



ORANGE Report

SAMPLE

Test

PLATINUM VERSION

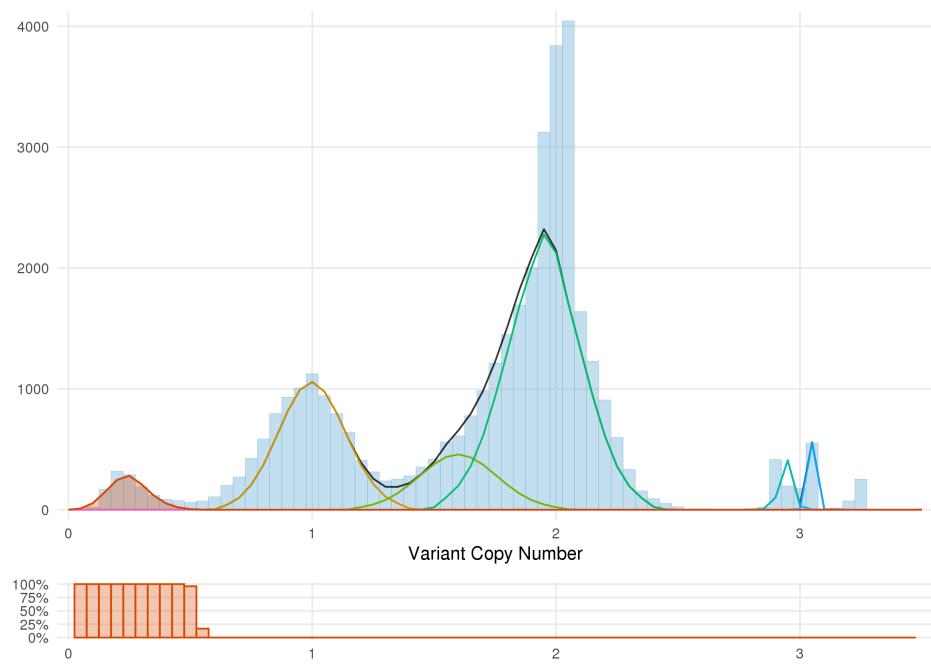
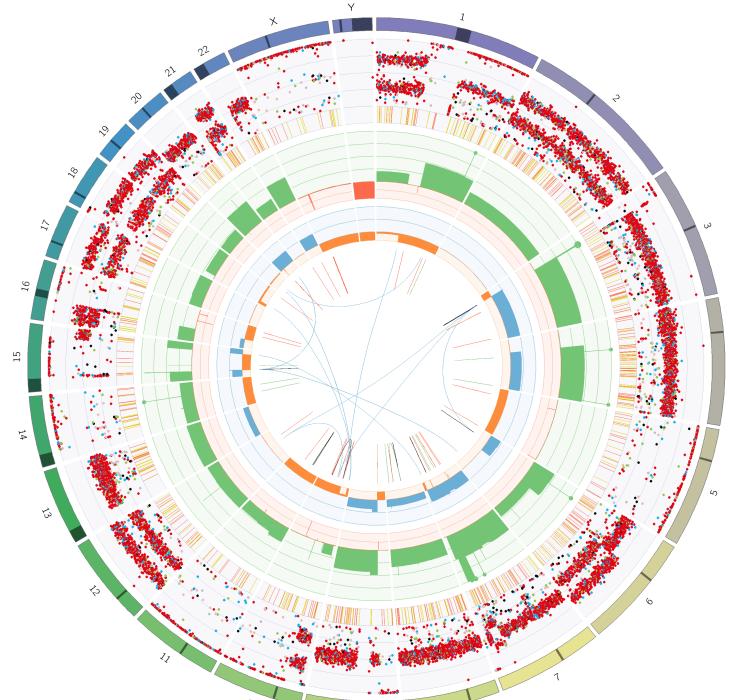
5.34

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:	5 (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:	*1 HOM (Normal Function)
Number of SVs:	75 (Pan 0.22 Skin 0.34)
Max complex cluster size:	8
Telomeric SGLs:	0
Number of LINE insertions:	3





