



ORANGE Report

SAMPLE

Test

PLATINUM VERSION

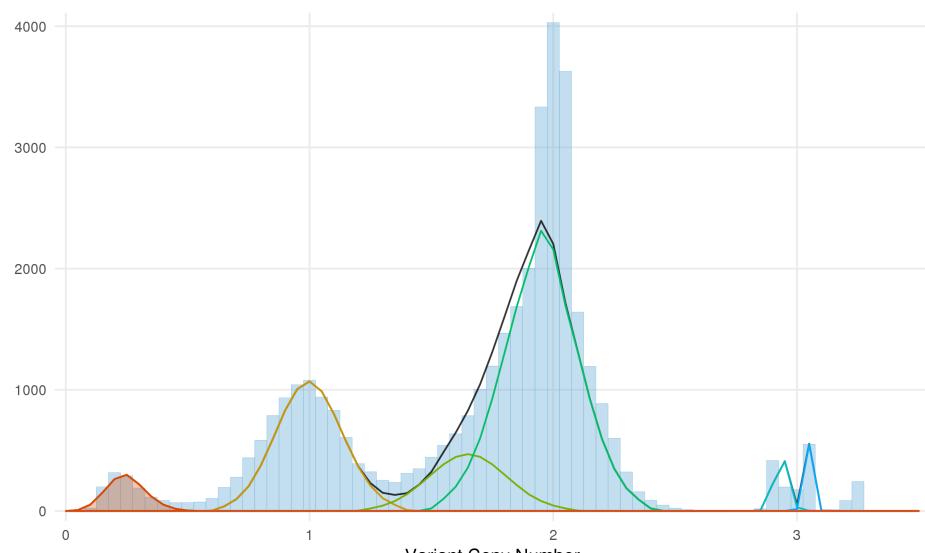
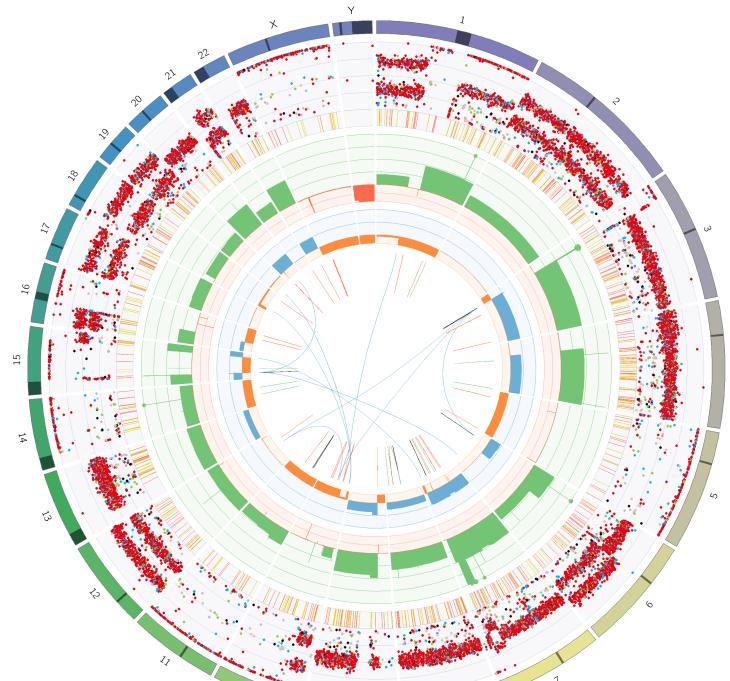
5.28

CONFIGURED PRIMARY TUMOR
skin melanoma (DOID 8923)

CUPPA CANCER TYPE
Melanoma (100%)

QC
PASS

Purity:	99% (97%-100%)
Ploidy:	3.1 (3.1-3.15)
Somatic variant drivers:	6 (BRAF, CDKN2A, TERT)
Germline variant drivers:	None
Copy number drivers:	1 (PTEN)
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
Tumor mutational load:	186 (High)
HR deficiency score:	0 (Proficient)
DPYD status:	*1_HOM (Normal Function)
Number of SVs:	72 (Pan 22% Skin 34%)
Max complex cluster size:	8
Telomeric SGLs:	0
Number of LINE insertions:	4
On-label treatments:	29 (A, B, C, D)
Off-label treatments:	61 (A, B, C, D)





