Somatic Mutations in Known Driver Genes

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene** | **Mutation** | **Confidence** | **References** |
| BRAF | p.Val600Glu | 4 | 1,2,3,4 |
| SF3B1 | p.Pro718Leu | 3 | 1,2,4 |
| DLEC1 | p.Asp215Asn | 2 | 3,5 |
| FAM46C | p.Thr209Asn | 2 | 1,4 |
| GLI1 | p.Ser1094Phe | 2 | 3,5 |
| HSP90AA1 | p.His612Asn | 2 | 1,4 |
| RPS6KA2 | p.Glu319Lys | 2 | 3,5 |
| TP63 | p.Met499Ile | 2 | 1,5 |
| ACHE | p.Thr95Ile | 1 | 5 |
| CNTRL | p.Gln2033Lys | 1 | 1 |
| EPHB4 | p.Pro346Leu | 1 | 5 |
| ETV5 | p.Tyr445Cys | 1 | 1 |
| LPP | p.Ala119Gly | 1 | 1 |
| MADD | p.Ser1620Phe | 1 | 5 |
| PABPC3 | p.Gly234Arg | 1 | 4 |
| PCSK5 | p.Cys747Tyr | 1 | 4 |
| RAD51B | p.Arg385Lys | 1 | 1 |
| ROBO2 | p.Ala16Val | 1 | 4 |
| TNPO1 | p.Gln38His | 1 | 4 |

Direct Association (Mutation in drug target)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **Mutation** | **Therapy** | **Confidence** | **References** |
| BRAF | p.Val600Glu | sorafenib | 9 | 6,7,8,9,10,11,12,13,14 |
| BRAF | p.Val600Glu | dabrafenib | 4 | 12,14,15 |
| BRAF | p.Val600Glu | vemurafenib | 4 | 12,14,16,17 |
| BRAF | p.Val600Glu | regorafenib | 3 | 12,18 |
| TNFRSF8 | p.Pro215Ser | brentuximab vedotin | 2 | 12,19 |
| BRAF | p.Val600Glu | gsk2118436 | 1 | 14 |
| BRAF | p.Val600Glu | r7204 | 1 | 14 |
| EPHB4 | p.Pro346Leu | vandetanib | 1 | 12 |
| KCNH2 | p.Leu468Phe | amsacrine | 1 | 20 |

Indirect Association (other Mutations with known effect on drug)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Mutation** | **Therapy** | **Disease** | **Evidence** | **References** |
| BRAF | AGK-BRAF | Sorafenib | Melanoma | C | 29 |
| BRAF | AGK-BRAF | Vemurafenib | Melanoma | D | 29 |
| BRAF | L597R | Vemurafenib | Melanoma | C | 30 |
| BRAF | MUTATION | Trametinib | Cancer | D | 39 |
| BRAF | PAPSS1-BRAF | Trametinib | Melanoma | D | 38 |
| BRAF | PAPSS1-BRAF | Vemurafenib | Melanoma | D | 38 |
| BRAF | TRIM24-BRAF | Trametinib | Melanoma | D | 38 |
| BRAF | V600 | BAY 86-9766 | Melanoma | C | 32 |
| BRAF | V600 | Dabrafenib,Trametinib | Melanoma | B | 22 |
| BRAF | V600 | Panitumumab | Colorectal Cancer | B | 21 |
| BRAF | V600 | RO4987655 | Melanoma | B | 26 |
| BRAF | V600D | Dabrafenib | Melanoma | B | 23 |
| BRAF | V600E | BEZ235 (NVP-BEZ235, Dactolisib),Selumetinib (AZD6244) | Melanoma | D | 40 |
| BRAF | V600E | Capecitabine,Vemurafenib,Bevacizumab | Colorectal Cancer | D | 37 |
| BRAF | V600E | Cetuximab | Colorectal Cancer | B | 25 |
| BRAF | V600E | Cobimetinib | Cancer | D | 41 |
| BRAF | V600E | Dabrafenib | Non-small Cell Lung Carcinoma | C | 28 |
| BRAF | V600E | Dabrafenib,Trametinib | Melanoma | B | 24 |
| BRAF | V600E | Pictilisib | Melanoma | C | 31 |
| BRAF | V600E | PLX4720,GDC0941 | Colorectal Cancer | D | 35 |
| BRAF | V600E | PLX4720,Nutlin-3 | Colorectal Cancer | D | 36 |
| BRAF | V600E | Sorafenib,Panitumumab | Colorectal Cancer | D | 33 |
| BRAF | V600E | Vemurafenib | Colorectal Cancer | D | 37 |
