

Figure S1. *ARID1A* mutated melanoma harbor more C>T substitutions than *ARID1A*-wild type melanoma.

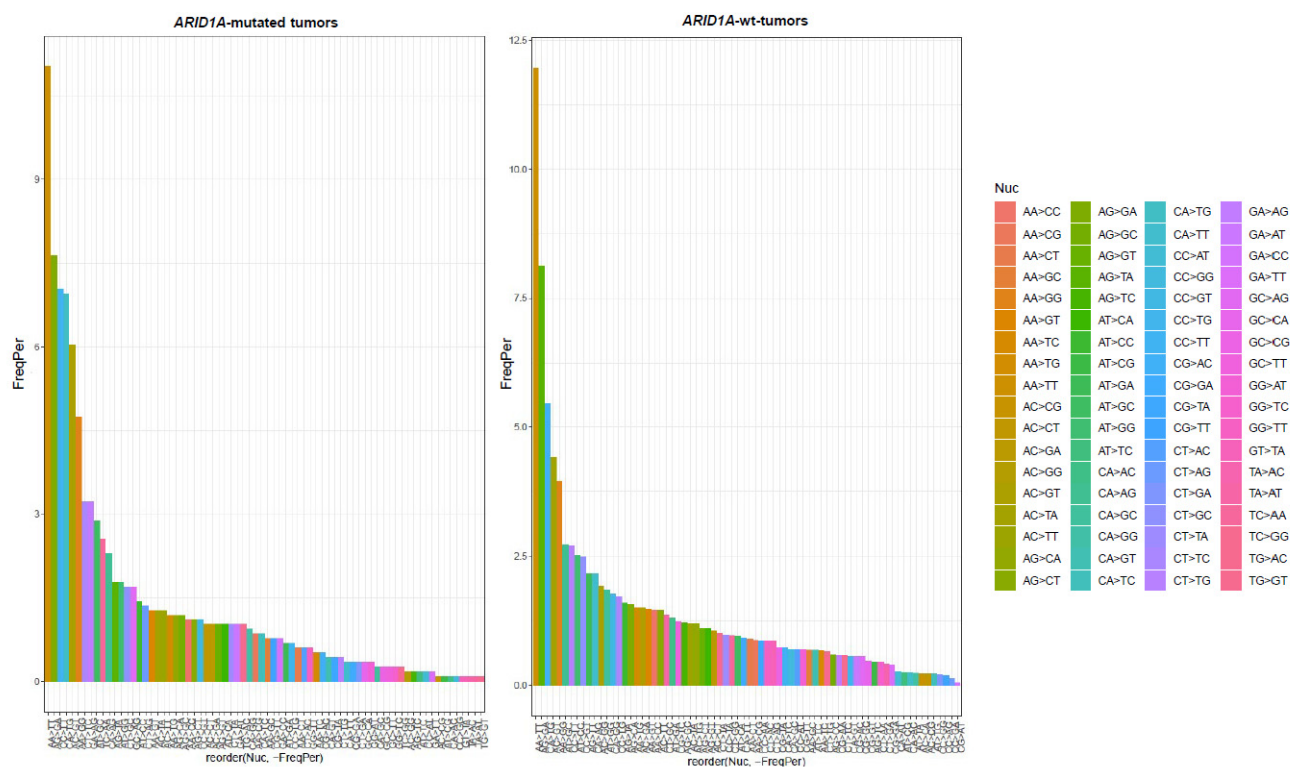


Figure S2. *ARID1A* mutated melanoma harbor more CC>TT UV-induced dinucleotide substitutions compared to *ARID1A*-wild type melanoma.

