



ORANGE Report (Research Use Only)

SAMPLE

Test

PIPELINE VERSION

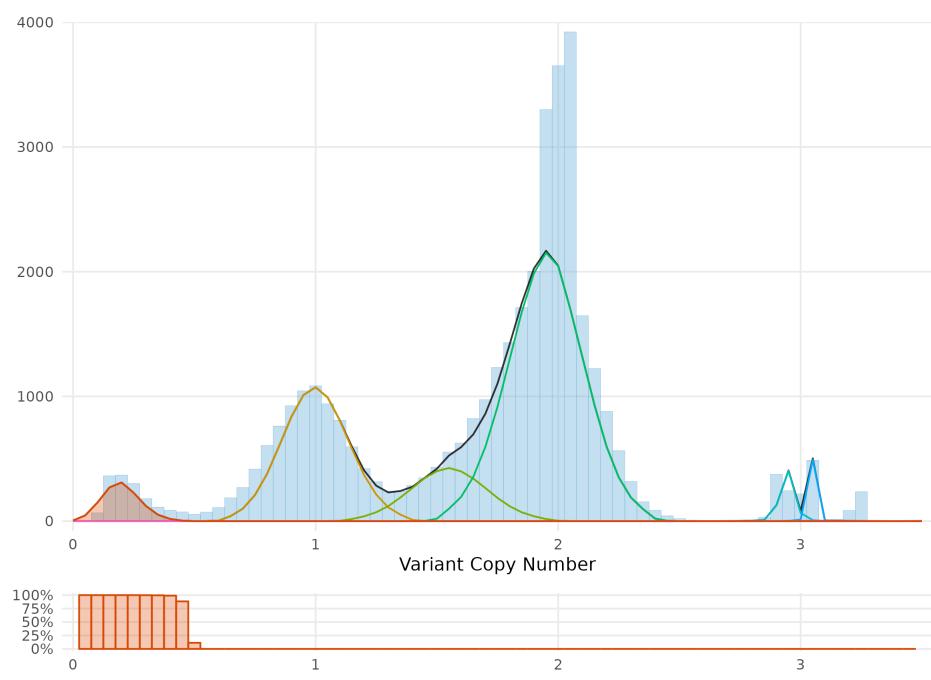
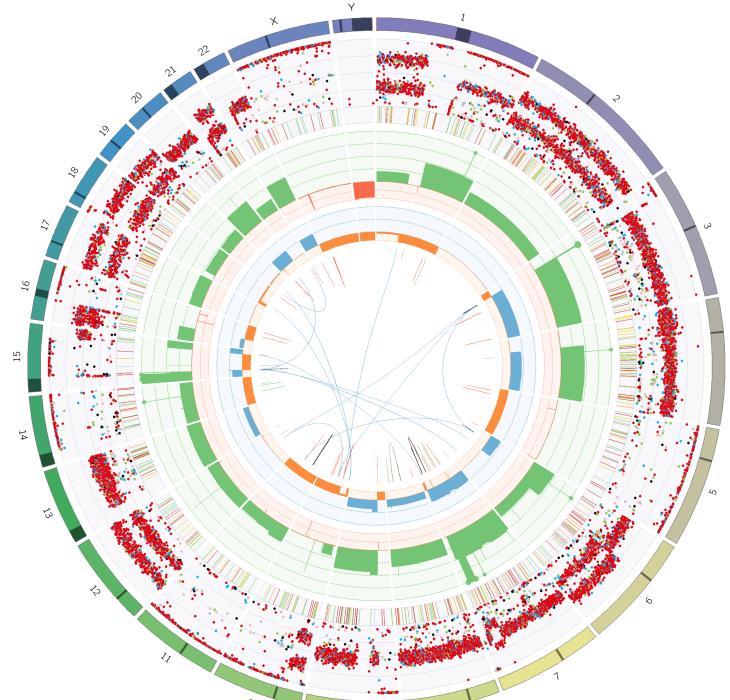
6.0

CONFIGURED PRIMARY TUMOR
skin melanoma (DOID 8923)

CUPPA CANCER TYPE
Skin: Melanoma (100%)

QC
PASS

Purity:	99% (97%-100%)
Ploidy:	3.10 (3.05-3.15)
Somatic variant drivers:	6 (BRAF, CDKN2A, TERT)
Germline variant drivers:	None
Somatic copy number drivers:	1 (PTEN)
Germline copy number drivers:	None
Somatic disruption drivers:	None
Germline disruption drivers:	None
Fusion drivers:	None
Viral presence:	None
Whole genome duplicated:	Yes
Microsatellite indels per Mb:	0.1 (Stable)
Tumor mutations per Mb:	13.7 (High)
Tumor mutational load:	184 (High)
HR deficiency score:	0.0 (Proficient)
DPYD status:	*1 HOM (Normal Function)
UGT1A1 status:	NA
Number of SVs:	86 (Pan 0.22 Skin 0.34)
Max complex cluster size:	8
Telomeric SGLs:	0
Number of LINE insertions:	0