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Somatic Findings

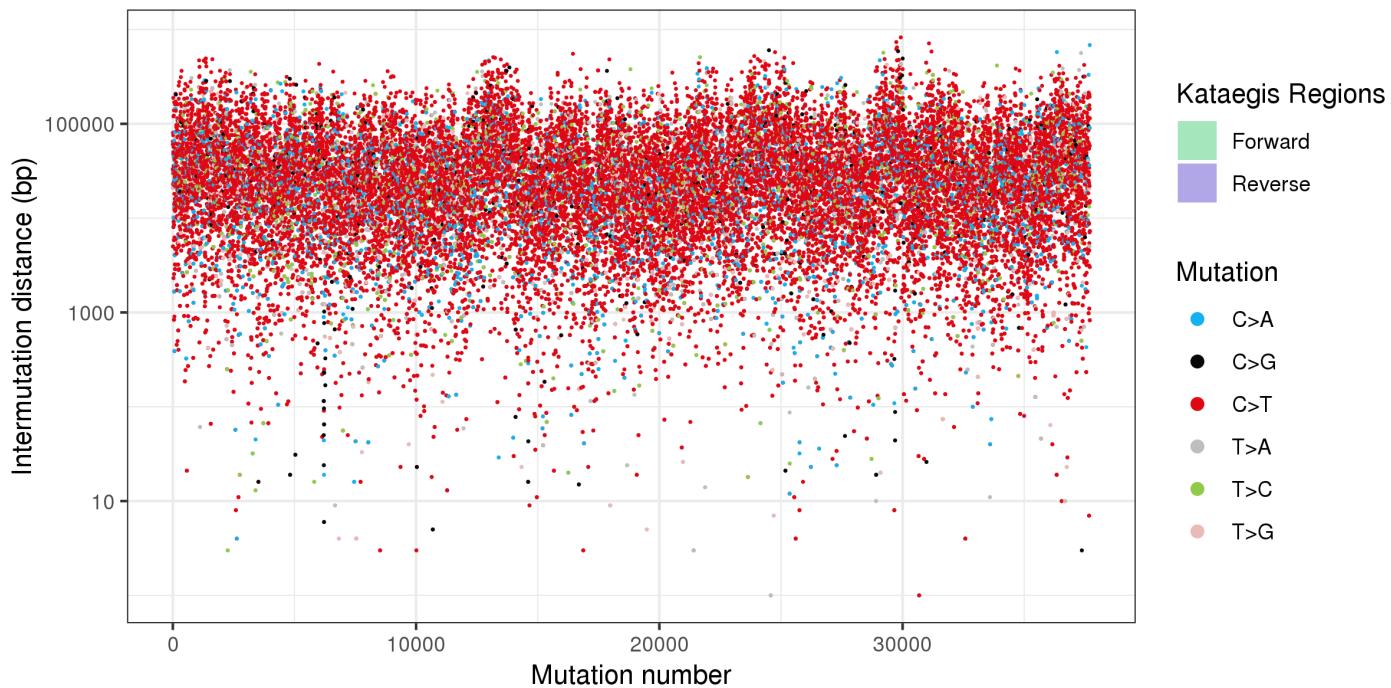
Driver variants (6)

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 upstream	1.7	2.0	0.0	Yes	Yes	100%	100%	4410	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 (3)

VARIANT	VCN	CN	MACN	BIALLELIC	HOTSPOT	DL	CL	PHASE ID	RNA DEPTH
ALB c.1059-53dupT	1.8	3.9	1.9	No	No		100%		NA
HDAC2 p.R409*	0.9	2.9	1.0	No	No		100%		NA
STK19 p.D89N	2.0	3.8	1.8	No	Yes		100%		NA

Kataegis plot



Driver amps/dels (1)

CHR	REGION	GENE	TYPE	CN	TPM	PERC (TYPE)	FC (TYPE)	PERC (DB)	FC (DB)
10	q23.31	PTEN	partial loss	0	NA	NA	NA	NA	NA



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Other regions with amps (1)

CHR	REGION	GENE	TYPE	CN	TPM	PERC (TYPE)	FC (TYPE)	PERC (DB)	FC (DB)
3	p24.2	CFL1P7	full gain	12	NA	NA	NA	NA	NA

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

CHR	REGION	GENE	TYPE	CN	TPM	PERC (TYPE)	FC (TYPE)	PERC (DB)	FC (DB)
16	q21	CNOT1	partial loss	0	NA	NA	NA	NA	NA

Driver fusions (0)

NONE

Other potentially interesting fusions (0)

