C =123 T =16	C =0.885 T =0.115	0.115	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chr16	3842002	Higher	C	G	*CREBBP*	SNP	NM_004380.2	c.1310G > C	p.S437T	659	C =516 G =137	C =0.783 G =0.208	0.208	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.58	Zinc_finger,_TAZ-type_(2),	Q92793	0.183			N/A
Lesion 2	chr16	9916303	Higher	A	AAG	*GRIN2A*	INS	NM_001134408.1			775	A =424 AAG =351	A =0.547 AAG =0.453	0.453	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr16	9934670	Higher	CAAAAA	C,CAAA	*GRIN2A*	DEL	NM_001134408.1			1102	CAAAAA =73 C =289 CAAA =227	CAAAAA =0.066 C =0.262 CAAA =0.206	0.262	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr16	68863592	Higher	C	T	*CDH1*	SNP	NM_004360.3	c.2331C > T	p.D777	719	C =516 T =203	C =0.718 T =0.282	0.282	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chr17	7573035	Higher	A	AACGG	*TP53*	INS	NM_001126118.1			37	A =8 AACGG =8	A =0.216 AACGG =0.216	0.216	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr17	29541437	Higher	T	C	*NF1*	SNP	NM_001128147.2			57	T =0 C =57	T =0.0 C =1.0	1	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr17	29670190	Higher	C	G	*NF1*	SNP	NM_001042492.2			129	C =68 G =61	C =0.527 G =0.473	0.473	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr17	37879706	Higher	C	T	*ERBB2*	SNP	NM_004448.2	c.2081C > T	p.T694M	177	C =133 T =44	C =0.751 T =0.249	0.249	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.05		B4DTR1,P04626-4,P04626	0.891,0.955,0.815			N/A
Lesion 2	chr18	48584660	Higher	T	C	*SMAD4*	SNP	NM_005359.5			25	T =20 C =5	T =0.8 C =0.2	0.2	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr19	11123731	Higher	C	T	*SMARCA4*	SNP	NM_003072.3	c.2381C > T	p.T794M	2367	C =1793 T =574	C =0.757 T =0.243	0.243	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0	DEAD-like_helicase_(2),SNF2-related_(1),	B1A8Z6,B1A8Z4,B1A8Z7,Q9HBD4,B1A8Z5,A7E2E1,P51532	0.994,0.996,0.996,0.994,0.998,0.996,0.996			N/A
Lesion 2	chr19	11136206	Higher	C	T	*SMARCA4*	SNP	NM_003072.3			55	C =37 T =18	C =0.673 T =0.327	0.327	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr19	11141497	Higher	TG	T	*SMARCA4*	DEL	NM_003072.3		p.-1159	1487	TG =986 T =488	TG =0.663 T =0.328	0.328	0.00001	Frame_shift	High	Utr_3_prime					2		N/A
Lesion 2	chr19	17950432	Higher	C	T	*JAK3*	SNP	NM_000215.3	c.1295G > A	p.R432H	2500	C =2259 T =238	C =0.904 T =0.095	0.095	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.01	SH2_motif_(2),	B4DK43,P52333-2,P52333	0.503,0.702,0.191			N/A
Lesion 2	chr20	36030923	Higher	T	C	*SRC*	SNP	NM_198291.1	c.1202T > C	p.L401P	2496	T =1781 C =711	T =0.714 C =0.285	0.285	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.03	Serine-threonine/tyrosine-protein_kinase_(1),Protein_kinase-like_domain_(1),Tyrosine-protein_kinase,_catalytic_domain_(1),Protein_kinase,_catalytic_domain_(1),	P12931	1			N/A
Lesion 2	chr20	57430214	Higher	C	T	*GNAS*	SNP	NM_080425.2	c.1894C > T	p.R632C	525	C =423 T =102	C =0.806 T =0.194	0.194	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.01		Q5JWF2	0.566	1		N/A
Lesion 2	chr22	41537234	Higher	G	T	*EP300*	SNP	NM_001429.3			55	G =0 T =55	G =0.0 T =1.0	1	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr22	41542830	Higher	GA	G	*EP300*	DEL	NM_001429.3			164	GA =77 G =50	GA =0.47 G =0.305	0.305	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chr22	41572824	Higher	C	T	*EP300*	SNP	NM_001429.3	c.5109C > T	p.H1703	1500	C =1045 T =454	C =0.697 T =0.303	0.303	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 2	chrX	1315034	Higher	C	T	*CRLF2*	SNP	NM_022148.2			1980	C =1429 T =549	C =0.722 T =0.277	0.277	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chrX	44935934	Higher	TTTTC	T	*KDM6A*	DEL	NM_021140.2			21	TTTTC =5 T =16	TTTTC =0.238 T =0.762	0.762	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 2	chrX	44938563	Higher	G	A	*KDM6A*	SNP	NM_021140.2	c.3111G > A	p.Q1037	62	G =0 A =62	G =0.0 A =1.0	1	0.00001	Synonymous_Coding	Low	Utr_3_prime					1		N/A
Lesion 2	chr1	120465398	Lower	A	T	*NOTCH2*	SNP	NM_024408.3	c.4863T > A	p.S1621	591	A =319 T =269	A =0.54 T =0.455	0.455	0.00067	Synonymous_Coding	Low	Hap_Score_More_Than_200							N/A