| BRAF | V600E | Vemurafenib | Melanoma | D | 34 |
| BRAF | V600E AMPLIFICATION | Selumetinib (AZD6244) | Colorectal Cancer | E | 42 |
| BRAF | V600E+V600M | Dabrafenib | Melanoma | C | 27 |

Somatic Mutations with known pharmacogenetic effect

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Mutation** | **Therapy** | **Disease** | **Evidence** | **References** |
| BRAF | V600E | Cetuximab | Colorectal Cancer | B | 25 |
| BRAF | V600E | Dabrafenib,Trametinib | Melanoma | B | 24 |
| BRAF | V600E | Dabrafenib | Non-small Cell Lung Carcinoma | C | 28 |
| BRAF | V600E | Pictilisib | Melanoma | C | 31 |
| BRAF | V600E | BEZ235 (NVP-BEZ235, Dactolisib),Selumetinib (AZD6244) | Melanoma | D | 40 |
| BRAF | V600E | Capecitabine,Vemurafenib,Bevacizumab | Colorectal Cancer | D | 37 |
| BRAF | V600E | Cobimetinib | Cancer | D | 41 |
| BRAF | V600E | PLX4720,GDC0941 | Colorectal Cancer | D | 35 |
| BRAF | V600E | PLX4720,Nutlin-3 | Colorectal Cancer | D | 36 |
| BRAF | V600E | Sorafenib,Panitumumab | Colorectal Cancer | D | 33 |
| BRAF | V600E | Vemurafenib | Colorectal Cancer | D | 37 |
| BRAF | V600E | Vemurafenib | Melanoma | D | 34 |

Appendix

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene** | **Mutation** | **COSMIC** | **dbSNP** |
| TNFRSF8 | p.Pro215Ser | ["COSM14024"] | rs267597959 |
| KIAA0319L | p.Pro278Ser | ["COSM36587"] | rs267598576 |
| FAM46C | p.Thr209Asn | [] | character(0) |
| S100A7A | p.Gly98Trp | ["COSM36721"] | rs267598049 |
| PKLR | p.Gly251Ser | ["COSM36782"] | rs267598065 |
| SMG5 | p.Pro549Leu | ["COSM21714"] | rs267598072 |
| MAEL | p.Ser431Cys | ["COSM36684"] | rs267598149 |
| ZBTB41 | p.Phe164Val | ["COSM36692"] | rs267598277 |
| LMOD1 | p.Glu188Lys | ["COSM36838"] | rs267598302 |
| SYT14 | p.Ser437Phe | ["COSM36786"] | rs267598356 |
| OBSCN | p.Ala4609Thr | ["COSM21034","COSM36848"] | rs267598401 |
| OR2T8 | p.Met197Arg | [] | rs4474294 |
| OR2T3 | p.Ala214Thr | [] | rs1770109 |
| SLC4A5 | p.Ser428Phe | ["COSM2999241","COSM2999242"] | rs111392973 |
| SLC4A5 | p.Ser428Thr | [] | rs267599454 |
| SNRNP200 | p.Arg1538Cys | ["COSM36589"] | rs267599495 |
| SEMA4C | p.Arg407Trp | ["COSM36666"] | rs267599501 |
| ANKRD36 | p.Ser1120Cys | [] | rs768768868 |
| KIAA1211L | p.Gly746Glu | [] | rs866719486 |
| IL1RL1 | p.Glu294Lys | ["COSM36680"] | rs267598807 |
| DPP10 | p.Ile93Asn | [] | character(0) |
| AMER3 | p.Ala276Asp | [] | rs267598874 |
| NXPH2 | p.Pro64Ser | ["COSM36843"] | rs267598905 |
| XIRP2 | p.Gly127Arg | ["COSM36673"] | rs267598980 |
| TTN | p.Pro10904Ser | [] | rs267599054 |
| TTN | p.Ala1347Thr | ["COSM2708938","COSM2708939","COSM2708940","COSM2708941","COSM2708942"] | rs267599092 |
| SF3B1 | p.Pro718Leu | ["COSM36655"] | rs267599150 |
| FZD7 | p.Pro285Ser | ["COSM24315"] | rs267599158 |
| ZDBF2 | p.Gly575Arg | [] | character(0) |
| AGFG1 | p.Gly364Arg | ["COSM25632","COSM3364621","COSM3364622"] | rs267599235 |