NONE

Driver viruses (0)

NONE

Other viral presence (0)

NONE

Homozygous disruptions (0)

NONE

Gene disruptions (1)

LOCATION	GENE	RANGE	TYPE	JUNCTION CN	UNDISRUPTED CN
10q23.31	PTEN	Intron 5 -> Intron 6	DEL	2.0	0.0

Potentially interesting LOH events in case of MSI or HRD (0)

NONE

Structural drivers (3)

GENE	EVENT TYPE
CDKN2A	LOH_SV_TELO
PTEN	DEL
PTEN	LOH_SV_TELO

Structural driver plots (3)



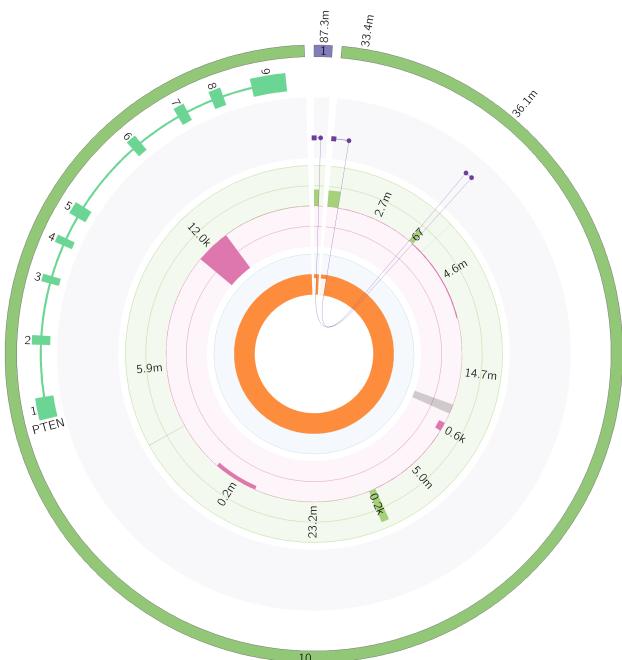
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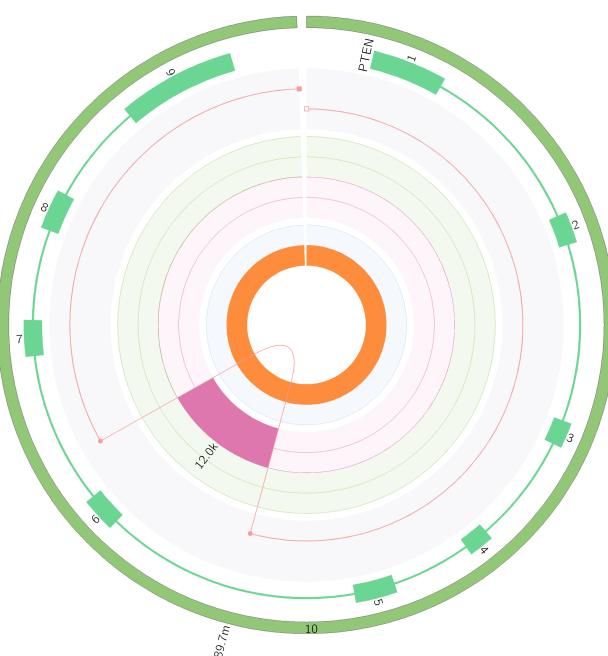
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CHR 1 CHR 10



CHR 10 CHR 10



CHR 9 CHR 9



Germline Findings

Driver variants (0)

NONE

Other potentially relevant variants (3)

VARIANT	VCN	CN	MACN	RNA DEPTH	BIALLELIC	HOTSPOT	GENOTYPE
CYP2D6 p.?	1.8	4.0	2.0	NA	No	Yes	HET
CYP3A4 c.522-191C>T	2.5	4.0	2.0	NA	No	Yes	HET
CYP3A4 upstream	4.0	4.0	2.0	NA	Yes	Yes	HOM

Driver germline deletions (0)

NONE

Driver germline disruptions (0)

NONE

Genes with missed variant likelihood > 1% (0)

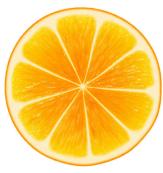
NONE

Germline CN aberrations (0)

NONE

Pharmacogenetics (1)

GENE	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	1602	NA	2	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	None
C*03:04	213	768	NA	2	None
C*07:01	225	767	NA	1.8	None



