# 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 |
| RPS6KA2 | p.Glu319Lys | 2 | 3,5 |
| ACHE | p.Thr95Ile | 1 | 5 |
| 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 |
| TNPO1 | p.Gln38His | 1 | 4 |

# Somatic Mutations in Pharmaceutical Target Proteins

## 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 |
| BRAF | p.Val600Glu | gsk2118436 | 1 | 14 |
| BRAF | p.Val600Glu | r7204 | 1 | 14 |
| EPHB4 | p.Pro346Leu | vandetanib | 1 | 12 |

## Indirect Association (other Mutations with known effect on drug)

| **Gene** | **Therapy** | **References** |
| --- | --- | --- |
| BRAF | BAY 86-9766 | 26 |
| BRAF | Dabrafenib | 21,23 |
| BRAF | Panitumumab | 19 |
| BRAF | RO4987655 | 22 |
| BRAF | Selumetinib (AZD6244) | 29 |
| BRAF | Sorafenib | 24 |
| BRAF | Trametinib | 27,27,28 |
| BRAF | Trametinib,Dabrafenib | 20 |
| BRAF | Vemurafenib | 25,24,27 |

# Somatic Mutations with known pharmacogenetic effect

| **Gene** | **Mutation** | **Therapy** | **Disease** | **Evidence** | **References** |
| --- | --- | --- | --- | --- | --- |
| BRAF | V600E | Cetuximab | Colorectal Cancer | B | 31 |
| BRAF | V600E | Trametinib,Dabrafenib | Melanoma | B | 30 |
| BRAF | V600E | Dabrafenib | Non-small Cell Lung Carcinoma | C | 32 |
| BRAF | V600E | Pictilisib | Melanoma | C | 33 |
| BRAF | V600E | Bevacizumab,Vemurafenib,Capecitabine | Colorectal Cancer | D | 38 |
| BRAF | V600E | BEZ235 (NVP-BEZ235, Dactolisib),Selumetinib (AZD6244) | Melanoma | D | 39 |
| BRAF | V600E | Cobimetinib | Cancer | D | 40 |
| BRAF | V600E | Nutlin-3,PLX4720 | Colorectal Cancer | D | 37 |
| BRAF | V600E | PLX4720,PD0325901 | Colorectal Cancer | D | 36 |
| BRAF | V600E | Sorafenib | Colorectal Cancer | D | 34 |
| BRAF | V600E | Vemurafenib | Colorectal Cancer | D | 38 |
| BRAF | V600E | Vemurafenib | Melanoma | D | 35 |