Lesion 2	chr1	120465409	Lower	A	G	*NOTCH2*	SNP	NM_024408.3			590	A =224 G =365	A =0.38 G =0.619	0.619	0.00001	Intron	Modifier	Hap_Score_More_Than_200							N/A
Lesion 2	chr2	29448410	Lower	T	G	*ALK*	SNP	NM_004304.4	c.3089A > C	p.H1030P	691	T =153 G =522	T =0.221 G =0.755	0.755	0.00003	Non_synonymous_coding	Moderate	Hap_Score_More_Than_200			Q9UM73	0.004			N/A
Lesion 2	chr2	48023115	Lower	T	C	*MSH6*	SNP	NM_000179.2	c.540T > C	p.D180	1,760	T =1201 C =559	T =0.682 C =0.318	0.318	0.00001	Synonymous_Coding	Low	Fs_More_Than_60							N/A
Lesion 2	chr7	2966390	Lower	T	A	*CARD11*	SNP	NM_032415.4	c.1790A > T	p.D597V	2,494	T =2001 A =270	T =0.802 A =0.108	0.108	0.00001	Non_synonymous_coding	Moderate	Fs_More_Than_60;Hap_Score_More_Than_200	0.26		Q9BXL7	0.003			N/A
Lesion 2	chr16	3860640	Lower	A	G	*CREBBP*	SNP	NM_004380.2	c.939T > C	p.D313	2,493	A =1094 G =1399	A =0.439 G =0.561	0.561	0.00001	Synonymous_Coding	Low	Hap_Score_More_Than_200							N/A
Lesion 2	chr16	3860647	Lower	G	T	*CREBBP*	SNP	NM_004380.2	c.932C > A	p.P311H	2,491	G =1750 T =739	G =0.703 T =0.297	0.297	0.00001	Non_synonymous_coding	Moderate	Hap_Score_More_Than_200	0.19		Q4LE28,Q92793	0.453,0.146			N/A
Lesion 3	chr1	27101282	Higher	G	A	*ARID1A*	SNP	NM_006015.4	c.4564G > A	p.A1522T	1862	G =1301 A =559	G =0.699 A =0.3	0.3	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime							N/A
Lesion 3	chr1	120465428	Higher	G	A	*NOTCH2*	SNP	NM_024408.3			35	G =20 A =14	G =0.571 A =0.4	0.4	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr2	29446184	Higher	C	G	*ALK*	SNP	NM_004304.4			53	C =16 G =37	C =0.302 G =0.698	0.698	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr2	30143051	Higher	CG	C	*ALK*	DEL	NM_004304.4		p.-158	771	CG =600 C =168	CG =0.778 C =0.218	0.218	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 3	chr2	212248357	Higher	G	A	*ERBB4*	SNP	NM_005235.2	c.3910C > T	p.R1304W	2498	G =1944 A =552	G =0.778 A =0.221	0.221	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0		Q15303-4,Q15303-2,Q15303-3,Q15303	0.996,0.999,0.996,0.99	1		N/A
Lesion 3	chr3	10188302	Higher	G	A	*VHL*	SNP	NM_000551.3	c.445G > A	p.A149T	2304	G =1797 A =504	G =0.78 A =0.219	0.219	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.13	von_Hippel-Lindau_disease_tumor_suppressor,__beta_domain_(1),von_Hippel-Lindau_disease_tumour_suppressor,_beta/alpha_domain_(2),	P40337	0.916	2		N/A
Lesion 3	chr3	41266487	Higher	G	A	*CTNNB1*	SNP	NM_001904.3	c.284G > A	p.R95Q	1470	G =1122 A =348	G =0.763 A =0.237	0.237	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.09		B4DSW9,P35222	0.975,0.888			N/A
Lesion 3	chr3	47103677	Higher	C	T	*SETD2*	SNP	NM_014159.6	c.6269G > A	p.R2090Q	2188	C =1669 T =519	C =0.763 T =0.237	0.237	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.1		F2Z317,Q9BYW2	0.92,0.92			N/A
Lesion 3	chr3	47161812	Higher	C	T	*SETD2*	SNP	NM_014159.6	c.4314G > A	p.V1438	464	C =359 T =105	C =0.774 T =0.226	0.226	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 3	chr4	1807395	Higher	C	T	*FGFR3*	SNP	NM_001163213.1	c.1650C > T	p.G550	44	C =30 T =14	C =0.682 T =0.318	0.318	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 3	chr6	138196799	Higher	CT	C	*TNFAIP3*	DEL	NM_006290.3			736	CT =556 C =180	CT =0.755 C =0.245	0.245	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr7	55229263	Higher	G	A	*EGFR*	SNP	NM_201284.1	c.1570G > A	p.V524I	2497	G =1948 A =548	G =0.78 A =0.219	0.219	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.03	Growth_factor,_receptor_(1),	Q504U8,P00533,P00533-3,P00533-4	0.008,0.016,0.032,0.046			N/A
Lesion 3	chr7	55238300	Higher	C	T	*EGFR*	SNP	NM_201284.1			2455	C =1939 T =513	C =0.79 T =0.209	0.209	0.00001	Utr_3_prime	Modifier	Utr_3_prime							N/A
Lesion 3	chr7	140434620	Higher	A	AAAAG	*BRAF*	INS	NM_004333.4			2475	A =913 AAAAG =808	A =0.369 AAAAG =0.326	0.326	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr7	148543525	Higher	A	G	*EZH2*	SNP	NM_152998.2			24	A =4 G =20	A =0.167 G =0.833	0.833	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr9	36840623	Higher	G	A	*PAX5*	SNP	NM_016734.1	c.1110C > T	p.Y370	659	G =0 A =659	G =0.0 A =1.0	1	0.00001	Synonymous_coding	Low	Utr_3_prime	0.07		E7ERW5,E7EQT0	0.0,0.001			N/A
