



ORANGE Report

SAMPLE

Test

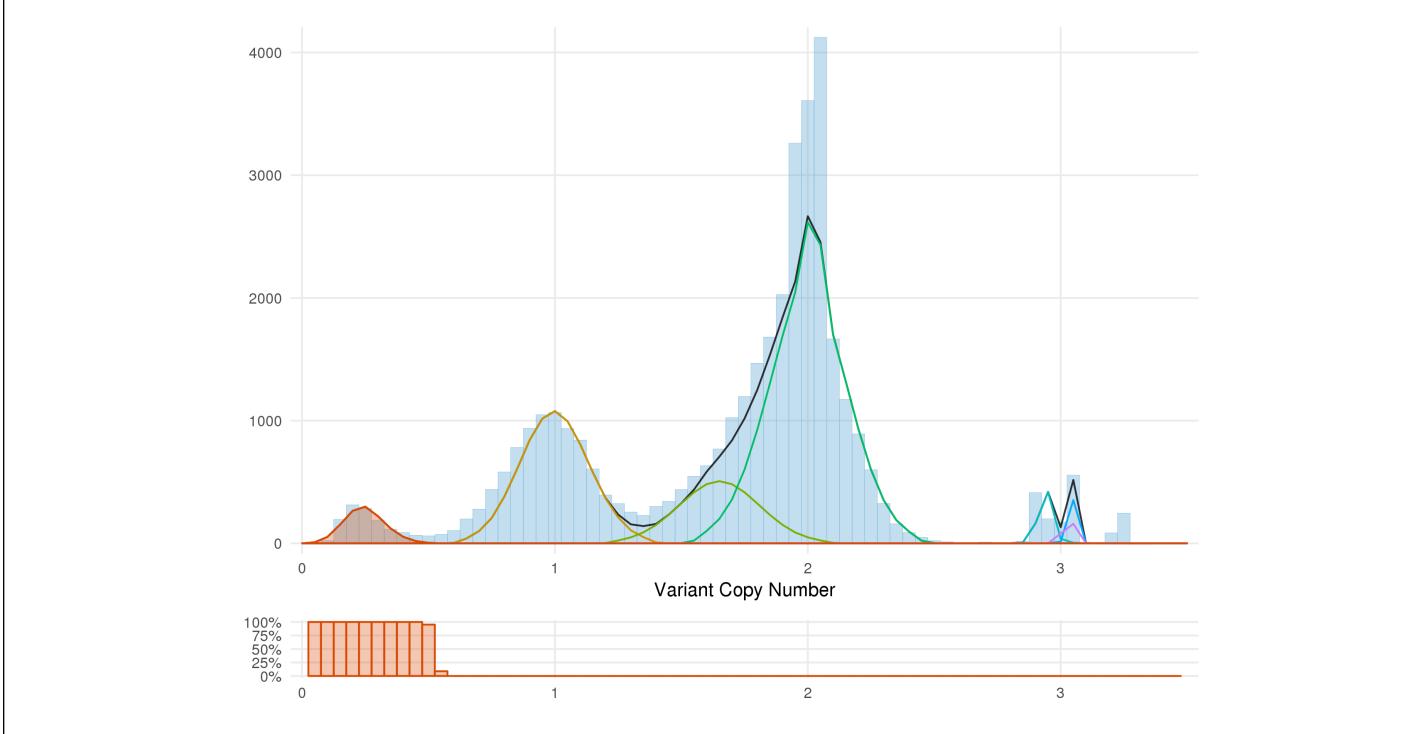