| SLC16A14 | p.Glu247Lys | ["COSM36712"] | rs267599250 |
| ARL4C | p.Gly71Ser | ["COSM21657"] | rs61752230 |
| SH3BP4 | p.Ala890Val | ["COSM36639"] | rs267599278 |
| RNPEPL1 | p.Asp186Asn | [] | rs267599287 |
| KIF1A | p.Ser141Ala | [] | character(0) |
| DLEC1 | p.Asp215Asn | ["COSM1566798","COSM36702"] | rs149190717 |
| SLC22A13 | p.Ser32Phe | ["COSM36695"] | rs267599783 |
| MYRIP | p.Pro572Ser | ["COSM36739"] | rs267599820 |
| VPRBP | p.Pro309Leu | [] | rs267599884 |
| TLR9 | p.Gly514Ser | ["COSM36649"] | rs267599888 |
| ROBO2 | p.Ala16Val | [] | character(0) |
| CMSS1 | p.Val156Ile | ["COSM36607"] | rs200457602 |
| SIDT1 | p.Met221Ile | ["COSM36653"] | rs267599548 |
| PRR23C | p.Glu262Lys | ["COSM36858"] | rs759730911 |
| CLSTN2 | p.Gln262His | ["COSM36631"] | rs267599628 |
| SAMD7 | p.Arg67Trp | ["COSM36663"] | rs191885635 |
| GNB4 | p.Pro107Leu | ["COSM13667"] | rs267599699 |
| ETV5 | p.Tyr445Cys | ["COSM23333"] | rs267599722 |
| LPP | p.Ala119Gly | [] | character(0) |
| TP63 | p.Met499Ile | ["COSM23541"] | rs267599730 |
| MUC4 | p.Pro1056His | [] | rs753583962 |
| EXOC1 | p.Pro774Ser | ["COSM36662"] | rs267600192 |
| REST | p.Pro752Thr | ["COSM24349"] | rs267600197 |
| SMR3B | p.Arg58Lys | ["COSM1310225","COSM36745"] | rs267600235 |
| SMARCAD1 | p.Val890Asp | ["COSM13923"] | rs267600302 |
| ADAM29 | p.Gly589Glu | ["COSM26290"] | rs267600094 |
| CARD6 | p.Leu638Phe | ["COSM14006"] | rs267600630 |
| TNPO1 | p.Gln38His | ["COSM36775","COSM5648790"] | rs267600680 |
| F2RL2 | p.Leu141Phe | ["COSM27249","COSM36780"] | rs267600693 |
| VCAN | p.Asp203Asn | ["COSM36758"] | rs267600718 |
| EDIL3 | p.Gln187Lys | ["COSM26295"] | rs267600722 |
| PCDHB7 | p.Asp374His | [] | character(0) |
| GRIA1 | p.Gly828Glu | ["COSM36714","COSM4854071","COSM4854072"] | rs267600500 |
| ADAM19 | p.Pro900Leu | [] | rs61757467 |
| MBOAT1 | p.Lys293Asn | [] | character(0) |
| VARS2 | p.Val234Ala | [] | character(0) |
| STK19 | p.Asp89Asn | ["COSM226579"] | rs267600971 |
| HLA-DOA | NA | [] | character(0) |
| SPDEF | p.Asp283His | [] | character(0) |
| SPDEF | p.Ser229Leu | ["COSM36760"] | rs200344679 |
| SCUBE3 | p.Gly702Glu | ["COSM36691"] | rs267600995 |
| BTBD9 | p.Arg46Cys | ["COSM36793"] | rs267601008 |
| DNAH8 | p.Arg1085Gln | ["COSM3077055","COSM3626601","COSM36781"] | rs267601013 |
| GUCA1B | p.Gly120Glu | [] | rs139823805 |
| TTBK1 | p.Pro855Ser | ["COSM21040"] | rs267601046 |
| GPR111 | p.Ile290Leu | ["COSM36619"] | rs267601055 |
| BAI3 | p.Asp755Asn | ["COSM22119"] | rs267601102 |
| EPB41L2 | p.Pro568Ser | ["COSM36576"] | rs144342263 |
| KATNA1 | p.Pro241Leu | [] | rs267600852 |
| KATNA1 | p.Pro241Ser | [] | rs267600853 |
| RPS6KA2 | p.Glu319Lys | ["COSM21036","COSM3024932","COSM3024933"] | rs267600891 |
| EVX1 | NA | [] | character(0) |
| NPSR1 | p.Asp11His | ["COSM3228516","COSM3228517","COSM36651","COSM4362160","COSM4362161"] | rs267601495 |
| ANLN | p.Gln649Arg | ["COSM36632"] | rs267601502 |
| ABCA13 | p.Gly4948Asp | ["COSM36817"] | rs267601533 |