Somatic Findings

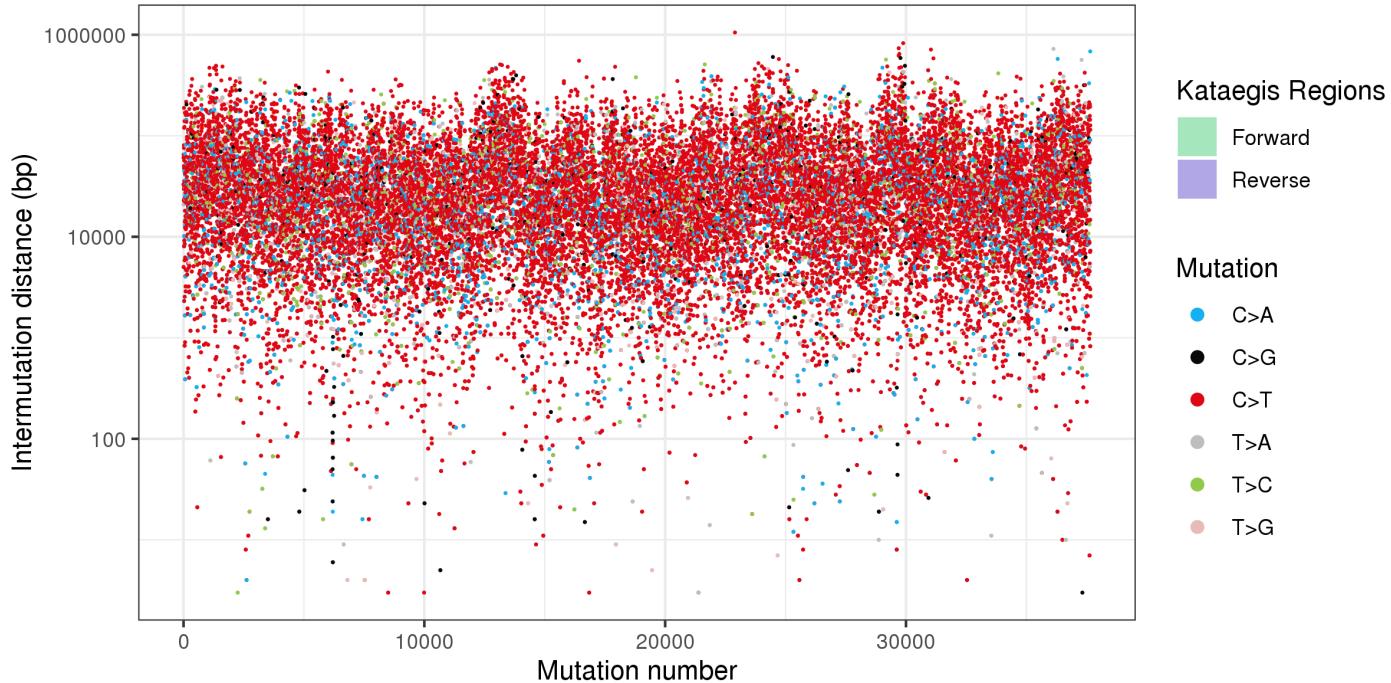
Driver variants (6)

VARIANT	VCN	CN	MACN	BIALLELIC	HOTSPOT	DL	CL	PHASE ID	RNA DEPTH
BRAF p.V600E	4.1	6.0	2.0	No	Yes	100%	100%		NA
CDKN2A p.A68fs	2.0	2.0	0.0	Yes	Near	100%	100%		NA
CDKN2A (alt) p.G83fs	2.0	2.0	0.0	Yes	Near	100%	100%		NA
TERT c.-125_-124delCCinsTT	1.7	2.0	0.0	Yes	Yes	100%	100%	4725	NA
SF3B1 p.P718L	2.0	3.0	1.0	No	No	15%	100%		NA
TP63 p.M499I	1.7	4.0	2.0	No	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	No	No		100%		NA
STK19 p.D89N	2.0	3.8	1.8	No	Yes		100%		NA

Kataegis plot



Driver amps/dels (1)

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

Potentially interesting near-driver amps (0)

NONE



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Other regions with amps (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 loss	0.1	NA	NA	NA	NA	NA

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
10q23.31	PTEN	Intron 5 Upstream	DEL	68	2.0	0.0
10q23.31	PTEN	Intron 6 Downstream	DEL	68	2.0	0.0

Other potentially interesting gene disruptions (0)

NONE

Potentially interesting LOH events (0)