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RNA Findings

NA



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Cohort Comparison

	Acute myeloid leukemia	Angiomyxoma	Bile duct/Ca/bile duct	Bone/Soft tissue: Other	Breast	Cartilaginous neoplasm	Chronic lymphocytic leukemia	Colon/Rectum/Appendix/Small intestine	Esophagus/Stomach	GIST	Glioma	Head and neck: other	Kidney	Leiomyosarcoma	Liposarcoma	Liver	Lung: NET	Lung: Non-small Cell	Lung: Small Cell	Lymphoid tissue	Meningioma	Mesothelioma	Myeloproliferative neoplasm	Osteosarcoma	Ovary/Fallopian tube	Pancreas	Pancreas: NET	Piloicytic astrocytoma	Prostate	Salivary gland/Adenoid cystic	Skin: Other	Small intestine/colon/rectum: NET	Thyroid gland	Urinary tract	Uterus: Endometrium	
SNV 96 PAIRWISE SIMILARITY	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	1%	0%	0%	0%	0%	0%	0%	0%	0%	97%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%				
GENOMIC POSITION SIMILARITY	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	100%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%				
FEATURE	0%	0%	1%	0%	0%	0%	0%	0%	0%	0%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	98%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%				
DNA COMBINED	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	100%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%				
SEX (MALE)	62%	16%	49%	53%	1%	78%	67%	56%	83%	65%	68%	76%	70%	29%	60%	76%	46%	44%	52%	57%	59%	61%	82%	46%	46%	0%	52%	60%	48%	100%	50%	67%	59%	76%	73%	0%

SNV SIGNATURES

SIG 7 UV (24251)	34700%	1920%	4140%	98%	1260%	176000%	49600%	1670%	2580%	24700%	50000%	144%	2910%	9970%	14300%	5700%	1140%	791%	1600%	2350%	39800%	34%	7890%	457000%	7990%	4330%	3580%	9450%	201000%	5660%	2930%	63%	10600%	27800%	747%	6130%	
SIG 6 MMR (0)	50%	22%	36%	44%	36%	44%	44%	31%	40%	40%	49%	27%	42%	42%	50%	42%	38%	34%	46%	42%	44%	45%	38%	40%	44%	30%	43%	38%	42%	40%	43%	48%	32%	38%	39%	22%	
SIG 4 SMOKING (2115)	664%	99%	107%	650%	120%	10000%	10000%	99%	189%	145%	10000%	93%	124%	99%	10000%	96%	97%	41%	9%	10000%	50000%	99%	169%	10000%	227%	101%	166%	127%	49700%	152%	98%	99%	10000%	322%	92%	376%	105%
SIG 2 13 AID APOBEC (3860)	20900%	67%	103%	98%	85%	41600%	10300%	100%	98%	80%	99%	88%	152%	518%	458%	1980%	82%	125%	99%	4110%	34%	865%	16100%	99%	100%	165%	98%	35000%	225%	99%	92%	677%	96%	59%	105%		
SIG 17 (1119)	1390%	97%	94%	97%	95%	22100%	208%	541%	24%	98%	10000%	97%	100%	285%	366%	100%	10000%	93%	97%	81%	10300%	97%	1560%	39300%	95%	99%	99%	18000%	99%	93%	92%	701%	353%	90%	97%		
SIG 11 (1328)	2410%	99%	100%	97%	100%	5370%	1870%	100%	100%	542%	93%	100%	336%	98%	252%	267%	385%	99%	123%	99%	923%	87%	431%	1260%	384%	100%	161%	98%	14600%	271%	55%	55%	219%	98%	212%		
SIG 10 POLE (0)	45%	24%	25%	37%	25%	50%	42%	15%	25%	32%	48%	16%	31%	41%	48%	37%	45%	38%	46%	30%	24%	45%	39%	42%	39%	44%	28%	42%	38%	35%	29%	40%	48%	22%	28%	41%	
SIG 1 (0)	0%	-1000%	4%	3%	2%	-10000%	-10000%	3%	10%	2%	1%	4%	6%	2%	-10000%	22%	7%	24%	42%	8%	-10000%	41%	-10000%	5%	2%	0%	4%	-10000%	0%	2%	22%	-10000%	8%	4%	6%		