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Somatic Findings

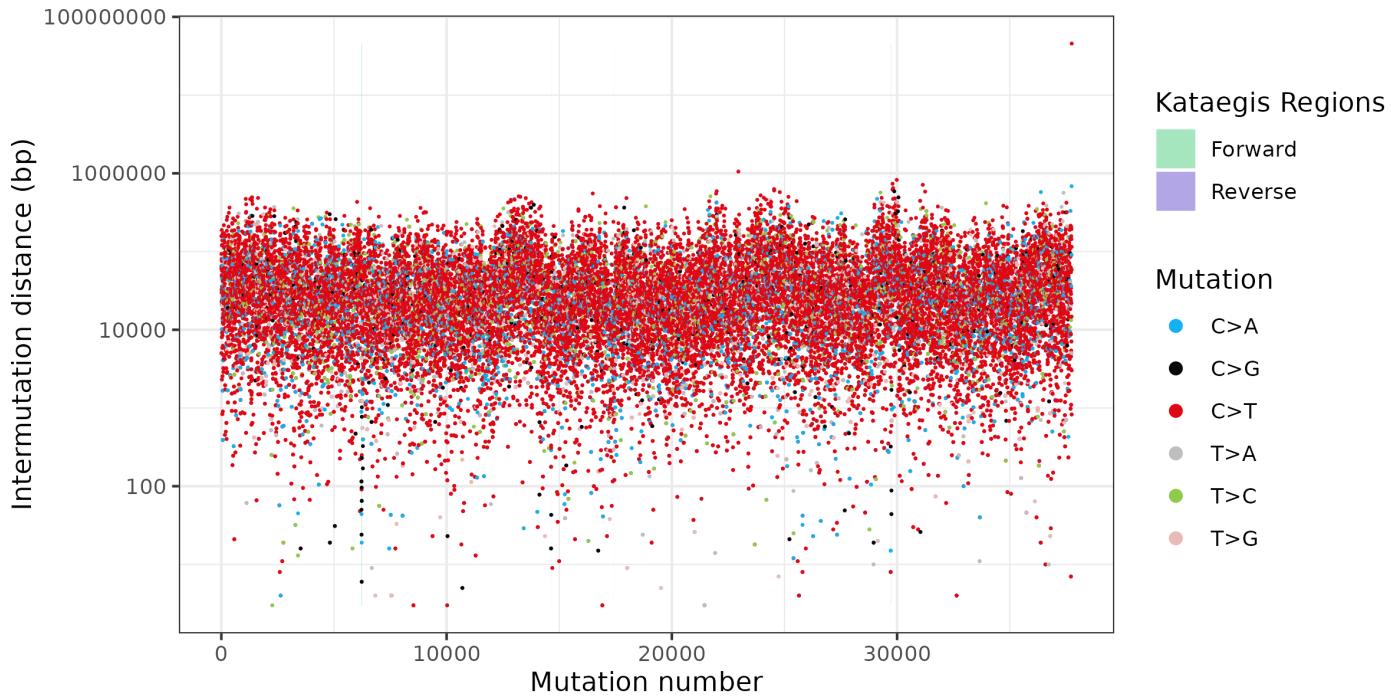
Driver variants (7)

VARIANT	VCN	CN	MACN	BIALLELIC	HOTSPOT	DL	CL	PHASE ID	RNA DEPTH
BRAF p.V600E	4.1	6.0	2.0	2%	Yes	100%	100%		NA
CDKN2A p.A68fs	2.0	2.0	0.0	100%	Near	100%	100%		NA
CDKN2A (alt) p.G83fs	2.0	2.0	0.0	100%	Near	100%	100%		NA
TERT c.-125_-124delCCinsTT	1.7	2.0	0.0	92%	Yes	100%	100%	4304	NA
HDAC2 p.R409*	0.9	2.9	1.0	2%	No	34%	100%		NA
SF3B1 p.P718L	2.0	3.0	1.0	2%	No	15%	100%		NA
TP63 p.M499I	1.8	4.0	2.0	2%	No	0%	100%		NA

Other potentially relevant variants (2)

VARIANT	VCN	CN	MACN	BIALLELIC	HOTSPOT	DL	CL	PHASE ID	RNA DEPTH
ALB c.1059-52dupT	1.8	3.9	1.9	2%	No		100%		NA
STK19 p.D89N	2.0	3.8	1.8	2%	Yes		100%		NA

Kataegis plot



Driver amplifications and homozygous deletions (1)

LOCATION	GENE	TYPE	CN	TPM	PERC (TYPE)	FC (TYPE)	PERC (DB)	FC (DB)
10q23.31	PTEN	partial del	0.0	NA	NA	NA	NA	NA

Potentially interesting near-driver amplifications (0)

NONE



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Other regions with amplifications (1)

LOCATION	GENE	TYPE	CN	TPM	PERC (TYPE)	FC (TYPE)	PERC (DB)	FC (DB)
3p24.2	CFL1P7	full gain	12.1	NA	NA	NA	NA	NA

Regions with deletions in genes in other autosomal regions (1)

LOCATION	GENE	TYPE	CN	TPM	PERC (TYPE)	FC (TYPE)	PERC (DB)	FC (DB)
16q21	CNOT1	partial del	0.0	NA	NA	NA	NA	NA

Potentially interesting chromosomal rearrangements

CHROMOSOMAL REARRANGEMENT	DETECTED?
1q trisomy	No
1p19q co-deletion	No

Driver fusions (0)

NONE

Other potentially interesting fusions (0)

NONE

Potentially interesting in-frame fusions in case no high drivers detected

High driver likelihood events are detected in this sample, therefore this section is empty

Driver viruses (0)

NONE

Other viral presence (0)

NONE

Homozygous disruptions (0)

NONE

Driver gene disruptions (2)

LOCATION	GENE	RANGE	TYPE	CLUSTER ID	JUNCTION CN	UNDISRUPTED CN
10	PTEN	Intron 5 Upstream	DEL	73	2.0	0.0
10	PTEN	Intron 6 Downstream	DEL	73	2.0	0.0

Other potentially interesting gene disruptions (0)

NONE



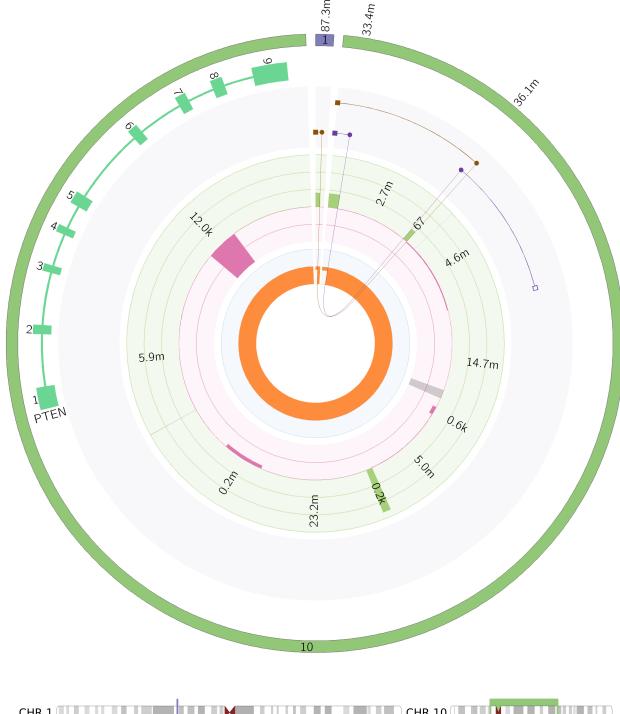
Potentially interesting LOH events (0)