NONE



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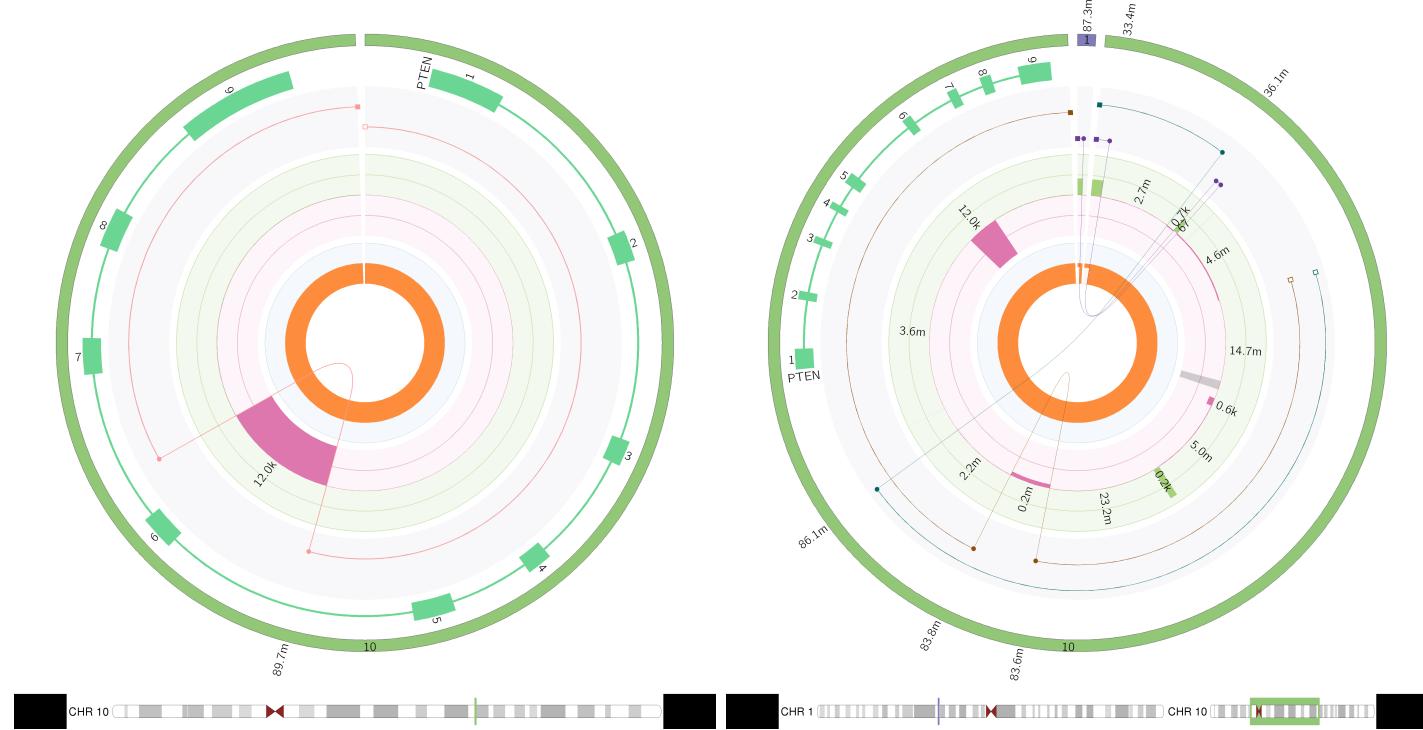
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Signature allocations (12)

SIGNATURE	ETIOLOGY	ALLOCATION	PERCENT
Sig7	Ultraviolet light exposure	23286.3	62%
Sig2	APOBEC activity	3702.7	10%
Sig18	Reactive oxygen species	2057.3	5%
Sig4	Tobacco smoking	2038.8	5%
Sig8	Unknown	1984.8	5%
Sig11	Temozolomide treatment	1313.3	3%
Sig12	Unknown	1137.1	3%
Sig17	Unknown	1083.2	3%
Sig28	Unknown	514.4	1%
Sig24	Aflatoxin exposure	289.0	1%
Sig20	Unknown	253.1	1%
MISALLOC	-	4611.5	12%

Structural driver plots (3)