PERCENTILES

SNV COUNT (37701)	1470%	91%	96%	97%	95%	2630%	860%	86%	83%	274%	92%	93%	99%	99%	327%	106%	384%	61%	40%	96%	1130%	38%	227%	2120%	211%	99%	99%	98%	5190%	97%	108%	56%	180%	111%	79%	87%
MS INDELS TMB (0.12)	634%	18%	48%	83%	62%	985%	134%	1%	16%	99%	48%	44%	88%	85%	94%	83%	99%	27%	12%	48%	99%	64%	94%	985%	98%	78%	40%	93%	2300%	37%	68%	36%	91%	21%	31%	
TELOMERIC SGL (0)	50%	32%	39%	26%	34%	50%	50%	38%	29%	49%	38%	40%	46%	2%	29%	42%	30%	25%	40%	46%	48%	28%	44%	50%	50%	42%	43%	39%	44%	35%	30%	44%				
SIMPLE DUP 32B 20B (3)	98%	15%	26%	6%	15%	100%	100%	7%	28%	20%	4%	30%	12%	4%	6%	56%	17%	8%	85%	84%	10%	20%	93%	53%	30%	55%	48%	98%	24%	5%	7%	12%	3%	14%	28%	
MAX COMPLEX SIZE (8)	94%	22%	21%	38%	8%	76%	96%	28%	8%	51%	8%	36%	48%	9%	30%	50%	40%	10%	32%	63%	80%	25%	7%	100%	7%	24%	20%	77%	99%	8%	33%	37%	74%	70%	14%	53%
LINE (4)	133%	17%	52%	88%	48%	200%	200%	2%	10%	96%	98%	26%	91%	92%	77%	86%	81%	32%	52%	98%	100%	88%	95%	133%	75%	38%	52%	94%	100%	26%	41%	32%	94%	65%	6%	46%

FEATURES

BRAF (1)	0%	1%	2%	1%	1%	0%	6%	13%	2%	2%	1%	1%	0%	0%	1%	0%	0%	7%	2%	2%	0%	52%	0%	0%	0%	2%	2%	7%	0%	0%	10%	4%	1%			
CDKN2A (1)	0%	15%	44%	23%	8%	0%	4%	37%	39%	68%	48%	23%	4%	4%	8%	9%	41%	3%	10%	0%	52%	69%	0%	19%	10%	70%	12%	0%	2%	13%	24%	8%	24%	45%	7%	
PTEN (1)	0%	8%	6%	2%	14%	0%	0%	10%	6%	5%	40%	4%	11%	12%	3%	5%	6%	10%	4%	4%	23%	0%	0%	12%	5%	1%	4%	0%	42%	10%	16%	0%	6%	47%		
SF3B1 (0.15)	0%	1%	5%	0%	2%	0%	8%	0%	1%	0%	0%	0%	1%	0%	1%	1%	14%	1%	0%	0%	2%	0%	0%	1%	0%	1%	0%	0%	1%	0%	0%	0%	0%	0%	0%	
TERT (1)	0%	16%	8%	6%	1%	0%	1%	2%	0%	2%	70%	17%	12%	0%	28%	16%	0%	7%	0%	0%	8%	68%	5%	0%	2%	6%	1%	0%	0%	0%	0%	0%	0%	0%		
TP53 (0.00)	0%	0%	0%	0%	0%	0%	0%	1%	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%	
INDEL_ALB (1)	0%	0%	6%	2%	1%	0%	0%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%	62%	0%	1%	2%	1%	0%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%



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Clinical Evidence

* Treatments are reported up to a maximum evidence level of B.

Applicable on-label evidence

TREATMENT	RESPONSIVE EVIDENCE	RESISTANCE EVIDENCE
Cobimetinib + Vemurafenib	BRAF p.V600E (A - CGI)	
Dabrafenib	BRAF p.V600E (A - CGI)	
Dabrafenib + Trametinib	BRAF p.V600E (A - CGI, CIViC)	
Trametinib	BRAF p.V600E (A - CGI)	
Vemurafenib	BRAF p.V600E (A - CGI, CIViC)	
Buparlisib + Carboplatin + Paclitaxel	PTEN partial loss (B - CIViC)	
RO4987655	BRAF p.V600E (B - CIViC)	