Lesion 3	chr9	36923395	Higher	G	A	*PAX5*	SNP	NM_016734.1	c.867C > T	p.I289	1864	G =1617 A =241	G =0.867 A =0.129	0.129	0.00001	Synonymous_coding	Low	Utr_3_prime					1		N/A
Lesion 3	chr9	80343587	Higher	GAAAA	G	*GNAQ*	DEL	NM_002072.3			70	GAAAA =12 G =20	GAAAA =0.171 G =0.286	0.286	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr9	98242237	Higher	G	A	*PTCH1*	SNP	NM_001083607.1			865	G =674 A =191	G =0.779 A =0.221	0.221	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr9	139401322	Higher	G	A	*NOTCH1*	SNP	NM_017617.3	c.3747C > T	p.G1249	253	G =174 A =78	G =0.688 A =0.308	0.308	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 3	chr9	139407932	Higher	A	G	*NOTCH1*	SNP	NM_017617.3	c.2265T > C	p.N755	2489	A =1216 G =1270	A =0.489 G =0.51	0.51	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 3	chr9	139410209	Higher	G	GAGAACC	*NOTCH1*	INS	NM_017617.3			108	G =2 GAGAACC =39	G =0.019 GAGAACC =0.361	0.361	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr11	108172463	Higher	A	G	*ATM*	SNP	NM_000051.3	c.5266A > G	p.T1756A	74	A =53 G =21	A =0.716 G =0.284	0.284	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.56	Armadillo-type_fold_(1),	Q13315	0.008			N/A
Lesion 3	chr11	119156254	Higher	C	T	*CBL*	SNP	NM_005188.3	c.1919C > T	p.T640M	2491	C =1846 T =644	C =0.741 T =0.259	0.259	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.06		P22681	0.128			N/A
Lesion 3	chr13	32937325	Higher	G	A	*BRCA2*	SNP	NM_000059.3	c.7986G > A	p.T2662	147	G =121 A =26	G =0.823 A =0.177	0.177	0.00001	Synonymous_Coding	Low	Utr_3_prime							N/A
Lesion 3	chr13	32954261	Higher	G	A	*BRCA2*	SNP	NM_000059.3	c.9235G > A	p.V3079I	70	G =49 A =21	G =0.7 A =0.3	0.3	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.68	Nucleic_acid-binding,_OB-fold-like_(1),BRCA2,_oligonucleotide/oligosaccharide-binding_3_(1),	P51587	0.132			N/A
Lesion 3	chr13	49051012	Higher	C	T	*RB1*	SNP	NM_000321.2			45	C =0 T =45	C =0.0 T =1.0	1	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr15	66727392	Higher	G	T	*MAP2K1*	SNP	NM_002755.3	c.108G > T	p.K36N	120	G =88 T =32	G =0.733 T =0.267	0.267	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.05		B4DFY5,Q02750	0.95,0.556			N/A
Lesion 3	chr16	9857379	Higher	CT	C	*GRIN2A*	DEL	NM_001134407.1		p.-1341	905	CT =659 C =244	CT =0.728 C =0.27	0.27	0.00001	Frame_shift	High	Utr_3_prime					2		N/A
Lesion 3	chr16	9862767	Higher	G	A	*GRIN2A*	SNP	NM_001134408.1	c.2536C > T	p.R846C	1255	G =946 A =308	G =0.754 A =0.245	0.245	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime		Glutamate_[NMDA]_receptor,_epsilon_subunit,_C-terminal_(1),	F5GZ52,Q17RZ6,Q12879	0.999,0.999,0.996			N/A
Lesion 3	chr16	68867289	Higher	A	C	*CDH1*	SNP	NM_004360.3	c.2536A > C	p.S846R	1891	A =1432 C =456	A =0.757 C =0.241	0.241	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0	Cadherin,_cytoplasmic_domain_(1),	Q9UII8,P12830	1.0,1.0			N/A
Lesion 3	chr17	7573035	Higher	A	AACGG	*TP53*	INS	NM_001126118.1			23	A =2 AACGG =6	A =0.087 AACGG =0.261	0.261	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr17	29560251	Higher	G	A	*NF1*	SNP	NM_001042492.2			430	G =348 A =82	G =0.809 A =0.191	0.191	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr17	29670190	Higher	C	G	*NF1*	SNP	NM_001042492.2			21	C =8 G =13	C =0.381 G =0.619	0.619	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr17	37864627	Higher	G	A	*ERBB2*	SNP	NM_004448.2	c.279G > A	p.Q93	2430	G =1815 A =615	G =0.747 A =0.253	0.253	0.00001	Synonymous_coding	Low	Utr_3_prime							N/A
Lesion 3	chr17	37881681	Higher	G	A	*MIR4728*	SNP	NR_039881.2			21	G =14 A =7	G =0.667 A =0.333	0.333	0.00001	Upstream	Modifier	Utr_3_prime							N/A
Lesion 3	chr17	41244016	Higher	TA	T	*BRCA1*	DEL	NM_007300.3		p.-1177	2498	TA =1980 T =518	TA =0.793 T =0.207	0.207	0.00001	Frame_shift	High	Utr_3_prime							N/A
Lesion 3	chr19	11101865	Higher	G	A	*SMARCA4*	SNP	NM_003072.3	c.1285G > A	p.A429T	403	G =316 A =87	G =0.784 A =0.216	0.216	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	1		B1A8Z6,B1A8Z4,B1A8Z7,Q9HBD4,B1A8Z5,A7E2E1,P51532	0.006,0.006,0.006,0.019,0.006,0.006,0.006			N/A