NONE

Signature allocations (12)

SIGNATURE	ETIOLOGY	ALLOCATION	PERCENT
Sig7	Ultraviolet light exposure	23350.7	62%
Sig2	APOBEC activity	3749.5	10%
Sig8	Unknown	2056.2	5%
Sig18	Reactive oxygen species	2012.6	5%
Sig4	Tobacco smoking	2011.8	5%
Sig11	Temozolomide treatment	1263.2	3%
Sig12	Unknown	1121.8	3%
Sig17	Unknown	1109.9	3%
Sig28	Unknown	526.6	1%
Sig24	Aflatoxin exposure	309.0	1%
Sig20	Unknown	241.7	1%
MISALLOC	-	4610.5	12%

Structural driver plots (3)



CHR 10

CHR 1

CHR 10



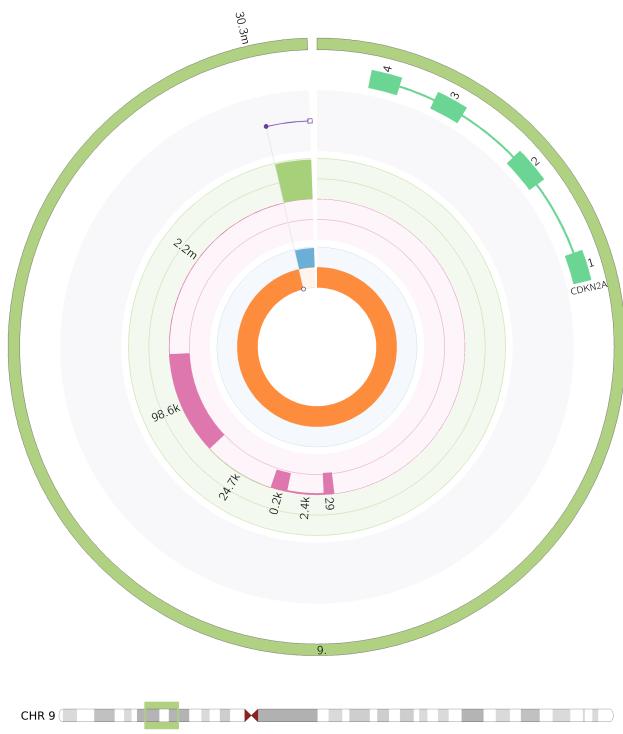
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Germline Findings

Driver variants (0)

NONE

Other potentially relevant variants (3)

VARIANT	VCN	CN	MACN	RNA DEPTH	BIALLELIC	HOTSPOT	GENOTYPE
CYP2D6 c.506-1G>A splice	1.8	4.0	2.0	NA	No	Yes	HET
CYP3A4 c.522-191C>T	2.4	4.0	2.0	NA	No	Yes	HET
CYP3A4 upstream	4.0	4.0	2.0	NA	Yes	Yes	HOM

Potentially pathogenic germline deletions (0)

NONE

Potentially pathogenic germline LOH events (0)

NONE

Potentially pathogenic germline homozygous disruptions (0)

NONE

Potentially pathogenic germline gene disruptions (0)

NONE

Genes with missed variant likelihood > 1% (0)

NONE

Germline CN aberrations (0)

NONE

Pharmacogenetics (1)

GENE	HAPLOTYPE	GENOTYPE	FUNCTION	LINKED DRUGS	SOURCE
DYPD	*1	HOM	Normal Function	5-Fluorouracil;Capecitabine;Tegafur	PHARMGKB



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Immunology

HLA QC

QC Status: PASS

HLA Alleles (6)

ALLELE	REF FRAGS	TUMOR FRAGS	RNA FRAGS	TUMOR CN	SOMATIC #MUTATIONS
A*01:01	210	1609	NA	2.0	NONE
A*01:01	211	1609	NA	1.8	NONE
B*08:01	217	753	NA	1.8	NONE
B*40:02	196	726	NA	2.0	NONE
C*03:04	213	772	NA	2.0	NONE
C*07:01	225	772	NA	1.8	NONE

Genetic Immune Escape

ESCAPE MECHANISM	DETECTED?
HLA-1 loss-of-function	No
Antigen presentation pathway inactivation	No
IFN gamma pathway inactivation	No
(Potential) PD-L1 overexpression	No
CD58 inactivation	No
Epigenetics driven immune escape via SETDB1	No



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Cohort Comparison

Probabilities by classifier

Cancer group (strips) and subtype (label)

	Bone/Soft tissue	Breast	CNS	Pynecology	HPB	Head and neck	Kidney	Lung	Myeloid	NET	Skin
DNA	[GROUP] DNA COMBINED DNA COMBINED GENOMIC POSITION SNV96 EVENT	Anogenital - Carriaginous neoplasm - GIST - Leiomyosarcoma - Liposarcoma - Osteosarcoma - Undiff. sarcoma - Other Triple negative Other	- Gioma - Medulloblastoma - Pilocytic astrocytoma - Esophagus/Stomach - Colorectum/Small intestine/Appendix - Endometrium - Ovary/Fallopian tube - Gallbladder - Liver - Pancreas - Adenoid cystic - Salivary gland - Other - Chromophobe - Other - Non-small cell: LUAD - Non-small cell: LUSC - Small cell - Lymphoid tissue - Mesotheliom - Acute myeloid leukemia - Myeloproliferative neoplasms - Colorectum/Small intestine - Lung - Pancreas - Prostate - Melanoma - Other - Thyroid gland - Urothelial tract	Probability 1.00 0.75 0.50 0.25 0.00							