Applicable off-label evidence

TREATMENT	RESPONSIVE EVIDENCE	RESISTANCE EVIDENCE
Anti-EGFR monoclonal antibody		PTEN partial loss (B - CGI)
Bevacizumab		BRAF p.V600E (B - CIViC)
CI-1040	BRAF p.V600E (B - CIViC)	
Cetuximab		BRAF p.V600E (B - CGI, CIViC) PTEN partial loss (B - CIViC)
Cetuximab + Irinotecan + Vemurafenib	BRAF p.V600E (B - CIViC)	
Everolimus		PTEN partial loss (B - CIViC)
Fluorouracil		BRAF p.V600E (B - CIViC)
Irinotecan		BRAF p.V600E (B - CIViC)
Lapatinib + Trastuzumab		PTEN partial loss (B - CIViC)
Oxaliplatin		BRAF p.V600E (B - CIViC)
Panitumumab		BRAF p.V600E (B - CGI, CIViC)
Selumetinib	BRAF p.V600E (B - CIViC)	
Sorafenib	BRAF p.V600E (B - CIViC)	
Trastuzumab		PTEN partial loss (B - CIViC)

Applicable trials

NONE



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Other potentially interesting on-label evidence

TREATMENT	RESPONSIVE EVIDENCE	RESISTANCE EVIDENCE
Cobimetinib + Vemurafenib	BRAF p.V600E (B - CIViC)	
Dabrafenib	BRAF p.V600E (B - CIViC)	
Dabrafenib + Trametinib	BRAF p.V600E (B - CIViC)	
Trametinib	BRAF p.V600E (B - CIViC)	
Vemurafenib	BRAF p.V600E (B - CIViC)	

Other potentially interesting off-label evidence

TREATMENT	RESPONSIVE EVIDENCE	RESISTANCE EVIDENCE
Dabrafenib	BRAF p.V600E (A - CGI)	
Dabrafenib + Trametinib	BRAF p.V600E (A - CGI, CIViC)	
Vemurafenib	BRAF p.V600E (A - CGI)	
Chemotherapy		PTEN partial loss (B - CIViC)

Other potentially interesting trials

NONE



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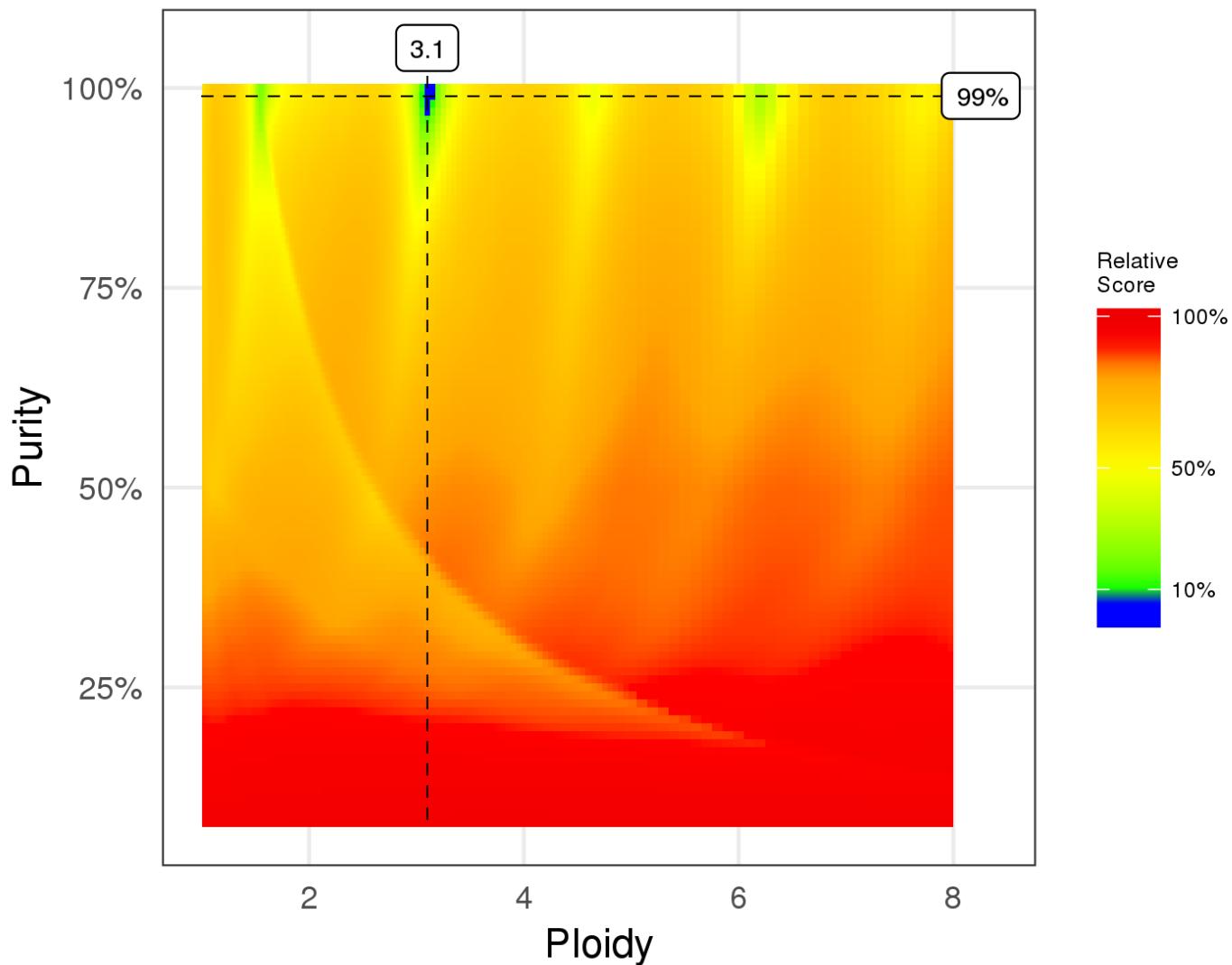
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Quality Control