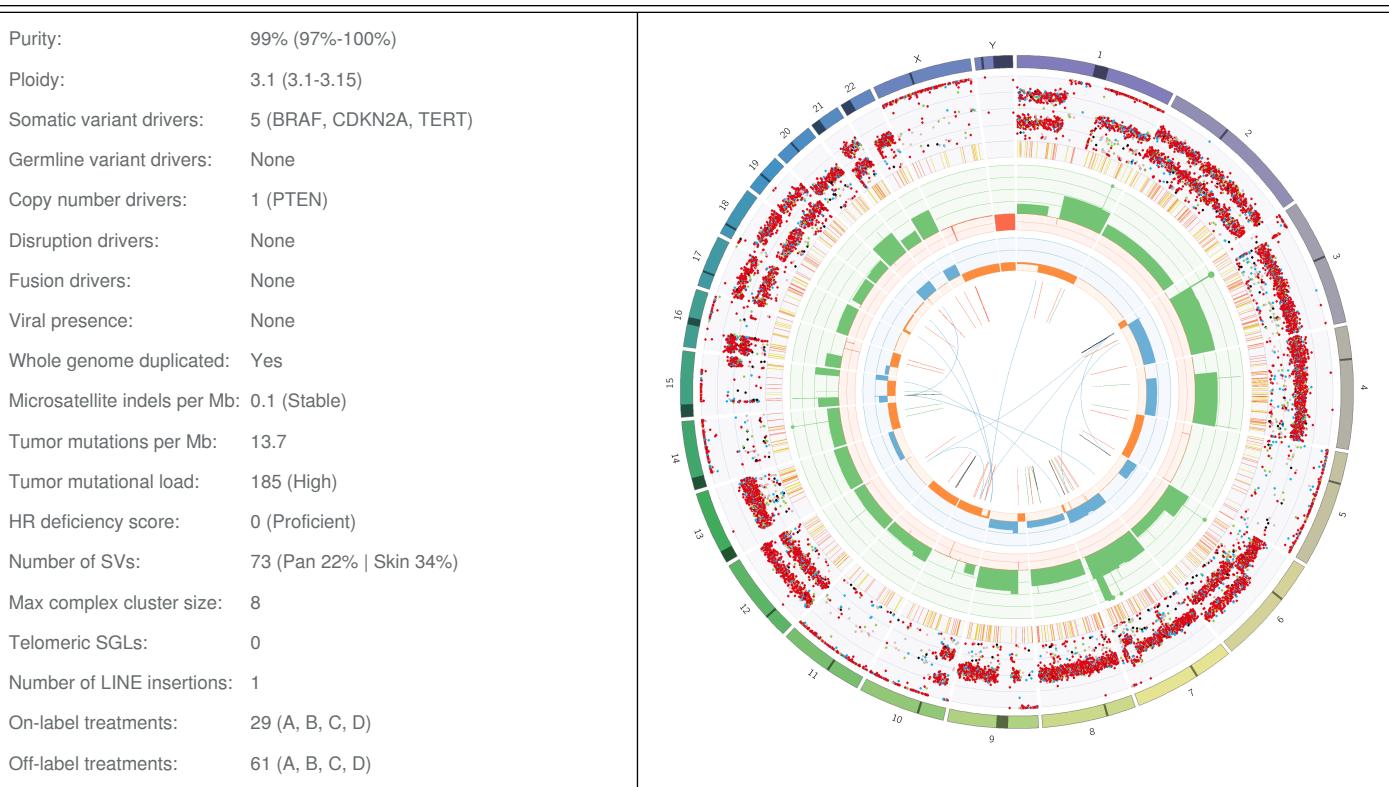
PLATINUM VERSION