Lesion 3	chr19	11136215	Higher	C	G	*SMARCA4*	SNP	NM_003072.3			25	C =7 G =17	C =0.28 G =0.68	0.68	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr19	11138447	Higher	C	A	*SMARCA4*	SNP	NM_003072.3			1417	C =1064 A =353	C =0.751 A =0.249	0.249	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr19	11150219	Higher	G	A	*SMARCA4*	SNP	NM_001128849.1	c.4256G > A	p.R1419H	2403	G =1769 A =634	G =0.736 A =0.264	0.264	0.00001	Non_synonymous_coding	Moderate	Utr_3_prime	0.04		Q9HBD4	0.522	1		N/A
Lesion 3	chrX	44920541	Higher	ATT	A	*KDM6A*	DEL	NM_021140.2			178	ATT =97 A =77	ATT =0.545 A =0.433	0.433	0.00001	Intron	Modifier	Utr_3_prime							N/A
Lesion 3	chr1	27107284	Lower	C	T	*ARID1A*	SNP	NM_139135.2			2058	C =1616 T =434	C =0.785 T =0.211	0.211	0.00001	Utr_3_prime	Modifier	Hap_score_more_than_200							N/A
Lesion 3	chr9	21971210	Lower	G	T	*CDKN2A*	SNP	NM_058197.4			957	G =669 T =139	G =0.699 T =0.145	0.145	0.00001	Intron	Modifier	Hap_Score_More_Than_200							N/A
Lesion 3	chr9	21971213	Lower	A	C	*CDKN2A*	SNP	NM_058197.4			940	A =300 C =634	A =0.319 C =0.674	0.674	0.00001	Intron	Modifier	Hap_score_more_than_200							N/A
Lesion 3	chr14	81610191	Lower	G	A	*TSHR*	SNP	NM_000369.2	c.1789G > A	p.V597I	1127	G =987 A =140	G =0.876 A =0.124	0.124	0.00001	Non_synonymous_coding	Moderate	FS_more_than_60	1		F5GYU5	0.013	1		N/A

Table S2 Putative germline variants

Chrom	Pos GRCh37	Confidence	Ref	Variant	Gene name	Variant type	Transcript ID	Codon change	AA change	Filtered coverage	Allele coverage	Allele frequency	Variant frequency	P Value	SNPEff effect	SNPEff impact
chr1	11200508	chr1_11200508_C_T_MTOR	C	T	MTOR	SNP	NM_004958.3	c.4731G > A	p.A1577						Synonymous_Coding	Low
chr1	11288758	chr1_11288758_G_A_MTOR	G	A	MTOR	SNP	NM_004958.3	c.2997C > T	p.N999						Synonymous_Coding	Low
chr1	11301714	chr1_11301714_A_G_MTOR	A	G	MTOR	SNP	NM_004958.3	c.1437T > C	p.D479						Synonymous_Coding	Low
chr1	120611864	chr1_120611864_G_C_NOTCH2	G	C	NOTCH2	SNP	NM_001200001.1	c.57C > G	p.C19W						Non_synonymous_coding	Moderate
chr2	29416366	chr2_29416366_G_C_ALK	G	C	ALK	SNP	NM_004304.4	c.4587C > G	p.D1529E						Non_synonymous_coding	Moderate
chr2	29416481	chr2_29416481_T_C_ALK	T	C	ALK	SNP	NM_004304.4	c.4473A > G	p.K1491R						Non_synonymous_coding	Moderate
chr2	29416572	chr2_29416572_T_C_ALK	T	C	ALK	SNP	NM_004304.4	c.4381A > G	p.I1461V						Non_synonymous_coding	Moderate
chr2	29445458	chr2_29445458_G_T_ALK	G	T	ALK	SNP	NM_004304.4	c.3379C > A	p.Q1125						Synonymous_Coding	Low
chr2	29449819	chr2_29449819_C_T_ALK	C	T	ALK	SNP	NM_004304.4	c.3039G > A	p.T1012						Synonymous_Coding	Low
chr2	29452827	chr2_29452827_A_G_ALK	A	G	ALK	SNP	NM_004304.4	c.2530T > C	p.S845						Synonymous_Coding	Low
chr2	29543663	chr2_29543663_T_C_ALK	T	C	ALK	SNP	NM_004304.4	c.1506A > G	p.Q500						Synonymous_Coding	Low
chr2	29543736	chr2_29543736_A_G_ALK	A	G	ALK	SNP	NM_004304.4	c.1427T > C	p.V476A						Non_synonymous_coding	Moderate
chr2	29640529	chr2_29640529_A_T_ALK	A	T	ALK	SNP	NM_004304.4	c.702T > A	p.P234						Synonymous_Coding	Low
chr2	47703578	chr2_47703578_GT_G_MSH2	GT	G	MSH2	DEL	NM_000251.2		p.-693						Frame_Shift	High
chr2	48018081	chr2_48018081_A_G_MSH6	A	G	MSH6	SNP	NM_000179.2	c.276A > G	p.P92						Synonymous_Coding	Low
chr3	47125385	chr3_47125385_G_A_SETD2	G	A	SETD2	SNP	NM_014159.6	c.5985C > T	p.P1962L						Non_synonymous_coding	Moderate
chr3	47162661	chr3_47162661_A_G_SETD2	A	G	SETD2	SNP	NM_014159.6	c.3497T > C	p.M1155						Synonymous_Coding	Low
chr4	1803704	chr4_1803704_T_C_FGFR3	T	C	FGFR3	SNP	NM_000142.4	c.882T > C	p.N294						Synonymous_Coding	Low
chr4	1807479	chr4_1807479_G_T_FGFR3	G	T	FGFR3	SNP	NM_001163213.1	c.1653G > T	p.G551						Synonymous_Coding	Low
chr4	55141055	chr4_55141055_A_G_PDGFRA	A	G	PDGFRA	SNP	NM_006206.4	c.1701A > G	p.P567						Synonymous_Coding	Low
chr4	55161391	chr4_55161391_T_C_PDGFRA	T	C	PDGFRA	SNP	NM_006206.4	c.3222T > C	p.D1074						Synonymous_Coding	Low
chr5	1294086	chr5_1294086_C_T_TERT	C	T	TERT	SNP	NM_198253.2	c.915G > A	p.A305						Synonymous_Coding	Low
chr5	35871190	chr5_35871190_G_A_IL7R	G	A	IL7R	SNP	NM_002185.3	c.412G > A	p.V138I						Non_synonymous_coding	Moderate
chr5	35871293	chr5_35871293_A_G_IL7R	A	G	IL7R	SNP	NM_002185.3	c.515A > G	p.E172G						Non_synonymous_coding	Moderate
chr5	35876449	chr5_35876449_C_T_IL7R	C	T	IL7R	SNP	NM_002185.3	c.1241C > T	p.T414M						Non_synonymous_coding	Moderate