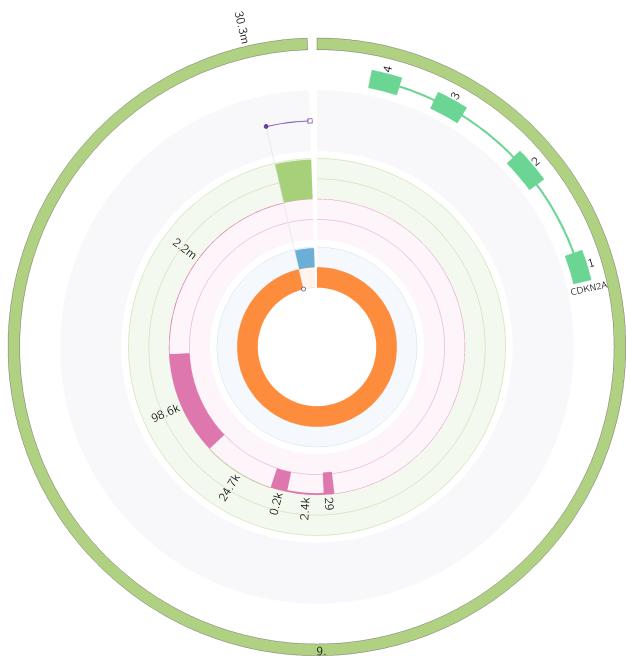
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Germline Findings

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 (2)

GENE	HAPLOTYPE	GENOTYPE	FUNCTION	LINKED DRUGS	SOURCE
DYPD	*1	HOM	Normal Function	5-Fluorouracil;Capecitabine;Tegafur	PHARMGKB
UGT1A1	*1	HOM	Normal Function	Irinotecan	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	1602	NA	2.0	NONE
A*01:01	211	1602	NA	1.8	NONE
B*08:01	216	750	NA	1.8	NONE
B*40:02	196	721	NA	2.0	NONE
C*03:04	213	768	NA	2.0	NONE
C*07:01	225	767	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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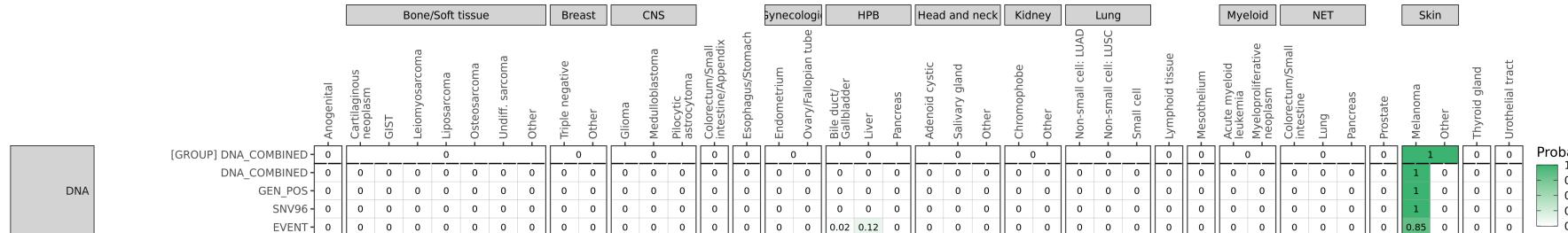
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Cohort Comparison

Probabilities by classifier

Cancer group (strips) and subtype (label)



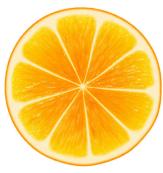
SNV96: Mutational signatures

EVENT: Feature contributions



DNA COMBINED: Training set performance

training_set	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
	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	
	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	