Table S1. Mutational overview of BRAF, NRAS, NF1, ARID1A, TERT promoter.

| BRAF | NRAS | NF1 | ARID1A | TERT Promoter |
|-----------------------------|-------------|-------------------|--------------------------------|----------------------|
| V600K; D66N | | G2052E; M1285I | P848L; S446F | 1295228 |
| V600K | Q61K | P2242S | S1153F | |
| V600K | | | F2103V | 1295228 |
| V600E; V600K | D33E | W2229*; W425* | G1849E; G410R | |
| V600E; S314F | | D2005G; W1685* | A837T; M828I | |
| V600E; R69K | | E2211K; L2116F | M628I; Q1172* | |
| V600E; R50K | | L2604F; V1677I | G1267R; H1624Y | |
| V600E; R165Q | S65N; V188M | D1485N; S2460L | M1224I; P582S | 1295250 |
| V600E; L144S | Q61R | F1289S; S1355L | G1282R; K1382R | 1295228 |
| V600E; G85D | | G849R; S1566N | D1231Y; G1996D | |
| V600E; G219E | R123G | K1263E; K2823E | M1215I; S539L | 1295250 |
| V600E; A133V | Q61L | R2349H; R752K | P1633S; P690L | 1295250 |
| V600E | | | D1193G | |
| V600E | | | H1624Y; P1132S | |
| V600E | | | P1966L | |
| V600E | | | P1567S | |
| V600E | | | N906K | |
| V600E | | V172I | D1286_R1287delinsC*; Y1285S | |
| V600E | | | G2040R | |
| V600E | | | R2236H | |
| V600E | | I1186T; S2543N | M1578I; P225S | |
| V600E | | Q1255*; S1500N | A1622T; T1198I | |
| V600E | | | P1710S; Q1856* | |
| V600E | | M1376V | R1202Q | |
| V600E | Q61K | | G1375S | 1295250 |
| V600E | | G72E | S258F | 1295250 |
| V600E | | | I1907F | 1295250 |
| V600E | | | R2183C | 1295250 |
| V600E | | | M828I; P1568S | 1295250 |
| V600E | | | P459S | 1295250 |
| V600E | | | P680L | 1295250 |
| V600E | | | E1033*; E1033* | 1295250 |
| V600E | | | S862F | 1295228 |
| V600E | | | L1607Q | 1295228 |
| V600E | | E244G; P2242L | P380S | 1295228 |
| V600E | | | P1563S | 1295228 |
| V600E | | | S735N | 1295228 |
| V600E | | | R1053C | 1295228 |
| V600E | | | R1020W | 1295228 |
| V600E | | | D1850fs; S1929fs | 1295228 |
| V600E | | | L1716F | 1295228 |
| V600D | | | R1906Q | 1295228 |
| V377I | | D832N; V253M | G1665E; R1566K | |
| S209_R210delins*; V600fs | | | L2112F | 1295250 |
| S16L | Q61K; R97K | V497M | P1567L; P819L | 1295228 |
| R278Q | G177E | G2811R; V2572I | S696F; S936N | |
| R278* | Q61L | A2333V; Q2636R | P1372L | |
| Q98* | | | P636L; S2179N | |