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# Appendix

| **Gene** | **Mutation** | **dbSNP** | **COSMIC** |
| --- | --- | --- | --- |
| FAM46C | p.Thr209Asn | character(0) | character(0) |
| S100A7A | p.Gly98Trp | rs267598049 | COSM36721 |
| PKLR | p.Gly251Ser | rs267598065 | COSM36782 |
| MAEL | p.Ser431Cys | rs267598149 | COSM36684 |
| ZBTB41 | p.Phe164Val | rs267598277 | COSM36692 |
| SYT14 | p.Ser437Phe | rs267598356 | COSM36786 |
| OR2T8 | p.Met197Arg | rs4474294 | character(0) |
| OR2T3 | p.Ala214Thr | rs1770109 | character(0) |
| SLC4A5 | p.Ser428Phe | rs111392973 | c("COSM2999241", "COSM2999242") |
| SNRNP200 | p.Arg1538Cys | rs267599495 | COSM36589 |
| DPP10 | p.Ile93Asn | character(0) | character(0) |
| SF3B1 | p.Pro718Leu | rs267599150 | COSM36655 |
| FZD7 | p.Pro285Ser | rs267599158 | COSM24315 |
| ZDBF2 | p.Gly575Arg | character(0) | character(0) |
| ARL4C | p.Gly71Ser | rs61752230 | COSM21657 |
| KIF1A | p.Ser141Ala | character(0) | character(0) |
| DLEC1 | p.Asp215Asn | rs149190717 | c("COSM1566798", "COSM36702") |
| VPRBP | p.Pro309Leu | rs267599884 | COSM36856 |
| TLR9 | p.Gly514Ser | rs267599888 | COSM36649 |
| PRR23C | p.Glu262Lys | rs759730911 | COSM36858 |
| CLSTN2 | p.Gln262His | rs267599628 | COSM36631 |
| SAMD7 | p.Arg67Trp | rs191885635 | COSM36663 |
| GNB4 | p.Pro107Leu | rs267599699 | COSM13667 |
| ETV5 | p.Tyr445Cys | rs267599722 | COSM23333 |
| LPP | p.Ala119Gly | character(0) | character(0) |
| EXOC1 | p.Pro774Ser | rs267600192 | COSM36662 |
| REST | p.Pro752Thr | rs267600197 | COSM24349 |
| SMR3B | p.Arg58Lys | rs267600235 | c("COSM1310225", "COSM36745") |
| ADAM29 | p.Gly589Glu | rs267600094 | COSM26290 |
| CARD6 | p.Leu638Phe | rs267600630 | COSM14006 |
| TNPO1 | p.Gln38His | rs267600680 | c("COSM36775", "COSM5648790") |
| VCAN | p.Asp203Asn | rs267600718 | COSM36758 |
| EDIL3 | p.Gln187Lys | rs267600722 | COSM26295 |
| PCDHB7 | p.Asp374His | character(0) | character(0) |
| GRIA1 | p.Gly828Glu | rs267600500 | c("COSM36714", "COSM4854071", "COSM4854072") |
| ADAM19 | p.Pro900Leu | rs61757467 | character(0) |
| MBOAT1 | p.Lys293Asn | character(0) | character(0) |
| SPDEF | p.Asp283His | character(0) | character(0) |
| SPDEF | p.Ser229Leu | rs200344679 | COSM36760 |
| SCUBE3 | p.Gly702Glu | rs267600995 | COSM36691 |
| BAI3 | p.Asp755Asn | rs267601102 | COSM22119 |
| KATNA1 | p.Pro241Leu | rs267600852 | character(0) |
| KATNA1 | p.Pro241Ser | rs267600853 | character(0) |
| RPS6KA2 | p.Glu319Lys | rs267600891 | c("COSM21036", "COSM3024932", "COSM3024933") |
| ANLN | p.Gln649Arg | rs267601502 | COSM36632 |
| EPHB4 | p.Pro346Leu | rs267601191 | COSM21032 |
| ACHE | p.Thr95Ile | rs267601193 | COSM36706 |
| BRAF | p.Val600Glu | rs113488022 | c("COSM18443", "COSM476", "COSM6137") |
| NAT2 | p.Glu264Lys | rs267601842 | COSM36677 |
| SCARA5 | p.Glu270Lys | rs267601883 | COSM36713 |
| GPR124 | p.Glu863Lys | rs267601912 | COSM36641 |
| REXO1L1P | p.Ser639Phe | character(0) | character(0) |
| CNBD1 | p.Leu135Arg | character(0) | character(0) |
| GRHL2 | p.Ser356Phe | rs267601682 | COSM36601 |
| ZC3H3 | p.Ser879Phe | rs267601811 | COSM36642 |
| ANKRD18A | p.Glu654Lys | rs267602244 | COSM36859 |
| PCSK5 | p.Cys747Tyr | rs267602276 | COSM36640 |
| NUTM2G | p.Gly36Asp | rs267602327 | COSM36612 |
| OR1J1 | p.Leu157Phe | rs267602118 | COSM36710 |
| ADAMTS13 | p.Arg398His | rs121908471 | COSM36777 |
| LHX3 | p.Gly92Glu | character(0) | COSM36599 |
| MADD | p.Ser1620Phe | rs267602903 | COSM26934 |
| OR4S2 | p.Arg120Cys | rs267602971 | COSM36685 |
| OR4D11 | p.Pro58Ala | rs267603040 | COSM36624 |
| SPTBN2 | p.Glu2047Lys | rs201985455 | c("COSM36751", "COSM4199893") |
| GRM5 | p.Glu941Lys | rs267603229 | character(0) |
| DCP1B | p.Pro98Ser | rs267603408 | COSM36575 |
| GLI1 | p.Ser1094Phe | rs267603606 | COSM24658 |
| TBC1D30 | p.Gly327Glu | rs267603627 | COSM36841 |
| KCNC2 | p.Leu298Ser | rs267603669 | COSM36754 |
| PABPC3 | p.Gly234Arg | rs267603790 | COSM36646 |
| CPB2 | p.Phe409Ser | rs267603833 | COSM36708 |
| CARKD | p.Pro205Ser | rs267603758 | COSM36577 |
| NOVA1 | p.Ala256Asp | rs267603974 | c("COSM1369439", "COSM25331") |
| SERPINA6 | p.Arg282Leu | rs267604111 | c("COSM1265285", "COSM26307", "COSM267404") |
| NUDT14 | p.Thr44Pro | rs267603899 | COSM36696 |
| TRPM1 | p.Glu1261Lys | rs267604151 | COSM36625 |
| PLIN1 | p.Leu191Arg | character(0) | COSM36595 |
| PRC1 | p.Gly507Glu | rs267604387 | COSM36743 |
| AMDHD2 | p.His587Arg | character(0) | character(0) |
| NLRC3 | p.Gly454Arg | rs267604538 | COSM36804 |
| TTLL6 | p.Arg280Lys | rs267604932 | COSM36852 |
| USH1G | p.Leu379Ser | rs267605044 | COSM36661 |
| PSMA8 | p.Gly36Glu | rs267605136 | COSM36586 |
| MBD3 | p.Asp283Asn | rs369581342 | character(0) |
| GTF2F1 | p.Gly411Arg | character(0) | character(0) |
| OLFM2 | p.Arg58Gln | rs267605828 | COSM36654 |
| CYP4F2 | p.Arg149Gln | rs140630977 | COSM1129961 |
| ZNF208 | p.His855Tyr | rs267605385 | character(0) |
| ARHGAP33 | p.Pro1068Leu | character(0) | character(0) |
| NOSIP | p.Pro297Leu | character(0) | character(0) |
| ZNF880 | p.Pro169Gln | rs267605631 | COSM1234752 |
| FLRT3 | p.Ile532Asn | character(0) | character(0) |
| DLGAP4 | p.Ala879Ser | rs267605913 | COSM36648 |
| SPO11 | p.Gly88Ser | rs267606012 | COSM36690 |
| TMEM50B | p.Ser113Phe | rs267606110 | COSM36665 |
| CECR2 | p.Gly474Arg | rs267606173 | COSM36851 |
| MEI1 | p.Gly507Glu | rs267606261 | COSM36800 |
| NHS | p.Arg373Gln | rs267606412 | c("COSM1118631", "COSM36761") |
| FGD1 | p.Arg636Trp | character(0) | COSM21850 |
| OGT | p.Leu367Ser | character(0) | character(0) |
| DCAF12L1 | p.Ser281Phe | rs267606338 | COSM36778 |