5.27

CONFIGURED PRIMARY TUMOR
skin melanoma (DOID 8923)

CUPPA CANCER TYPE
Melanoma (100%)

QC
PASS





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Somatic Findings

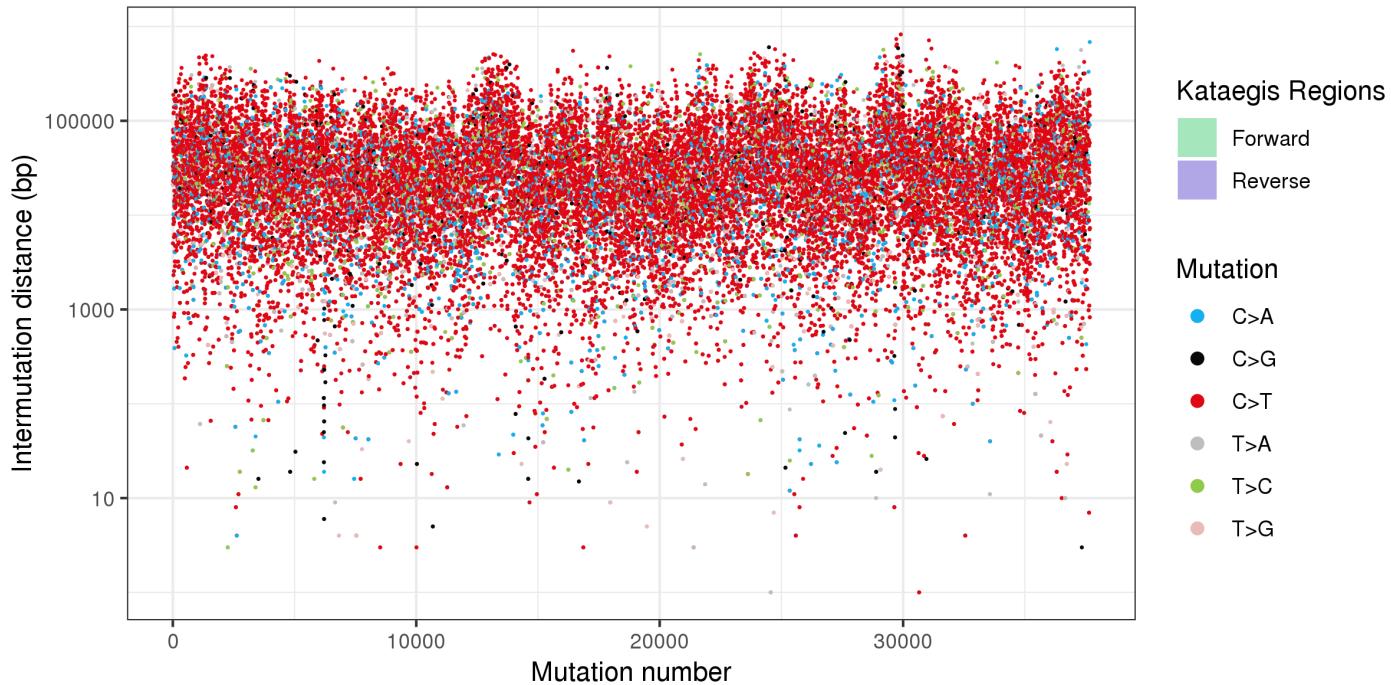
Driver variants (5)

| VARIANT | VCN | CN | MACN | RNA VAF | BIALLELIC | HOTSPOT | DL | CL | PHASE ID |
|----------------|-----|-----|------|---------|-----------|---------|------|------|----------|
| BRAF p.V600E | 4.1 | 6.0 | 2.0 | NA | No | Yes | 100% | 100% | |
| CDKN2A p.A68fs | 2.0 | 2.0 | 0.0 | NA | Yes | Near | 100% | 100% | |
| TERT upstream | 1.7 | 2.0 | 0.0 | NA | Yes | Yes | 100% | 100% | 482 |
| SF3B1 p.P718L | 2.0 | 3.0 | 1.0 | NA | No | No | 15% | 100% | |
| TP63 p.M499I | 1.7 | 4.0 | 2.0 | NA | No | No | 0% | 100% | |

Other potentially relevant variants (3)

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

Kataegis plot



Driver amps/dels (1)

| CHROMOSOME | REGION | GENE | TYPE | CN |
|------------|--------|------|--------------|----|
| 10 | q23.31 | PTEN | partial loss | 0 |



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Other regions with amps (1)

| CHROMOSOME | REGION | GENE | TYPE | CN |
|------------|--------|--------|-----------|----|
| 3 | p24.2 | CFL1P7 | full gain | 12 |

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

| CHROMOSOME | REGION | GENE | TYPE | CN |
|------------|--------|-------|--------------|----|
| 16 | q21 | CNOT1 | partial loss | 0 |

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 |

Structural drivers (3)

| GENE | EVENT TYPE |
|--------|-------------|
| CDKN2A | LOH_SV_TELO |
| PTEN | DEL |
| PTEN | LOH_SV_TELO |

Structural driver plots (3)