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|--------------|-------------|-------------------|-------------------|---------|
| P75L | | A1294T; A2333T | G827D; W1545* | 1295228 |
| P367S | Q61L | | S536F | 1295250 |
| P334Q | | | Q1145K | |
| P29S | E132K | P464L; V530I | P1326fs; P1407S | |
| P239L; S363F | | L2620F | S574F | 1295228 |
| P229S; P321S | A66V; G115R | A1294V; E1571K | A905T; P600L | |
| N140S | | P2758S; T1950I | G443S; Q1974* | |
| L313F; V281I | Q61R | A456T; H2658Y | Q449*; R2057W | |
| L286F; S136L | Q61R; Y157* | A1177V; P2696L | G838R; Q920* | |
| G73E | | | P545L | |
| E140K | G12A | P458L; W1512* | P535L; P554S | |
| D201N | P34L | V1182D | P1710S | 1295228 |
| D172E; L204R | | | L1915F | 1295228 |
| | V14I | A132T; L121F | D2051fs; R1989* | |
| | Q61R | A152V | P2095L; Q1631* | |
| | Q61R | | P383S | |
| | Q61K | | Q1131* | |
| | Q61K | | P418S | |
| | Q61K | | P2102L; S2104fs | |
| | Q61K | V1308L | P1562L | |
| | Q61K | | Q588*; R1202Q | |
| | Q150P; Q61R | P2792L | Q309P; Y311fs | |
| | G12S | | E1767* | |
| | A130T | E1929K; I183T | Q1098R | |
| | | | P2140L | |
| | | | G1015S; P1642S | |
| | | | P1326fs | |
| | | | V1526M | |
| | | | P739S | |
| | | M2526I | H477Y; S825N | |
| | | D896N; T1184fs | V700A | |
| | Q61R | | P1132A | 1295250 |
| | Q61L | | P1213S; P452S | 1295250 |
| | Q61L | | P1163S | 1295250 |
| | Q61L | | P1240S | 1295250 |
| | Q61K | | P729fs | 1295250 |
| | Q61K | | Q1894* | 1295250 |
| | Q61K | | D1794fs; Q1856* | 1295250 |
| | | R1870L; R440* | Q1537* | 1295250 |
| | | Q2636*; S2549L | Q1458* | 1295250 |
| | | Q1070* | P533S | 1295250 |
| | | | P2225L | 1295250 |
| | | Q756* | A2237P | 1295250 |
| | | | Q1200*; S682F | 1295250 |
| | | Q1218* | E1778_Glu1780del | 1295250 |
| | | K1263* | S1544P | 1295250 |
| | | Q2234*; W1997* | P1667L | 1295242 |
| | | R440*; V951I | S1338F | 1295242 |
| | Q61R | | Q1334_R1335insGln | 1295228 |
| | Q61L | | H1608Y | 1295228 |
| | Q61L | | P2077L | 1295228 |
| | Q61L | | P2114L | 1295228 |
| | Q61L | S2817F | S1338F | 1295228 |
| | Q61K; S87N | | A2181fs | 1295228 |
| | Q61K | | L1970F; S1516F | 1295228 |
| | Q61K | | D1972N | 1295228 |
| | Q61K | | S1868F | 1295228 |
| | L95P; Q61R | P1851S; S155G | E1787K; Q1346H | 1295228 |

| | | |
|-------------------|----------------|---------|
| R2812Q; Y794* | F2103L | 1295228 |
| C454Y | M1661I; P1325L | 1295228 |
| R1306Q; W1236* | S1868F | 1295228 |
| Q1255* | S499L | 1295228 |
| L300fs; Q1515* | A900T | 1295228 |
| S1991Y | P1115S | 1295228 |
| L161fs | R1461* | 1295228 |
| Q853*; S2754F | P1667S | 1295228 |
| R1241*; S1567L | P1307L; P1325F | 1295228 |
| | M1215I | 1295228 |

Table S2. Genes covered in the applied sequencing panel.