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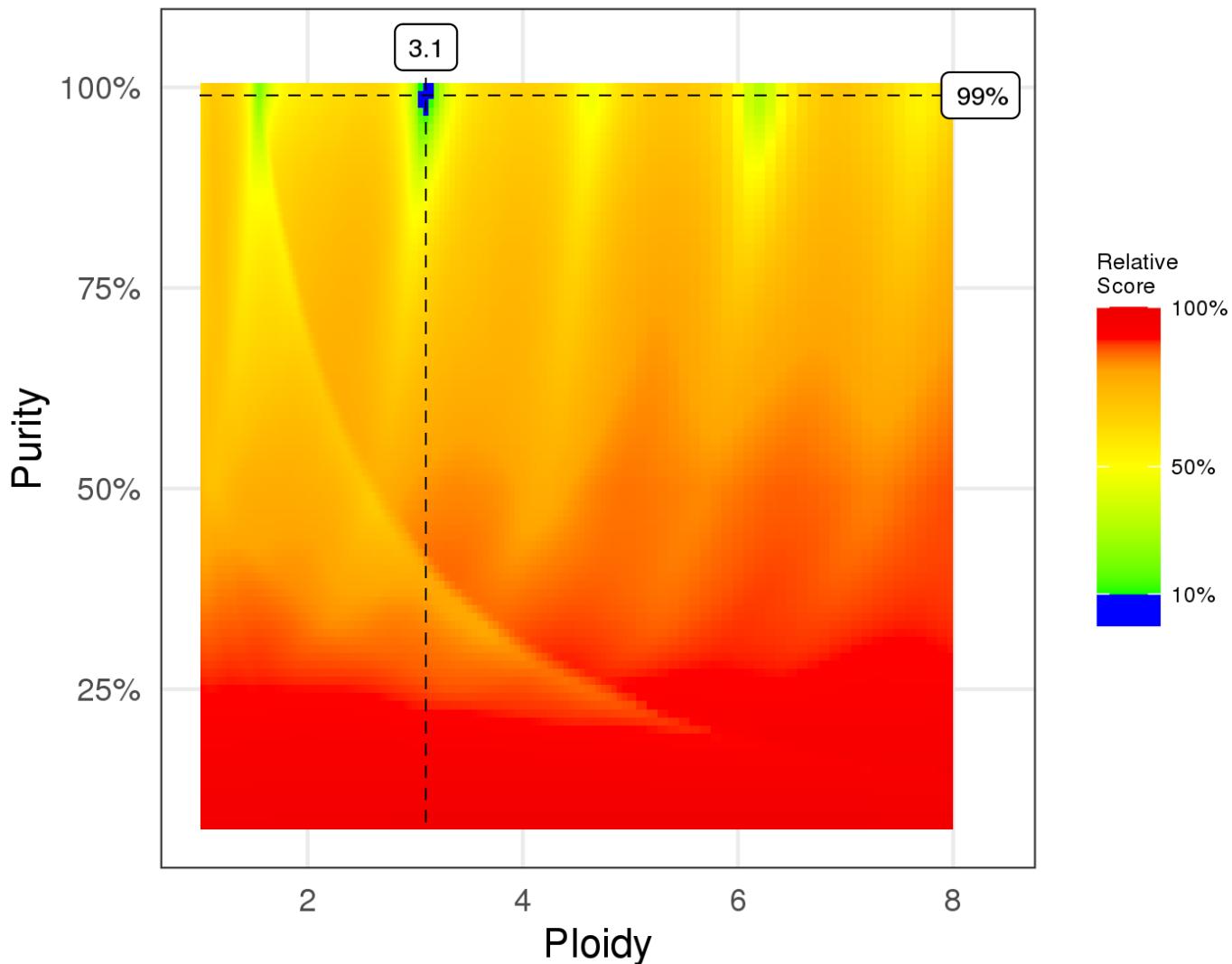
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Quality Control

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	740406212	0	5742696	99%
Tumor Sample	2671674230	0	21477075	100%