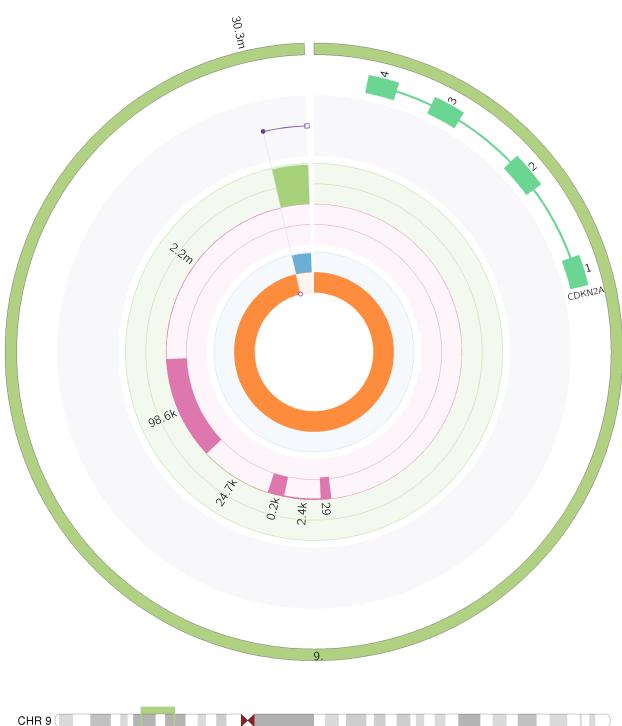
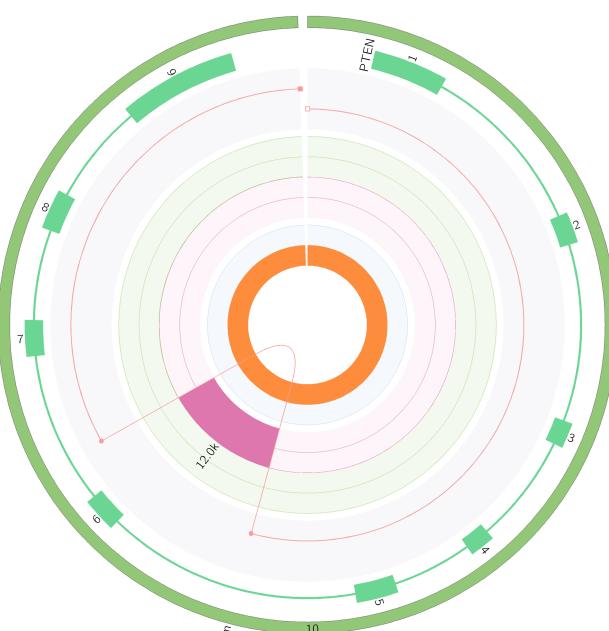
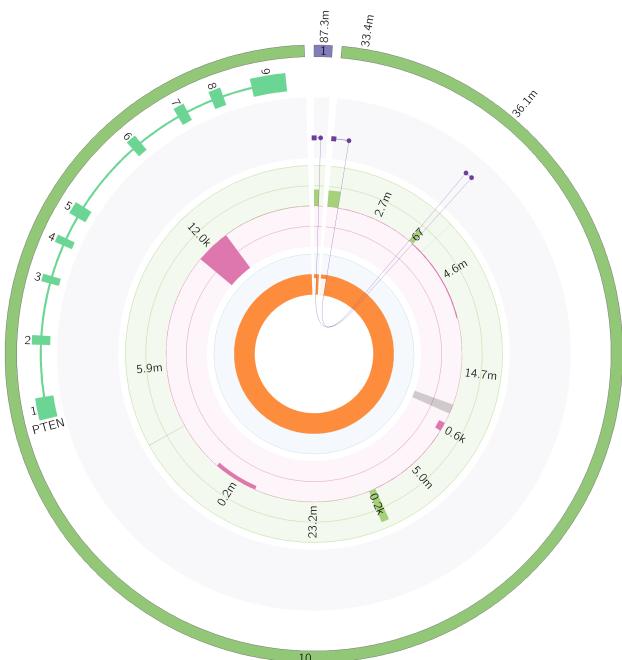
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Germline Findings

Driver variants (0)

NONE

Other potentially relevant variants (3)

| VARIANT | VCN | CN | MACN | RNA VAF | BIALLELIC | HOTSPOT | GENOTYPE |
|---------------------|-----|-----|------|---------|-----------|---------|----------|
| CYP2D6 c.506-1G>A | 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 |

Genes with missed variant likelihood > 1% (22)

| GENE | MVLH | GENE | MVLH | GENE | MVLH | GENE | MVLH |
|-------|------|----------|------|-------|------|--------|------|
| AMER1 | 3.8% | AR | 2.6% | ARAF | 2.0% | ATP2B3 | 2.0% |
| ATRX | 3.1% | BCOR | 2.2% | BTK | 3.1% | CASZ1 | 3.7% |
| DDX3X | 2.7% | EIF1AX | 1.9% | GATA1 | 1.9% | KDM5C | 1.7% |
| KDM6A | 3.3% | KRTAP5-5 | 1.2% | MED12 | 3.1% | PHF6 | 3.9% |
| RBM10 | 2.1% | RPS6KA3 | 3.7% | STAG2 | 2.5% | ZFX | 1.5% |
| ZMYM3 | 3.0% | ZRSR2 | 5.1% | | | | |