SNV96: Mutational signatures

	AID/APOBEC (SBS2/13) = 3894 (10.32%)	0.55	232	3.4	2.5	3	0.98	1.6	0.99	0.92	0.77	0.99	33	428	0.99	0.94	0.95	0.97	0.97	1.5	1	42	0.91	0.64	7.2	1	0.65	0.57	0.94	0.99	3.7	203	160	3.9	4.8	0.98	1	0.33	0.52	0.96	0.33	Quantile in subtype cohort
signature	Smoking (SBS4) = 2079 (5.51%)	0.98	Inf	15	0.99	186	2.2	10	5.8	1.7	1.2	Inf	15	Inf	0.99	1	3.7	1	1	0.95	4.2	5.5	0.98	0.93	866	1.2	0.46	0.16	0.1	Inf	1.6	6	Inf	0.99	1	1.5	1	0.33	0.52	0.96	0.33	>0 - 0.95 (in expected range)
	MMRD (SBS6) = 0 (%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.95 - 1.2 (above expected range)		
	UV (SBS7) = 24249 (64.23%)	19	1770	230	99	104	8.1	2.7	0.99	26	6.3	475	396	2021	39	26	61	43	23	57	35	350	0.97	18	158	30	7.9	22	17	23	63	324	3e+04	142	89	92	0.33	0.55	0.225	1	0.95 - 1.2 (above expected range)	
	ROS/5FU (SBS17) = 1148 (3.04%)	0.97	221	0.99	2.1	1.7	0.95	0.91	0.95	0.93	0.94	Inf	107	177	0.57	0.26	0.99	1	0.95	1	0.95	294	0.92	0.97	0.99	1	0.93	1.2	0.97	0.89	8.1	13	410	0.98	2.8	0.99	0.99	0.98	0.96	0.99	0.92	>1.2 (well above expected range)

EVENT: Feature contributions

tmb	snv count = 37753 indels per mb = 0.1	0.2	0.2	1.1	0.2	0.06			1.9		0.4	1.4	5	4	12		0.9	0.4	3	2.2	0.9	6.8	5.4	0.7				
trait	is male = TRUE whole genome duplication = TRUE	0.4	1.9	0.8	0.6	1.6	0.8	1.1	0.8	0.06	0.1	0.9	0.8	0.7	1.4	0.1	0.07	0.8	1.1	0.8	1.1	1.9	1.7	1.5	0.7			
driver (DL)	ALB indel (1) APC mut (absent) BRAF mut (1) CDKN2A mut (1) PTEN mut (1) SF3B1 mut (0,1) TERT mut (1) TP53 mut (absent)			2					13	118												1.1	0.9	0.9	0.9			
SV	LINE = 0 SIMPLE DEL 20KB 1MB = 22 SIMPLE DUP 32B 200B = 3 SIMPLE DUP 100KB 5MB = 2 MAX COMPLEX SIZE = 8 TELOMERIC SGL = 0.9	0.2	5.5	2.3	1.3	1.4	1.1	1.6	3.3	1.2	0.2	0.1	0.7	0.5	0.9	1.1	0.7		0.2	0.5	0.2	2.5	2	13	2.4	0.8	0.3	
		1.1	0.3	1.2	1.6	1.2	1.1		0.9	0.5	0.9	1.4	1.1		1.3			1.2	0.7	0.8	0.5	1.7	1.7	0.4	0.3	0.5	0.2	
				1.1	1.1				1.1									1.1	1.2	1.3			0.9	0.9		1.1		
					1.1	0.6	0.9	0.9	0.6	0.7	0.9	0.5	1.1	0.9	0.5	0.6	0.7	1.3	0.7	1.2	2.2			1.9	1.3	1.2	0.7	
						0.8				1.7								1.6	1.6	0.9			1.5	0.8	2.6	1.6	1.1	0.9
																		1.1	0.9		1.2		1.2	1.1	0.8	0.7	1.1	0.9
																		1.1	0.9		1.2		1.2	1.1	0.8	0.7	1.1	0.9

DNA COMBINED: Training set performance

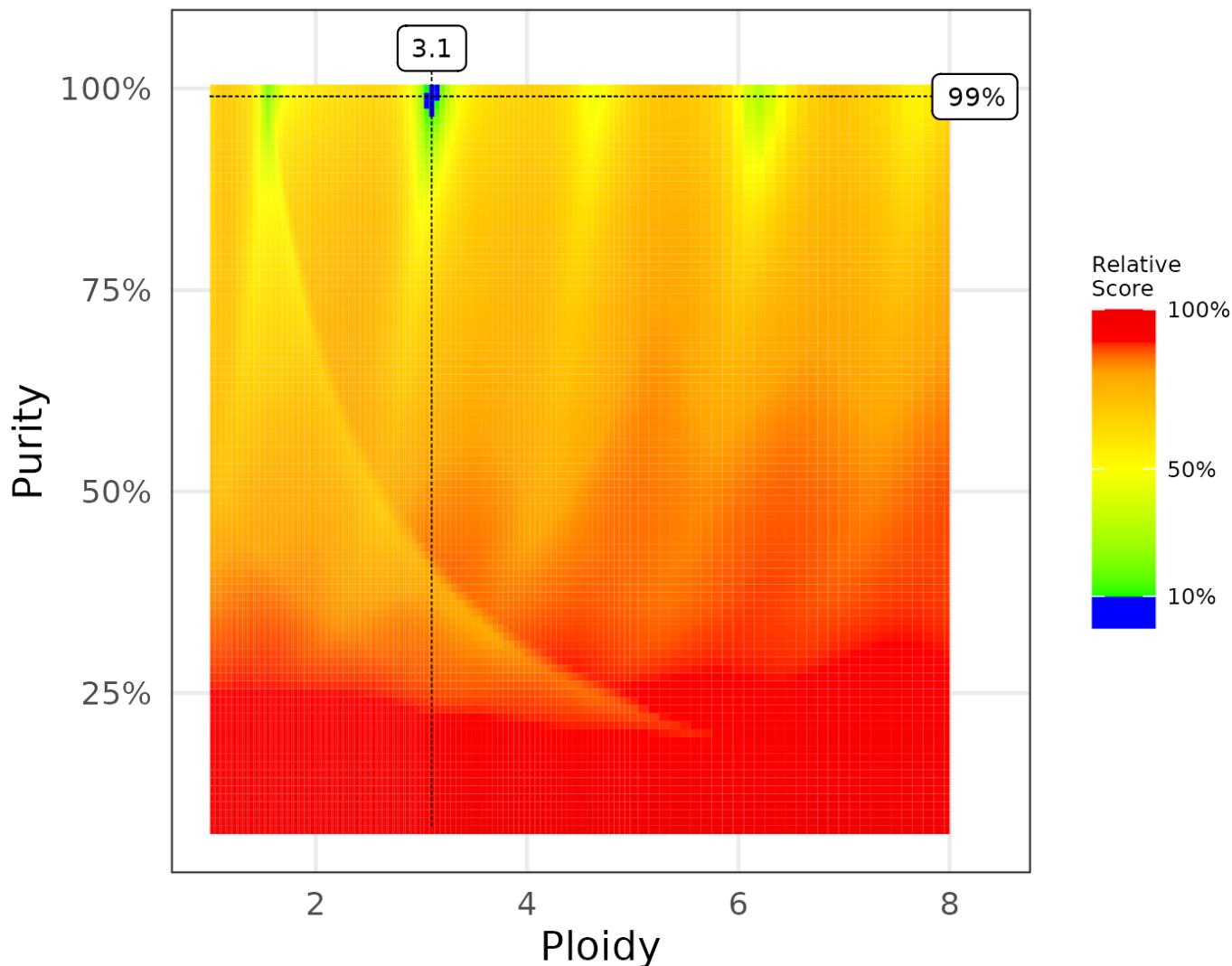
	Total no. of samples	128	9	66	80	59	47	37	157	183	908	159	138	58	837	349	85	320	131	341	372	10	26	101	44	277	254	78	56	216	77	12	18	56	46	118	607	408	49	71	241	1.00
training set	Recall (prop. of total correct)	0.74	0.33	0.95	0.76	0.85	0.57	0.43	0.68	0.7	0.94	0.96	0.94	0.74	0.96	0.85	0.61	0.91	0.54	0.96	0.88	0.5	0.27	0.66	0.77	0.94	0.91	0.65	0.84	0.99	0.91	0.75	0.67	0.79	0.74	0.8	0.99	0.99	0.73	0.73	0.88	0.00
	Precision (prop. of predicted correct)	0.77	0.75	0.91	0.77	0.81	0.77	0.35	0.64	0.77	0.91	0.94	0.86	0.91	0.96	0.87	0.83	0.84	0.76	0.93	0.86	0.62	0.47	0.6	0.94	0.95	0.89	0.77	0.85	0.96	0.92	0.64	0.55	0.77	0.79	0.73	0.96	0.96	0.82	0.87	0.92	0.00