chr5	67588148	chr5_67588148_G_A_PIK3R1	G	A	PIK3R1	SNP	NM_181504.3	c.1662G > A	p.M56I						Non_synonymous_coding	Moderate
chr5	112162854	chr5_112162854_T_C_APC	T	C	APC	SNP	NM_000038.5	c.1458T > C	p.Y486						Synonymous_Coding	Low
chr5	112175770	chr5_112175770_G_A_APC	G	A	APC	SNP	NM_001127510.2	c.4479G > A	p.T1493						Synonymous_Coding	Low
chr5	112176325	chr5_112176325_G_A_APC	G	A	APC	SNP	NM_001127510.2	c.5034G > A	p.G1678						Synonymous_Coding	Low
chr5	112176559	chr5_112176559_T_G_APC	T	G	APC	SNP	NM_001127510.2	c.5288T > G	p.S1756						Synonymous_Coding	Low
chr5	112176756	chr5_112176756_T_A_APC	T	A	APC	SNP	NM_001127510.2	c.5465T > A	p.V1822D						Non_synonymous_coding	Moderate
chr5	112177171	chr5_112177171_G_A_APC	G	A	APC	SNP	NM_001127510.2	c.5886G > A	p.P1960						Synonymous_Coding	Low
chr5	149456843	chr5_149456843_C_T_CSF1R	C	T	CSF1R	SNP	NM_005211.3	c.885G > A	p.V295						Synonymous_Coding	Low
chr5	149457678	chr5_149457678_G_A_CSF1R	G	A	CSF1R	SNP	NM_005211.3	c.726C > T	p.T242						Synonymous_Coding	Low
chr5	149460553	chr5_149460553_G_A_CSF1R	G	A	CSF1R	SNP	NM_005211.3	c.84T > C	p.P28						Synonymous_Coding	Low
chr6	117622184	chr6_117622184_G_C_ROS1	G	C	ROS1	SNP	NM_002944.2	c.6666C > G	p.S2229C						Non_synonymous_coding	Moderate
chr6	117622188	chr6_117622188_T_G_ROS1	T	G	ROS1	SNP	NM_002944.2	c.6662A > C	p.K2228Q						Non_synonymous_coding	Moderate
chr6	117622233	chr6_117622233_C_T_ROS1	C	T	ROS1	SNP	NM_002944.2	c.6617G > A	p.D2113N						Non_synonymous_coding	Moderate
chr6	117631431	chr6_117631431_T_G_ROS1	T	G	ROS1	SNP	NM_002944.2	c.6341A > C	p.R2083						Non_synonymous_coding	Moderate
chr6	117645537	chr6_117645537_T_C_ROS1	T	C	ROS1	SNP	NM_002944.2	c.5599A > G	p.I1867V						Non_synonymous_coding	Moderate
chr6	117708971	chr6_117708971_C_T_ROS1	C	T	ROS1	SNP	NM_002944.2	c.1986G > A	p.E662						Synonymous_Coding	Low
chr6	117715573	chr6_117715573_G_C_ROS1	G	C	ROS1	SNP	NM_002944.2	c.1609C > G	p.L547V						Non_synonymous_coding	Moderate
chr6	117725448	chr6_117725448_T_G_ROS1	T	G	ROS1	SNP	NM_002944.2	c.433A > C	p.T145P						Non_synonymous_coding	Moderate
chr6	117725578	chr6_117725578_T_A_ROS1	T	A	ROS1	SNP	NM_002944.2	c.303A > T	p.L101						Synonymous_Coding	Low
chr7	2957005	chr7_2957005_T_C_CARD11	T	C	CARD11	SNP	NM_032415.4	c.2602A > G	p.R874						Non_synonymous_coding	Low
chr7	55214348	chr7_55214348_C_T_EGFR	C	T	EGFR	SNP	NM_005228.3	c.474C > T	p.N158						Synonymous_Coding	Low
chr7	55249063	chr7_55249063_G_A_EGFR	G	A	EGFR	SNP	NM_005228.3	c.2361G > A	p.G787						Synonymous_Coding	Low
chr7	55256417	chr7_55256417_T_C_EGFR	T	C	EGFR	SNP	NM_005228.3	c.2708T > C	p.T903						Synonymous_Coding	Low
chr7	116340269	chr7_116340269_C_T_MET	C	T	MET	SNP	NM_001127500.1	c.1131C > T	p.I377						Synonymous_Coding	Low
chr7	128846328	chr7_128846328_G_C_SMO	G	C	SMO	SNP	NM_005631.4	c.1164G > C	p.G388						Synonymous_Coding	Low
chr7	140449160	chr7_140449160_T_C_BRAF	T	C	BRAF	SNP	NM_004333.4	c.1825A > G	p.I609						Synonymous_Coding	Low
chr7	140476804	chr7_140476804_G_A_BRAF	G	A	BRAF	SNP	NM_004333.4	c.1602C > T	p.G534						Synonymous_Coding	Low
chr9	133755528	chr9_133755528_A_G_ABL1	A	G	ABL1	SNP	NM_007313.2	c.1554A > G	p.E518						Synonymous_Coding	Low
chr9	133760029	chr9_133760029_C_G_ABL1	C	G	ABL1	SNP	NM_007313.2	c.2409C > G	p.P803						Synonymous_Coding	Low
chr9	133761001	chr9_133761001_A_G_ABL1	A	G	ABL1	SNP	NM_007313.2	c.3381A > G	p.P1127						Synonymous_Coding	Low
chr9	139391636	chr9_139391636_G_A_NOTCH1	G	A	NOTCH1	SNP	NM_017617.3	c.6559C > T	p.D2185						Synonymous_Coding	Low
chr9	139401233	chr9_139401233_C_T_NOTCH1	C	T	NOTCH1	SNP	NM_017617.3	c.3836G > A	p.R1279H						Non_synonymous_coding	Moderate
chr9	139418260	chr9_139418260_A_G_NOTCH1	A	G	NOTCH1	SNP	NM_017617.3	c.3127T > C	p.N104						Synonymous_Coding	Low
chr10	43606687	chr10_43606687_A_G_RET	A	G	RET	SNP	NM_020975.4	c.1296A > G	p.A432						Synonymous_Coding	Low
chr10	43613843	chr10_43613843_G_T_RET	G	T	RET	SNP	NM_020975.4	c.2307G > T	p.L769						Synonymous_Coding	Low
chr10	123298158	chr10_123298158_T_C_FGFR2	T	C	FGFR2	SNP	NM_022970.3	c.956A > G	p.V733						Non_synonymous_coding	Moderate
chr11	32417945	chr11_32417945_T_C_WT1	T	C	WT1	SNP	NM_024426.4	c.1107A > G	p.R369						Synonymous_Coding	Low