Germline CN aberrations (0)

NONE

Pharmacogenetics (1)

| GENE | GENOTYPE | FUNCTION | LINKED DRUGS | SOURCE |
|------|----------|-----------------|-------------------------------------|----------|
| DPYD | *1_HOM | Normal Function | 5-Fluorouracil;Capecitabine;Tegafur | PHARMGKB |



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Immunology

Coming soon: HLA types for patient + status in tumor

Coming soon: List of neo-epitopes with predicted binding affinity

Coming soon: Details about RNA tumor micro-environment



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Cohort Comparison

| | Acute myeloid leukemia | Angiogenesis | Bile duct/Ca/bile duct | Bone/Soft tissue: Other | Breast | Cartilaginous neoplasm | Chronic lymphocytic leukemia | Colon/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% | 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% | 0% | | | |
| FEATURE | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 1% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | 97% | 0% | 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% | 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 (24239) | 34700% | 1920% | 4140% | 98% | 1260% | 175000% | 49600% | 1670% | 2580% | 24700% | 50000% | 144% | 2910% | 9970% | 14300% | 5700% | 1140% | 791% | 1600% | 2350% | 38700% | 34% | 7890% | 4560000% | 7990% | 4330% | 3570% | 9450% | 201000% | 5660% | 2930% | 63% | 10600% | 27800% | 746% | 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 (2095) | 65% | 99% | 103% | 644% | 11% | 10000% | 10000% | 99% | 187% | 143% | 10000% | 93% | 122% | 99% | 10000% | 96% | 97% | 41% | 9% | 10000% | 4950% | 99% | 167% | 10000% | 224% | 100% | 166% | 125% | 49300% | 151% | 98% | 99% | 10000% | 319% | 92% | 375% | 105% |
| SIG 2 13 AID APOBEC (3858) | 20900% | 67% | 103% | 98% | 85% | 41500% | 10300% | 100% | 98% | 805% | 99% | 88% | 152% | 518% | 376% | 455% | 1980% | 82% | 123% | 99% | 4110% | 34% | 864% | 16100% | 99% | 100% | 165% | 98% | 35000% | 225% | 99% | 92% | 677% | 96% | 59% | 59% | 105% |
| SIG 17 (1117) | 1390% | 97% | 94% | 97% | 95% | 22100% | 208% | 541% | 24% | 98% | 10000% | 97% | 100% | 284% | 366% | 100% | 10000% | 93% | 97% | 81% | 10300% | 97% | 1560% | 39200% | 95% | 99% | 96% | 99% | 18000% | 99% | 93% | 92% | 700% | 353% | 90% | 97% | |
| SIG 11 (1350) | 2450% | 99% | 100% | 97% | 100% | 54600% | 1900% | 100% | 100% | 551% | 93% | 100% | 342% | 98% | 358% | 272% | 392% | 99% | 123% | 99% | 933% | 87% | 438% | 1280% | 390% | 100% | 163% | 98% | 14900% | 270% | 55% | 56% | 223% | 98% | 216% | 216% | |
| 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 (37675) | 1470% | 91% | 96% | 97% | 95% | 2630% | 859% | 86% | 83% | 273% | 92% | 93% | 99% | 99% | 327% | 106% | 384% | 61% | 40% | 96% | 1130% | 38% | 228% | 2110% | 211% | 99% | 99% | 98% | 5180% | 97% | 108% | 56% | 180% | 111% | 79% | 87% |
| MS INDELS TMB (0.12) | 62% | 18% | 47% | 82% | 61% | 96% | 132% | 1% | 16% | 98% | 45% | 43% | 87% | 85% | 93% | 82% | 99% | 27% | 11% | 47% | 99% | 64% | 94% | 867% | 97% | 76% | 39% | 93% | 2330% | 37% | 68% | 36% | 91% | 20% | 30% | |
| 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% | 51% | 17% | 38% | 36% | 34% | 50% | 42% | 43% | 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% | 8% | 80% | 94% | 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 (1) | 94% | 8% | 30% | 68% | 25% | 94% | 98% | 1% | 6% | 86% | 76% | 8% | 74% | 76% | 44% | 71% | 60% | 16% | 22% | 93% | 93% | 66% | 82% | 83% | 60% | 25% | 30% | 80% | 99% | 12% | 21% | 15% | 76% | 45% | 20% | |