QC	REF GENOME	FIT METHOD	MEAN DEPTH	CONTAMINATION	UNS. SEGMENTS	DELETED GENES
PASS	V37	NORMAL	111	0%	0	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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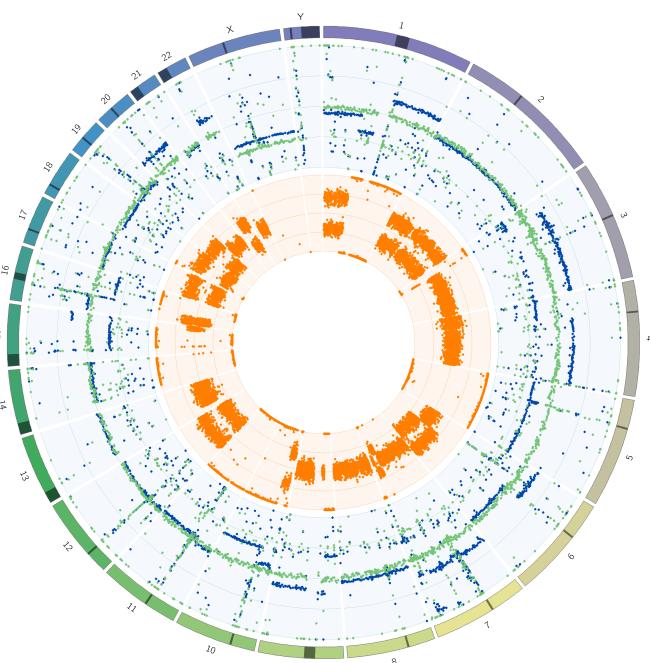
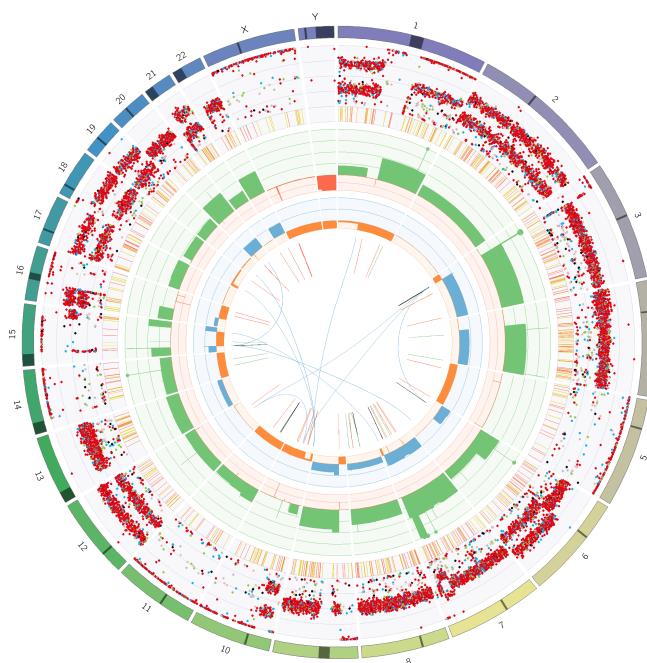
Coverage Stats

	MEAN COVERAGE	SD COVERAGE	MEDIAN COVERAGE	MAD COVERAGE
Ref Sample	31.4	10.1	32	5
Tumor Sample	108.1	35.0	109	24