Quality Control

QC	REF GENOME	FIT METHOD	MEAN DEPTH	CONTAMINATION	UNS. SEGMENTS (%)	DELETED GENES
PASS	V37	NORMAL	111	0%	0 (0%)	4

Purity/Ploidy Scores



Flagstats

	UNIQUE RC	SECONDARY RC	SUPPLEMENTARY RC	MAPPED PROPORTION
Ref Sample	691880238	0	871753	100%
Tumor Sample	2513301754	0	3179178	100%



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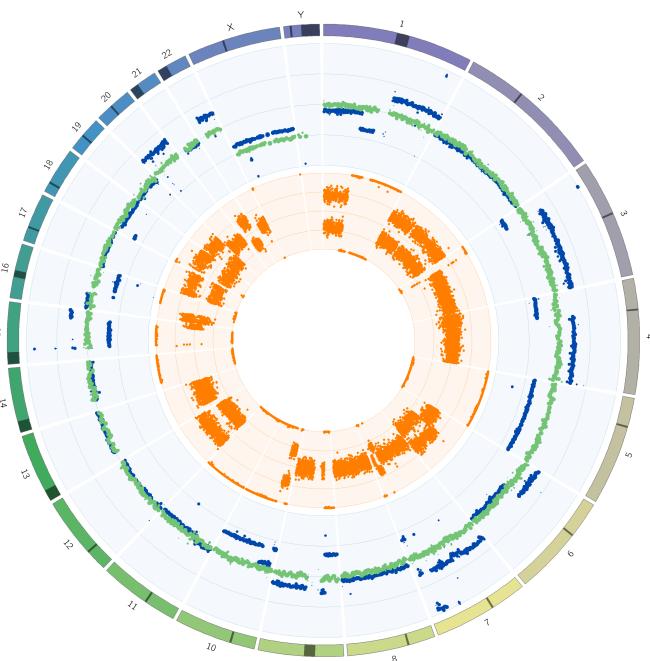
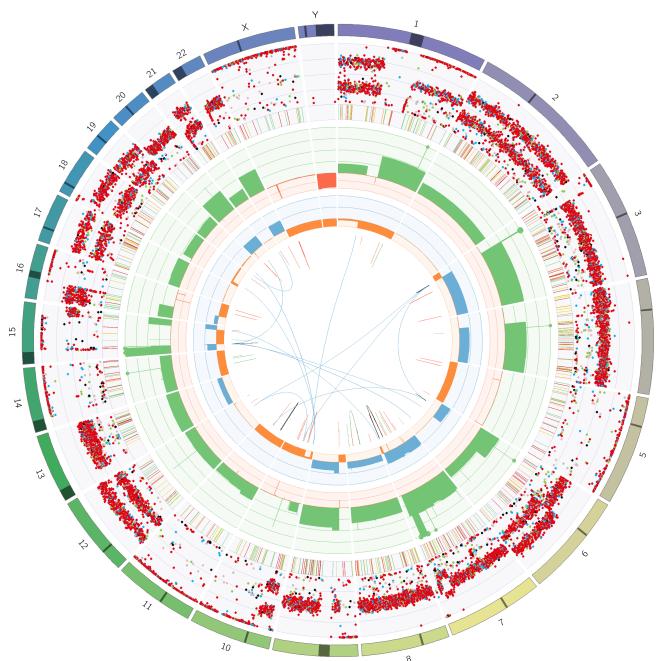
Coverage Stats

	MEAN COVERAGE	SD COVERAGE	MEDIAN COVERAGE	MAD COVERAGE
Ref Sample	31.3	9.4	32	5
Tumor Sample	107.6	34.9	109	23