FEATURES

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------|----|-----|-----|-----|-----|----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|-----|-----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|
| BRAF (1) | 0% | 1% | 2% | 1% | 1% | 0% | 6% | 13% | 2% | 2% | 1% | 1% | 0% | 0% | 1% | 0% | 7% | 2% | 2% | 0% | 52% | 0% | 0% | 2% | 2% | 0% | 0% | 10% | 4% | 1% | 0% | 1% | 0% | 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% | 0% | | |
| 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% | 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% | 13% | 38% | 0% | 33% | 70% | 7% | |
| 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% | 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% | 0% |



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Clinical Evidence

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

Applicable on-label evidence

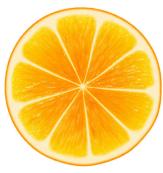
| TREATMENT | RESPONSIVE EVIDENCE | RESISTANCE EVIDENCE |
|---------------------------------------|-------------------------------|---------------------|
| Cobimetinib + Vemurafenib | BRAF p.V600E (A - CGI) | |
| Dabrafenib | BRAF p.V600E (A - CGI) | |
| Dabrafenib + Trametinib | BRAF p.V600E (A - CGI, 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 (D - CIViC) 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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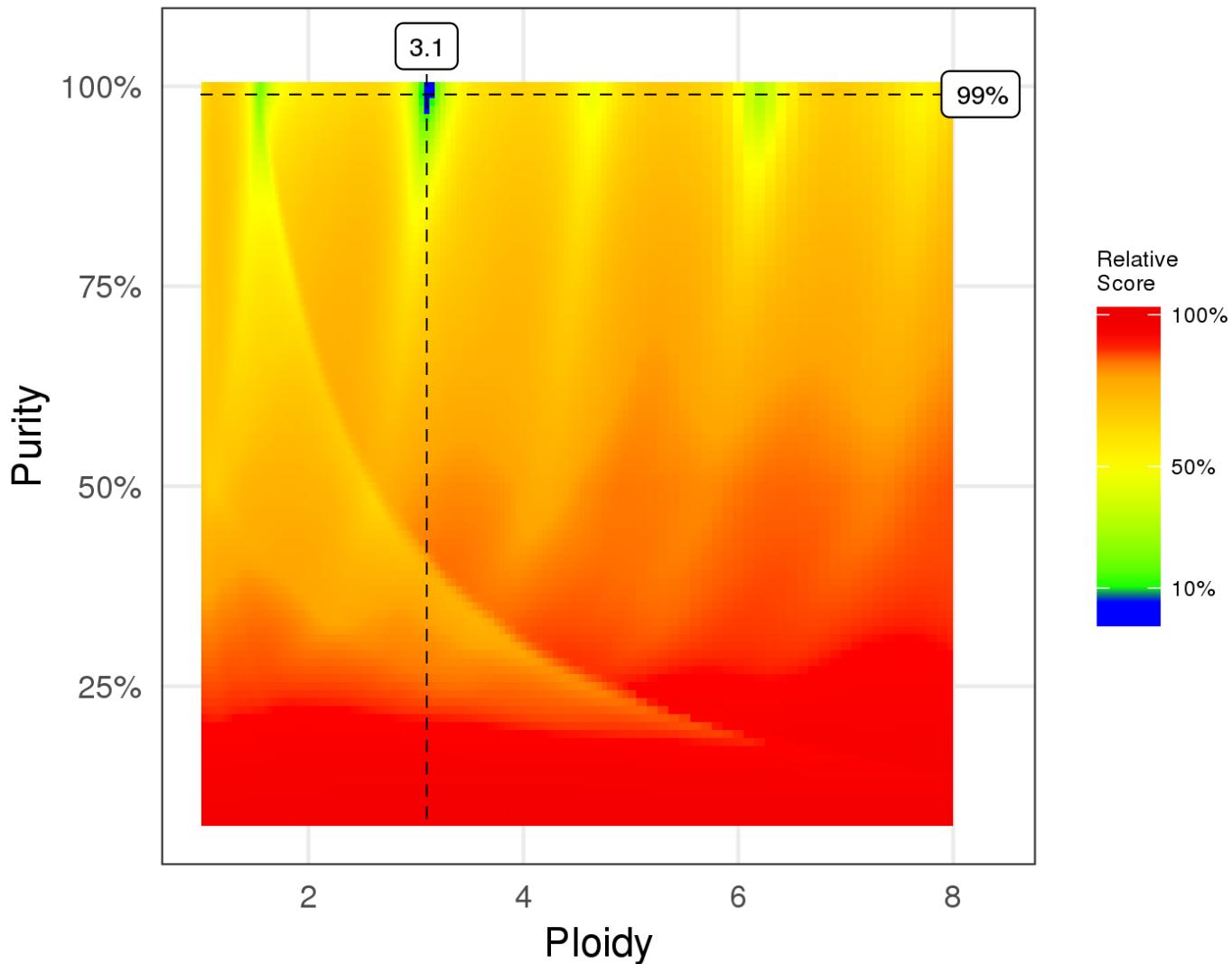
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Quality Control