chr11	64573018	chr11_64573018_T_C_MEN1	T	C	MEN1	SNP	NM_130799.2	c.1621A > G	p.T541A						Non_synonymous_coding	Moderate
chr11	64573557	chr11_64573557_A_G_MEN1	A	G	MEN1	SNP	NM_130804.2	c.1314T > C	p.H438						Synonymous_Coding	Low
chr11	108183167	chr11_108183167_A_G_ATM	A	G	ATM	SNP	NM_000051.3	c.5948A > G	p.N1983S						Non_synonymous_coding	Moderate
chr12	25368462	chr12_25368462_C_T_KRAS	C	T	KRAS	SNP	NM_033360.2	c.483G > A	p.R161						Synonymous_Coding	Low
chr12	121435342	chr12_121435342_C_T_HNF1A	C	T	HNF1A	SNP	NM_000545.5	c.1375C > T	p.L459						Synonymous_Coding	Low
chr12	121435427	chr12_121435427_G_A_HNF1A	G	A	HNF1A	SNP	NM_000545.5	c.1460G > A	p.S487N						Non_synonymous_coding	Moderate
chr12	121437114	chr12_121437114_G_A_HNF1A	G	A	HNF1A	SNP	NM_000545.5	c.1545G > A	p.T515						Synonymous_Coding	Low
chr13	28624294	chr13_28624294_C_T_FLT3	G	A	FLT3	SNP	NM_004119.2	c.2692C > T	p.T227M						Non_synonymous_coding	Moderate
chr13	28636084	chr13_28636084_G_A_FLT3	G	A	FLT3	SNP	NM_004119.2	c.286C > T	p.D96						Synonymous_Coding	Low
chr13	32900729	chr13_32900729_A_C_BRCA2	A	C	BRCA2	SNP	NM_000059.3	c.1114A > C	p.N372H						Non_synonymous_coding	Moderate
chr13	32911988	chr13_32911988_A_G_BRCA2	A	G	BRCA2	SNP	NM_000059.3	c.339A > G	p.K113Z						Synonymous_Coding	Low
chr13	32929232	chr13_32929232_A_G_BRCA2	A	G	BRCA2	SNP	NM_000059.3	c.7242A > G	p.S2414						Synonymous_Coding	Low
chr14	81562998	chr14_81562998_T_C_TSHR	T	C	TSHR	SNP	NM_000369.2	c.561T > C	p.N187						Synonymous_Coding	Low
chr14	81610583	chr14_81610583_G_C_TSHR	G	C	TSHR	SNP	NM_000369.2	c.2161G > C	p.E721D						Non_synonymous_coding	Moderate
chr15	90631596	chr15_90631596_C_T_IDH2	C	T	IDH2	SNP	NM_002168.2	c.673G > A	p.D225N						Non_synonymous_coding	Moderate
chr16	9916204	chr16_9916204_C_G_GRIN2A	C	G	GRIN2A	SNP	NM_001134408.1	c.2089G > C	p.R697						Synonymous_Coding	Low
chr16	68857441	chr16_68857441_C_T_CDH1	C	T	CDH1	SNP	NM_004360.3	c.2076T > C	p.A692						Synonymous_Coding	Low
chr17	7579472	chr17_7579472_G_C_TP53	G	C	TP53	SNP	NM_000546.5	c.215C > G	p.P72R						Non_synonymous_coding	Moderate
chr17	29508775	chr17_29508775_G_A_NF1	G	A	NF1	SNP	NM_001128147.2	c.7120G > A	p.L2374						Synonymous_Coding	Low
chr19	3118239	chr19_3118239_C_T_GNA11	C	T	GNA11	SNP	NM_002067.2	c.771C > T	p.T257						Synonymous_Coding	Low
chr19	11105608	chr19_11105608_T_C_SMARCA4	T	C	SMARCA4	SNP	NM_003072.3	c.1524T > C	p.H508						Synonymous_Coding	Low
chr19	11145691	chr19_11145691_C_T_SMARCA4	C	T	SMARCA4	SNP	NM_003072.3	c.4553C > T	p.D1351						Synonymous_Coding	Low
chr19	52729000	chr19_52729000_A_G_PPP1R1A	A	G	PPP1R1A	SNP	NM_014225.5	c.160A > G	p.L54A						Synonymous_Coding	Low
chr20	31923959	chr20_31923959_T_C_ASXL1	T	C	ASXL1	SNP	NM_015338.5	c.2441T > C	p.L815P						Non_synonymous_coding	Moderate
chr20	31924274	chr20_31924274_T_C_ASXL1	T	C	ASXL1	SNP	NM_015338.5	c.3758T > C	p.S1253						Synonymous_Coding	Low
chr20	36030939	chr20_36030939_G_C_SRC	G	C	SRC	SNP	NM_198291.1	c.1218G > C	p.A406						Synonymous_Coding	Low
chr20	57478807	chr20_57478807_C_T_GNAS	C	T	GNAS	SNP	NM_080425.2	c.2322C > T	p.I774						Synonymous_Coding	Low
chr20	57484241	chr20_57484241_C_T_GNAS	C	T	GNAS	SNP	NM_080425.2	c.2446C > T	p.R828						Synonymous_Coding	Low
chr20	57485812	chr20_57485812_C_T_GNAS	C	T	GNAS	SNP	NM_001077488.2	c.1116C > T	p.N372						Synonymous_Coding	Low
chr22	41551039	chr22_41551039_T_A_EP300	T	A	EP300	SNP	NM_001429.3	c.3182T > A	p.I1061						Synonymous_Coding	Low
chr22	41572867	chr22_41572867_A_G_EP300	A	G	EP300	SNP	NM_001429.3	c.5152A > G	p.N1718D						Non_synonymous_coding	Moderate
chr22	41573886	chr22_41573886_T_C_EP300	T	C	EP300	SNP	NM_001429.3	c.6171T > C	p.T2057						Synonymous_Coding	Low
chr1	11167893	chr1_11167893_T_C_MTOR5NP	T	C	MTOR	SNP	NM_004958.3								Intron	Modifier
chr1	120466398	chr1_120466398_A_T_NOTCH2SNP	A	T	NOTCH2	SNP	NM_024408.3	c.4863T > A	p.S1621						Intron	Modifier
chr1	120465409	chr1_120465409_A_G_NOTCH2SNP	A	G	NOTCH2	SNP	NM_024408.3	0	0						Intron	Modifier
chr10	43595998	chr10_43595998_A_G_RETSNP	A	G	RET	SNP	NM_020975.4	c.135A > G	p.A45						Synonymous_Coding	Low
chr10	43600689	chr10_43600689_A_G_RETSNP	A	G	RET	SNP	NM_020975.4	0	0						Intron	Modifier