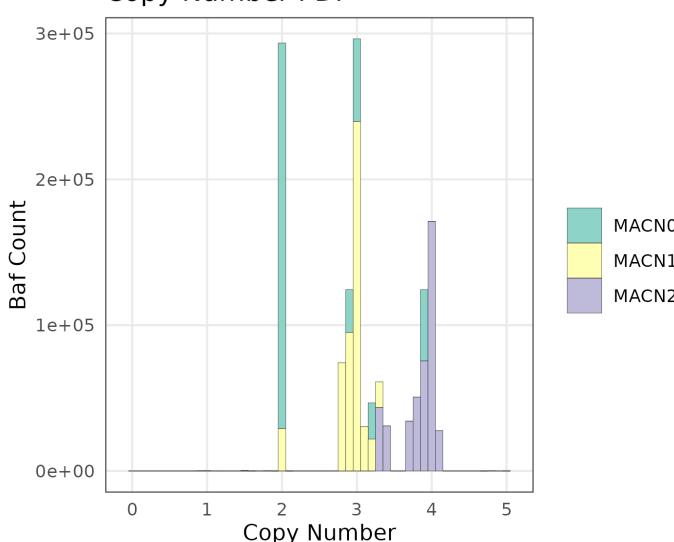
Excluded Percentages

	ADAPTER	BASEQ	CAPPED	DUPE	MAPQ	OVERLAP	UNPAIRED	TOTAL
Ref Sample	0%	0%	0%	11%	2%	0%	0%	13%
Tumor Sample	0%	0%	0%	15%	2%	1%	0%	18%

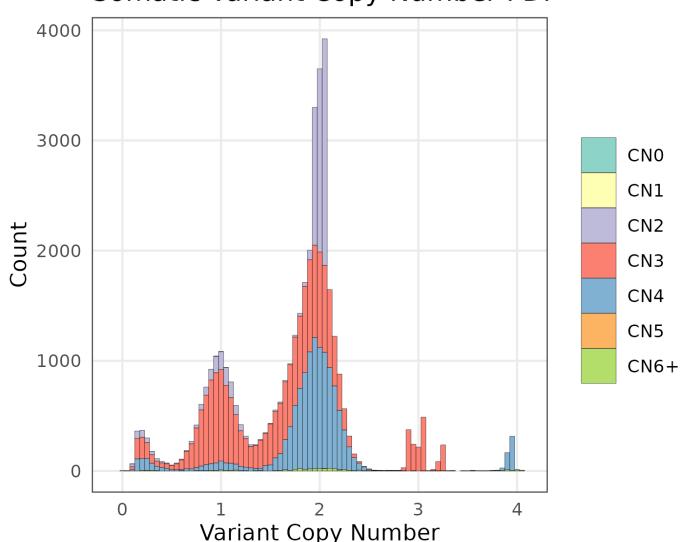
QC plots



Copy Number PDF



Somatic Variant Copy Number PDF





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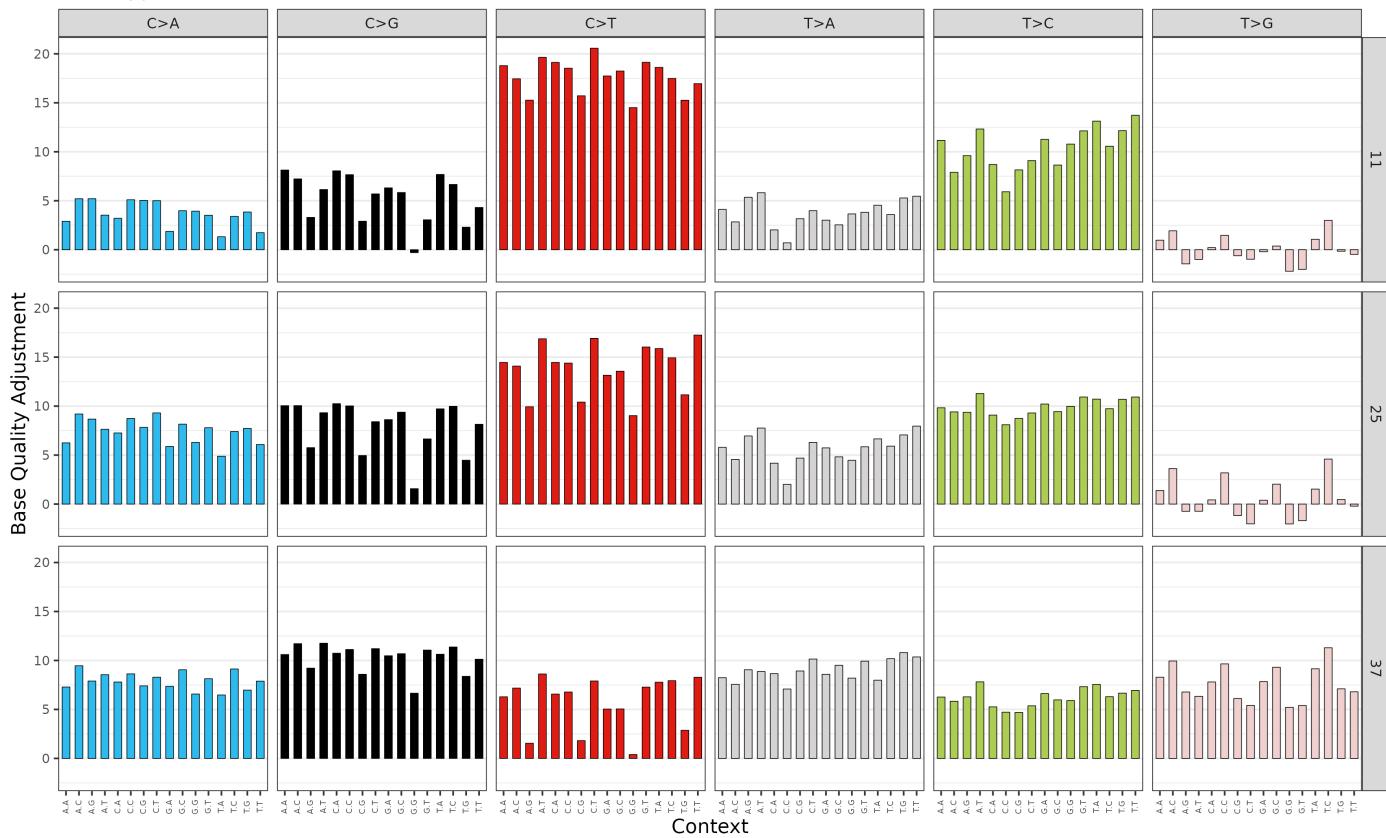
Test