| EPHB4 | p.Pro346Leu | ["COSM21032"] | rs267601191 |
| ACHE | p.Thr95Ile | ["COSM36706"] | rs267601193 |
| RELN | p.Glu331Lys | ["COSM36731","COSM3876866"] | rs267601217 |
| BRAF | p.Val600Glu | ["COSM18443","COSM476","COSM6137"] | rs113488022 |
| RP11-1220K2.2 | p.Asp1426Glu | [] | character(0) |
| ZNF862 | p.Gln583Lys | ["COSM36833"] | rs267601404 |
| KCNH2 | p.Leu468Phe | ["COSM36578"] | rs267601414 |
| NAT2 | p.Glu264Lys | ["COSM36677"] | rs267601842 |
| ADRA1A | p.Val311Ile | ["COSM2787551","COSM2787552","COSM2787553","COSM36671"] | rs267601877 |
| SCARA5 | p.Glu270Lys | ["COSM36713"] | rs267601883 |
| GPR124 | p.Glu863Lys | ["COSM36641"] | rs267601912 |
| MCM4 | NA | [] | character(0) |
| BHLHE22 | p.Ser227Gly | [] | rs62519838 |
| REXO1L1P | p.Ser639Phe | [] | character(0) |
| CNGB3 | p.Glu64Gly | [] | character(0) |
| CNBD1 | p.Leu135Arg | [] | character(0) |
| GRHL2 | p.Ser356Phe | ["COSM36601"] | rs267601682 |
| OC90 | p.Lys257Glu | ["COSM23378","COSM36839"] | rs267601777 |
| ZC3H3 | p.Ser879Phe | ["COSM36642"] | rs267601811 |
| DMRT2 | p.Pro470Ser | ["COSM36855"] | rs267602063 |
| ANKRD18A | p.Glu654Lys | ["COSM36859"] | rs267602244 |
| PCSK5 | p.Cys747Tyr | ["COSM36640"] | rs267602276 |
| ZNF367 | p.Asn12Lys | [] | character(0) |
| NUTM2G | p.Gly36Asp | ["COSM36612"] | rs267602327 |
| CYLC2 | p.Asp167Asn | ["COSM36727"] | rs267602064 |
| PTBP3 | p.Pro43Leu | [] | rs267602088 |
| PTBP3 | p.Pro43Ser | ["COSM36676","COSM4463186"] | rs267602089 |
| CNTRL | p.Gln2033Lys | [] | character(0) |
| OR1J1 | p.Leu157Phe | ["COSM36710"] | rs267602118 |
| OR1J2 | p.Leu260Phe | ["COSM36753"] | rs267602119 |
| GAPVD1 | p.Leu35Phe | ["COSM36617"] | rs267602131 |
| ADAMTS13 | p.Arg398His | ["COSM36777"] | rs121908471 |
| LHX3 | p.Gly92Glu | ["COSM36599"] | character(0) |
| KIAA1217 | p.Ser925Ala | [] | character(0) |
| OR52A1 | p.Leu152Ile | [] | character(0) |
| OTOG | p.Pro1482Ser | ["COSM36821"] | rs267602806 |
| MPPED2 | p.Leu81Phe | ["COSM36672"] | rs267602842 |
| MADD | p.Ser1620Phe | ["COSM26934"] | rs267602903 |
| OR4S2 | p.Arg120Cys | ["COSM36685"] | rs267602971 |
| TNKS1BP1 | p.Pro291Ser | ["COSM36722"] | rs267603015 |
| OR4D11 | p.Pro58Ala | ["COSM36624"] | rs267603040 |
| SLC22A8 | p.Asn450Ser | [] | character(0) |
| SPTBN2 | p.Glu2047Lys | ["COSM36751","COSM4199893"] | rs201985455 |
| GRM5 | p.Glu941Lys | [] | rs267603229 |
| DCP1B | p.Pro98Ser | ["COSM36575"] | rs267603408 |
| KCNA6 | p.Pro514Ser | ["COSM36724"] | rs267603494 |
| CD163 | p.Pro310Leu | ["COSM36725"] | rs267603681 |
| GLI1 | p.Ser1094Phe | ["COSM24658"] | rs267603606 |
| TBC1D30 | p.Gly327Glu | ["COSM36841"] | rs267603627 |
| KCNC2 | p.Leu298Ser | ["COSM36754"] | rs267603669 |
| RBM19 | p.Glu115Lys | ["COSM36748"] | rs267603319 |
| PABPC3 | p.Gly234Arg | ["COSM36646"] | rs267603790 |
| CPB2 | p.Phe409Ser | ["COSM36708"] | rs267603833 |
| OXGR1 | p.Gly22Val | ["COSM1368119","COSM36698"] | rs267603871 |