| Nr. | Gene | Chr | Start | End | Primary Melanoma type | Nr. Targets |
|-----|-------------------|-----|-----------|-----------|-----------------------|-------------|
| 1 | <i>TERT</i> prom. | 5 | 1295200 | 1295280 | cutaneous | 2 |
| 2 | <i>BRAF</i> | 7 | 140419127 | 140624564 | cutaneous | 95 |
| 3 | <i>NRAS</i> | 1 | 115247085 | 115259515 | cutaneous | 7 |
| 4 | <i>HRAS</i> | 11 | 532242 | 537287 | cutaneous | 8 |
| 5 | <i>KRAS</i> | 12 | 25357723 | 25403870 | cutaneous | 14 |
| 6 | <i>KIT</i> | 4 | 55524085 | 55606881 | cutaneous | 34 |
| 7 | <i>RAC1</i> | 7 | 6414126 | 6443608 | cutaneous | 9 |
| 8 | <i>NF1</i> | 17 | 29421945 | 29709134 | cutaneous | 111 |
| 9 | <i>TP53</i> | 17 | 7565097 | 7590863 | cutaneous | 18 |
| 10 | <i>CDKN2A</i> | 9 | 21967751 | 21995300 | cutaneous | 26 |
| 11 | <i>GNAQ</i> | 9 | 80331003 | 80646374 | uveal | 14 |
| 12 | <i>GNA11</i> | 19 | 3094408 | 3124002 | uveal | 14 |
| 13 | <i>PTEN</i> | 10 | 89622870 | 89731687 | cutaneous | 14 |
| 14 | <i>CDK4</i> | 12 | 58141510 | 58149796 | cutaneous | 11 |
| 15 | <i>ARID1A</i> | 1 | 27022522 | 27108601 | cutaneous | 67 |
| 16 | <i>ARID2</i> | 12 | 46123448 | 46301823 | cutaneous | 56 |
| 17 | <i>SMARCA4</i> | 19 | 11071598 | 11176071 | cutaneous | 60 |
| 18 | <i>MAP2K1</i> | 15 | 66679155 | 66784650 | cutaneous | 35 |
| 19 | <i>MAP2K2</i> | 19 | 4090319 | 4124126 | cutaneous | 35 |
| 20 | <i>CTNNB1</i> | 3 | 41236328 | 41301587 | cutaneous | 27 |
| 21 | <i>PIK3CA</i> | 3 | 178865902 | 178957881 | cutaneous | 37 |
| 22 | <i>EZH2</i> | 7 | 148504464 | 148581441 | cutaneous | 30 |
| 23 | <i>IDH1</i> | 2 | 209100951 | 209130798 | cutaneous | 15 |
| 24 | <i>FBXW7</i> | 4 | 153242410 | 153457253 | cutaneous | 33 |
| 25 | <i>WT1</i> | 11 | 32409321 | 32457176 | cutaneous | 21 |
| 26 | <i>SF3B1</i> | 2 | 198254508 | 198299815 | uveal | 48 |
| 27 | <i>BAP1</i> | 3 | 52435024 | 52444366 | uveal | 30 |
| 28 | <i>PIK3R1</i> | 5 | 67511548 | 67597649 | cutaneous | 32 |
| 29 | <i>MITF</i> | 3 | 69788586 | 70017488 | cutaneous | 31 |
| 30 | <i>TERT</i> | 5 | 1253147 | 1295068 | cutaneous | 36 |

Table S3. Clinical characteristics of patients receiving non-adjuvant systemic therapy.

| Variable (n = 37) | |
|-------------------|-----------|
| Age | |
| Median | 64 |
| Range | 38 - 87 |
| ≤60 | 14 (37.8) |
| >60 | 23 (62.2) |
| Sex | |
| Female | 15 (40.5) |
| Male | 22 (59.5) |
| Primary Tumor | |
| Cutaneous | 29 (78.4) |
| Mucosal | 1 (2.7) |
| Occult | 7 (18.9) |
| Ulceration | |
| Present | 14 (37.8) |
| Missing | 8 (21.7) |

| | |
|-----------------------------------|-----------|
| Unknown | 15 (40.5) |
| Sentinel Lymph Node Biopsy | |
| Positive | 7 (18.9) |
| Negative | 12 (32.4) |
| Not performed | 18 (48.6) |
| PD-L1 | |
| Positive | 10 (27.0) |
| Negative | 21 (56.8) |
| Unknown | 6 (16.2) |
| LDH at therapy start | |
| Elevated | 4 (10.8) |
| WNL | 19 (51.4) |
| Unknown | 14 (37.8) |
| Therapies | |
| PD1 Mono | 11 (29.7) |
| PD1 + CTLA4 | 16 (43.2) |
| Dabra Trame | 7 (18.9) |
| Vemura Cobi | 2 (5.4) |
| Enco Bine | 1 (2.7) |
| Metastatic organs | |
| <3 Organs | 25 (67.5) |
| ≥3 Organs | 12 (32.5) |