| QC | FIT METHOD | MEAN DEPTH | CONTAMINATION | UNS. CN SEGMENTS | DELETED GENES |
|------|------------|------------|---------------|------------------|---------------|
| PASS | 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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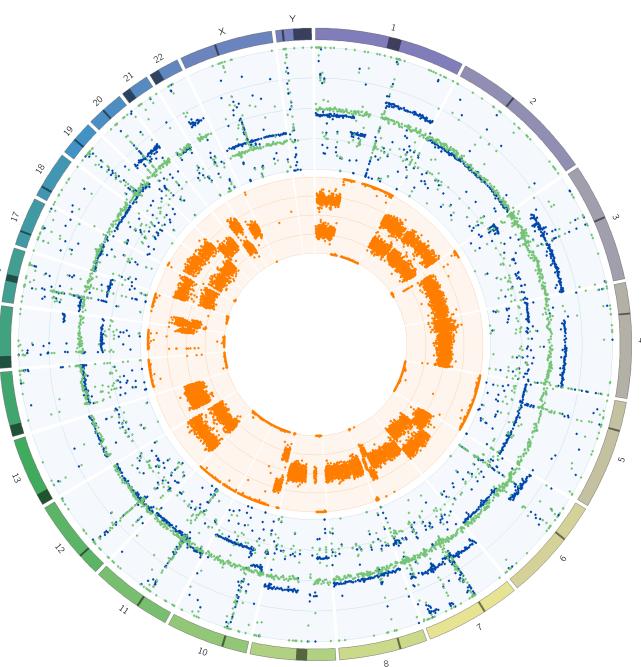
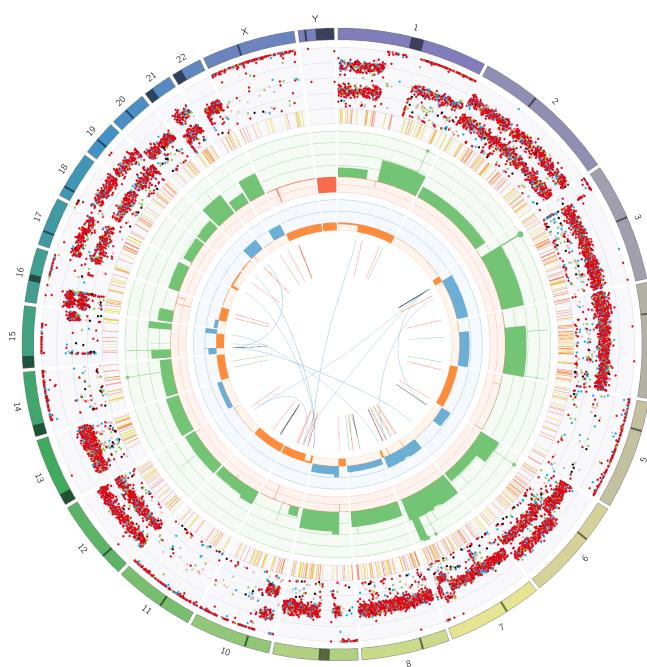
Coverage Stats