| CARKD | p.Pro205Ser | ["COSM36577"] | rs267603758 |
| NOVA1 | p.Ala256Asp | ["COSM1369439","COSM25331"] | rs267603974 |
| ARHGAP5 | p.Thr437Ile | [] | rs56259828 |
| RAD51B | p.Arg385Lys | [] | rs267604035 |
| SERPINA6 | p.Arg282Leu | ["COSM1265285","COSM26307","COSM267404"] | rs267604111 |
| HSP90AA1 | p.His612Asn | [] | character(0) |
| NUDT14 | p.Thr44Pro | ["COSM36696"] | rs267603899 |
| TRPM1 | p.Glu1261Lys | ["COSM36625"] | rs267604151 |
| PLIN1 | p.Leu191Arg | ["COSM36595"] | character(0) |
| PRC1 | p.Gly507Glu | ["COSM36743"] | rs267604387 |
| AMDHD2 | p.His587Arg | [] | character(0) |
| NLRC3 | p.Gly454Arg | ["COSM36804"] | rs267604538 |
| DPEP2 | p.Pro480Ser | ["COSM36719"] | rs267604603 |
| CCDC144A | p.Met803Ile | ["COSM36830"] | rs267604757 |
| MYO15A | p.Leu3152Phe | ["COSM36737"] | rs267604764 |
| C17orf50 | NA | [] | rs267604816 |
| TTLL6 | p.Arg280Lys | ["COSM36852"] | rs267604932 |
| USH1G | p.Leu379Ser | ["COSM36661"] | rs267605044 |
| PSMA8 | p.Gly36Glu | ["COSM36586"] | rs267605136 |
| MBD3 | p.Asp283Asn | [] | rs369581342 |
| GTF2F1 | p.Gly411Arg | [] | character(0) |
| MUC16 | p.Met2821Ile | ["COSM2701120","COSM36853"] | rs267605807 |
| MUC16 | p.Leu2819Met | [] | character(0) |
| MUC16 | p.Leu1434Ile | [] | character(0) |
| OLFM2 | p.Arg58Gln | ["COSM36654"] | rs267605828 |
| PKN1 | p.Arg191Cys | ["COSM21035"] | rs267605306 |
| CYP4F2 | p.Arg149Gln | ["COSM1129961"] | rs140630977 |
| ZNF208 | p.His855Tyr | [] | rs267605385 |
| ARHGAP33 | p.Pro1068Leu | [] | character(0) |
| CYP2A13 | p.Arg485Gln | ["COSM36742"] | rs267605496 |
| PSG1 | p.Thr43Ile | [] | character(0) |
| NOSIP | p.Pro297Leu | [] | character(0) |
| ZNF614 | p.Gly267Ser | ["COSM36678"] | rs267605628 |
| ZNF880 | p.Pro169Gln | ["COSM1234752"] | rs267605631 |
| ZNF28 | p.Ile572Thr | ["COSM36679"] | rs267605644 |
| ZSCAN5A | p.Ala179Thr | [] | character(0) |
| FLRT3 | p.Ile532Asn | [] | character(0) |
| DLGAP4 | p.Ala879Ser | ["COSM36648"] | rs267605913 |
| ZNF217 | p.Pro651Ser | ["COSM25218","COSM2763526"] | rs267606004 |
| SPO11 | p.Gly88Ser | ["COSM36690"] | rs267606012 |
| TPTE | p.Asp545Asn | [] | rs267606168 |
| TMEM50B | p.Ser113Phe | ["COSM36665"] | rs267606110 |
| TRAPPC10 | p.Gly983Asp | ["COSM36726"] | rs267606147 |
| CECR2 | p.Gly474Arg | ["COSM36851"] | rs267606173 |
| IGLL5 | p.Arg23Cys | [] | rs382768 |
| TRIOBP | p.Arg497Gln | ["COSM36827"] | rs755186518 |
| MEI1 | p.Gly507Glu | ["COSM36800"] | rs267606261 |
| CELSR1 | p.Leu2698Phe | ["COSM36703"] | character(0) |
| NHS | p.Arg373Gln | ["COSM1118631","COSM36761"] | rs267606412 |
| FGD1 | p.Arg636Trp | ["COSM21850"] | character(0) |
| PJA1 | p.His586Tyr | [] | rs267606501 |
| OGT | p.Leu367Ser | [] | character(0) |
| DCAF12L1 | p.Ser281Phe | ["COSM36778"] | rs267606338 |
| ZNF280C | p.His379Tyr | [] | rs267606348 |
| PNMA3 | p.Pro342Leu | ["COSM36769"] | rs267606390 |

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