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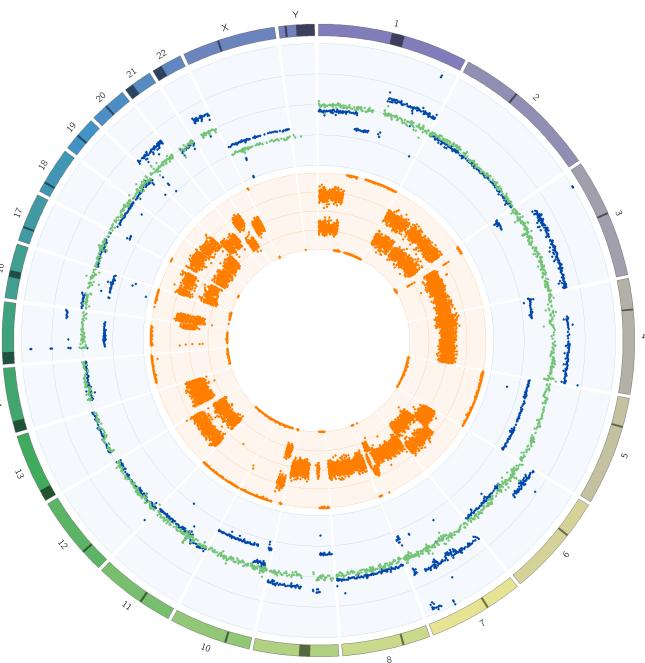
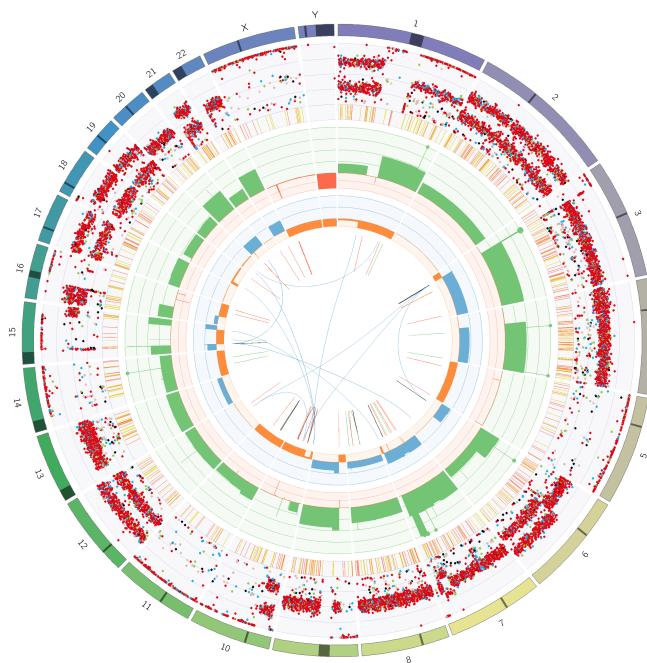
Coverage Stats

	MEAN COVERAGE	SD COVERAGE	MEDIAN COVERAGE	MAD COVERAGE
Ref Sample	31.4	10.1	32	5
Tumor Sample	108.0	35.0	109	24

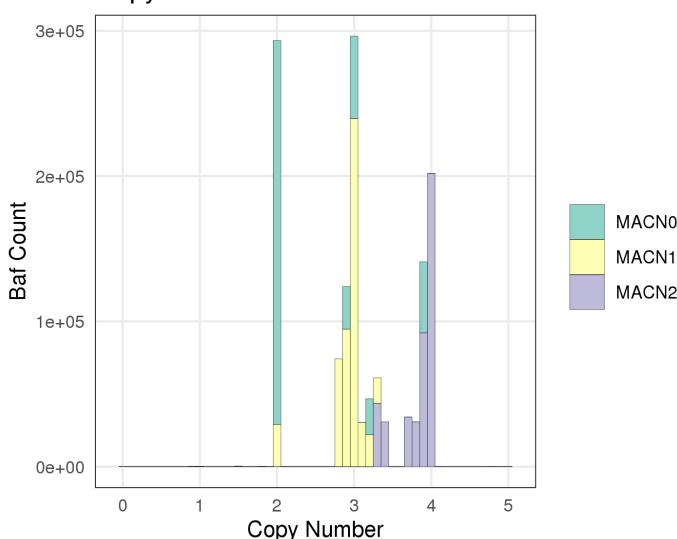
Excluded Percentages

	ADAPTER	BASEQ	CAPPED	DUPE	MAPQ	OVERLAP	UNPAIRED	TOTAL
Ref Sample	0%	0%	1%	11%	5%	1%	0%	18%
Tumor Sample	0%	0%	1%	15%	5%	1%	0%	22%