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

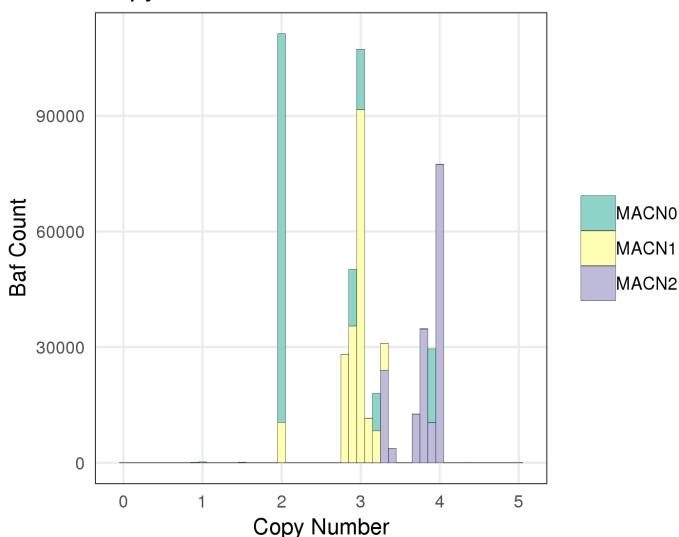
Excluded Percentages

| | 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% |

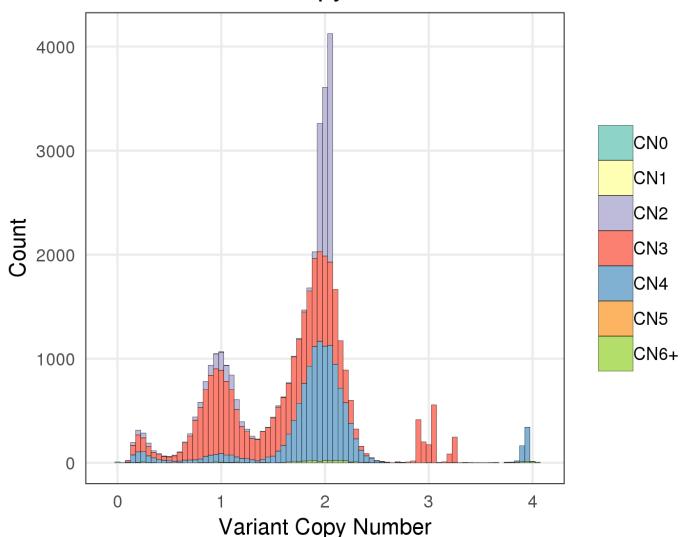
QC plots



Copy Number PDF



Somatic Variant Copy Number PDF





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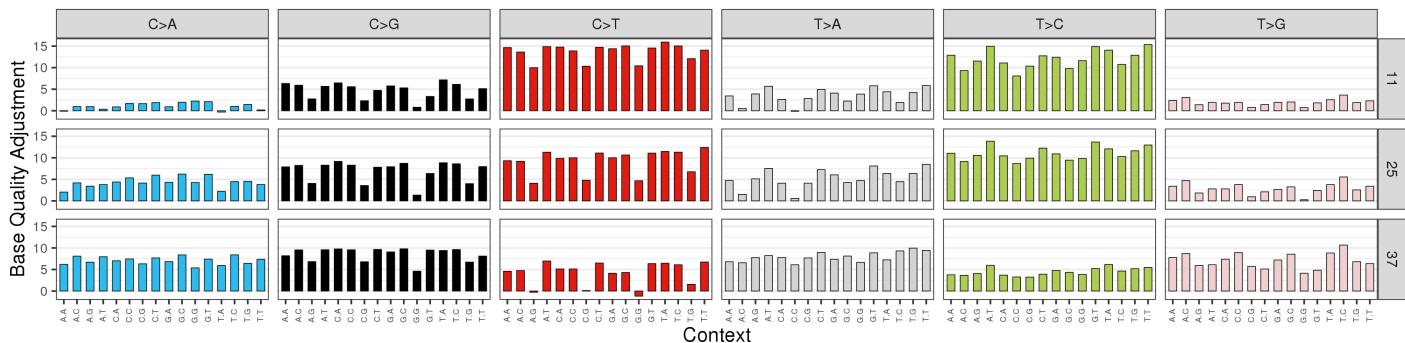
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Reference Sample BQR plot



Tumor Sample BQR plot