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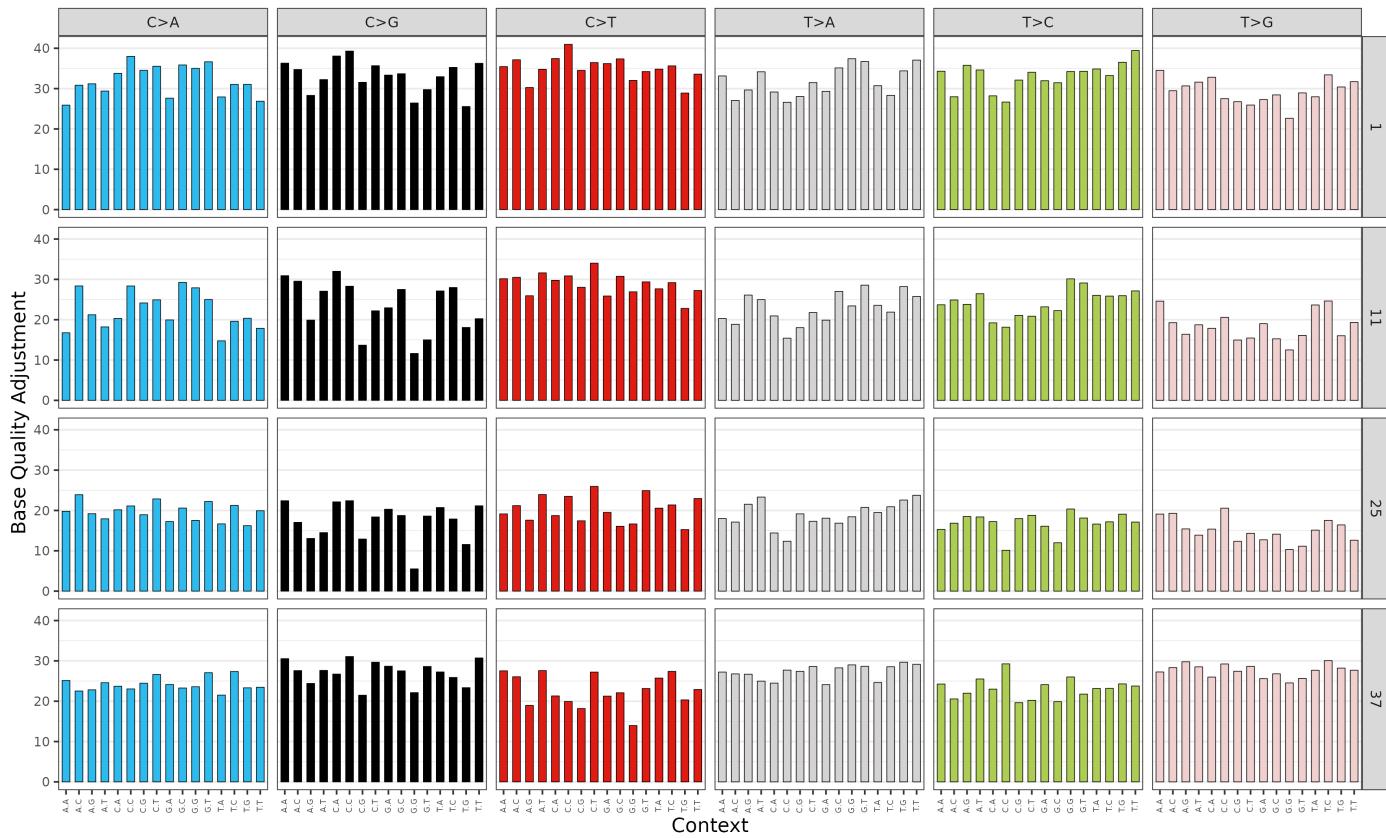
6.0

Reference Sample BQR plot

Read type: NONE



Read type: SINGLE





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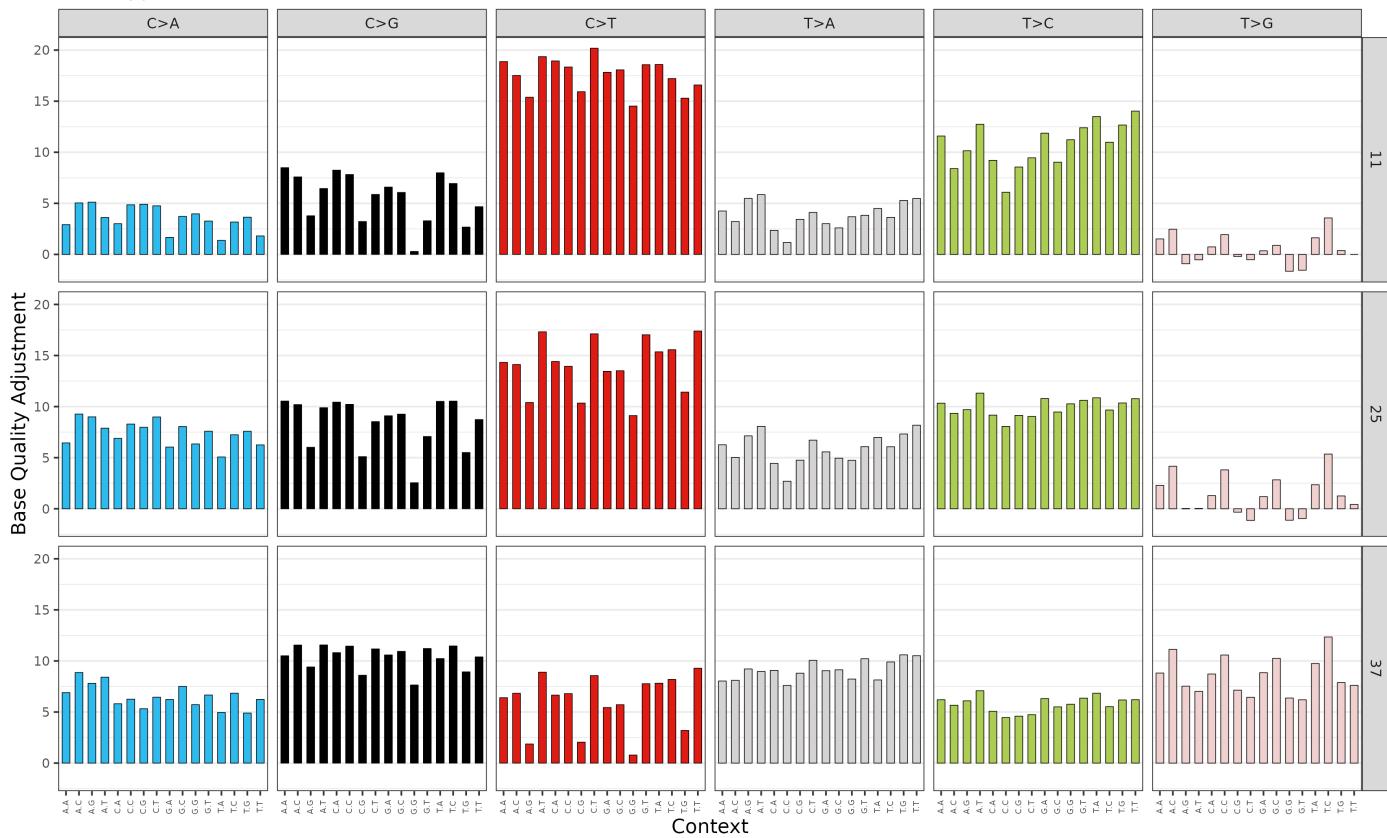
Test