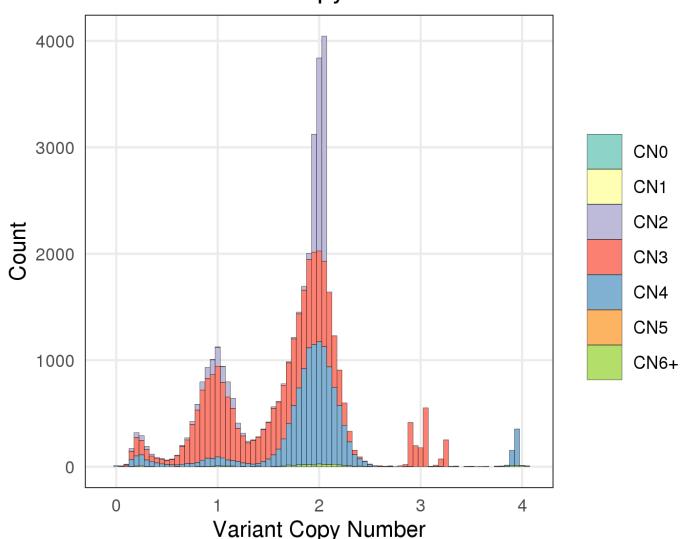
QC plots

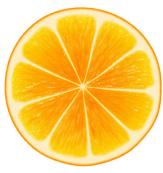


Copy Number PDF



Somatic Variant Copy Number PDF





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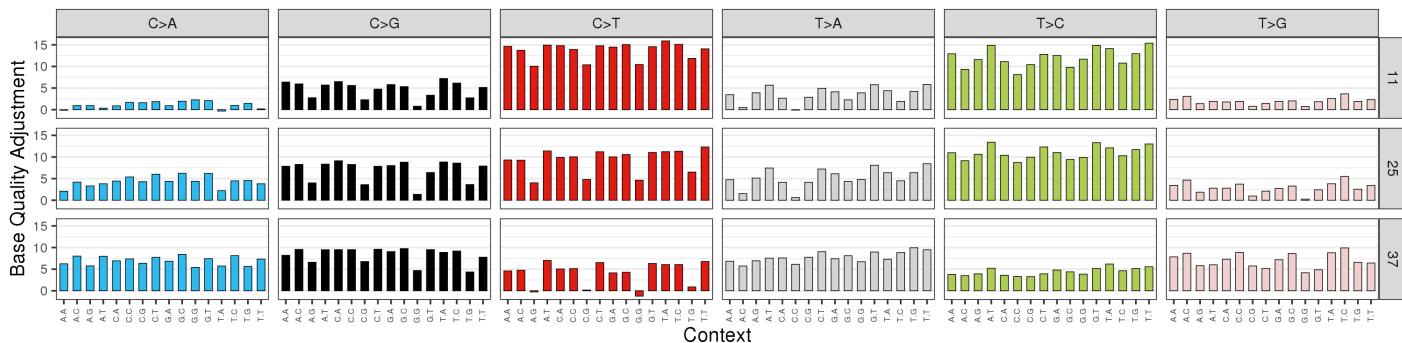
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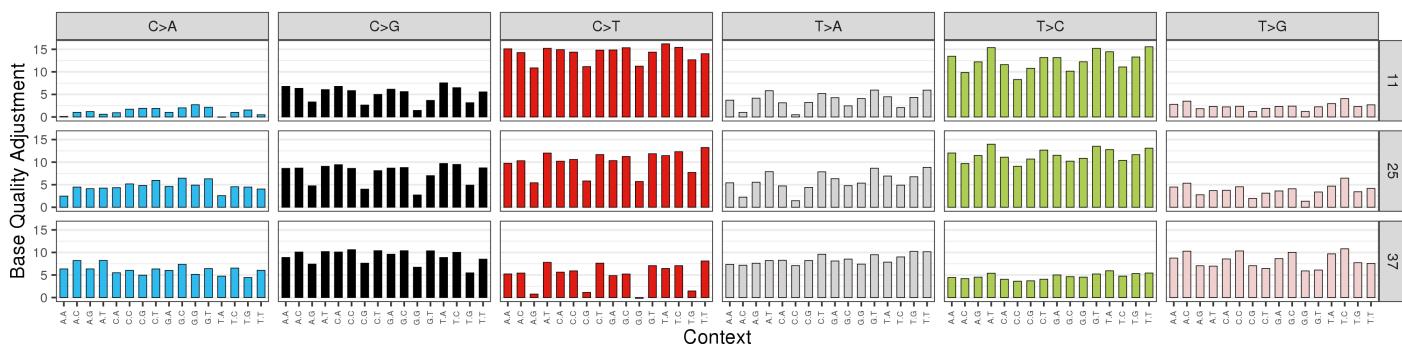
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Reference Sample BQR plot



Tumor Sample BQR plot



Tumor detection requirements

At least one requirement needs to be met to indicate detection of tumor, in case of highly diploid candidate solutions (proportion ≥ 0.97)

Tumor maximum diploid proportion	0.02
Number of hotspot mutations	3
Number of hotspot structural variants	0
Sum of small variants allele read counts	2273196
Sum of structural variant tumor fragment counts (excluding single breakends)	4908
Sum of B-allele frequency points in germline diploid regions regions with tumor ratio < 0.8 OR > 1.2	675344