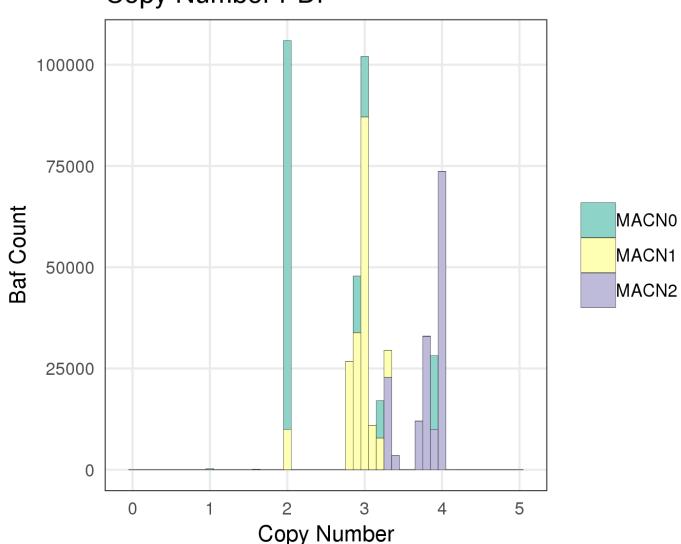
Excluded Percentages

	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%

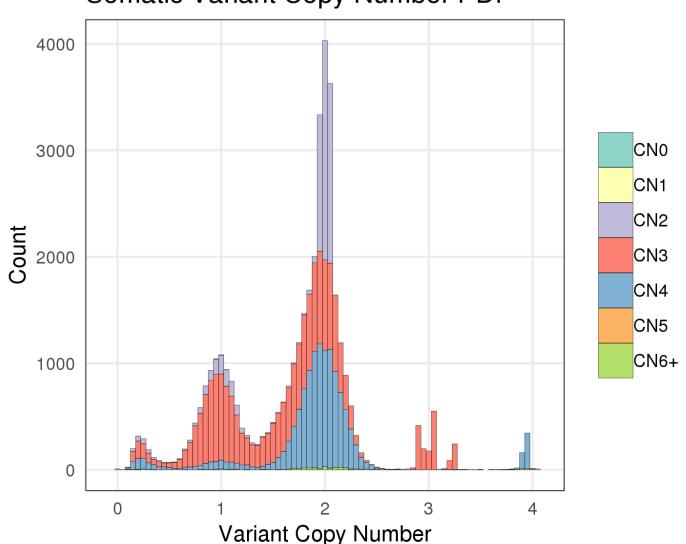
QC plots



Copy Number PDF



Somatic Variant Copy Number PDF





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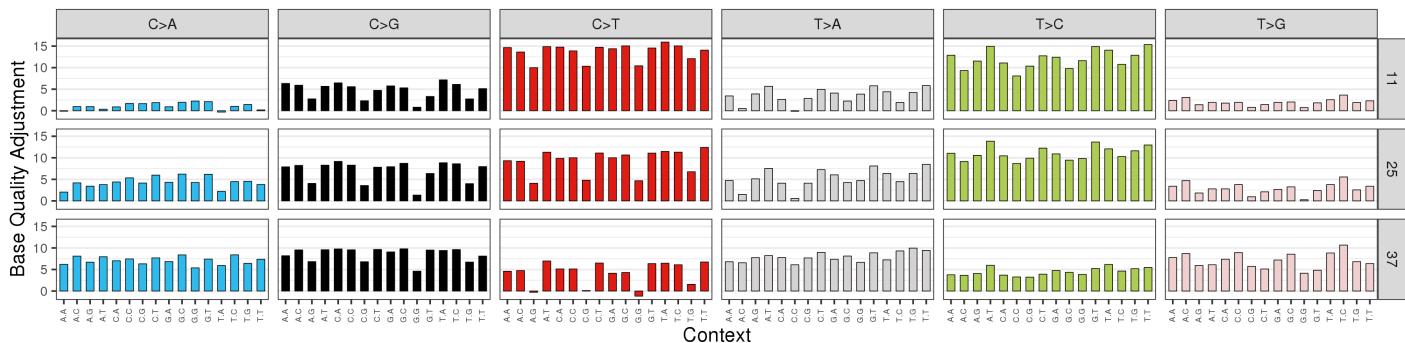
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Reference Sample BQR plot



Tumor Sample BQR plot

