## Table D.10 Examples of pharmacogenomic associations

| Drug | Gene | Protein | Clinical significance |
|---|---|---|---|
| Abacavir | HLA | Human leucocyte antigen (HLA) system (also called the major histocompatibility complex, MHC) | Patients with HLA-B*5701, HLA-DR7 and HLA-DQ3 haplotype likely to experience a potentially life threatening hypersensitivity reaction |
| ACE inhibitors | Bradykinin $beta_2$ receptor | Bradykinin $beta_2$ receptor | Polymorphism in promoter region: 58 thymine(T)/cytosine(C). Patients homozygous for TT genotype are more susceptible to ACE Inhibitor–induced cough than those homozygous for CC genotype |
| Azathioprine, 6-mercaptopurine | TPMT | TPMT | Patients with low or undetectable TPMT activity are at risk of severe toxicity |
| β-blockers and Calcium antagonists | Gly460Tr | | Variant is sensitive to salt and reacts with high blood pressure when given salt. In those patients beta blocker and calcium antagonists will never result in risk reduction, and thiazides are the drugs of choice |
| Codeine | CYP2D6 | CYP2D6 | Patients with two inactive alleles do not achieve analgesia |
| Diuretics: frusemide and hydrochlorothiazide | α-adducin | α-adducin | Patients with Gly460Trp mutation have significantly increased blood pressure reduction. Blood pressure also more susceptible to changes in salt balance |
| Fluorouracil (5-FU) | DPYD | Dihydropyrimidine dehydrogenase | Deficiency leads to 5-FU toxicity (neutropenia, thrombocytopenia, neurological damage) |
| Irinotecan | UGT1A1 | UGT1A1 | Patients homozygous for 7 TA repeats in the promoter sequence are greater than 9 times more likely to experience severe irinotecan-induced neutropenia than other patients |
| Isoniazid | NAT2 | Arylamine N-acetyltransferase type 2 (NAT2) | Rapid acetylators metabolise isoniazid faster, so require a higher dose for same effect |
| Salbutamol | ADR$\beta_2$ | Beta$_2$ adrenergic receptor | Patients homozygous for Gly17Arg mutation experience a decline in respiratory function with regular use of salbutamol |
| Sibutramine | GNB3 CC | | Carriers respond much better to obesity treatment with sibutramine than non-carriers |
| Trastuzumab | HER2 | Human epidermal growth factor receptor type II (HER2) | Tumours not over-expressing HER2 will not respond to trastuzumab. Tumour regression with trastuzumab therapy in up to 35% of patients with tumours that strongly over-express HER2 |
| Warfarin | CYP2C9 | CYP2C9 | Patients with defective alleles require significantly lower maintenance doses, have longer times to dose stabilisation, and are at higher risk for serious and life-threatening bleeding than are patients without these variants |
| Warfarin | VKORC | Vitamin K epoxide reductase complex 1 | Variants stratify patients into low-, intermediate- and high-sensitivity groups |



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