chr10	43607756	chr10_43607756_G_A_RETSNP	G	A	RET	SNP	NM_020975.4	0	0						Intron	Modifier
chr10	43607759	chr10_43607759_GC_G_RET3DEL	GC	G	RET	DEL	NM_020975.4	0	0						Intron	Modifier
chr10	43612226	chr10_43612226_C_T_RETSNP	C	T	RET	SNP	NM_020975.4	0	0						Intron	Modifier
chr10	43622217	chr10_43622217_T_C_RETSNP	T	C	RET	SNP	NM_020630.4	0	0						Utr_3_prime	Modifier
chr11	108088459	chr11_108088459_TAA_T_ATM3DEL	TAA	T	ATM	DEL	NM_000051.3	0	0						Intron	Modifier
chr11	119148573	chr11_119148573_G_T_CBLSNP	G	T	CBL	SNP	NM_005188.3	0	0						Intron	Modifier
chr11	119155649	chr11_119155649_G_C_CBLSNP	G	C	CBL	SNP	NM_005188.3	0	0						Intron	Modifier
chr11	32449661	chr11_32449661_G_A_WT1SNP	G	A	WT1	SNP	NM_024426.4	0	0						Intron	Modifier
chr12	121426594	chr12_121426594_A_G_HNF1ASNP	A	G	HNF1A	SNP	NM_000545.5	0	0						Intron	Modifier
chr12	121426901	chr12_121426901_G_C_HNF1ASNP	G	C	HNF1A	SNP	NM_000545.5	0	0						Intron	Modifier
chr12	121435475	chr12_121435475_G_A_HNF1ASNP	G	A	HNF1A	SNP	NM_000545.5	0	0						Intron	Modifier
chr12	121437221	chr12_121437221_T_C_HNF1ASNP	T	C	HNF1A	SNP	NM_000545.5	0	0						Intron	Modifier
chr13	28580267	chr13_28580267_C_T_FLT3SNP	C	T	FLT3	SNP	NM_004119.2	0	0						Intron	Modifier
chr13	28609825	chr13_28609825_A_G_FLT3SNP	A	G	FLT3	SNP	NM_004119.2	0	0						Intron	Modifier
chr13	28609846	chr13_28609846_A_T_FLT3SNP	A	T	FLT3	SNP	NM_004119.2	0	0						Intron	Modifier
chr13	28610183	chr13_28610183_A_G_FLT3SNP	A	G	FLT3	SNP	NM_004119.2	0	0						Intron	Modifier
chr13	32895572	chr13_32895572_G_A_BRCA2SNP	G	A	BRCA2	SNP	NM_000059.3	0	0						Utr_3_Prime	Modifier
chr13	32900265	chr13_32900265_G_A_BRCA2SNP	G	A	BRCA2	SNP	NM_000059.3	0	0						Intron	Modifier
chr13	32913055	chr13_32913055_A_G_BRCA2SNP	A	G	BRCA2	SNP	NM_000059.3	c.4563A > G	p.L1521						Synonymous_Coding	Low
chr13	32936646	chr13_32936646_T_C_BRCA2SNP	T	C	BRCA2	SNP	NM_000059.3	0	0						Intron	Modifier
chr13	32953388	chr13_32953388_T_C_BRCA2SNP	T	C	BRCA2	SNP	NM_000059.3	0	0						Intron	Modifier
chr13	48919358	chr13_48919358_T_G_RB1SNP	T	G	RB1	SNP	NM_000321.2	0	0						Intron	Modifier
chr14	105241378	chr14_105241378_C_T_AKT1SNP	C	T	AKT1	SNP	NM_005163.2	0	0						Intron	Modifier
chr14	81559965	chr14_81559965_A_G_TSHR5NP	A	G	TSHR	SNP	NM_001142626.2	0	0						Intron	Modifier
chr16	3777990	chr16_3777990_GA_G_CREBBPDEL	GA	G	CREBBP	DEL	NM_004380.2	0	0						Utr_3_prime	Modifier
chr16	3795363	chr16_3795363_G_A_CREBBPSNP	G	A	CREBBP	SNP	NM_004380.2	0	0						Intron	Modifier
chr16	3860640	chr16_3860640_A_G_CREBBPSNP	A	G	CREBBP	SNP	NM_004380.2	c.9397 > C	p.D313						Synonymous_Coding	Low
chr16	50825642	chr16_50825642_T_A_CYLD5NP	T	A	CYLD	SNP	NM_015247.2	0	0						Intron	Modifier
chr16	50827601	chr16_50827601_A_G_CYLD5NP	A	G	CYLD	SNP	NM_015247.2	0	0						Intron	Modifier
chr17	29543987	chr17_29543987_A_AT_NF1INS	A	AT	NF1	INS	NM_001128147.2	0	0						Intron	Modifier
chr17	29546175	chr17_29546175_T_C_NF1SNP	T	C	NF1	SNP	NM_001128147.2	0	0						Intron	Modifier
chr17	29556837	chr17_29556837_T_C_NF1SNP	T	C	NF1	SNP	NM_001042492.2	0	0						Intron	Modifier
chr17	29653293	chr17_29653293_T_C_EVI2A5NP	T	C	EVI2A	SNP	NM_014210.3	0	0						Upstream	Modifier
chr17	29654876	chr17_29654876_T_A_NF1SNP	T	A	NF1	SNP	NM_001042492.2	0	0						Intron	Modifier
chr17	29663614	chr17_29663614_GTT_G_NF1DEL	GTT	G	NF1	DEL	NM_001042492.2	0	0						Intron	Modifier
chr17	29679246	chr17_29679246_G_A_NF1SNP	G	A	NF1	SNP	NM_001042492.2	0	0						Intron	Modifier
chr17	37979762	chr17_37979762_G_A_MRM1ZB5NP	G	A	MRM1ZB	SNP	NR_039891.2	0	0						Upstream	Modifier
chr17	37984037	chr17_37984037_C_G_ERBB2SNP	C	G	ERBB2	SNP	NM_004448.2	c.3508C > G	p.P1170A						Non_synonymous_coding	Moderate
chr17	66529027	chr17_66529027_G_T_PRKAR1A5NP	G	T	PRKAR1A	SNP	NM_212472.2	0	0						Intron	Modifier
chr17	7573929	chr17_7573929_GA_G_TP53DEL	GA	G	TP53	DEL	NM_001126118.1	0	0						Intron	Modifier
chr19	11113997	chr19_11113997_G_T_SMARCA4SNP	G	T	SMARCA4	SNP	NM_003072.3	0	0						Intron	Modifier
chr19	17945696	chr19_17945696_C_T_JAK3SNP	C	T	JAK3	SNP	NM_000215.3	c.2164G > A	p.V722I						Non_synonymous_coding	Moderate
chr19	3110049	chr19_3110049_T_G_GNA11SNP	T	G	GNA11	SNP	NM_002067.2	0	0						Intron	Modifier