Pipeline Version

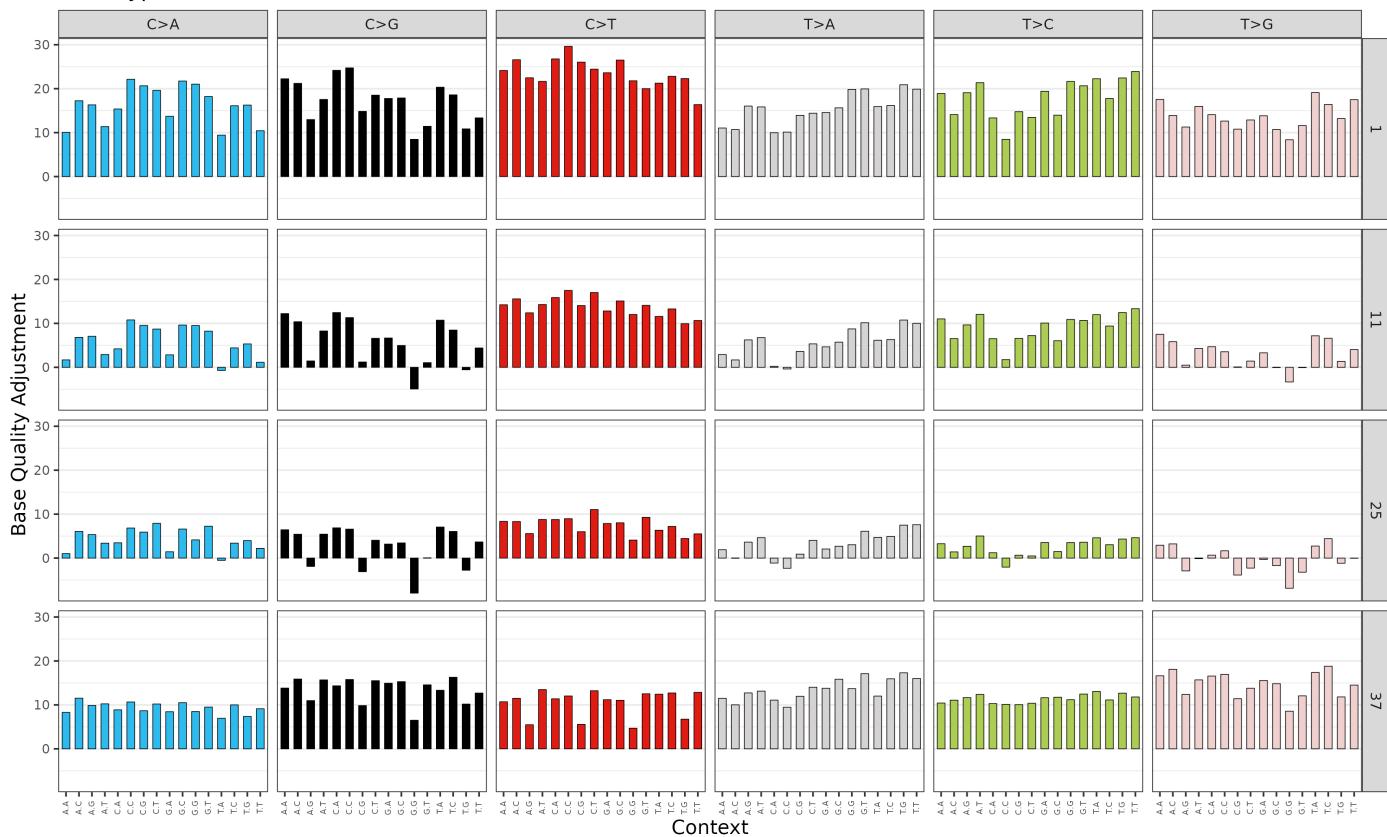
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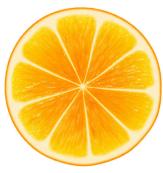
Tumor Sample BQR plot

Read type: NONE



Read type: SINGLE





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Tumor Detection Statistics

Tumor maximum diploid proportion	0.02
Number of hotspot mutations	3
Number of hotspot structural variants	0
Sum of small variant allele read counts	2287733
Sum of structural variant tumor fragment counts (excluding single breakends)	6408
Sum of B-allele frequency points in germline diploid regions with tumor ratio < 0.8 OR > 1.2	682755