chr19	3113305	chr19_3113305_G_C_GNA11SNP	G	C	GNA11	SNP	NM_002067.2	0	0						Intron	Modifier
chr2	212569983	chr2_212569983_G_A_ERBB4SNP	G	A	ERBB4	SNP	NM_005235.2	0	0						Intron	Modifier
chr2	25463483	chr2_25463483_G_A_DNMT3ASNP	G	A	DNMT3A	SNP	NM_175629.2	0	0						Intron	Modifier
chr2	25469913	chr2_25469913_C_T_DNMT3ASNP	C	T	DNMT3A	SNP	NM_175629.2	0	0						Intron	Modifier
chr2	29498210	chr2_29498210_A_G_ALK3NP	A	G	ALK	SNP	NM_004304.4	0	0						Intron	Modifier
chr2	48023115	chr2_48023115_T_C_MSH6SNP	T	C	MSH6	SNP	NM_000179.2	c.5467 > C	p.D1823						Synonymous_Coding	Low
chr2	48030838	chr2_48030838_A_T_MSH6SNP	A	T	MSH6	SNP	NM_000179.2	0	0						Intron	Modifier
chr2	48032874	chr2_48032874_ACTAT_A_MSH6DEL	ACTAT	A	MSH6	DEL	NM_000179.2	0	0						Intron	Modifier
chr2	48032937	chr2_48032937_T_C_MSH6SNP	T	C	MSH6	SNP	NM_000179.2	0	0						Intron	Modifier
chr20	30954295	chr20_30954295_A_G_ASXL1SNP	A	G	ASXL1	SNP	NM_015338.5	0	0						Intron	Modifier
chr20	31025163	chr20_31025163_A_G_ASXL1SNP	A	G	ASXL1	SNP	NM_015338.5	0	0						Utr_3_prime	Modifier
chr20	31025231	chr20_31025231_T_C_ASXL1SNP	T	C	ASXL1	SNP	NM_015338.5	0	0						Utr_3_prime	Modifier
chr20	36031097	chr20_36031097_A_G_SRC3NP	A	G	SRC	SNP	NM_198291.1	0	0						Intron	Modifier
chr20	57415110	chr20_57415110_A_G_GNAS5NP	A	G	GNAS	SNP	NM_016592.2	0	0						Utr_5_Prime	Modifier
chr22	41548008	chr22_41548008_A_G_EP3005NP	A	G	EP300	SNP	NM_001429.3	c.2986A > G	p.I997V						Non_synonymous_coding	Moderate
chr22	41566595	chr22_41566595_C_T_EP3005NP	C	T	EP300	SNP	NM_001429.3	0	0						Intron	Modifier
chr22	41568480	chr22_41568480_T_C_EP3005NP	T	C	EP300	SNP	NM_001429.3	0	0						Intron	Modifier
chr22	41572541	chr22_41572541_C_T_EP3005NP	C	T	EP300	SNP	NM_001429.3	0	0						Intron	Modifier
chr3	178922274	chr3_178922274_C_A_PIK3CA3NP	C	A	PIK3CA	SNP	NM_006218.2	0	0						Intron	Modifier
chr4	1803307	chr4_1803307_T_C_FGFR3SNP	T	C	FGFR3	SNP	NM_022965.3	0	0						Intron	Modifier
chr4	1803824	chr4_1803824_C_G_FGFR3SNP	C	G	FGFR3	SNP	NM_022965.3	0	0						Intron	Modifier
chr4	1806311	chr4_1806311_C_T_FGFR3SNP	C	T	FGFR3	SNP	NM_022965.3	0	0						Intron	Modifier
chr4	55161254	chr4_55161254_C_T_PDGFRA5NP	C	T	PDGFRA	SNP	NM_006206.4	0	0						Intron	Modifier
chr4	55161517	chr4_55161517_A_G_PDGFRA5NP	A	G	PDGFRA	SNP	NM_006206.4	0	0						Utr_3_prime	Modifier
chr4	55946081	chr4_55946081_A_G_KDR5NP	A	G	KDR	SNP	NM_002253.2	0	0						Utr_3_prime	Modifier
chr4	55948108	chr4_55948108_A_G_KDR5NP	A	G	KDR	SNP	NM_002253.2	0	0						Intron	Modifier
chr4	55966053	chr4_55966053_A_C_KDR5NP	A	C	KDR	SNP	NM_002253.2	0	0						Intron	Modifier
chr5	149437190	chr5_149437190_C_G_CSF1R5NP	C	G	CSF1R	SNP	NM_005211.3	0	0						Intron	Modifier
chr5	67569746	chr5_67569746_G_A_PIK3R15NP	G	A	PIK3R1	SNP	NM_181523.2	0	0						Intron	Modifier
chr6	117639419	chr6_117639419_T_C_ROS15NP	T	C	ROS1	SNP	NM_002944.2	0	0						Intron	Modifier
chr6	117641246	chr6_117641246_C_A_ROS15NP	C	A	ROS1	SNP	NM_002944.2	0	0						Intron	Modifier
chr6	117676063	chr6_117676063_A_G_ROS15NP	A	G	ROS1	SNP	NM_002944.2	0	0						Intron	Modifier
chr6	117737390	chr6_117737390_G_A_ROS15NP	G	A	ROS1	SNP	NM_002944.2	0	0						Intron	Modifier
chr6	136197331	chr6_136197331_A_C_TNFAIP35NP	A	C	TNFAIP3	SNP	NM_006290.3	0	0						Intron	Modifier
chr7	128843277	chr7_128843277_G_C_SMO5NP	G	C	SMO	SNP	NM_005631.4	0	0						Intron	Modifier
chr7	140449071	chr7_140449071_C_G_BRAF5NP	C	G	BRAF	SNP	NM_004333.4	0	0						Intron	Modifier
chr7	2962241	chr7_2962241_G_A_CARD11SNP	G	A	CARD11	SNP	NM_032415.4	0	0						Intron	Modifier
chr7	55214443	chr7_55214443_G_A_EGFR5NP	G	A	EGFR	SNP	NM_201284.1	0	0						Intron	Modifier
chr9	139410177	chr9_139410177_T_C_NOTCH15NP	T	C	NOTCH1	SNP	NM_017617.3	0	0						Intron	Modifier
chr9	139410424	chr9_139410424_A_G_NOTCH15NP	A	G	NOTCH1	SNP	NM_017617.3	0	0						Intron	Modifier
chr9	139412197	chr9_139412197_A_G_NOTCH15NP	A	G	NOTCH1	SNP	NM_017617.3	0	0						Intron	Modifier
chr9	21968199	chr9_21968199_C_G_CDKN2A5NP	C	G	CDKN2A	SNP	NM_058197.4	0	0						Utr_3_prime	Modifier
chr9	37020602	chr9_37020602_A_C_PAX5SNP	A	C	PAX5	SNP	NM_016734.1	0	0						Intron	Modifier
chrX	1331495	chrX_1331495_G_C_CRLF2SNP	G	C	CRLF2	SNP	NM_001012288.1	0	0						Utr_5_Prime	Modifier